(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 January 2014 (16.01.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/012074 A2

(51) International Patent Classification:
C07D 231/12 (2006.01) *C07D 403/14* (2006.01)
C07D 403/12 (2006.01)

(21) International Application Number:
PCT/US2013/050398

(22) International Filing Date:
12 July 2013 (12.07.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/670,979 12 July 2012 (12.07.2012) US

(71) Applicant: **EUCLISES PHARMACEUTICALS, INC.** [—/US]; 4320 Forest Park, Suite 303, St. Louis, MO 63108 (US).

(72) Inventors: **MARTINEZ, Eduardo, J.**; 632 Dayton Road, Bryn Mawr, PA 19010 (US). **TALLEY, John, J.**; 6519 Walsh St., St. Louis, MO 63109 (US). **JEROME, Kevin, D.**; 5982 Mergenthal Ct., St. Charles, MO 63304 (US). **BOEHM, Terri, L.**; 928 Cleta Drive, Ballwin, MO 63021 (US).

(74) Agent: **LEE, Kisuk**; Harness, Dickey & Pierce, P.L.C., 7700 Bonhomme Avenue, Suite 400, St. Louis, MO 63105 (US).

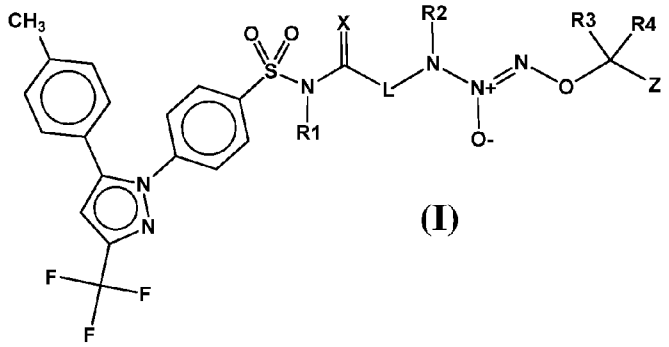
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) Title: NO-RELEASING NONOATE (NITROGEN-BOUND) SULFONAMIDE-LINKED-COXIB ANTI-CANCER AGENTS



(I)

(57) Abstract: The present invention provides NO-releasing NONOate(nitrogen bound)sulfonamide- linked-coxib anti-cancer agents, having the structure of Formula (I): wherein R^1, X, L, R^2, R^3, R^4, and Z are as defined in the detailed description; pharmaceutical compositions comprising at least one compound of Formula (I); and methods useful for healing wounds, preventing and treating cancer, or treating actinic keratosis, cystic fibrosis or acne, using a compound of Formula (I).

WO 2014/012074 A2

NO-RELEASING NONOATE(NITROGEN-BOUND)SULFONAMIDE-LINKED-COXIB ANTI-CANCER AGENTS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 61/670,979, filed on 12 July 2012. The entire disclosure of the above application is incorporated herein by reference.

FIELD

[0002] The present invention generally relates to NO-releasing coxib compounds, pharmaceutical compositions comprising the compounds, methods useful for treating a subject by administering a therapeutically effective amount of the compounds, and methods for making the compounds. More specifically, the present invention relates to a class of NO-releasing NONOate(nitrogen-bound)sulfonamide-linked-coxib cardioprotective compounds, pharmaceutical compositions thereof, and methods useful for healing wounds, preventing and treating cancer, and treating actinic keratosis, cystic fibrosis and acne.

BACKGROUND

[0003] Despite decades of effort, cancer remains an especially difficult disease for development of therapeutics. According to the Cancer Prevention Coalition (University of Illinois), cancer rates have increased 24% in the past thirty years even after adjusting for aging of the population. Remarkably, despite significant progress during this period the overall five-year survival rates have remained virtually static (approximately 50% depending on the cancer). Thus new drugs are required to develop more effective life-saving cancer therapies.

[0004] Celecoxib, a selective COX-2 inhibitor, is one of the world's most successful drugs, alleviating pain and inflammation for millions of patients. In addition, COX-2 over-expression has been found in several types of human cancers such as colon, breast, lung, prostate and pancreas, and appears to control many cellular processes. COX-2 plays a role in carcinogenesis, apoptosis and angiogenesis, and therefore represents an excellent drug target for the development of novel medicines for prevention and/or treatment of human cancers. Currently, celecoxib is approved for limited use in the reduction of polyps in familial adenomatous polyposis (FAP).

[0005] The Adenoma Prevention with Celecoxib (APC) trial demonstrated human efficacy of celecoxib in the prevention of sporadic colorectal adenoma. However, this trial also showed that the elevated dose of celecoxib required for anti-cancer efficacy was accompanied by concomitant increase in adverse cardiovascular (CV) events (Bertagnolli, et al., Cancer Prev. Res. (Phila) 2, 310-321(2009)).

[0006] Development of more potent or selective COX-2 inhibitors does not improve CV safety; this liability is thought to be a mechanism-based effect. This was demonstrated in the VIGOR trial by Vioxx®, an extremely potent and highly selective COX-2 inhibitor withdrawn from the market in 2004 due to CV concerns about increased risk of heart attack and stroke with long term, high dose use. These facts have undermined the development of novel COX-2 inhibitors and slowed research to expand their utility to other disease indications, such as cancer.

[0007] Nitric oxide (NO) is an important endogenous signaling molecule and vasodilator. NO is synthesized from L-arginine by the enzyme NO synthase (NOS), which exists in three distinct isoforms, namely the constitutively expressed endothelial (eNOS) and neuronal (nNOS) forms, and the mainly inducible form (iNOS). Arginine administration has been shown to reduce blood pressure and renal vascular resistance in essential hypertensive patients with normal or insufficient renal function (*Am. J. Hypertens.* 12, 8-15 (1999)). It has also been shown that NO deficiency promotes vascular side-effects of celecoxib and other COX inhibitors (Blood 108, 4059-4062 (2006)).

[0008] The role of NO in cancer is complex; however, pharmacological evidence using NO-releasing compounds of NSAID's has shown increased anti-tumor efficacy in cell culture and animal cancer models. The different molecular mechanisms of NO are expected to simultaneously enhance anti-cancer efficacy of celecoxib and improve CV safety by preventing an increase in blood pressure associated with COX-2 inhibition, while maintaining gastric-sparing properties superior to NSAID's.

[0009] Diverse molecular mechanisms of NO delivery are well known. For example, Kashfi, et al. reported that nitric oxide-donating nonsteroidal anti-inflammatory drugs (NO-sulindac, NO-ibuprofen, NO-indomethacin and NO-aspirin) inhibit the growth of various cultured human cancer cells; providing evidence of a tissue type-independent effect (J. Pharmacol. Exp. Ther. 303, 1273-1282 (2002)).

[0010] In another example, Ouyang, et al. reported that nitric oxide-donating aspirin prevented pancreatic cancer in a hamster tumor model (Cancer Res. 66, 4503-4511 (2006)).

[0011] COX inhibition and cancer: Two isoforms of cyclooxygenase (COX) are known to exist, a constitutive form (COX-1) present in nearly all tissues and an inducible form (COX-2) upregulated in response to inflammatory stimuli. The discovery of COX-2 led to the development of selective COX-2 inhibitors as anti-inflammatory drugs (coxibs), which were shown to be largely devoid of antiplatelet activity and gastrointestinal ulcerogenicity believed to be associated with inhibition of COX-1.

[0012] NSAID's are among the most widely used treatments for pain, fever and inflammation, and have long been known to reduce the risk of cancer in multiple organ sites. The use of aspirin in treatment and prevention of cancer has wide-spread support in the medical community; however, the risks of regular aspirin use are also well established and the risk-benefit profile is not sufficient to recommend aspirin treatment for cancer prevention. With the advent of coxibs, research has focused on COX-2 as a target for the treatment and prevention of certain cancers. Compelling data from the APC trial, described above, demonstrated that celecoxib was useful in preventing sporadic colorectal adenoma in patients at high risk for colorectal cancer.

[0013] The role of COX-2 in lung cancer: Lung cancer is the leading cause of cancer-related deaths in the US and is responsible for more deaths than breast, prostate and colon cancers combined. Current research suggests that COX-2 and epidermal growth factor receptor, (EGFR), are important mediators in non-small cell lung cancer (NSCLC). In human NSCLC patients, a combination of erlotinib (a tyrosine kinase inhibitor), and celecoxib showed high response rates and demonstrable clinical benefit. NSCLC currently represents one of the preferred indications for COX-2 inhibition cancer therapy.

[0014] Mechanism of COX-2 in cancer: A key feature of COX-2 biology is its ability alone to cause cancer formation in a number of transgenic mouse models. COX-2 derived PGE_2 plays a prominent role in tumor growth and the most abundant prostanoid in many human malignancies. Metabolism of arachidonic acid by COX-2 leads to the formation of several prostglandins (PGs) that bind to tumor suppressor p53, preventing p53-mediated apoptosis. COX-2 derived PGE_2 promotes epithelial-to-mesenchymal transition and thus increases resistance to EGFR tyrosine kinase inhibitors in lung cancer.

[0015] Nitric oxide and cardiovascular safety: Nitric oxide exhibits a number of important pharmacological actions including vascular relaxation (vasodilatation) and inhibition of platelet aggregation and adhesion. Inhibition of NO synthesis leads to an increase in systemic blood pressure. NO also prevents atherogenesis by inhibiting vascular smooth muscle cell proliferation and preventing low-density lipoprotein oxidation and macrophage activation. Vascular NO generation is important in controlling blood pressure, and a growing body of evidence indicates that NO signaling is a key factor in counteracting the onset and development of several CV diseases including hypertension, myocardial infarction and stroke. NO can be used to counteract CV liabilities associated with COX-2 inhibition.

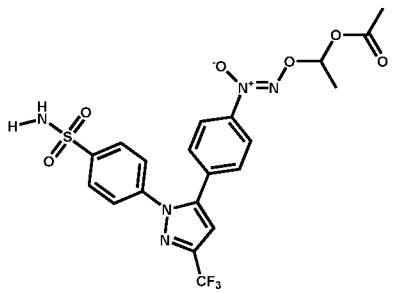
[0016] Nitric oxide and gastric sparing properties: NO-releasing COX inhibitors were originally created to improve gastrointestinal (GI) tolerability (*Inflammopharmacology* 11(4), 415-22 (2003)). Naproxcinod is a NO-releasing pro-drug of the NSAID naproxen. Naproxcinod showed significantly improved GI tolerability compared to naproxen alone in a chronic rat study (Life Sciences 62, 235-240 (1998)). In another example, L-arginine, coadministered with the NSAID ibuprofen, showed a protective effect on gastric mucosa against ibuprofen-induced mucosal lesions (*Free Radic. Res.* 38(9), 903-11 (2004)).

[0017] Nitric oxide and cancer: NO modulates the activity of transcription factor NF-κB, which represents a potential mechanism for inflammation control, but also regulation of apoptotic mechanisms. NO promotes apoptosis and can reverse tumor cell resistance to chemotherapeutic agents. Studies with NO-releasing NSAID's have shown that NO contributes to anti-cancer activity in cell culture and enhanced *in vivo* efficacy in rodent cancer models. For example, Steele, et al. reported the chemopreventive efficacy of nitric oxide-naproxen in rodent models of colon, urinary bladder and mammary cancers, (Cancer Prev. Res. (Phila) 2, 951-956 (2009)).

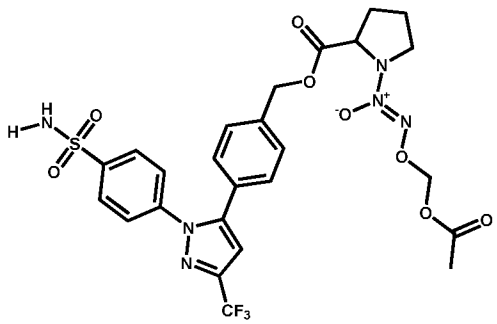
[0018] Nitric oxide-releasing prodrugs capable of producing desirable therapeutic effects regarding enhanced anti-inflammatory activity, reduced intestinal, cardiac and renal toxicity are reported by Tam et al. US 2008/0288176. The compounds described therein include sulfonamide nitrogen-linked amide prodrugs derived from amino acids, specifically aspartic or glutamic acid, and sulfonamide nitrogen-linked carbamate prodrugs using hydroxyproline substituted with a oxymethylene diazen-1-ium-1,2-diolate. Typically, the diazen-1-ium-1,2-diolate may be attached to celecoxib via an acyloxymethylene radical (i.e., O-Linked).

[0019] Nitric oxide-releasing prodrugs useful in the treatment of inflammation and the reduction of adverse cardiovascular and/or ulcerogenic events associated with chronic use of COX-2 inhibitors are reported by Velazquez et al. WO2007/127725. Also disclosed is a method of preventing or treating cancer or treating inflammation or an inflammation-related condition. Compounds proposed therein include proline-based acyloxymethylene diazen-1-ium-1,2-diolate prodrugs of NSAIDS and celecoxib compound.

[0020] Nitric oxide-releasing prodrugs useful in the treatment of inflammation and the reduction of adverse cardiovascular and/or ulcerogenic events associated with chronic use of COX-2 inhibitors are reported by Abdellatif et al, Bioorg. Med. Chem. (20) 4544-4549 (2010). The compounds described therein include celecoxib substituted with an acetyloxymethylenediazeniumdiolate radical attached to non-sulfonamide substituted phenyl, yielding the structure:

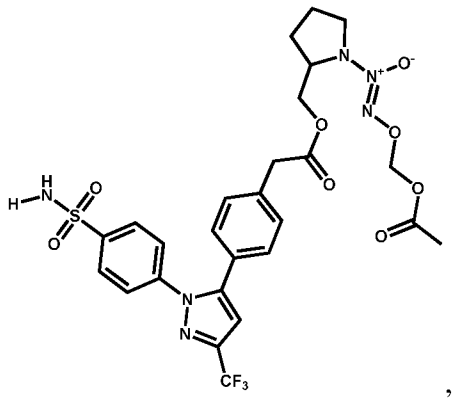


[0021] Nitric oxide-releasing prodrugs useful in the treatment of inflammation and the reduction of adverse cardiovascular and/or ulcerogenic events associated with chronic use of COX-2 inhibitors are reported by Abdellatif et al, Bioorg. Med. Chem. (16) 9694-98 (2008). The compounds described therein include celecoxib substituted with an acetyloxymethylenediazeniumdiolatepyrrolidinylcarbonyloxymethylene radical attached to non-sulfonamide substituted phenyl, yielding the structure:

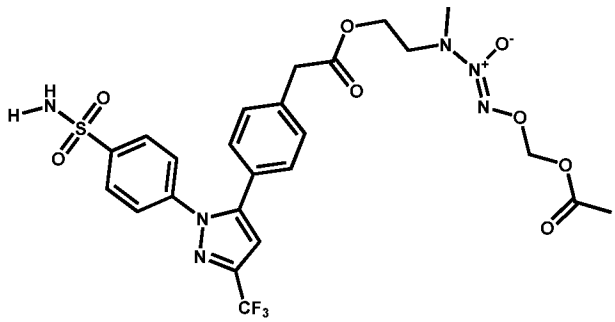


[0022] Nitric oxide-releasing prodrugs useful in the treatment of inflammation and the reduction of adverse cardiovascular and/or ulcerogenic events associated with chronic use of

COX-2 inhibitors are reported by Abdellatif et al, Bioorg. Med. Chem. (14) 5182-88 (2009). The compounds described therein include celecoxib substituted with a acetyloxymethylenediazeniumdiolatepyrrolidinylmethyleneoxycarbonylmethylene or a acetyloxymethylenediazeniumdiolateaminoethyleneoxycarbonylmethylene radical attached to non-sulfonamide containing phenyl, yielding the following structures, respectively:

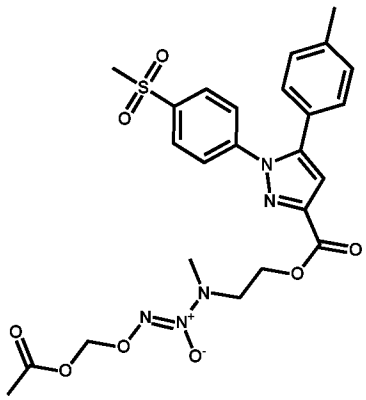


,



.

[0023] Nitric oxide-releasing prodrugs useful in the treatment of inflammation and the reduction of adverse cardiovascular and/or ulcerogenic events associated with chronic use of COX-2 inhibitors are reported by Abdellatif et al, Bioorg. Med. Chem. (16) 6528-34 (2008). The compounds described therein include methylsulfonylcelecoxib substituted with a acetyloxymethylenediazeniumdiolateaminoethyleneoxycarbonyl radical attached to pyrazolyl, yielding the structure:

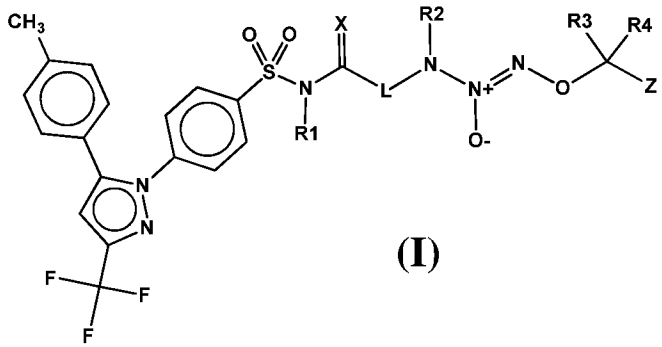


SUMMARY

[0024] Herein described is a family of NO-releasing coxib conjugates which provides a therapeutic benefit to a subject with a disease indication, such as cancer, actinic keratosis, cystic fibrosis or acne, or provides a wound healing benefit to a subject. Such NO-releasing coxib

conjugate can improve CV safety, permit higher dose of cancer-treating compound, enhance cancer-treating efficacy, and/or maintain gastric-sparing properties superior to NSAID's.

[0025] In one embodiment, there is provided a compound of Formula (I):



(I)

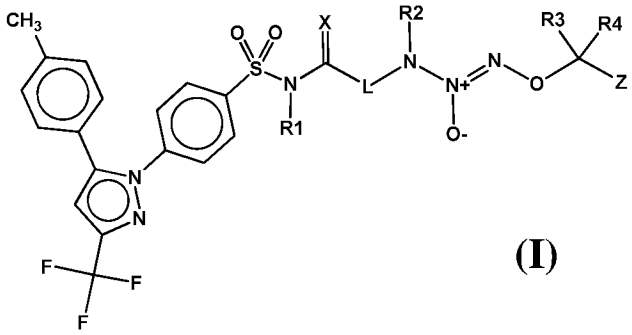
and pharmaceutically acceptable salts thereof, wherein R^1, X, L, R^2, R^3, R^4, and Z are as defined in the detailed description.

[0026] Compounds of the present invention can exist in tautomeric, geometric or stereoisomeric forms. An ester, metabolite, oxime, prodrug, onium, hydrate, solvate and N-oxide forms of a compound of Formula (I) are also embraced by the invention. The present invention considers all such compounds, including, but not limited to, cis- and trans-geometric isomers (e.g., Z- and E-geometric isomers, respectively), R- and S-enantiomers, diastereomers, d-isomers, l-isomers, atropisomers, epimers, conformers, rotamers, mixtures of isomers and racemates thereof, as falling within the scope of the invention.

DETAILED DESCRIPTION

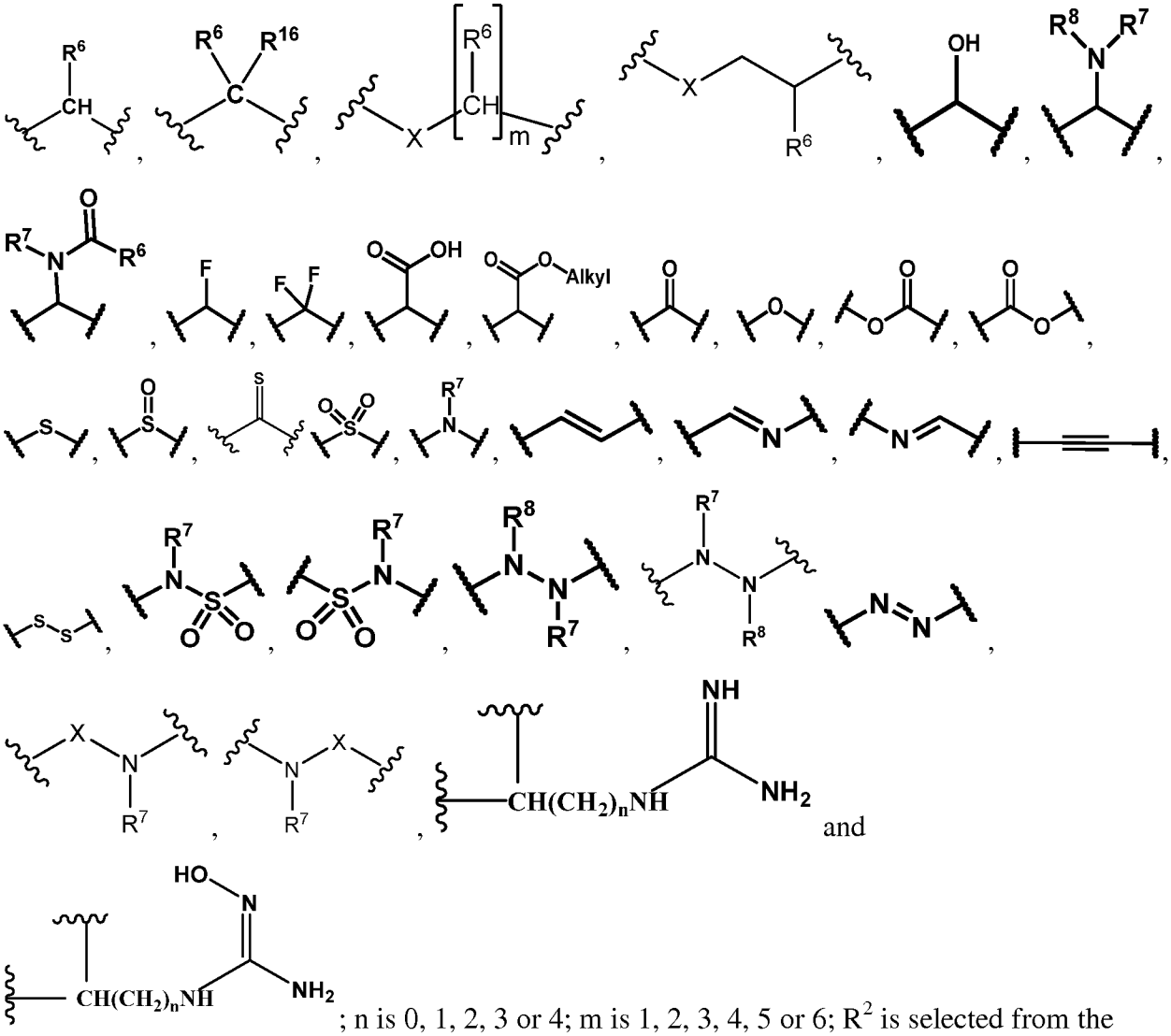
A. Compounds

[0027] The present invention provides compounds, or pharmaceutically acceptable salts,



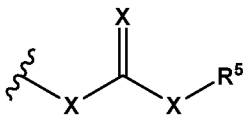
(I)

wherein R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-; X is O or S; –L– is C_{1-15}alkylene, wherein one or more $–CH_2–$ radicals may be replaced with a radical selected from the group consisting of:

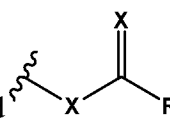


and

; n is 0, 1, 2, 3 or 4; m is 1, 2, 3, 4, 5 or 6; R^2 is selected from the group consisting of H, alkyl, aryl, heterocyclyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, carboxyalkyl and hydroxyalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl, or R^3 may be taken together with R^4 to form a carbocyclic ring having 3 to 7 ring atoms including optionally one or more O, N, or S atoms as ring atoms; Z is selected from the group consisting of phthalimido, succinimido,



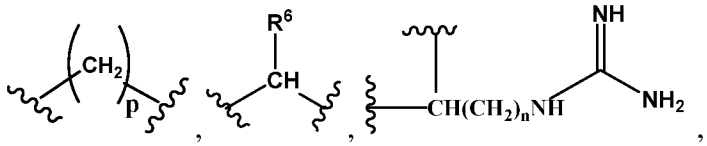
and



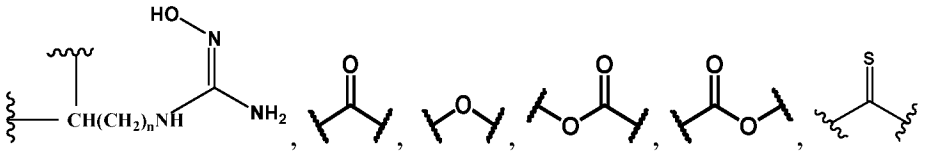
, wherein phthalimido or succinimido is optionally

substituted by halo, alkyl, alkyl-O, aryl and heteroaryl; R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; each of R^6 and R^{16} is independently selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or each of R^6 and R^{16} may independently be taken together with R^2, R^7 or R^8 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and each of R^7 and R^8 is independently selected from the group consisting of H, alkyl, hydroxyalkyl, aryl, heterocyclyl, alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, carboxyalkylcarbonyl, alkyloxycarbonylalkylcarbonyl, alkylsulfonyl, arylsulfonyl and heteroarylsulfonyl, or R^7 may be taken together with R^2, R^6 or R^8 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms.

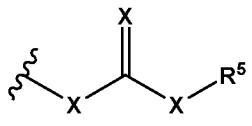
[0028] In another family of the compounds of Formula (I), R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-; X is O or S; –L– is one or more radicals selected from the group consisting of:

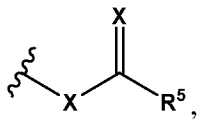


,



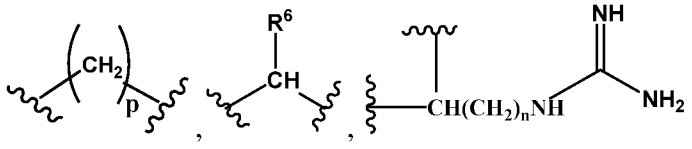
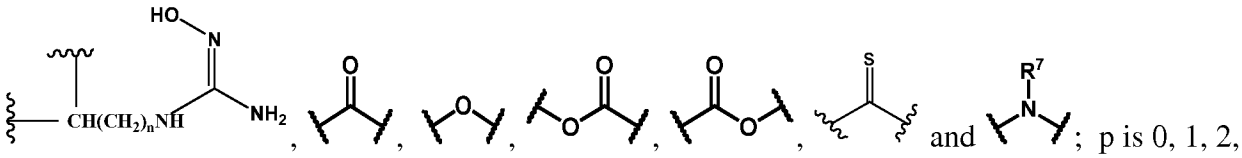
and ; p is 0, 1, 2, 3 or 4; n is 0, 1, 2, 3 or 4; R^2 is selected from the group consisting of H, alkyl, aryl, heterocyclyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, carboxyalkyl and hydroxyalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

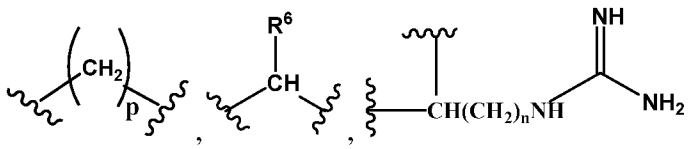
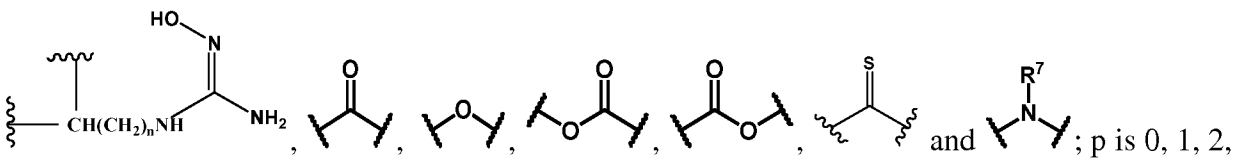
Z is selected from the group consisting of phthalimido, succinimido, 

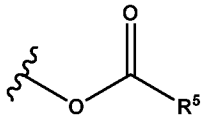
and 

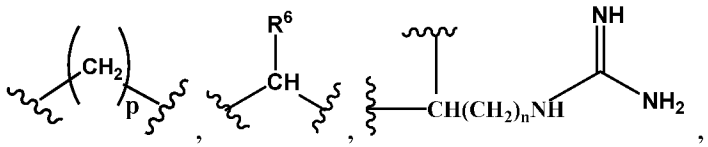
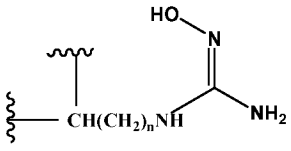
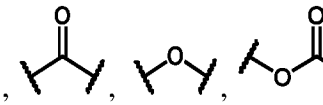
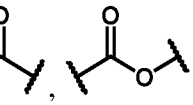
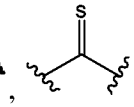
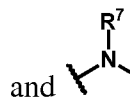
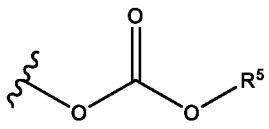
, wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl; R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 may be taken together with R^2 to form a nitrogen-

containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and R^7 is selected from the group consisting of H, alkyl, hydroxyalkyl, aryl, heterocyclyl, alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, carboxyalkylcarbonyl, alkyloxycarbonylalkylcarbonyl, alkylsulfonyl, arylsulfonyl and heteroarylsulfonyl, or R^7 may be taken together with R^2 or R^6 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms.

[0029] In another family of the compounds of Formula (I), R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-; X is O; –L– is one or more radicals selected from the group consisting of:  ,  ; p is 0, 1, 2, 3 or 4; n is 0, 1, 2, 3 or 4; R^2 is selected from the group consisting of H, alkyl and cycloalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is phthalimido or succinimido, wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl; R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 may be taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and R7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl.

[0030] In another family of the compounds of Formula (I), R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-; X is O; –L– is one or more radicals selected from the group consisting of:  ,  ; p is 0, 1, 2, 3 or 4; n is 0, 1, 2, 3 or 4; R^2 is selected from the group consisting of H, alkyl and cycloalkyl;

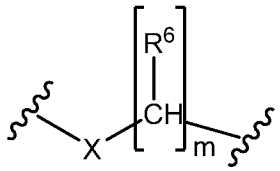
each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is  ; R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH– , or R^6 may be taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl.

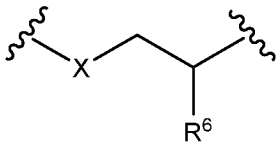
[0031] In another family of the compounds of Formula (I), R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-; X is O; –L– is one or more radicals selected from the group consisting of:  ,  ,  ,  ,  ,  and ; p is 0, 1, 2, 3 or 4; n is 0, 1, 2, 3 or 4; R^2 is selected from the group consisting of H, alkyl and cycloalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is  ; R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 may be taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl. Non-limiting examples include:

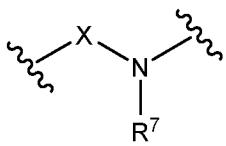
No.	Compound Name
407	(Z)-3,7-Dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
503	(Z)-3,11-Dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide

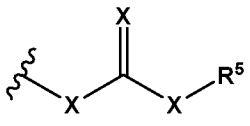
408	(Z)-3,7,11,11-Tetramethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
371	(Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
372	(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide

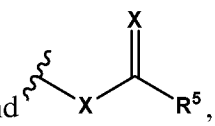
[0032] In another family of the compounds of Formula (I), R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-; X is O or S; –L– is one or more radicals selected from the group consisting of:



,


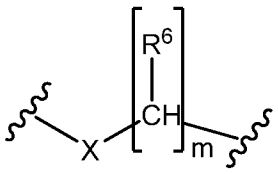
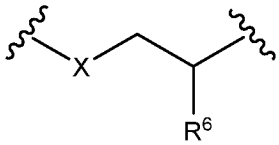
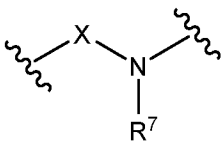
and


; m is 1, 2, 3, 4, 5 or 6; R^2 is selected from the group consisting of H, alkyl, aryl, heterocyclyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, carboxyalkyl and hydroxyalkyl; each of R3 and R4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is selected from the group consisting of phthalimido, succinimido,


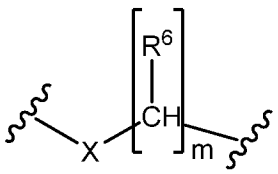
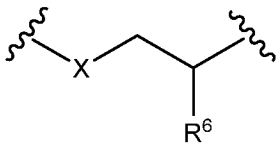
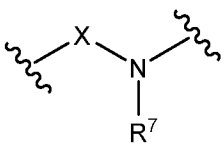
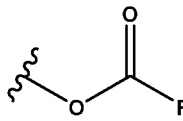
and


, wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl; R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 may be taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and R^7 is selected from the group consisting of H, alkyl, hydroxyalkyl, aryl, heterocyclyl, alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, carboxyalkylcarbonyl, alkyloxycarbonylalkylcarbonyl, alkylsulfonyl, arylsulfonyl and heteroarylsulfonyl, or R^7 may be taken together with R^2 or R^6 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms.

[0033] In another family of the compounds of Formula (I), R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-; X is O or S; –L– is one or more radicals selected from

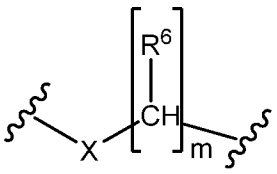
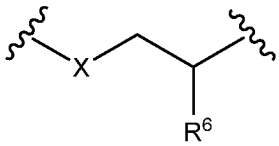
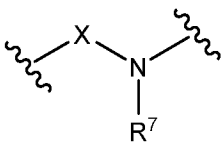
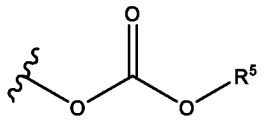
the group consisting of:  ,  ,  ; m is 1, 2, 3, 4, 5 or 6; R^2 is selected from the group consisting of H, alkyl and cycloalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is phthalimido or succinimido, wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl; R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 may be taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl. Non-limiting examples include:

No.	Compound Name
12	(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
11	(Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
8	(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-ethyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
10	(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-isopropyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
14	(Z)-3-(tert-Butyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide

[0034] In another family of the compounds of Formula (I), R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-; X is O or S; –L– is one or more radicals selected from the group consisting of:  ,  ,  ; m is 1, 2, 3, 4, 5 or 6; R^2 is selected from the group consisting of H, alkyl and cycloalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is  ; R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl;

R6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 may be taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl. Non-limiting examples include:

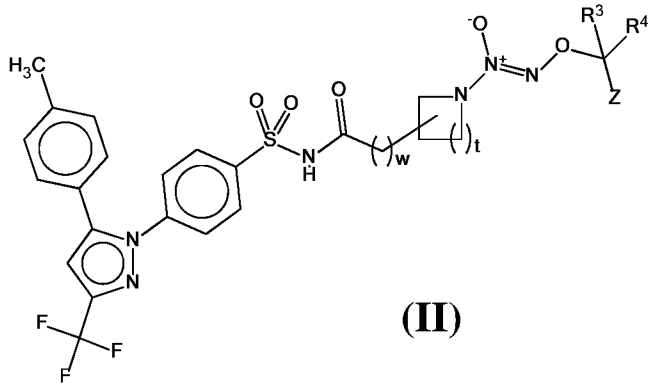
No.	Compound Name
199	(Z)-5-Methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
350-A	(Z)-5-Methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatetradec-6-ene 6-oxide
200	(Z)-7-Methyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
195	(Z)-3,7-Dimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
202	(Z)-5,12,12-Trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
197	(Z)-5,9,12,12-Tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide

[0035] In another family of the compounds of Formula (I), R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-; X is O or S; –L– is one or more radicals selected from the group consisting of:  ,  ,  ; m is 1, 2, 3, 4, 5 or 6; R^2 is selected from the group consisting of H, alkyl and cycloalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is  ; R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 may be taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl. Non-limiting examples include:

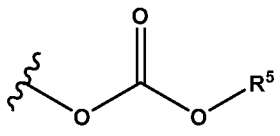
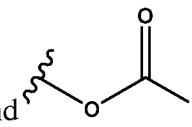
No.	Compound Name

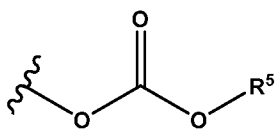
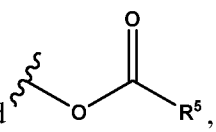
150-C	(Z)-5-Ethyl-13-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
150-D	(Z)-5-Ethyl-9,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
93	(Z)-5,9,13,13-Tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
89	(Z)-5-Ethyl-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
91	(Z)-5-Isopropyl-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
95	(Z)-5-(tert-Butyl)-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
150-B	(Z)-5,9,13-Trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide

[0036] The present invention is also directed to a subclass of compounds of Formula (II):



(II)

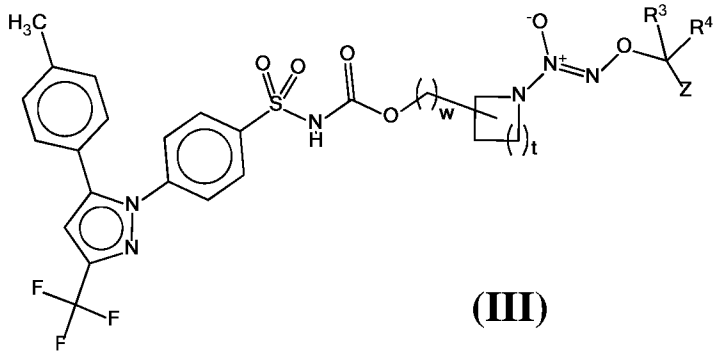
wherein w is 0, 1, or 2; t is 1, 2, 3, or 4; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is selected from the group consisting of phthalimido, succinimido,  and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl; and R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl.

[0037] In another family of the compounds of Formula (II), w is 0, 1, or 2; t is 1 or 2; each of R^3 and R^4 is independently selected from the group consisting of H and alkyl; Z is selected from the group consisting of phthalimido,  and  ,

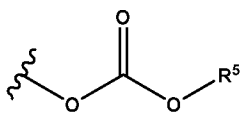
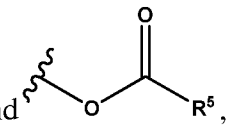
wherein phthalimido is optionally substituted by halo, alkyl and alkyl-O; and R5 is selected from the group consisting of alkyl, phenyl and benzyl. Non-limiting examples include:

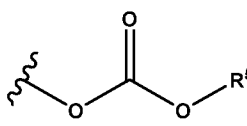
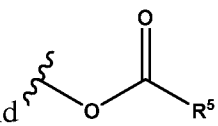
No.	Compound Name
430	(Z)-2-(1-((Ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
432	(Z)-2-(1-((tert-Butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
414	(Z)-2,2,6,10-Tetramethyl-4,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide

[0038] The present invention is also directed to a subclass of compounds of Formula (II):



(III)

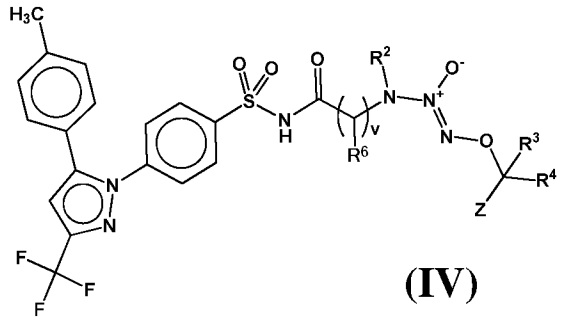
wherein w is 0, 1, or 2; t is 1, 2, 3 or 4; each of R^3 and R^4 is independently selected from the group consisting of H and alkyl; Z is selected from the group consisting of phthalimido, succinimido,  and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl; and R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl.

[0039] In another family of the compounds of Formula (III), w is 0, 1, or 2; t is 1 or 2; each of R^3 and R^4 is independently selected from the group consisting of H and alkyl; Z is selected from the group consisting of phthalimido,  and  , wherein phthalimido is optionally substituted by halo, alkyl and alkyl-O; and R5 is selected from the group consisting of alkyl, phenyl and benzyl. Non-limiting examples include:

No.	Compound Name
32	(S,Z)-2-((1,3-Dioxoisoindolin-2-yl)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide

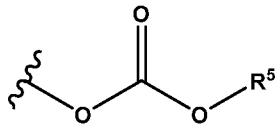
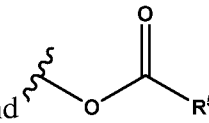
126	(Z)-2-(1-((tert-Butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide

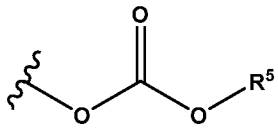
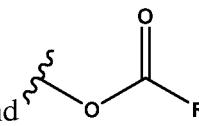
[0040] The present invention is also directed to a subclass of compounds of Formula (IV):



(IV)

wherein v is 1, 2, 3 or 4; R^2 is selected from the group consisting of H, alkyl and cycloalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is selected from the group consisting of phthalimido, succinimido,

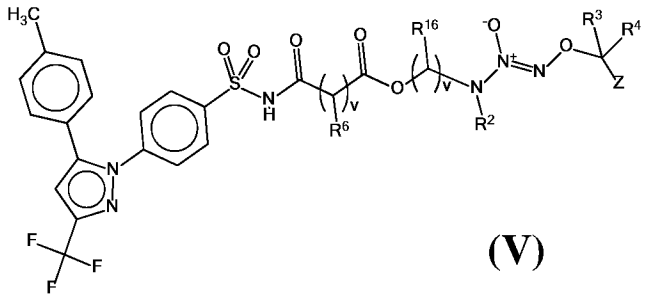
 and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl; R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; and R^6 is selected from the group consisting of H, alkyl and aralkyl.

[0041] In another family of the compounds of Formula (IV), v is 1 or 2; R^2 is selected from the group consisting of H, alkyl and cycloalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is selected from the group consisting of phthalimido,  and  , wherein phthalimido is optionally substituted by halo, alkyl and alkyl-O; and R^5 is selected from the group consisting of alkyl, phenyl and benzyl; and R^6 is selected from the group consisting of H, alkyl and aralkyl. Non-limiting examples include:

No.	Compound Name
355	(Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide
602	(Z)-3-Methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-

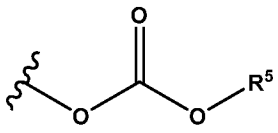
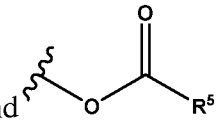
	yl)phenylsulfonamido)ethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide

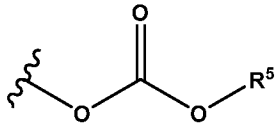
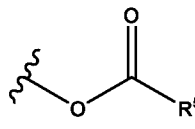
[0042] The present invention is also directed to a subclass of compounds of Formula (V):



(V)

wherein v is 1, 2, 3 or 4; R^2 is selected from the group consisting of H, alkyl and cycloalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is selected from the group consisting of phthalimido, succinimido,

 and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl; R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; and each of R^6 and R^{16} is independently selected from the group consisting of H, alkyl and aralkyl.

[0043] In another family of the compounds of Formula (V), v is 1 or 2; R^2 is selected from the group consisting of H, alkyl and cycloalkyl; each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl; Z is selected from the group consisting of phthalimido,  and  , wherein phthalimido is optionally substituted by halo, alkyl and alkyl-O; R^5 is selected from the group consisting of alkyl, phenyl and benzyl; and each of R^6 and R^{16} is independently selected from the group consisting of H and alkyl. Non-limiting examples include:

No.	Compound Name
764	(Z)-6,10-Dimethyl-4,14,17-trioxo-17-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7,13-tetraoxa-8,9,10-triazaheptadec-8-ene 9-oxide

B. Other Embodiments

[0044] In another embodiment, there is provided a pharmaceutical composition comprising a compound of Formula (I) and a pharmaceutically-acceptable carrier.

[0045] In another embodiment, the pharmaceutical composition further comprises one or more additional pharmaceutically active compounds.

[0046] In another embodiment, there is provided a method for treating or preventing a disease condition comprising administering to a subject a therapeutically effective amount of a compound of Formula (I), wherein the condition to be treated or prevented includes, for example, cancer. Further non-limiting examples include non-small cell lung cancer, skin cancer, liver cancer, colorectal cancer (and FAP), squamous cell cancer, bladder cancer, breast cancer, biliary tract cancer, cervical cancer, prostate cancer, small cell lung cancer, ovarian cancer, pancreatic cancer, gastrointestinal cancer and CNS cancer.

[0047] In another embodiment, there is provided a method for healing wounds, comprising administering to a subject a therapeutically effective amount of a compound of Formula (I).

[0048] In another embodiment, there is provided a method for treating a condition, comprising administering to a subject a therapeutically effective amount of a compound of Formula (I), wherein the condition to be treated includes, for example, actinic keratosis, cystic fibrosis and/or acne.

[0049] In another embodiment, there is provided a method for treating a condition comprising administering to a subject a therapeutically effective amount of a compound of Formula (I), wherein the condition to be treated includes, for example, autoimmune disorder, inflammatory disorder and/or auto-inflammatory disorder.

[0050] In another embodiment, there is provided a method that comprises administering a combination of a compound of Formula (I) and at least one additional pharmaceutically active compound.

[0051] In another embodiment, there is provided a use of a compound of Formula (I) for manufacture of a medicament for treatment of a disease condition in a subject.

[0052] In another embodiment, there is provided a method for preparing a compound of Formula (I).

[0053] In another embodiment, there is provided an intermediate useful in making a compound of Formula (I).

[0054] In another embodiment, there is provided a method of enhancing cancer-treating efficacy by activating both NO and COX-2-inihibitor anti-tumor mechanisms in a subject, by administering a therapeutically effective amount of a compound of Formula (I).

[0055] In another embodiment, there is provided a method of treating a subject suffering from a disease condition caused by COX-2 over-expression, including but not limited to cancer, by administering a therapeutically effective amount of a compound of Formula (I).

[0056] In another embodiment, there is provided a method of improving CV safety in a subject, by administering a therapeutically effective amount of a compound of Formula (I).

[0057] In another embodiment, there is provided a method of treating a subject suffering from a disease condition, including but not limited to cancer, by administering a high-dose of a compound of Formula (I).

[0058] In another embodiment, there is provided a method of cardio-protection in a subject, comprising administering a therapeutically effective amount of a compound of Formula (I).

[0059] In another embodiment, there is provided a method of releasing NO in a subject, comprising administering a therapeutically effective amount of a compound of Formula (I).

[0060] In another embodiment, there is provided a method of cardio-protection in a subject, comprising administering a therapeutically effective amount of a compound of Formula (I), which releases NO in the subject, preferably by sustained release.

[0061] In another embodiment, there is provided a method of cardio-protection in a subject, comprising administering a therapeutically effective amount of a compound of Formula (I), which releases NO in the subject, preferably by sustained release.

[0062] In another embodiment, there is provided a method of cardio-protection in a subject, comprising administering a therapeutically effective amount of a compound of Formula (I), which releases NO in the subject, preferably by sustained release, wherein the NO release is likely caused by an enzymatic mechanism acting on the NONOate moiety of the compound of Formula (I).

[0063] In another embodiment, there is provided a method of cardio-protection in a subject, comprising administering a therapeutically effective amount of a compound of Formula (I), which releases NO in the subject, preferably by sustained release, wherein the NO release is

likely caused by a non-enzymatic mechanism acting on the NONOate moiety of the compound of Formula (I).

[0064] In another embodiment, there is provided a method of treating a subject suffering from a disease condition, including but not limited to cancer, comprising administering a therapeutically effective amount of a compound of Formula (I), without causing substantial adverse, cardiovascular events.

[0065] In another embodiment, there is provided a method of treating a subject suffering from a disease condition, including but not limited to cancer, comprising administering a therapeutically effective amount of a compound of Formula (I), without causing substantial changes in blood pressure, while maintaining gastric-sparing properties.

C. General Synthetic Schemes

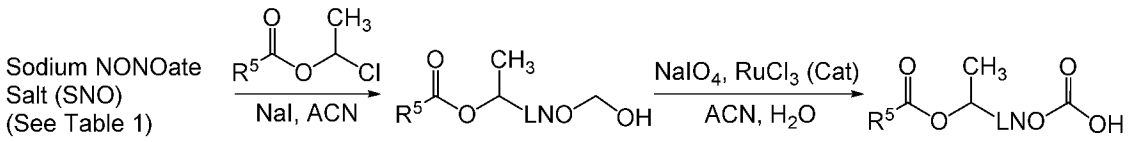
[0066] Compounds of the present invention can be prepared using methods illustrated in general synthetic schemes and experimental procedures detailed below. These general synthetic schemes and experimental procedures are presented for purposes of illustration and are not intended to be limiting. Starting materials used to prepare compounds of the present invention are commercially available or can be prepared using routine methods known in the art. Scheme 1 illustrates synthesis of Capped-NONOate Alcohols and Carboxylic Acid, Scheme 2 illustrates synthesis of NONOate-oxycarbonyl-sulfonamide-linked coxib species-compounds, Scheme 3 illustrates synthesis of NONOate-carbonyl-sulfonamide-linked coxib species-compounds, and Scheme 4 illustrates synthesis of NONOate-succinyl-sulfonamide-linked coxib compounds.

[0067] **Conversion of N-Boc-protected amino alcohols to N-alkylamino alcohols**: (S)-2-Boc-alaninol, (S)-2-Boc-leucinol, (S)-2-(Boc-amino)-3-phenyl-1-propanol, (S)-2-Boc-3-methyl-1-butanol, and (S)-2-Boc-isoleucinol are converted to (S)-2-N-methyl-alaninol, (S)-2-N-methyl-leucinol, (S)-2-(N-methylamino)-3-phenyl-1-propanol, (S)-2-N-methyl-3-methyl-1-butanol, and (S)-2-N-methyl-isoleucinol) respectively using established procedures (*See also* Reddy, G.V., Rao, G.V., Sreevani, V. and Iyengar, D.S. *Tetrahedron Letters* 2000, *41*, 949–951). A N-protected amino alcohol (1.0 eq.), paraformaldehyde (3 eq.), and p-toluenesulfonic acid (0.1 eq.) are dissolved in toluene and refluxed for 30 min using a Dean Stark trap. The solvent is evaporated under reduced pressure to give a crude residue that is purified by silica gel column chromatography to give afford pure N-protected oxazolines. The N-protected oxazoline (1 eq.) is dissolved in dry ACN under nitrogen atmosphere and treated with sodium cyanoborohydride (1

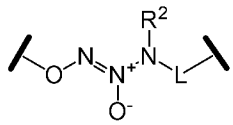
eq.) followed by trimethylsilyl chloride (1 eq.). The reaction mixture is stirred at room temperature for 30 min and the solvent is evaporated under reduced pressure. The residue is suspended in ethyl acetate and washed with a solution of 0.5 N sodium hydroxide. The organic layer is separated and the aqueous layer is extracted again with ethyl acetate. The combined organic layers are washed with brine, dried over sodium sulfate, filtered, and evaporated under reduced pressure. The residue is purified by silica gel column chromatography to afford pure Boc-N-methyl amino alcohols. Boc-Deprotection is accomplished using standard conditions stirring at room temperature in 5:1-methylene chloride(methylene chloride)/trifluoroacetic acid (TFA)(v/v). After 4 hrs the reaction is evaporated, the residue is dissolved in ethyl acetate and washed with saturated sodium bicarbonate solution. The organic layer is separated and the aqueous layer is extracted again with ethyl acetate. The organic layers are pooled, dried over sodium sulfate, filtered to remove solids, and evaporated to dryness resulting in N-methylamino alcohols. In addition to paraformaldehyde, numerous aldehydes such as paraldehyde, benzaldehyde, isobutyraldehyde, trimethylacetaldehyde, 2-methylbutyraldehyde, 2-ethylbutyraldehyde, etc. are commercially available and can be use in this reaction to generate starting materials (*See* Table 1).

[0068] **Sodium NONOate (SNO) Salts** (*see* also Velázquez, C.A., Chen, Q., Citro, M.L., Keefer, L.K. and Knaus, E.E. *J Med Chem* 2008, *51*, 1954-1961): A N-methylamino alcohol (*See* Table 1) (10 g, 0.13 mol) is added to a solution of sodium methoxide (7.2 g, 0.13 mol, 30.5 mL of a 25% w/v solution in MeOH) and ether (150 mL) with stirring at 25 °C. The flask is evacuated and then charged with nitric oxide (NO) (40 psi internal pressure) with stirring at 25 °C for 72 hrs. The product is isolated by filtration and then suspended in ether (100 mL) with stirring for 15 min. The suspension is filtered, collected and dried under reduced pressure until a constant weight is achieved. Starting materials and corresponding sodium NONOate salts are listed in Table 1.

[0069] **Scheme 1: Synthesis of O-Capped-NONOate Alcohols and Carboxylic Acid**



SNO = A sodium NONOate Salt (See Table 1)
R^5 = Phenyl or Ethoxy
R^2 = H or Alkyl
LNO = NONOate Linker Corresponding to Selected SNO, for example:



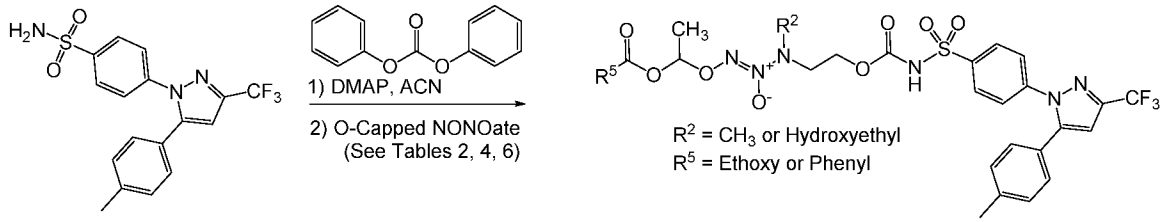
[0070] **Alpha-Chloroalkyl Ester Formation** (*See also* Ulich, L.H. and Adams, R. *J. Am. Chem. Soc.* 1921, *43*, 660–667): An acyl chloride (1.0 eq) and aldehyde (1.2 eq) is mixed in a round-bottomed flask equipped with a reflux water condenser. A minute quantity of anhydrous zinc chloride is added resulting in considerable heat evolution (in many cases causing the reaction mixture to boil gently). The reaction is heated further to 90 °C for 3 to 4 hrs and at the end of this time the reaction mixture is distilled with a fractionating column preferably under diminished pressure. The distillate is then redistilled either under atmospheric or diminished pressure to yield halogenated alkyl esters. In addition to paraformaldehyde, numerous aldehydes such as paraldehyde, benzaldehyde, isobutyraldehyde, trimethylacetaldehyde, 2-methylbutyraldehyde, 2-ethylbutyraldehyde, etc. are commercially available and can be use in this reaction.

[0071] **Capping Sodium NONOates with Electrophiles** (*see* also Velázquez, C.A., Chen, Q., Citro, M.L., Keefer, L.K. and Knaus, E.E. *J Med Chem* 2008, *51*, 1954-1961): A NONOate sodium salt from Table 1 (1.0 eq.) is suspended in ACN and a solution of electrophile (e.g. chloromethylphthalimide, chloromethyl acetate, 1-chloroethyl ethylcarbonate) is added at room temperature in ACN followed by solid sodium iodide (1.4 eq). The resulting mixture is stirred at room temperature for 12 hrs and then evaporated under reduced pressure. The residue is suspended in ethyl acetate and washed with a solution of 0.2 N sodium thiosulfate. The organic layer is separated and the aqueous layer is extracted again with ethyl acetate. The combined organic layers are washed with brine, dried over sodium sulfate, filtered, and the filtrate is evaporated under reduced pressure. The residue is purified by silica gel column chromatography to afford O-capped NONOates shown in Tables 2, 4, and 6.

[0072] **Oxidation of Primary Alcohol NONOates to Carboxylic Acids** (*See also*, Chakrapani, H., Maciag, A.E., Citro, M.L., Keefer, L.K. and Saavedra, J.E. *Org Lett* 2008, *10*, 5155-5158): Capped NONOate (1.0 eq.) is dissolved in ACN and water (2:3 v/v) and treated

with sodium periodate ($NaIO_4$) (4.0 eq.) and ruthenium trichloride hydrate ($RuCl_3$) (0.04 eq). The reaction mixture is diluted with ethyl acetate (1 volume) and stirred overnight. The reaction mixture is diluted with ethyl acetate and filtered through Celite. The filtrate is extracted with 5 % aqueous sodium bicarbonate and washed with methylene chloride. The aqueous layer is acidified with dilute hydrochloric acid and washed with methylene chloride. The combined organic layers are separated, dried, filtered and concentrated under reduced pressure. The residue is purified by silica gel column chromatography to afford O-capped NONOates shown in Tables 3, 5, and 7.

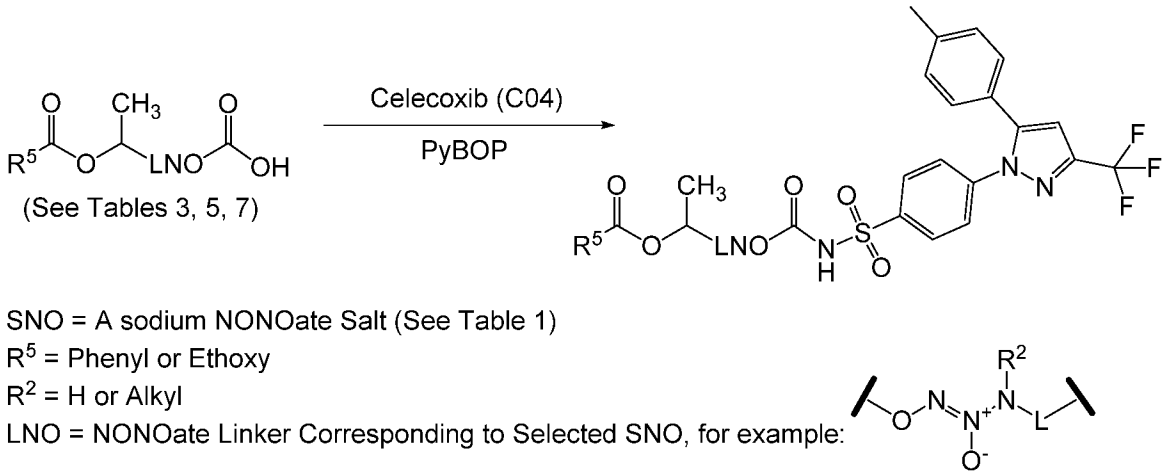
[0073] Scheme 2: Synthesis of NONOate-Oxycarbonyl-Sulfonamide-Linked Coxib Species-Compounds.



[0074] NONOate-Oxycarbonyl (Carbamate-Linked Coxib) (*See also* Sączewski, F., Kuchnio, A., Samsel, M., Łobocka, M., Kiedrowska, A., Lisewska, K., Sączewski, J., Gdaniec, M. and Bednarski, P.J. *Molecules* 2010, *15*, 1113-1126): Celecoxib (**C02**) (1.0 eq.) and 4-dimethylaminopyridine (DMAP) (2.0 eq) are dissolved in ACN and treated with diphenyl carbonate (1.05 eq.). The reaction mixture is stirred 12 hrs at room temperature. The solid that precipitates is collected by suction filtration, washed with dry ACN and dried to give pure celecoxib carbamoylide (See Example **C03**).

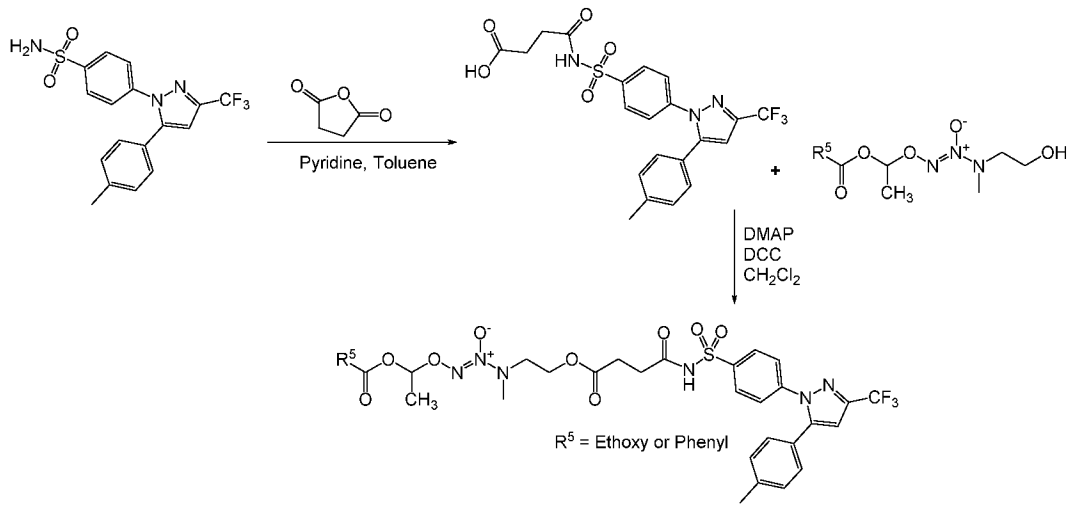
[0075] **C03** (1.0 eq.) is dissolved in ACN and an O-capped NONOate from Tables 2, 4, and 6 is added in ACN solution and the mixture is heated to 50 °C. The reaction mixture is cooled to room temperature and the solvent is evaporated under reduced pressure to dryness. The residue is dissolved in ethyl acetate and washed with a solution of 0.2 N hydrochloric acid. The organic layer is separated and the aqueous layer is extracted again with ethyl acetate. The combined organic layers are washed with brine, dried over sodium sulfate, filtered, and evaporated under reduced pressure. The residue is purified by silica gel column chromatography to afford species-compounds shown in Tables 8, 9, and 10.

[0076] Scheme 3: Synthesis of NONOate-Carbonyl-Sulfonamide-Linked Coxib Species-Compounds.



[0077] NONOate(Nitrogen-Bound)Sulfonamide-Linked (Amide-Linked Coxib): Celecoxib sodium salt (**C04**) (2.0 eq.) is suspended in methylene chloride, benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (**PyBOP**) (1.2 eq.) and NONOate carboxylic acid (1.0 eq.) is added and the reaction is stirred at room temperature overnight. The methylene chloride is removed under reduced pressure and the residue is taken up in ethyl acetate. The organic layer is washed with water, brine, dried over magnesium sulfate, filtered and concentrated. The residue is purified by silica gel column chromatography to afford species-compounds shown in Tables 11, 12, and 13.

[0078] Scheme 4: Synthesis of NONOate-Succinyl-Sulfonamide-Linked Coxib Species-Compounds.



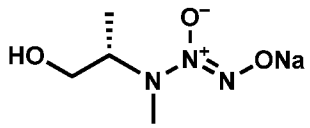
[0079] NONOate-Succinyl-Sulfonamide-Linked (Amide-Linked Succinamide Coxib): Celecoxib (**C02**) (1.0 eq.) is dissolved in toluene. Succinic anhydride (5.0 eq.) and pyridine (1.5 eq.) are added and refluxed overnight. After acidic work-up the solution is dried

over magnesium sulfate and evaporated. The product is chromatographed to afford the succinyl diimide celecoxib derivative (*See* Example **C05**).

[0080] **Succinyl-Sulfonamide-Linked NONOates**: **C05** (1.0 eq.) and an O-capped NONOate (1.2 eq.; *See* Tables 2, 4, and 6) are dissolved in methylene chloride. Dicyclohexylcarbodiimide (**DCC**) (1.0 eq.) and DMAP (1.0 eq.) are added at room temperature and stirred for 12 hrs. The reaction mixture is evaporated and dissolved in ethyl acetate. The organic layer is washed with saturated potassium hydrogen sulfate solution and brine, dried over magnesium sulfate and evaporated. The residue is purified by silica gel column chromatography to afford species-compounds shown in Table 14.

SODIUM NONOATES

[0081] **(S,Z)-1-Hydroxy-3-(1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide sodium salt (N001)**

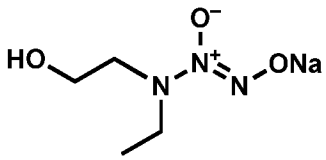


[0082] A solution of iodine (4.92 g, 19.39 mmol) in tetrahydrofuran (10 mL) was slowly added dropwise to a suspension of *N*-methyl-L-alanine (2.00 g, 10.39 mmol) and sodium borohydride (1.83 g, 48.49 mmol) in tetrahydrofuran (50 mL), pre-cooled in an ice-bath. Once the addition was complete the reaction mixture was heated to reflux. After 18 hours the reaction was allowed to cool to ambient temperature and then methanol (5 mL) was slowly added. The mixture was stirred at ambient temperature for 30 minutes and then concentrated under reduced pressure. The residue was dissolved in 20% KOH (w/w) (30 mL) and then stirred at ambient temperature for 4 hours. The aqueous reaction mixture was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure to provide a clear oil (2.07 g, 100% yield).

[0083] Crude alaninol (19.39 mmol) was added to a solution of sodium methoxide (1.05 g, 19.39 mmol, 4.5 mL of a 25% w/v solution in MeOH) and ether (25 mL) with stirring at 25 °C. The flask was evacuated and then charged with nitric oxide (NO) (40 psi internal pressure) with stirring at 25 °C for 2 days. The product was isolated by filtration and the filtrate was concentrated under reduced pressure. The residue was treated with acetonitrile and the precipitate that developed was collected by filtration. This process was repeated a second time

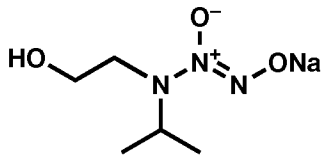
and the solids collect were combined with the original product to give an off-white solid (0.935 g, 28% yield).

[0084] **(Z)-3-Ethyl-1-hydroxy-3-(2-hydroxyethyl)triaz-1-ene 2-oxide sodium salt (N004)**



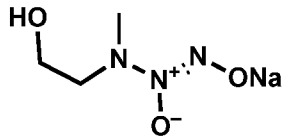
[0085] 2-(Ethylamino) ethanol (5.0 g, 56.1 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N001**: (9.58 g, 50% yield). ^{1}H NMR (400 MHz, D_2O) δ 3.41 (t, 5.6 Hz, 2H), 2.94 (t, J=5.7 Hz, 2H), 2.84 (q, J=7.1 Hz, 2H), 0.83 (t, 7.1 Hz, 3H).

[0086] **(Z)-1-Hydroxy-3-(2-hydroxyethyl)-3-isopropyltriaz-1-ene 2-oxide sodium salt (N005)**



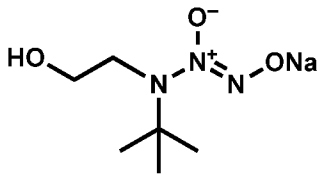
[0087] 2-(Isopropylamino) ethanol (13.0 g, 126 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N001**: (4.02 g, 17% yield). ^{1}H NMR (400 MHz, D_2O) δ 3.44 (t, 5.8 Hz, 2H), 3.21-3.15 (m, 1H), 3.08 (t, J=5.9 Hz, 2H), 1.00 (d, J=6.3 Hz, 6H).

[0088] **(Z)-1-Hydroxy-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide sodium salt (N006)**



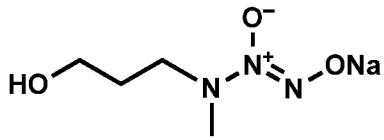
[0089] *N*-methylethanolamine (2.0 g, 26.63 mmol) was added to a solution of sodium methoxide (1.44 g, 26.63 mmol, 6.0 mL of a 25% w/v solution in methanol) and ether (30 mL) with stirring at 25 °C. The flask was evacuated and then charged with nitric oxide (NO) (40 psi internal pressure) and stirred at 25 °C for 24 hrs. The product was isolated by filtration and then suspended in ether (30 mL) and stirred for 15 min. The suspension was filtered, collected and dried at 25 °C under reduced pressure to give **(N006)** as a white fine powder (2.72 g, 65% yield). ^{1}H NMR (400 MHz, D_2O) δ 3.42-3.40 (m, 2H), 2.95-2.92 (m, 2H), 2.63 (s, 3H).

[0090] **(Z)-3-(tert-Butyl)-1-hydroxy-3-(2-hydroxyethyl)triaz-1-ene 2-oxide sodium salt (N007)**



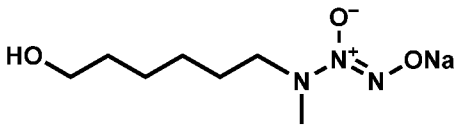
[0091] 2-(t-Butylamino) ethanol (10.0 g, 85.6 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N001**: (3.07 g, 18% yield). ^{1}H NMR (400 MHz, D_2O) δ 8.38 (s, 1H), 3.41 (t, 5.9 Hz, 2H), 3.12 (t, J=5.9 Hz, 2H), 1.11 (s, 9H).

[0092] **(Z)-1-Hydroxy-3-(3-hydroxypropyl)-3-methyltriaz-1-ene 2-oxide sodium salt (N009)**



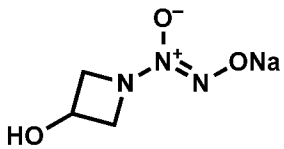
[0093] N-Methylamino-1-propanol (4.75 g, 53.29 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N001**: (2.80 g, 31% yield).

[0094] **(Z)-1-Hydroxy-3-(6-hydroxyhexyl)-3-methyltriaz-1-ene 2-oxide sodium salt (N012)**



[0095] 6-(Methylamino)hexan-1-ol (1.0 g, 7.62 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N001**: (1.67 g as colorless oil, 100% yield. ^{1}H NMR (400 MHz, D_2O) δ 3.54-3.48 (m, 2H), 2.84-2.79 (m, 2H), 2.63 (s, 3H), 1.51-1.42 (m, 4H), 1.31-1.21 (m, 4H).

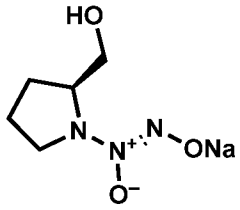
[0096] **(Z)-2-Hydroxy-1-(3-hydroxyazetidin-1-yl)diazene oxide sodium salt (N013)**



[0097] 3-Hydroxyazetidine hydrochloride (5.0 g, 46.1 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N001**: (8.98 g, >100%

yield(contaminated with ~25% NaCl)). ^{1}H NMR (400 MHz, D_2O) δ 4.43-4.38 (m, 1H), 4.04-4.00 (m, 2H), 3.88-3.84 (m, 2H).

[0098] (*S,Z*)-2-Hydroxy-1-(2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide sodium salt (N016)



[0099] (*S*)-(+)-2-Pyrrolidinemethanol (5.0 g, 49.4 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N001**: (4.36 g, 48% yield). ^{1}H NMR (400 MHz, d-DMSO) δ 3.37-3.19 (br m, 4H), 2.97-2.90 (br m, 2H), 1.87-1.50 (m, 4H). LC t_r=0.90 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C).

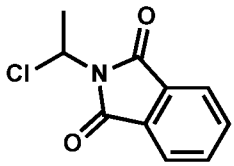
[00100] Table 1. Sodium NONOates.

Amine	NONOate #	NONOate Name
(S)-2-(methylamino)propan-1-ol	N001	(S,Z)-1-hydroxy-3-(1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide sodium salt
(S)-3-methyl-2-(methylamino)butan-1-ol	N002	(S,Z)-1-hydroxy-3-(1-hydroxy-3-methylbutan-2-yl)-3-methyltriaz-1-ene 2-oxide sodium salt
(S)-azetidine-2-methanol	N003	(S,Z)-2-hydroxy-1-(2-(hydroxymethyl)azetidin-1-yl)diazene oxide sodium salt
2-(ethylamino)ethanol	N004	(Z)-3-ethyl-1-hydroxy-3-(2-hydroxyethyl)triaz-1-ene 2-oxide sodium salt
2-(isopropylamino)ethanol	N005	(Z)-1-hydroxy-3-(2-hydroxyethyl)-3-isopropyltriaz-1-ene 2-oxide sodium salt
2-(methylamino)ethanol	N006	(Z)-1-hydroxy-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide sodium salt
2-(tert-butylamino)ethanol	N007	(Z)-3-(tert-butyl)-1-hydroxy-3-(2-hydroxyethyl)triaz-1-ene 2-oxide sodium salt
2-methyl-2-(methylamino)propan-1-ol	N008	(Z)-1-hydroxy-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide sodium salt
3-(methylamino)propan-1-ol	N009	(Z)-1-hydroxy-3-(3-hydroxypropyl)-3-methyltriaz-1-ene 2-oxide sodium salt
4-(methylamino)butan-1-ol	N010	(Z)-1-hydroxy-3-(4-hydroxybutyl)-3-methyltriaz-1-ene 2-oxide sodium salt
5-(methylamino)pentan-1-ol	N011	(Z)-1-hydroxy-3-(5-hydroxypentyl)-3-methyltriaz-1-ene 2-oxide sodium salt
6-(methylamino)hexan-1-ol	N012	(Z)-1-hydroxy-3-(6-hydroxyhexyl)-3-methyltriaz-1-ene 2-oxide sodium salt
azetidin-3-ol	N013	(Z)-2-hydroxy-1-(3-hydroxyazetidin-1-yl)diazene oxide sodium salt

azetidine-3-methanol	N014	(Z)-2-hydroxy-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide sodium salt
Diethanolamine	N015	(Z)-1-hydroxy-3,3-bis(2-hydroxyethyl)triaz-1-ene 2-oxide sodium salt
L-prolinol	N016	(S,Z)-2-hydroxy-1-(2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide sodium salt
N-methyl L-isoleucinol	N017	(Z)-1-hydroxy-3-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide sodium salt
N-methyl L-leucinol	N018	(S,Z)-1-hydroxy-3-(1-hydroxy-4-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide sodium salt
N-methyl L-phenylalaninol	N019	(S,Z)-1-hydroxy-3-(1-hydroxy-3-phenylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide sodium salt
piperidin-3-ol	N020	(Z)-2-hydroxy-1-(3-hydroxypiperidin-1-yl)diazene oxide sodium salt
piperidin-4-ol	N021	(Z)-2-hydroxy-1-(4-hydroxypiperidin-1-yl)diazene oxide sodium salt
piperidine-3-methanol	N022	(Z)-2-hydroxy-1-(3-(hydroxymethyl)piperidin-1-yl)diazene oxide sodium salt
piperidine-4-methanol	N023	(Z)-2-hydroxy-1-(4-(hydroxymethyl)piperidin-1-yl)diazene oxide sodium salt
pyrrolidin-3-ol	N024	(Z)-2-hydroxy-1-(3-hydroxypyrrolidin-1-yl)diazene oxide sodium salt
pyrrolidine-3-methanol	N025	(Z)-2-hydroxy-1-(3-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide sodium salt

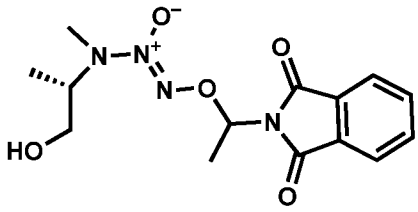
DIIMIDE-CAPPED ALOCHOL NONOATES

[00101] 1-(Chloroethyl) phthalimide



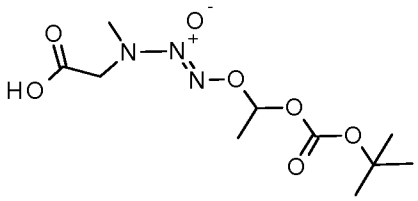
[00102] *N*-Vinyl phthalimide (0.100 g, 0.577 mol) was treated with 4*N* HCl/dioxane (0.433 mL, 1.73 mmol) at 25 °C. After 3 hours the reaction mixture was concentrated under reduced pressure to provide an off white solid (112 g, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.89 (m, 2H), 7.83-7.77 (m, 2H), 6.32 (q, J=6.8 Hz, 1H), 2.19 (d, J=6.8 Hz, 2H), LC t_r=3.05 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C).

[00103] (*Z*)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-((S)-1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide (N026)



[00104] NONOate salt **N001** (0.350 g, 2.05 mmol) suspended in acetonitrile (2.5 mL), pre-cooled in an ice-bath, was treated with a solution of 1-(chloroethyl) phthalimide (0.323 g, 1.54 mmol) in acetonitrile (2.5 mL) and then sodium iodide (0.231 g, 1.54 mmol) was added. The resulting mixture was stirred for 30 minutes then the ice-bath was removed and the mixture was stirred for an additional hour. The acetonitrile was removed under reduced pressure. The residue was suspended in ethyl acetate and then washed with a 0.2 *N* solution of sodium thiosulfate. The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated. The residue was subjected to chromatography using ethyl acetate in hexanes to provide a tan oily solid (42 mg, 8.5% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94-7.88 (m, 2H), 7.81-7.76 (m, 2H), 6.29 (dq, J=2.3, 6.6 Hz, 1H), 4.09-3.90 (m, 1H), 3.63-3.49 (m, 2H), 2.88 (d, J=5.6 Hz, 2H), 2.05 (d, J=6.6 Hz, 3H), 1.63-1.54 (br s, 1H), 1.04 (d, J=6.8 Hz, 3H). LC t_r=2.86 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 345 (M+Na calcd for $C_{14}H_{18}N_4O_5$ requires 345).

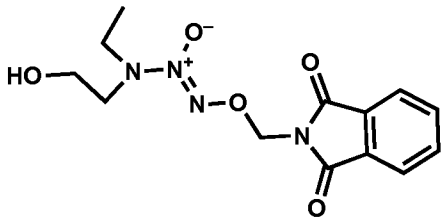
[00105] **(S,Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-(1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide (N027)**



[00106] NONOate salt **N001** (0.270 g, 1.58 mmol) suspended in acetonitrile (3.0 mL) was treated with a solution of *N*-(chloromethyl)phthalimide (0.280 g, 1.43 mmol) in acetonitrile (3.0 mL) and then sodium iodide (0.215 g, 1.43 mmol) was added. The resulting mixture was stirred at 25 °C overnight. *N,N*-dimethylformamide (1.0 mL) was added to the reaction mixture which was then heated to 60 °C for 1 hour. The acetonitrile was removed under reduced pressure. The residue was suspended in ethyl acetate and then washed with a 0.2 *N* solution of sodium thiosulfate. The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated. The residue was subjected to prep-chromatography using ethyl acetate in hexane to

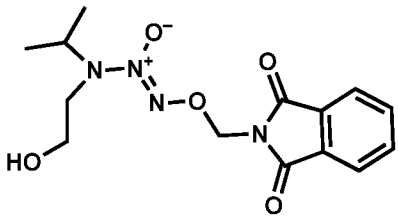
provide a tan oily solid (14 mg, 3.0% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92-7.87 (m, 2H), 7.78-7.73 (m, 2H), 5.67 (s, 2H), 2.97 (s, 1H), 2.19 (s, 2H), 1.59 (s, 6H). LC t_r=2.65 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 331 (M+Na calcd for $C_{13}H_{16}N_4O_5$ requires 331).

[00107] (Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)methoxy)-3-ethyl-3-(2-hydroxyethyl)triaz-1-ene 2-oxide (N033)



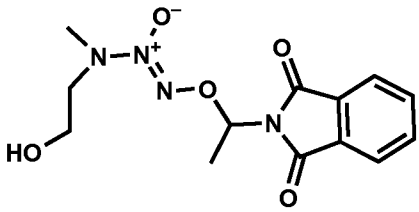
[00108] N-(chloromethyl) phthalimide (503 mg, 2.57 mmol) and **N004** (400 mg, 2.34 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N027**: (452 mg, 63% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.78 (m, 4H), 5.80 (s, 2H), 3.68-3.66 (m, 2H), 3.36-3.31 (m, 4H), 1.12 (t, J=7.1 Hz, 3H). LC t_r=2.68 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C).

[00109] (Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-(2-hydroxyethyl)-3-isopropyltriaz-1-ene 2-oxide (N035)



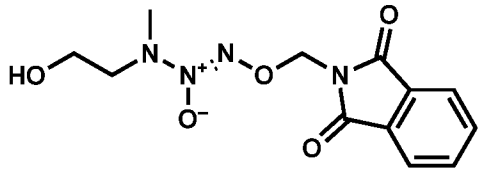
[00110] N-(chloromethyl) phthalimide (197 mg, 1.19 mmol) and **N005** (200 mg, 1.08 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N027**: (177 mg, 51% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.77 (m, 4H), 5.80 (s, 2H), 3.95-3.87 (m, 1H), 3.63-3.60 (m, 2H), 3.30 (t, J=5.2 Hz, 2H), 1.15 (d, J=6.5 Hz, 6H). LC t_r=2.84 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C).

[00111] (Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide (N036)



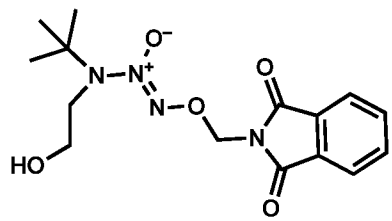
[00112] **N006** (0.312 g, 1.99 mmol) and 1-(chloroethyl) phthalimide (0.500 g, 2.39 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N026**: (227 mg, 31% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94-7.88 (m, 2H), 7.82-7.76 (m, 2H), 6.27 (q, J=6.6 Hz, 1H), 3.76 (br q, J=5.1 Hz, 2H), 3.43 (t, J=5.4 Hz, 2H), 3.01 (s, 3H), 2.04 (d, J=6.6 Hz, 3H). LC t_r=2.68 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 331 (M+Na calcd for $C_{13}H_{16}N_4O_5$ requires 331).

[00113] **(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide (N037)**



[00114] N-(chloromethyl) phthalimide (259 mg, 1.33 mmol) and **N006** (250 mg, 1.59 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N026**: (257 mg, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.89 (m, 2H), 7.81-7.75 (m, 2H), 5.74 (s, 2H), 3.74 (t, J=5.1 Hz, 2H), 3.47 (t, J=5.2 Hz, 2H), 3.07 (s, 3H), 2.08 (br s, 1H). LC t_r=2.78 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 317 (M+Na calcd for $C_{12}H_{14}N_4O_5$ requires 317).

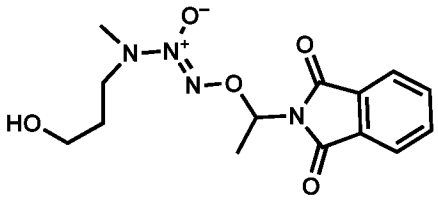
[00115] **(Z)-3-(tert-Butyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(2-hydroxyethyl)triaz-1-ene 2-oxide (N039)**



[00116] N-(chloromethyl) phthalimide (216 mg, 1.10 mmol) and **N007** (200 mg, 1.00 mmol) were converted to the title compound by a procedure similar to that described in the

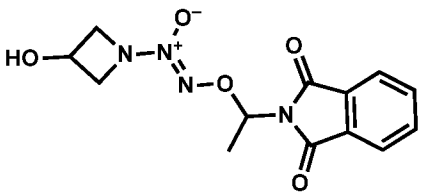
synthesis of **N027**: (223 mg, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98-7.74 (m, 4H), 5.84 (s, 2H), 3.51-3.48 (m, 2H), 3.24-3.20 (m, 2H), 1.58 (s, 9H). LC t_r=3.06 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C).

[00117] (Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-(3-hydroxypropyl)-3-methyltriaz-1-ene 2-oxide (N042)



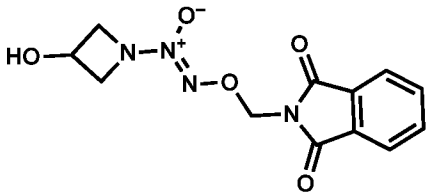
[00118] **N009** (0.395 g, 2.31 mmol) and 1-(chloroethyl) phthalimide (0.441 g, 210 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N026**: (90 mg, 13% yield). LC t_r=2.80 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 345 (M+Na calcd for $C_{14}H_{18}N_4O_5$ requires 345).

[00119] (Z)-2-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide (N050)



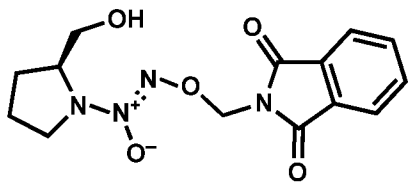
[00120] 1-(Chloroethyl) phthalimide (500 mg, 2.39 mmol) and **N013** (444 mg, 2.86 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N026**: (89 mg, 12% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92-7.89 (m, 2H), 7.80-7.78 (m, 2H), 5.72 (q, J=6.6 Hz, 1H), 4.48-4.42 (m, 1H), 4.30-4.24 (m, 2H), 4.01-3.92 (m, 2H), 2.02 (d, J=6.6 Hz, 3H). LC t_r=2.71 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 ml/min with detection 254 nm, at 23° C). ES(pos)MS m/z 329 (M+Na calcd for $C_{13}H_{14}N_4O_5$ requires 329).

[00121] (Z)-2-(1-(1,3-Dioxoisoindolin-2-yl)methoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide (N051)



[00122] N-(chloromethyl) phthalimide (1.05 g, 5.38 mmol) and **N013** (1.0 g, 6.45 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N027**: (614 mg, 39% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.92 (m, 2H), 7.82-7.79 (m, 2H), 5.72 (s, 2H), 4.58-4.49 (m, 1H), 4.36-4.29 (m, 2H), 4.06-3.99 (m, 2H), 2.53 (d, J=6.3 Hz, 1H). LC t_r=2.45 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 ml/min with detection 254 nm, at 23° C). ES(pos)MS m/z 315 (M+Na calcd for $C_{12}H_{12}N_4O_5$ requires 315).

[00123] **(S,Z)-2-((1,3-Dioxoisoindolin-2-yl)methoxy)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide (N057)**



[00124] N-(chloromethyl) phthalimide (587 mg, 3.00 mmol) and **N016** (500 mg, 2.73 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N027**: (307 mg, 35% yield). ^{1}H NMR (400 MHz, d-DMSO) δ 7.97-7.94 (m, 2H), 7.83-7.80 (m, 2H), 5.74 (s, 2H), 4.17-4.06 (m, 1H), 3.77-3.57 (m, 4H), 2.81 (t, J=5.9 Hz, 1H), 2.11-2.04 (m, 1H), 1.98-1.91 (m, 1H), 1.85-1.78 (m, 2H). LC t_r=2.73 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C).

[00125] **Table 2. Diimide-Capped Alcohol NONOates.**

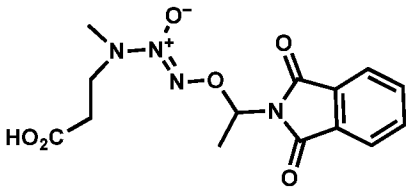
NONOate Salt	Capping Reagent	NONOate #	NONOate Name
N001	1-Chloroethyl-phthalimide	N026	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-((S)-1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N001	N-Chloromethyl-phthalimide	N027	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N002	1-Chloroethyl-phthalimide	N028	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-((S)-1-hydroxy-3-methylbutan-2-yl)-3-methyltriaz-1-ene 2-oxide
N002	N-Chloromethyl-phthalimide	N029	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-3-((S)-1-hydroxy-3-methylbutan-2-yl)-3-methyltriaz-1-ene 2-oxide
N003	1-Chloroethyl-phthalimide	N030	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-((S)-2-(hydroxymethyl)azetidin-1-yl)diazene oxide

N003	N-Chloromethyl-phthalimide	N031	(S,Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(2-(hydroxymethyl)azetidin-1-yl)diazene oxide
N004	1-Chloroethyl-phthalimide	N032	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-ethyl-3-(2-hydroxyethyl)triaz-1-ene 2-oxide
N004	N-Chloromethyl-phthalimide	N033	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-3-ethyl-3-(2-hydroxyethyl)triaz-1-ene 2-oxide
N005	1-Chloroethyl-phthalimide	N034	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(2-hydroxyethyl)-3-isopropyltriaz-1-ene 2-oxide
N005	N-Chloromethyl-phthalimide	N035	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(2-hydroxyethyl)-3-isopropyltriaz-1-ene 2-oxide
N006	1-Chloroethyl-phthalimide	N036	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide
N006	N-Chloromethyl-phthalimide	N037	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide
N007	1-Chloroethyl-phthalimide	N038	(Z)-3-(tert-butyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(2-hydroxyethyl)triaz-1-ene 2-oxide
N007	N-Chloromethyl-phthalimide	N039	(Z)-3-(tert-butyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(2-hydroxyethyl)triaz-1-ene 2-oxide
N008	1-Chloroethyl-phthalimide	N040	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N008	N-Chloromethyl-phthalimide	N041	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N009	1-Chloroethyl-phthalimide	N042	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(3-hydroxypropyl)-3-methyltriaz-1-ene 2-oxide
N009	N-Chloromethyl-phthalimide	N043	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-3-(3-hydroxypropyl)-3-methyltriaz-1-ene 2-oxide
N010	1-Chloroethyl-phthalimide	N044	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(4-hydroxybutyl)-3-methyltriaz-1-ene 2-oxide
N010	N-Chloromethyl-phthalimide	N045	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-3-(4-hydroxybutyl)-3-methyltriaz-1-ene 2-oxide
N011	1-Chloroethyl-phthalimide	N046	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(5-hydroxypentyl)-3-methyltriaz-1-ene 2-oxide
N011	N-Chloromethyl-phthalimide	N047	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-3-(5-hydroxypentyl)-3-methyltriaz-1-ene 2-oxide
N012	1-Chloroethyl-phthalimide	N048	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(6-hydroxyhexyl)-3-methyltriaz-1-ene 2-oxide
N012	N-Chloromethyl-phthalimide	N049	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-3-(6-hydroxyhexyl)-3-methyltriaz-1-ene 2-oxide
N013	1-Chloroethyl-phthalimide	N050	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide
N013	N-Chloromethyl-phthalimide	N051	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide
N014	1-Chloroethyl-phthalimide	N052	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide
N014	N-Chloromethyl-phthalimide	N053	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide
N015	1-Chloroethyl-phthalimide	N054	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3,3-bis(2-hydroxyethyl)triaz-1-ene 2-oxide
N015	N-Chloromethyl-	N055	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3,3-bis(2-

	phthalimide		hydroxyethyl)triaz-1-ene 2-oxide
N016	1-Chloroethyl-phthalimide	N056	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N016	N-Chloromethyl-phthalimide	N057	(S,Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N017	1-Chloroethyl-phthalimide	N058	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide
N017	N-Chloromethyl-phthalimide	N059	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide
N018	1-Chloroethyl-phthalimide	N060	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-((S)-1-hydroxy-4-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide
N018	N-Chloromethyl-phthalimide	N061	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(1-hydroxy-4-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide
N019	1-Chloroethyl-phthalimide	N062	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-((S)-1-hydroxy-3-phenylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N019	N-Chloromethyl-phthalimide	N063	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(1-hydroxy-3-phenylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N020	1-Chloroethyl-phthalimide	N064	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-hydroxypiperidin-1-yl)diazene oxide
N020	N-Chloromethyl-phthalimide	N065	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-hydroxypiperidin-1-yl)diazene oxide
N021	1-Chloroethyl-phthalimide	N066	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(4-hydroxypiperidin-1-yl)diazene oxide
N021	N-Chloromethyl-phthalimide	N067	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-1-(4-hydroxypiperidin-1-yl)diazene oxide
N022	1-Chloroethyl-phthalimide	N068	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(hydroxymethyl)piperidin-1-yl)diazene oxide
N022	N-Chloromethyl-phthalimide	N069	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-(hydroxymethyl)piperidin-1-yl)diazene oxide
N023	1-Chloroethyl-phthalimide	N070	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(4-(hydroxymethyl)piperidin-1-yl)diazene oxide
N023	N-Chloromethyl-phthalimide	N071	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-1-(4-(hydroxymethyl)piperidin-1-yl)diazene oxide
N024	1-Chloroethyl-phthalimide	N072	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-hydroxypyrrolidin-1-yl)diazene oxide
N024	N-Chloromethyl-phthalimide	N073	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-hydroxypyrrolidin-1-yl)diazene oxide
N025	1-Chloroethyl-phthalimide	N074	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N025	N-Chloromethyl-phthalimide	N075	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide

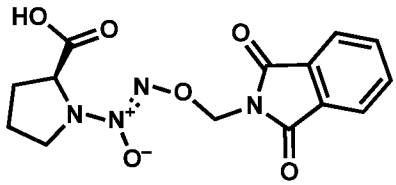
DIIMIDE-CAPPED CARBOXYLIC ACID NONOATES

[00126] **(Z)-3-(2-Carboxyethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide (N080)**



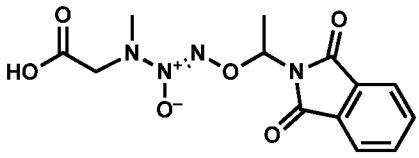
[00127] Sodium metaperiodate (0.225 g, 1.05 mmol) was added to a mixture of **N042** (0.081 g, 0.251 mmol) and ruthenium(III)chloride (cat) in acetonitrile (1.0 mL), ethyl acetate (1.0 mL) and water (1.5 mL). The resulting mixture was stirred at ambient temperature for 3.5 hours and then diluted with water and filtered through a pad of celite®. The aqueous reaction mixture was then extracted into ethyl acetate. The combined organic layers were washed with water, brine, dried over sodium sulfate, filtered and concentrated under reduced pressure to provide a colorless oil (82 mg, 97% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J=5.5 Hz, 2H), 7.90 (d, J=5.5 Hz, 2H), 7.78 (d, J=5.5 Hz, 1H), 7.76 (d, J=5.5 Hz, 2H), 6.27 (q, J=6.6 Hz, 1H), 3.61-3.55 (dt, J=2.2,6.8 Hz, 2H), 2.99 (s, 3H), 2.61-2.55 (dt, J=1.5,6.8 Hz, 2H), 2.04 (d, J=6.6 Hz, 3H). LC tr=2.85 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C).

[00128] **(S,Z)-1-(2-Carboxypyrrolidin-1-yl)-2-((1,3-dioxoisoindolin-2-yl)methoxy)diazene oxide (N091)**



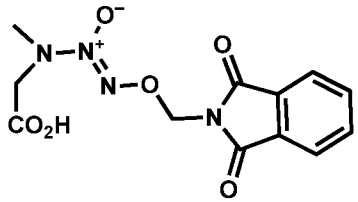
[00129] **N057** (200 mg, 0.62 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N080**: (165 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.77 (m, 4H), 5.74 (s, 2H), 4.59-4.53 (m, 1H), 3.84-3.79 (m, 2H), 3.69-3.62 (m, 2H), 2.31-2.25 (m, 2H). LC t_r=2.71 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 ml/min with detection 254 nm, at 23° C). ES(pos)MS m/z 357 (M+Na calcd for $C_{14}H_{14}N_4O_6$ requires 357).

[00130] **(Z)-3-(Carboxymethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide (N096)**



[00131] **N036** (0.227 g, 0.736 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N080**: (224 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.89 (m, 4H), 7.88-7.83 (m, 4H), 6.23 (q, J=6.6 Hz, 1H), 4.27-4.13 (m, 2H), 3.15 (s, 3H), 1.97 (d, J=6.6 Hz, 3H). LC t_r=2.80 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C).

[00132] **(Z)-3-(Carboxymethyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide (N097)**



[00133] **N037** (328 mg, 1.11 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N080**: (253 mg, 74% yield). ^{1}H NMR (400 MHz, CD3OD) δ 7.97-7.87 (m, 4H), 5.71 (s, 2H), 4.27 (s, 2H), 3.23 (s, 3H). LC t_r=2.59 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 331 (M+Na calcd for $C_{12}H_{12}N_4O_6$ requires 331).

[00134] **Table 3. Diimide-Capped Carboxylic Acid NONOates.**

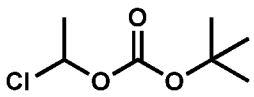
Starting NONOate	NONOate #	NONOate Name
N030	N076	(Z)-1-((S)-2-carboxyazetidin-1-yl)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)diazene oxide
N031	N077	(S,Z)-1-(2-carboxyazetidin-1-yl)-2-((1,3-dioxoisoindolin-2-yl)methoxy)diazene oxide
N040	N078	(Z)-3-(2-carboxypropan-2-yl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N041	N079	(Z)-3-(2-carboxypropan-2-yl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N042	N080	(Z)-3-(2-carboxyethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N043	N081	(Z)-3-(2-carboxyethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N044	N082	(Z)-3-(3-carboxypropyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N045	N083	(Z)-3-(3-carboxypropyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N046	N084	(Z)-3-(4-carboxybutyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-

		methyltriaz-1-ene 2-oxide
N047	N085	(Z)-3-(4-carboxybutyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N048	N086	(Z)-3-(5-carboxypentyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N049	N087	(Z)-3-(5-carboxypentyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N052	N088	(Z)-1-(3-carboxyazetidin-1-yl)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)diazene oxide
N053	N089	(Z)-1-(3-carboxyazetidin-1-yl)-2-((1,3-dioxoisoindolin-2-yl)methoxy)diazene oxide
N056	N090	(Z)-1-((S)-2-carboxypyrrolidin-1-yl)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)diazene oxide
N057	N091	(S,Z)-1-(2-carboxypyrrolidin-1-yl)-2-((1,3-dioxoisoindolin-2-yl)methoxy)diazene oxide
N032	N092	(Z)-3-(carboxymethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-ethyltriaz-1-ene 2-oxide
N033	N093	(Z)-3-(carboxymethyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-ethyltriaz-1-ene 2-oxide
N034	N094	(Z)-3-(carboxymethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-isopropyltriaz-1-ene 2-oxide
N035	N095	(Z)-3-(carboxymethyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-isopropyltriaz-1-ene 2-oxide
N036	N096	(Z)-3-(carboxymethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N037	N097	(Z)-3-(carboxymethyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N026	N098	(Z)-3-((S)-1-carboxyethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N027	N099	(S,Z)-3-(1-carboxyethyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N058	N100	(Z)-3-((1S,2R)-1-carboxy-2-methylbutyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N059	N101	(Z)-3-((1S,2R)-1-carboxy-2-methylbutyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N060	N102	(Z)-3-((S)-1-carboxy-3-methylbutyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N061	N103	(S,Z)-3-(1-carboxy-3-methylbutyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N062	N104	(Z)-3-((S)-1-carboxy-2-phenylethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N063	N105	(S,Z)-3-(1-carboxy-2-phenylethyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N028	N106	(Z)-3-((S)-1-carboxy-2-methylpropyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyltriaz-1-ene 2-oxide
N029	N107	(S,Z)-3-(1-carboxy-2-methylpropyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyltriaz-1-ene 2-oxide
N038	N108	(Z)-3-(tert-butyl)-3-(carboxymethyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)triaz-1-ene 2-oxide
N039	N109	(Z)-3-(tert-butyl)-3-(carboxymethyl)-1-((1,3-dioxoisoindolin-2-

		yl)methoxy)triaz-1-ene 2-oxide
N068	N110	(Z)-1-(3-carboxypiperidin-1-yl)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)diazene oxide
N069	N111	(Z)-1-(3-carboxypiperidin-1-yl)-2-((1,3-dioxoisoindolin-2-yl)methoxy)diazene oxide
N070	N112	(Z)-1-(4-carboxypiperidin-1-yl)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)diazene oxide
N071	N113	(Z)-1-(4-carboxypiperidin-1-yl)-2-((1,3-dioxoisoindolin-2-yl)methoxy)diazene oxide
N074	N114	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)diazene oxide
N075	N115	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-((1,3-dioxoisoindolin-2-yl)methoxy)diazene oxide

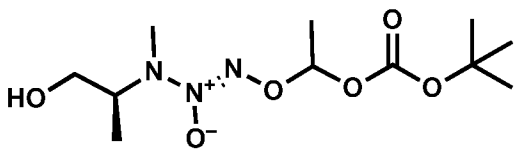
CARBONATE-CAPPED ALCOHOL NONOATES

[00135] 1-Chloroethyl t-butyl carbonate



[00136] t-Butanol (3.34 mL, 35 mmol) and pyridine (3.39 mL, 42 mmol) were dissolved in 90 mL methylene chloride and cooled to -78 °C. 1-Chloroethyl chloroformate (5.0 g, 35 mmol) was added dropwise and the reaction was slowly allowed to warm to room temperature, then stirred for 3 days. The rxn was evaporated, dissolved in ethyl acetate, then washed with water and brine, dried over magnesium sulfate and evaporated. It was noted that product evaporated under high vacuum. The product was distilled to yield 1-chloroethyl t-butyl carbonate a colorless oil (2.46 g, 39% yield).). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (d, J=5.6 Hz, 1H), 1.82 (d, J=5.6 Hz, 3H), 1.53 (s, 9H).

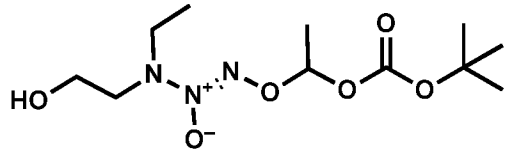
[00137] (2S,Z)-1-Hydroxy-2,3,7,11,11-pentamethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N118)



[00138] **N001** (0.350 g, 2.05 mmol) suspended in acetonitrile (2.0 mL) was treated with a solution of 1-chloroethyl t-butyl carbonate (0.336 g, 1.86 mmol) in acetonitrile (1.0 mL) and then sodium iodide (1.25 g, 8.37 mmol) was added. The resulting mixture was heated to 60 °C for 3 hours. The acetonitrile was removed under reduced pressure. The residue was suspended in ethyl acetate and then washed with a 0.2 *N* solution of sodium thiosulfate. The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated. The residue was

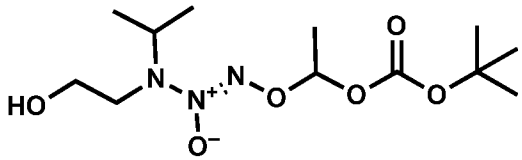
subjected to prep-chromatography using ethyl acetate in hexanes to provide an amber oil (29 mg, 5.3% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (dq, J=2.5, 5.6 Hz, 1H), 4.21-3.75 (m, 1H), 3.71-3.54 (m, 2H), 2.98 (d, J=3.5 Hz, 3H), 1.65 (d, J=5.6 Hz, 3H), 1.52 (s, 9H), 1.15-1.11 (m, 3H). LC t_r=3.20 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 316 (M+Na calcd for $C_{11}H_{23}N_3O_6$ requires 316).

[00139] (Z)-3-Ethyl-1-hydroxy-7,11,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N129)



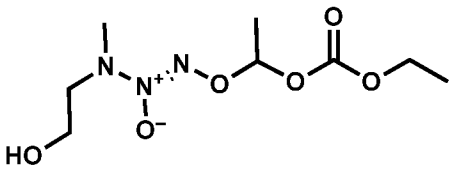
[00140] 1-Chloroethyl t-butyl carbonate (500 mg, 2.77 mmol) and **N004** (521 mg, 3.05 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N118**: (421 mg, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (q, J=5.6 Hz, 1H), 3.72-3.70 (m, 2H), 3.38-3.13 (m, 4H), 1.66 (d, J=5.6 Hz, 3H), 1.52 (s, 9H), 1.16 (t, J=7.1 Hz, 3H). LC t_r=3.19 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 316 (M+Na calcd for $C_{11}H_{23}N_3O_6$ requires 316).

[00141] (Z)-1-Hydroxy-3-isopropyl-7,11,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N131)



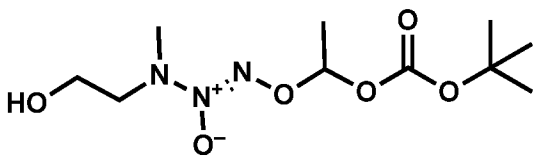
[00142] **N005** (500 mg, 2.7 mmol) and 1-chloroethyl t-butyl carbonate (488 mg, 2.7 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N118**: (465 mg, 56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (q, J=5.6 Hz, 1H), 3.85-3.79 (m, 1H), 3.68-3.65 (m, 2H), 3.38-3.23 (m, 2H), 1.65 (d, J=5.6 Hz, 3H), 1.52 (s, 9H), 1.18 (dd, J=5.6, 3.8 Hz, 6H). LC t_r=3.40 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 330 (M+Na calcd for $C_{12}H_{25}N_3O_6$ requires 330).

[00143] (Z)-1-Hydroxy-3,7-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N132)



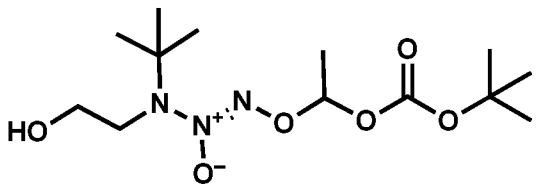
[00144] **N006** (0.250 g, 1.59 mmol) was suspended in acetonitrile (3.0 mL) and to this was added a solution of 1-chloroethyl ethyl carbonate (0.291 g, 1.91 mmol) in acetonitrile (2.0 mL) and sodium iodide (0.286 g, 1.91 mmol) and the resulting mixture was stirred at 25 °C overnight. The acetonitrile was removed under reduced pressure and the residue was suspended in ethyl acetate and then washed with a 0.2 *N* solution of sodium thiosulfate. The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated. The residue was chromatographed using 50% ethyl acetate in hexanes to give an oily residue (61 mg, 15% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (q, J=5.6 Hz, 1H), 4.22 (q, J=7.1 Hz, 2H), 3.76 (t, J=5.1 Hz, 2H), 3.53-3.42 (m, 2H), 3.08 (s, 3H), 2.19-1.76 (br s, 1H), 1.64 (d, J=5.6 Hz, 3H), 1.32 (t, J=7.1 Hz, 3H). LC t_r=2.60 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 274 (M+Na calcd for $C_8H_{17}N_3O_6$ requires 274).

[00145] **(Z)-1-Hydroxy-3,7,11,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N133)**



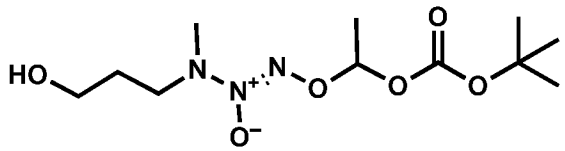
[00146] 1-Chloroethyl t-butyl carbonate (2.0 g, 11.07 mmol) and **N006** (1.4 g, 7.26 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N118**: (1.75 g, 51% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (q, J=5.6 Hz, 1H), 3.80 (t, J=5.0 Hz, 2H), 3.50 (dt, J=5.0, 1.2 Hz, 2H), 3.10 (s, 3H), 1.64 (d, J=5.6 Hz, 3H), 1.52 (s, 9H). LC t_r=3.02 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 302 (M+Na calcd for $C_{10}H_{21}N_3O_6$ requires 302).

[00147] **(Z)-3-(2-Hydroxyethyl)-2,2,7,11,11-pentamethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N135)**



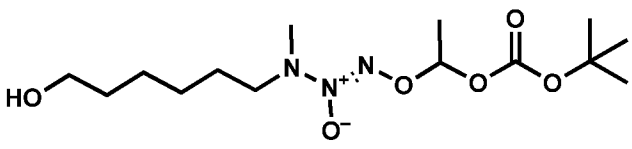
[00148] **N007** (500 mg, 2.51 mmol) and 1-chloroethyl t-butyl carbonate (454 mg, 2.51 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N118**: (240 mg, 30% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (q, J=5.6 Hz, 1H), 3.56 (t, J=4.9 Hz, 2H), 3.30-3.20 (m, 2H), 1.65 (d, J=5.6 Hz, 3H), 1.51 (s, 9H), 1.26 (s, 9H). LC t_r=3.61 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 344 (M+Na calcd for $C_{13}H_{27}N_3O_6$ requires 344).

[00149] **(Z)-13-Hydroxy-2,2,6,10-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide (N139)**



[00150] **N009** (2.30 g, 13.44 mmol) suspended in acetonitrile (10.0 mL) was treated with a solution of 1-chloroethyl t-butyl carbonate (1.87 g, 10.35 mmol) in acetonitrile (10.0 mL) and then sodium iodide (1.55 g, 10.35 mmol) was added. The resulting mixture was stirred at ambient temperature for 4 days then heated to 60 °C for 32.5 hours. The acetonitrile was removed under reduced pressure. The residue was suspended in ethyl acetate and then washed with a 0.2 *N* solution of sodium thiosulfate. The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated. The residue was subjected to chromatography using ethyl acetate in hexanes to provide a yellow oil (390 mg, 13% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (q, J=5.6 Hz, 1H), 3.78-3.71 (dt, J=2.8,6.8 Hz, 2H), 3.04 (s, 3H), 2.03-1.94 (br t, 1H), 1.85-1.76 (m, 2H), 1.65 (d, J=5.6 Hz, 3H), 1.52 (s, 9H). LC t_r=3.12 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 316 (M+Na calcd for $C_{11}H_{23}N_3O_6$ requires 316).

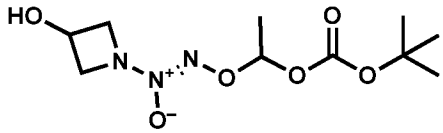
[00151] **(Z)-16-Hydroxy-2,2,6,10-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazahexadec-8-ene 9-oxide (N149)**



[00152] 1-Chloroethyl t-butyl carbonate (192 mg, 1.17 mmol) and **N012** (250 mg, 1.17 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N118**: (614 mg, 39% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (q, J=5.6 Hz, 1H), 3.66 (t, J=6.5 Hz, 2H), 3.36-3.32 (m, 2H), 3.00 (s, 3H), 1.63 (d, J= 5.6 Hz, 3H), 1.60-1.53 (m,

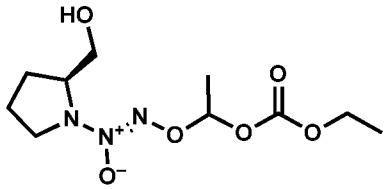
4H), 1.51 (s, 9H), 1.42-1.37 (m, 4H). LC t_r=3.62 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 ml/min with detection 254 nm, at 23° C). ES(pos)MS m/z 358 (M+Na calcd for $C_{14}H_{29}N_3O_6$ requires 358).

[00153] (Z)-2-(1-((tert-Butoxycarbonyl)oxy)ethoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide (N152)



[00154] 1-Chloroethyl t-butyl carbonate (430 mg, 2.38 mmol) and **N013** (444 mg, 2.86 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N118**: (121 mg, 18% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44-6.35 (bm, 1H), 4.63-4.49 (bm, 1H), 4.42-4.29 (bm, 2H). 4.10-3.99 (bm, 2H), 2.43-2.34 (bs, 1H), 1.69-1.59 (bs, 3H), 1.52 (bs, 9H). LC t_r=3.03 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 ml/min with detection 254 nm, at 23° C). ES(pos)MS m/z 300 (M+Na calcd for $C_{10}H_{19}N_3O_6$ requires 300).

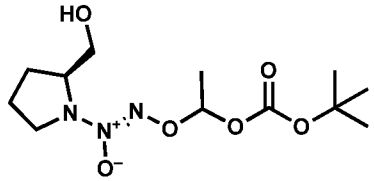
[00155] (Z)-2-(1-((Ethoxycarbonyl)oxy)ethoxy)-1-((*S*)-2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide (N164)



[00156] 1-Chloroethyl ethyl carbonate (5.0 g, 32.8 mmol) was dissolved in 125 mL acetonitrile. Sodium iodide (22.1 g, 147.5 mmol) was added and stirred at 60 °C for 1.5 hours. The reaction was evaporated, diluted with ether and filtered. The filtrate was evaporated to a dark red oil, to afford 1-iodoethyl ethyl carbonate (4.12 g, 51% yield). **N016** (2.07 g, 11.3 mmol) and freshly made 1-iodoethyl ethyl carbonate (4.12 g, 16.9 mmol) were dissolved in 15 mL acetonitrile and stirred at room temperature overnight. The reaction was evaporated, diluted with ethyl acetate, washed with 0.2N $Na_2S_2O_3$ and brine, dried over magnesium sulfate and evaporated. Chromatography was performed using 50% ethyl acetate/hexanes to yield a colorless oil (890 mg, 28% yield). ^{1}H NMR (400 MHz, d-DMSO) δ 6.28 (dq, J=2.6, 5.6 Hz, 1H), 4.76 (dt, J=2.9, 5.7 Hz, 1H), 4.12 (q, J=7.1 Hz, 2H), 3.97-3.86 (m, 1H), 3.55-3.31 (m, 4H), 1.96-1.77 (m, 4H), 1.47 (d, J=5.5 Hz, 3H), 1.17 (dt, J=18.4, 7.1 Hz, 3H). LC t_r=2.98 minutes (C-18 column, 5

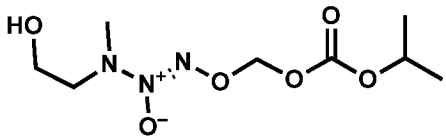
to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 300 (M+Na calcd for $C_{10}H_{19}N_3O_6$ requires 300).

[00157] (Z)-2-(1-((tert-Butoxycarbonyl)oxy)ethoxy)-1-((*S*)-2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide (N166)



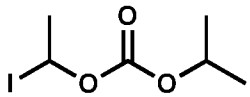
[00158] 1-Chloroethyl t-butyl carbonate (448 mg, 2.48 mmol) and **N016** (500 mg, 2.73 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N118**: (223 mg, 29% yield). ^{1}H NMR (400 MHz, d-DMSO) δ 6.43 (dq, J=1.0, 5.6 Hz, 1H), 4.19-4.07 (m, 1H), 3.82-3.56 (m, 3H), 2.91-2.79 (m, 1H), 2.13-2.05 (m, 2H), 2.00-1.93 (m, 2H), 1.87-1.79 (m, 2H), 1.64 (d, J=5.6 Hz, 3H), 1.52 (d, J=1.4, 9H). LC t_r=3.30 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C).

[00159] (Z)-1-Hydroxy-3,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N190-A)



[00160] Chloromethyl isopropyl carbonate (1.75 g, 11.47 mmol) and **N006** (1.98 g, 12.62 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N118**: (1.9 g, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (s, 1H), 4.95 (dq, J=6.3, 6.3 Hz, 1H), 3.83-3.80 (m, 2H), 3.57-3.53 (m, 2H), 3.14 (s, 3H), 1.30 (d, J=6.3 Hz, 6H). LC t_r=2.61 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 274 (M+Na calcd for $C_8H_{17}N_3O_6$ requires 274).

[00161] 1-Iodoethyl isopropyl carbonate

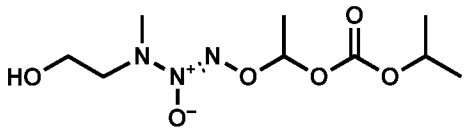


[00162] To a solution of 2-propanol (2.66 mL, 34.97 mmol) and pyridine (3.39 mL, 41.96 mmol), pre-cooled in a dry-ice/acetone bath was slowly added 1-chloroethyl chloroformate. The resulting mixture was allowed to slowly warm to 25 °C overnight, with stirring. After

concentration under reduced pressure the mixture was dissolved in ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated under reduced pressure to give 1-chloroethyl isopropyl carbonate as a pink/orange oil (5.11 g, 88% yield).

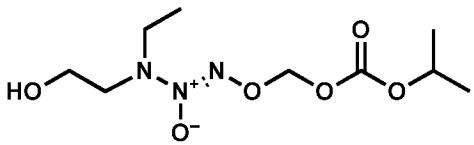
[00163] Sodium iodide (20.69 g, 138.0 mmol) was added to the crude solution of chloroethyl isopropyl carbonate (5.11 g, 30.67 mmol) in acetonitrile (50 mL). The resulting mixture was heated to 60 °C for 2 hours and then allowed to cool to 25 °C. The reaction mixture was concentrated under reduced pressure and the resulting mixture was treated with diethyl ether. The solids were filtered off and the filtrate was concentrated under reduced pressure to obtain 1-iodoethyl isopropyl carbonate as a dark orange oil (5.43 g, 69% yield).

[00164] **(Z)-1-Hydroxy-3,7,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N190-B)**



[00165] **N006** (0.250 g, 1.59 mmol) and 1-iodoethyl isopropyl carbonate (0.492 g, 1.91 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N164**, with the exception no sodium iodide was added: (141 mg, 33% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (q, J=5.6 Hz, 1H), 4.89 (sep, J=6.3 Hz, 1H), 3.77 (t, J=5.2 Hz, 2H), 3.53-3.42 (m, 2H), 3.08 (s, 3H), 1.64 (d, J=5.6 Hz, 3H), 1.31 (d, J=6.3 Hz, 3H). LC t_r=2.96 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 288 (M+Na calcd for $C_9H_{19}N_3O_6$ requires 288).

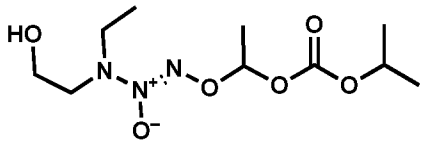
[00166] **(Z)-3-Ethyl-1-hydroxy-11-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N190-C)**



[00167] 1-Chloromethyl isopropyl carbonate (1.0 g, 6.55 mmol) and **N004** (1.23 g, 7.21 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N118**: (312 mg, 18% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (s, 2H), 4.97-4.92 (m, 1H), 3.74-3.71 (m, 2H), 3.39-3.32 (m, 4H), 1.33 (d, J=6.3 Hz, 6H), 1.16 (t, J=7.1 Hz, 3H). LC t_r=2.77 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min

with detection 254 nm, at 23° C). ES(pos)MS m/z 288 (M+Na calcd for $C_9H_{19}N_3O_6$ requires 288).

[00168] (Z)-3-Ethyl-1-hydroxy-7,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N190-D)



[00169] 1-Chloroethyl isopropyl carbonate (1.0 g, 6.0 mmol) and **N004** (1.13 g, 6.6 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N164**: (898 mg, 53% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.50 (q, J=5.6 Hz, 1H), 4.95-4.90 (m, 1H), 3.72-3.68 (m, 2H), 3.40-3.31 (m, 2H), 3.31-3.22 (m, 2H), 1.67 (d, J=5.6 Hz, 3H), 1.33 (dd, J=6.3, 1.6 Hz, 6H), 1.14 (t, J=7.1 Hz, 3H). LC t_r=3.90 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 302 (M+Na calcd for $C_{10}H_{21}N_3O_6$ requires 302).

[00170] Table 4. Carbonate-Capped Alcohol NONOates.

NONOate Salt	Capping Reagent	NONOate #	NONOate Name
N001	Chloroethyl ethyl carbonate	N116	(2S,Z)-1-hydroxy-2,3,7-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N001	Chloroethyl isopropyl carbonate	N117	(2S,Z)-1-hydroxy-2,3,7,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N001	Chloroethyl tert-butyl carbonate	N118	(2S,Z)-1-hydroxy-2,3,7,11,11-pentamethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N001	Chloromethyl isopropyl carbonate	N119	(S,Z)-1-hydroxy-2,3,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N001	Chloromethyl tert-butyl carbonate	N120	(S,Z)-1-hydroxy-2,3,11,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N002	Chloroethyl ethyl carbonate	N121	(11S,Z)-11-(hydroxymethyl)-6,10,12-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N002	Chloroethyl isopropyl carbonate	N122	(11S,Z)-11-(hydroxymethyl)-2,6,10,12-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N002	Chloroethyl tert-butyl carbonate	N123	(11S,Z)-11-(hydroxymethyl)-2,2,6,10,12-pentamethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N002	Chloromethyl isopropyl carbonate	N124	(S,Z)-11-(hydroxymethyl)-2,10,12-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N002	Chloromethyl tert-butyl carbonate	N125	(S,Z)-11-(hydroxymethyl)-2,2,10,12-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N003	Chloroethyl ethyl carbonate	N126	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(hydroxymethyl)azetidin-1-yl)diazene oxide

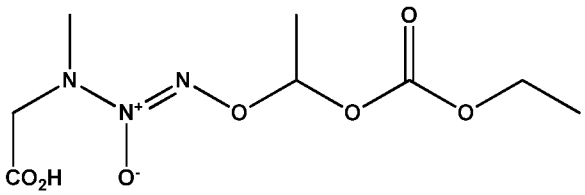
N003	Chloroethyl tert-butyl carbonate	N127	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(hydroxymethyl)azetidin-1-yl)diazene oxide
N004	Chloroethyl ethyl carbonate	N128	(Z)-3-ethyl-1-hydroxy-7-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N004	Chloroethyl tert-butyl carbonate	N129	(Z)-3-ethyl-1-hydroxy-7,11,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N005	Chloroethyl ethyl carbonate	N130	(Z)-1-hydroxy-3-isopropyl-7-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N005	Chloroethyl tert-butyl carbonate	N131	(Z)-1-hydroxy-3-isopropyl-7,11,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N006	Chloroethyl ethyl carbonate	N132	(Z)-1-hydroxy-3,7-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N006	Chloroethyl tert-butyl carbonate	N133	(Z)-1-hydroxy-3,7,11,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N007	Chloroethyl ethyl carbonate	N134	(Z)-3-(2-hydroxyethyl)-2,2,7-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N007	Chloroethyl tert-butyl carbonate	N135	(Z)-3-(2-hydroxyethyl)-2,2,7,11,11-pentamethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N008	Chloroethyl ethyl carbonate	N136	(Z)-1-hydroxy-2,2,3,7-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N008	Chloroethyl tert-butyl carbonate	N137	(Z)-1-hydroxy-2,2,3,7,11,11-hexamethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N009	Chloroethyl ethyl carbonate	N138	(Z)-13-hydroxy-6,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N009	Chloroethyl tert-butyl carbonate	N139	(Z)-13-hydroxy-2,2,6,10-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N010	Chloroethyl ethyl carbonate	N140	(Z)-14-hydroxy-6,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N010	Chloroethyl isopropyl carbonate	N141	(Z)-14-hydroxy-2,6,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N010	Chloroethyl tert-butyl carbonate	N142	(Z)-14-hydroxy-2,2,6,10-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N011	Chloroethyl ethyl carbonate	N143	(Z)-15-hydroxy-6,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N011	Chloroethyl isopropyl carbonate	N144	(Z)-15-hydroxy-2,6,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N011	Chloroethyl tert-butyl carbonate	N145	(Z)-15-hydroxy-2,2,6,10-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N011	Chloromethyl isopropyl carbonate	N146	(Z)-15-hydroxy-2,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N011	Chloromethyl tert-butyl carbonate	N147	(Z)-15-hydroxy-2,2,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N012	Chloroethyl ethyl carbonate	N148	(Z)-16-hydroxy-6,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazahexadec-8-ene 9-oxide
N012	Chloroethyl tert-butyl carbonate	N149	(Z)-16-hydroxy-2,2,6,10-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazahexadec-8-ene 9-oxide
N013	Chloroethyl ethyl carbonate	N150	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide
N013	Chloroethyl isopropyl carbonate	N151	(Z)-1-(3-hydroxyazetidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide

N013	Chloroethyl tert-butyl carbonate	N152	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide
N013	Chloromethyl isopropyl carbonate	N153	(Z)-1-(3-hydroxyazetidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
N013	Chloromethyl tert-butyl carbonate	N154	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide
N014	Chloroethyl ethyl carbonate	N155	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide
N014	Chloroethyl isopropyl carbonate	N156	(Z)-1-(3-(hydroxymethyl)azetidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
N014	Chloroethyl tert-butyl carbonate	N157	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide
N014	Chloromethyl isopropyl carbonate	N158	(Z)-1-(3-(hydroxymethyl)azetidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
N014	Chloromethyl tert-butyl carbonate	N159	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide
N015	Chloroethyl ethyl carbonate	N160	(Z)-1-hydroxy-3-(2-hydroxyethyl)-7-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N015	Chloroethyl isopropyl carbonate	N161	(Z)-1-hydroxy-3-(2-hydroxyethyl)-7,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N015	Chloromethyl isopropyl carbonate	N162	(Z)-1-hydroxy-3-(2-hydroxyethyl)-11-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N015	Chloromethyl tert-butyl carbonate	N163	(Z)-1-hydroxy-3-(2-hydroxyethyl)-11,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N016	Chloroethyl ethyl carbonate	N164	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N016	Chloroethyl isopropyl carbonate	N165	(Z)-1-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
N016	Chloroethyl tert-butyl carbonate	N166	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N016	Chloromethyl isopropyl carbonate	N167	(*S*)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
N016	Chloromethyl tert-butyl carbonate	N168	(S,Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N017	Chloroethyl ethyl carbonate	N169	(11S,12R,Z)-11-(hydroxymethyl)-6,10,12-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N017	Chloromethyl isopropyl carbonate	N170	(11S,12R,Z)-11-(hydroxymethyl)-2,10,12-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N018	Chloroethyl ethyl carbonate	N171	(11S,Z)-11-(hydroxymethyl)-6,10,13-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N018	Chloromethyl isopropyl carbonate	N172	(S,Z)-11-(hydroxymethyl)-2,10,13-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N019	Chloroethyl ethyl carbonate	N173	(2S,Z)-2-benzyl-1-hydroxy-3,7-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide

N019	Chloromethyl isopropyl carbonate	N174	(S,Z)-2-benzyl-1-hydroxy-3,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N020	Chloroethyl ethyl carbonate	N175	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-hydroxypiperidin-1-yl)diazene oxide
N020	Chloroethyl ethyl carbonate	N176	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(4-hydroxypiperidin-1-yl)diazene oxide
N021	Chloroethyl isopropyl carbonate	N177	(Z)-1-(4-hydroxypiperidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
N021	Chloromethyl isopropyl carbonate	N178	(Z)-1-(4-hydroxypiperidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
N022	Chloroethyl ethyl carbonate	N179	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N022	Chloroethyl isopropyl carbonate	N180	(Z)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
N023	Chloroethyl ethyl carbonate	N181	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(4-(hydroxymethyl)piperidin-1-yl)diazene oxide
N023	Chloroethyl isopropyl carbonate	N182	(Z)-1-(4-(hydroxymethyl)piperidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
N023	Chloroethyl tert-butyl carbonate	N183	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(4-(hydroxymethyl)piperidin-1-yl)diazene oxide
N023	Chloromethyl tert-butyl carbonate	N184	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(4-(hydroxymethyl)piperidin-1-yl)diazene oxide
N024	Chloroethyl ethyl carbonate	N185	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-hydroxypyrrolidin-1-yl)diazene oxide
N024	Chloroethyl tert-butyl carbonate	N186	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-hydroxypyrrolidin-1-yl)diazene oxide
N024	Chloromethyl tert-butyl carbonate	N187	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-hydroxypyrrolidin-1-yl)diazene oxide
N025	Chloroethyl ethyl carbonate	N188	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N025	Chloroethyl tert-butyl carbonate	N189	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N025	Chloromethyl isopropyl carbonate	N190	(Z)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
N006	Chloromethyl isopropyl carbonate	N190-A	(Z)-1-Hydroxy-3,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N006	Chloroethyl isopropyl carbonate	N190-B	(Z)-1-Hydroxy-3,7,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N004	Chloromethyl isopropyl carbonate	N190-C	(Z)-3-Ethyl-1-hydroxy-11-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N004	Chloroethyl isopropyl carbonate	N190-D	(Z)-3-Ethyl-1-hydroxy-7,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide

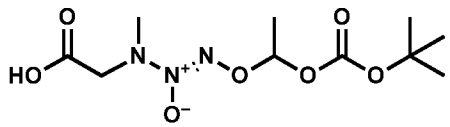
CARBONATE-CAPPED CARBOXYLIC ACID NONOATES

[00171] (Z)-1-Carboxy-2,6-dimethyl-8-oxo-5,7,9-trioxa-2,3,4-triazaundec-3-ene 3-oxide (N207)



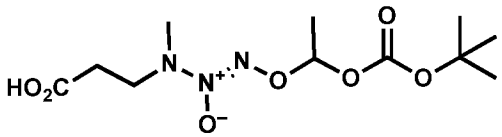
[00172] Sodium metaperiodate (0.467 g, 2.18 mmol) was added to a mixture of **N132** (0.130 g, 0.52 mmol) and ruthenium(III)chloride (cat) in acetonitrile (1.0 mL), ethyl acetate (1.0 mL) and water (1.5 mL). The resulting mixture was stirred at ambient temperature for 3.5 hours and then diluted with water and filtered through a pad of celite®. The aqueous reaction mixture was then extracted into ethyl acetate. The combined organic layers were washed with water, brine, dried over sodium sulfate, filtered and concentrated under reduced pressure to provide a colorless oil (111 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (q, J=5.6 Hz, 1H), 4.28 (q, J=18.1 Hz, 2H), 4.25 (q, J=7.1 Hz, 2H), 3.29 (s, 3H), 1.65 (d, J=5.6 Hz, 3H), 1.34 (t, J=7.1 Hz, 3H). LC t_r=2.74 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 288 (M+Na calcd for $C_8H_{15}N_3O_7$ requires 288), ES(neg)MS m/z 264 (M-H calcd for $C_8H_{15}N_3O_7$ requires 264).

[00173] **(Z)-1-Carboxy-2,6,10,10-tetramethyl-8-oxo-5,7,9-trioxa-2,3,4-triazaundec-3-ene 3-oxide (N208)**



[00174] **N133** (400 mg, 1.44 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N207**: (352 mg, 83% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (q, J=5.6 Hz, 1H), 4.29 (q, J=18.1 Hz, 2H), 3.28 (s, 3H), 1.63 (d, J=5.6 Hz, 3H), 1.52 (s, 9H). LC t_r=5.04 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 316 (M+Na calcd for $C_{10}H_{19}N_3O_7$ requires 316).

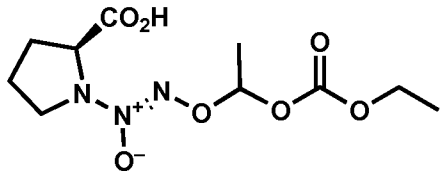
[00175] **(Z)-1-Carboxy-3,7,11,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (N214)**



[00176] Sodium metaperiodate (0.983 g, 4.60 mmol) was added to a mixture of **N139** (0.321 g, 1.09 mmol) and ruthenium(III)chloride (cat) in acetonitrile (2.5 mL), ethyl acetate (2.5

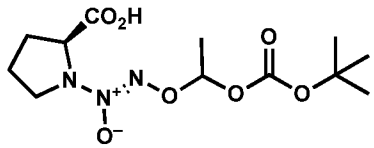
mL) and water (4.0 mL). The resulting mixture was stirred at ambient temperature for 5.0 hours and then diluted with water and filtered through a pad of celite. The aqueous reaction mixture was then extracted into ethyl acetate. The combined organic layers were washed with water, brine, dried over sodium sulfate, filtered and concentrated under reduced pressure to provide a brown solid (335 mg, 100% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (q, J=5.6 Hz, 1H), 3.72-3.60 (dt, J=3.2,6.8 Hz, 2H), 3.08 (s, 3H), 2.69 (t, J=6.8 Hz, 2H), 1.64 (d, J=5.6 Hz, 3H), 1.52 (s, 9H). LC t_r=3.21 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C).

[00177] (Z)-1-((S)-2-Carboxypyrrolidin-1-yl)-2-(1-((ethoxycarbonyl)oxy)ethoxy)diazene oxide (N230)



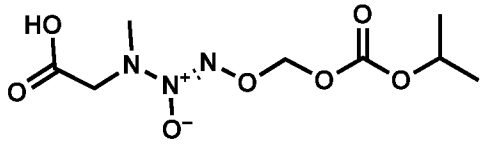
[00178] **N164** (150 mg, 0.54 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N207**, step 2: (146 mg, 93% yield). ^{1}H NMR (400 MHz, d-DMSO) δ 6.29-6.23 (m, 1H), 4.39-4.33 (m, 1H), 4.12 (dq, J=1.8, 7.1 Hz, 2H), 3.67-3.49 (m, 2H), 2.28-2.20 (m, 1H), 1.95-1.86 (m, 4H), 1.46 (dd, J=2.9, 5.5 Hz, 3H), 1.17 (ddt, J=19.3, 14.2, 2.3 Hz, 3H). LC t_r=2.92 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 314 (M+Na calcd for $C_{10}H_{17}N_3O_7$ requires 314).

[00179] (Z)-2-(1-((tert-Butoxycarbonyl)oxy)ethoxy)-1-((S)-2-carboxypyrrolidin-1-yl)diazene oxide (N232)



[00180] **N166** (150 mg, 0.49 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N207**: (74 mg, 47% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (q, J=5.6 Hz, 1H), 4.65-4.58 (m, 1H), 3.87-3.76 (m, 1H), 3.72-3.61 (m, 1H), 2.33-2.77 (m, 2H), 2.13-2.03 (m, 2H), 1.63 (d, J=5.6 Hz, 3H), 1.52 (s, 9H). LC t_r=3.28 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 342 (M+Na calcd for $C_{12}H_{21}N_3O_7$ requires 342).

[00181] **(Z)-1-Carboxy-2,10-dimethyl-8-oxo-5,7,9-trioxa-2,3,4-triazaundec-3-ene 3-oxide (N303)**



[00182] **N190-A** (250 mg, 1.0 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N207**: (238 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (s, 2H), 4.98-4.92 (m, 1H), 4.31 (s, 2H), 3.32 (s, 3H), 1.34 (d, J=5.6 Hz, 6H). LC t_r=2.84 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 288 (M+Na calcd for $C_8H_{15}N_3O_7$ requires 288).

[00183] **Table 5. Carbonate-Capped Carboxylic Acid Nonoates.**

Starting NONOate	NONOate #	NONOate Name
N116	N191	(2S,Z)-2-carboxy-3,7-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N117	N192	(2S,Z)-2-carboxy-3,7,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N118	N193	(2S,Z)-2-carboxy-3,7,11,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N119	N194	(S,Z)-2-carboxy-3,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N120	N195	(S,Z)-2-carboxy-3,11,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N121	N196	(11S,Z)-11-carboxy-6,10,12-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N122	N197	(11S,Z)-11-carboxy-2,6,10,12-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N123	N198	(11S,12R,Z)-11-carboxy-2,2,6,10,12-pentamethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N124	N199	(S,Z)-11-carboxy-2,10,12-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N125	N200	(S,Z)-11-carboxy-2,2,10,12-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N126	N201	(Z)-1-((S)-2-carboxyazetidin-1-yl)-2-(1-((ethoxycarbonyl)oxy)ethoxy)diazene oxide
N127	N202	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-((S)-2-carboxyazetidin-1-yl)diazene oxide
N128	N203	(Z)-3-(carboxymethyl)-7-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N129	N204	(Z)-3-(carboxymethyl)-7,11,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N130	N205	(Z)-3-(carboxymethyl)-2,7-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N131	N206	(Z)-3-(carboxymethyl)-2,7,11,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-

		triazadodec-4-ene 4-oxide
N132	N207	(Z)-1-carboxy-2,6-dimethyl-8-oxo-5,7,9-trioxa-2,3,4-triazaundec-3-ene 3-oxide
N133	N208	(Z)-1-carboxy-2,6,10,10-tetramethyl-8-oxo-5,7,9-trioxa-2,3,4-triazaundec-3-ene 3-oxide
N134	N209	(Z)-3-(carboxymethyl)-2,2,7-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N135	N210	(11S,Z)-11-carboxy-2,2,6,10,13-pentamethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N136	N211	(Z)-2-carboxy-2,3,7-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N137	N212	(Z)-2-carboxy-2,3,7,11,11-pentamethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N138	N213	(Z)-1-carboxy-3,7-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N139	N214	(Z)-1-carboxy-3,7,11,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N140	N215	(Z)-13-carboxy-6,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N141	N216	(Z)-13-carboxy-2,6,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N142	N217	(Z)-13-carboxy-2,2,6,10-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N143	N218	(Z)-14-carboxy-2,6,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N144	N219	(Z)-14-carboxy-2,6,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N145	N220	(Z)-14-carboxy-2,2,6,10-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N146	N221	(Z)-14-carboxy-2,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N147	N222	(Z)-14-carboxy-2,2,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N148	N223	(Z)-15-carboxy-6,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N149	N224	(Z)-15-carboxy-2,2,6,10-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N155	N225	(Z)-1-(3-carboxyazetidin-1-yl)-2-(1-((ethoxycarbonyl)oxy)ethoxy)diazene oxide
N156	N226	(Z)-1-(3-carboxyazetidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
N157	N227	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-carboxyazetidin-1-yl)diazene oxide
N158	N228	(Z)-1-(3-carboxyazetidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
N159	N229	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-carboxyazetidin-1-yl)diazene oxide
N164	N230	(Z)-1-((S)-2-carboxypyrrolidin-1-yl)-2-(1-((ethoxycarbonyl)oxy)ethoxy)diazene oxide
N165	N231	(Z)-1-((S)-2-carboxypyrrolidin-1-yl)-2-(1-

		((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
N166	N232	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-((S)-2-carboxypyrrolidin-1-yl)diazene oxide
N167	N233	(S,Z)-1-(2-carboxypyrrolidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
N168	N234	(S,Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(2-carboxypyrrolidin-1-yl)diazene oxide
N169	N235	(11S,12R,Z)-11-carboxy-6,10,12-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N170	N236	(11S,12R,Z)-11-carboxy-2,10,12-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N171	N237	(11S,Z)-11-carboxy-6,10,13-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N172	N238	(S,Z)-11-carboxy-2,10,13-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N173	N239	(2S,Z)-2-carboxy-3,7-dimethyl-9-oxo-1-phenyl-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N174	N240	(S,Z)-2-carboxy-3,11-dimethyl-9-oxo-1-phenyl-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N179	N241	(Z)-1-(3-carboxypiperidin-1-yl)-2-(1-((ethoxycarbonyl)oxy)ethoxy)diazene oxide
N180	N242	(Z)-1-(3-carboxypiperidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
N181	N243	(Z)-1-(4-carboxypiperidin-1-yl)-2-(1-((ethoxycarbonyl)oxy)ethoxy)diazene oxide
N182	N244	(Z)-1-(4-carboxypiperidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
N183	N245	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(4-carboxypiperidin-1-yl)diazene oxide
N184	N246	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(4-carboxypiperidin-1-yl)diazene oxide
N188	N247	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(1-((ethoxycarbonyl)oxy)ethoxy)diazene oxide
N189	N248	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-carboxypiperidin-1-yl)diazene oxide
N190	N249	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
	N250	(Z)-1-((S)-2-carboxyazetidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
	N251	(Z)-1-((S)-2-carboxyazetidin-1-yl)-2-(1-((methoxycarbonyl)oxy)ethoxy)diazene oxide
	N252	(S,Z)-1-(2-carboxyazetidin-1-yl)-2-(((ethoxycarbonyl)oxy)methoxy)diazene oxide
	N253	(S,Z)-1-(2-carboxyazetidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
	N254	(S,Z)-1-(2-carboxyazetidin-1-yl)-2-(((methoxycarbonyl)oxy)methoxy)diazene oxide
	N255	(S,Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(2-carboxyazetidin-1-yl)diazene oxide
	N256	(Z)-2-carboxy-2,3,7,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-

		4-ene 4-oxide
	N257	(Z)-10-carboxy-5,9,10-trimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N258	(Z)-2-carboxy-2,3-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N259	(Z)-2-carboxy-2,3,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N260	(Z)-10-carboxy-9,10-dimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N261	(Z)-2-carboxy-2,3,11,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N262	(Z)-1-carboxy-3,7,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N263	(Z)-11-carboxy-5,9-dimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N264	(Z)-1-carboxy-3-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N265	(Z)-1-carboxy-3,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N266	(Z)-11-carboxy-9-methyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N267	(Z)-1-carboxy-3,11,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N268	(Z)-12-carboxy-5,9-dimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazadodec-7-ene 8-oxide
	N269	(Z)-13-carboxy-10-methyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
	N270	(Z)-13-carboxy-2,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
	N271	(Z)-12-carboxy-9-methyl-3-oxo-2,4,6-trioxa-7,8,9-triazadodec-7-ene 8-oxide
	N272	(Z)-13-carboxy-2,2,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
	N273	(Z)-14-carboxy-2,6,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
	N274	(Z)-14-carboxy-10-methyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
	N275	(Z)-13-carboxy-9-methyl-3-oxo-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
	N276	(Z)-15-carboxy-2,6,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
	N277	(Z)-14-carboxy-2,6,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
	N278	(Z)-15-carboxy-10-methyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
	N279	(Z)-15-carboxy-2,10-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
	N280	(Z)-14-carboxy-9-methyl-3-oxo-2,4,6-trioxa-7,8,9-triazatetradec-7-ene 8-oxide
	N281	(Z)-15-carboxy-2,2,10-trimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazapentadec-

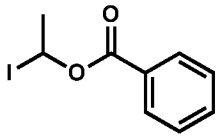
		8-ene 9-oxide
	N282	(Z)-1-(3-carboxyazetidin-1-yl)-2-(1-((methoxycarbonyl)oxy)ethoxy)diazene oxide
	N283	(Z)-1-(3-carboxyazetidin-1-yl)-2-(((ethoxycarbonyl)oxy)methoxy)diazene oxide
	N284	(Z)-1-(3-carboxyazetidin-1-yl)-2-(((methoxycarbonyl)oxy)methoxy)diazene oxide
	N285	(Z)-1-((S)-2-carboxypyrrolidin-1-yl)-2-(1-((methoxycarbonyl)oxy)ethoxy)diazene oxide
	N286	(S,Z)-1-(2-carboxypyrrolidin-1-yl)-2-(((ethoxycarbonyl)oxy)methoxy)diazene oxide
	N287	(S,Z)-1-(2-carboxypyrrolidin-1-yl)-2-(((methoxycarbonyl)oxy)methoxy)diazene oxide
	N288	(Z)-3-(carboxymethyl)-7,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N289	(Z)-9-(carboxymethyl)-5-methyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N290	(Z)-3-(carboxymethyl)-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N291	(Z)-3-(carboxymethyl)-11-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N292	(Z)-9-(carboxymethyl)-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N293	(Z)-3-(carboxymethyl)-11,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N294	(Z)-3-(carboxymethyl)-2,7,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N295	(Z)-9-(carboxymethyl)-5,10-dimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N296	(Z)-3-(carboxymethyl)-2-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N297	(Z)-3-(carboxymethyl)-2,11-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N298	(Z)-9-(carboxymethyl)-10-methyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N299	(Z)-3-(carboxymethyl)-2,11,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N300	(Z)-1-carboxy-2,6,10-trimethyl-8-oxo-5,7,9-trioxa-2,3,4-triazaundec-3-ene 3-oxide
	N301	(Z)-1-carboxy-2,6-dimethyl-8-oxo-5,7,9-trioxa-2,3,4-triazadec-3-ene 3-oxide
	N302	(Z)-1-carboxy-2-methyl-8-oxo-5,7,9-trioxa-2,3,4-triazaundec-3-ene 3-oxide
N190-A	N303	(Z)-1-carboxy-2,10-dimethyl-8-oxo-5,7,9-trioxa-2,3,4-triazaundec-3-ene 3-oxide
	N304	(Z)-1-carboxy-2-methyl-8-oxo-5,7,9-trioxa-2,3,4-triazadec-3-ene 3-oxide
	N305	(Z)-1-carboxy-2,10,10-trimethyl-8-oxo-5,7,9-trioxa-2,3,4-triazaundec-3-ene 3-oxide
	N306	(10S,Z)-10-carboxy-5,9-dimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N307	(S,Z)-2-carboxy-3-methyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-

		oxide
	N308	(S,Z)-10-carboxy-9-methyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N309	(11S,12R,Z)-11-carboxy-2,6,10,12-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
	N310	(10S,11R,Z)-10-carboxy-5,9,11-trimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
	N311	(11S,12R,Z)-11-carboxy-10,12-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
	N312	(10S,11R,Z)-10-carboxy-9,11-dimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
	N313	(11S,12R,Z)-11-carboxy-2,2,10,12-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
	N314	(11S,Z)-11-carboxy-2,6,10,13-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
	N315	(10S,Z)-10-carboxy-5,9,12-trimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
	N316	(S,Z)-11-carboxy-10,13-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
	N317	(S,Z)-10-carboxy-9,12-dimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
	N318	(S,Z)-11-carboxy-2,2,10,13-tetramethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
	N319	(2S,Z)-2-carboxy-3,7,11-trimethyl-9-oxo-1-phenyl-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N320	(10S,Z)-10-carboxy-5,9-dimethyl-3-oxo-11-phenyl-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N321	(2S,Z)-2-carboxy-3,7,11,11-tetramethyl-9-oxo-1-phenyl-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N322	(S,Z)-2-carboxy-3-methyl-9-oxo-1-phenyl-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N323	(S,Z)-10-carboxy-9-methyl-3-oxo-11-phenyl-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N324	(S,Z)-2-carboxy-3,11,11-trimethyl-9-oxo-1-phenyl-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N325	(10S,Z)-10-carboxy-5,9,11-trimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazadodec-7-ene 8-oxide
	N326	(11S,Z)-11-carboxy-2,2,6,10,12-pentamethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
	N327	(S,Z)-11-carboxy-10,12-dimethyl-4-oxo-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
	N328	(S,Z)-10-carboxy-9,11-dimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazadodec-7-ene 8-oxide
	N329	(Z)-3-(carboxymethyl)-2,2,7,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N330	(Z)-9-(carboxymethyl)-5,10,10-trimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N331	(Z)-3-(carboxymethyl)-2,2,7,11,11-pentamethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N332	(Z)-3-(carboxymethyl)-2,2-dimethyl-9-oxo-6,8,10-trioxa-3,4,5-

		triazadodec-4-ene 4-oxide
	N333	(Z)-3-(carboxymethyl)-2,2,11-trimethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N334	(Z)-9-(carboxymethyl)-10,10-dimethyl-3-oxo-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
	N335	(Z)-3-(carboxymethyl)-2,2,11,11-tetramethyl-9-oxo-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
	N336	(Z)-1-(3-carboxypiperidin-1-yl)-2-(1-((methoxycarbonyl)oxy)ethoxy)diazene oxide
	N337	(Z)-1-(3-carboxypiperidin-1-yl)-2-(((ethoxycarbonyl)oxy)methoxy)diazene oxide
	N338	(Z)-1-(3-carboxypiperidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
	N339	(Z)-1-(3-carboxypiperidin-1-yl)-2-(((methoxycarbonyl)oxy)methoxy)diazene oxide
	N340	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-carboxypiperidin-1-yl)diazene oxide
	N341	(Z)-1-(4-carboxypiperidin-1-yl)-2-(1-((methoxycarbonyl)oxy)ethoxy)diazene oxide
	N342	(Z)-1-(4-carboxypiperidin-1-yl)-2-(((ethoxycarbonyl)oxy)methoxy)diazene oxide
	N343	(Z)-1-(4-carboxypiperidin-1-yl)-2-(((isopropoxycarbonyl)oxy)methoxy)diazene oxide
	N344	(Z)-1-(4-carboxypiperidin-1-yl)-2-(((methoxycarbonyl)oxy)methoxy)diazene oxide
	N345	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)diazene oxide
	N346	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(1-((methoxycarbonyl)oxy)ethoxy)diazene oxide
	N347	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-carboxypyrrolidin-1-yl)diazene oxide
	N348	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(((ethoxycarbonyl)oxy)methoxy)diazene oxide
	N349	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(((methoxycarbonyl)oxy)methoxy)diazene oxide
	N350	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-carboxypyrrolidin-1-yl)diazene oxide

ESTER-CAPPED ALCOHOL NONOATES

[00184] **1-Iodoethyl benzoate**

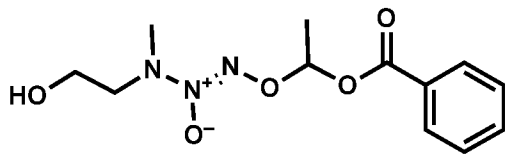


[00185] A solution of benzoyl chloride (7.0 g, 49.80 mmol) in dichloromethane (10 mL) was slowly added to a mixture of acetaldehyde (2.6 g, 59.05 mmol) and a catalytic amount of zinc chloride in dichloromethane (60 mL), pre-cooled in an ice bath. Once the addition was

complete the cooling bath was removed and the reaction was heated to 50 °C. After 2.5 hours the mixture was allowed to cool to ambient temperature and then concentrated under reduced pressure. Water was added and the reaction was extracted with methyl *t*-butyl ether. The combined organic layers were washed several times with saturated $NaHCO_3$ solution, brine, dried over sodium sulfate, filtered and concentrated under reduced pressure to obtain 1-chloroethyl benzoate as a pale yellow oil (7.82 g, 85% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 8.20-7.98 (m, 2H), 7.70-7.55 (m, 1H), 7.54-7.39 (m, 2H), 6.89-6.70 (m, 1H), 2.11-1.82 (m, 3H). LC t_r=4.27 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C).

[00186] 1-Chloroethyl benzoate (6.30 g, 34.12 mmol) and sodium iodide (23.0 g, 153.56 mmol) were combined in acetonitrile (150 mL) and heated to 60 °C for 2 hours. The reaction mixture was concentrated under reduced pressure. Diethyl ether and dichloromethane were added to the residue and the solids were filtered off and the filtrate was concentrated under reduced pressure. After silica gel chromatography using ethyl acetate in hexanes the residue was combined with sodium iodide (4.70 g, 31.39 mmol) in acetonitrile (50 mL) and heated to 60 °C for 1.5 hours. The reaction mixture was concentrated under reduced pressure. Diethyl ether was added, the solids were filtered off and the filtrate was concentrated under reduced pressure. Chromatography on silica gel using ethyl acetate in hexanes provided 1-iodoethyl benzoate as a pale yellow oil (3.67 g, 39% yield).

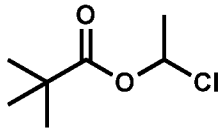
[00187] **(Z)-1-(1-(Benzoyloxy)ethoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide (N395)**



[00188] **N006** (0.250 g, 1.59 mmol) was suspended in acetonitrile (3.0 mL) and treated with a solution of 1-iodoethyl benzoate (0.367 g, 1.33 mmol) in acetonitrile (2.0 mL). The resulting mixture was stirred at 25 °C overnight then the acetonitrile was removed under reduced pressure. The residue was suspended in ethyl acetate and then washed with a 0.2 *N* solution of sodium thiosulfate. The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated. The residue was chromatographed using ethyl acetate in heptanes to provide a thick amber oil (82 mg, 22% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 8.09-8.03 (m, 2H), 7.62-7.55

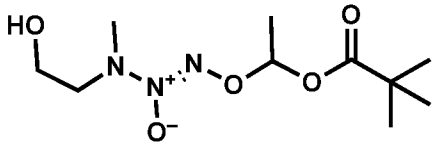
(m, 1H), 7.49-7.42 (m, 2H), 6.85 (q J=5.6 Hz, d1H), 3.72 (t, J=5.0 Hz, 2H), 3.48-3.42 (m, 2H), 3.04 (s, 3H), 1.74 (d, J=5.6 Hz, 3H). LC t_r=3.14 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 306 (M+Na calcd for $C_{12}H_{17}N_3O_5$ requires 306).

[00189] 1-Chloroethyl pivalate



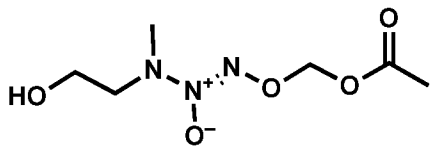
[00190] Trimethylacetyl chloride (7.0 g, 58.0 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of 1-iodoethyl benzoate above. Distillation gave pdt as a clear oil (2.72 g, 28% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (d, J=5.8 Hz, 1H), 1.82 (d, J=5.8 Hz, 3H), 1.25 (s, 9H).

[00191] (Z)-3-(2-Hydroxyethyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide (N397)



[00192] 1-Chloroethyl pivalate (524 mg, 3.18 mmol) and **N006** (500 mg, 3.18 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N132**: (552 mg, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60 (q, J=5.6 Hz, 1H), 3.79-3.76 (m, 2H), 3.50-3.47 (m, 2H), 3.08 (s, 3H), 1.61 (d, J=5.6 Hz, 3H), 1.23 (s, 9H). LC t_r=3.03 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 286 (M+Na calcd for $C_{10}H_{21}N_3O_5$ requires 286).

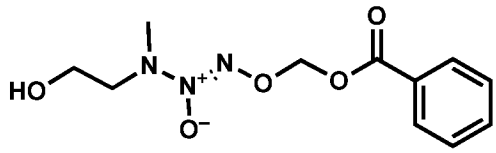
[00193] (Z)-1-(Acetoxymethoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide (N399)



[00194] Chloromethyl methyl acetate (1.0 g, 9.2 mmol) and **N006** (1.59 g, 10.0 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N132**: (348 mg, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (s, 2H), 3.80-3.78 (m, 2H), 3.53-3.50 (m, 2H), 3.11 (s, 3H), 2.13 (s, 3H). LC t_r=3.19 minutes (C-18 column, 5 to 95%

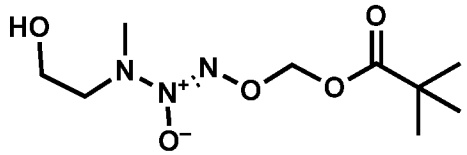
acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 230 (M+Na calcd for $C_6H_{13}N_3O_5$ requires 230).

[00195] (Z)-1-((Benzoyloxy)methoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide (N400)



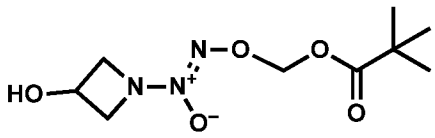
[00196] **N006** (0.250 g, 1.59 mmol) was suspended in acetonitrile (3.0 mL) was treated with a solution of iodomethyl benzoate (0.50 g, 1.91 mmol) in acetonitrile (2.0 mL), formed *in situ* from chloromethyl benzoate and NaI in refluxing acetone. The resulting mixture was stirred at 25 °C for 24 hours at which time the acetonitrile was removed under reduced pressure. The residue was suspended in ethyl acetate and then washed with a 0.2 *N* solution of sodium thiosulfate. The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated. The residue was chromatographed using 50% ethyl acetate in hexanes to provide an off white solid (125 mg, 29% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10-8.04 (m, 2H), 7.62-7.56 (m, 1H), 7.49-7.42 (m, 2H), 6.05 (s, 2H), 3.76 (t, J=5.0 Hz, 2H), 3.49 (t, J=5.2 Hz, 2H), 3.09 (s, 3H), 2.19-1.74 (br m, 1H). LC t_r=3.24 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 °C). ES(pos)MS m/z 292 (M+Na calcd for $C_{11}H_{15}N_3O_5$ requires 292).

[00197] (Z)-3-(2-Hydroxyethyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide (N402)



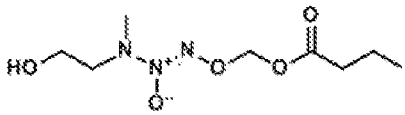
[00198] Chloromethyl t-butyl acetate (1.0 g, 6.6 mmol) and **N006** (1.4 g, 7.26 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N132**: (763 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (s, 2H), 3.79-3.76 (m, 2H), 3.51-3.48 (m, 2H), 3.09 (s, 3H), 1.22 (s, 9H). LC t_r=3.85 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 272 (M+Na calcd for $C_9H_{19}N_3O_5$ requires 272).

[00199] (Z)-1-(3-Hydroxyazetidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide (N464)



[00200] **N013** (300 mg, 2.27 mmol) and chloromethyl pivalate (244 mg, 1.62 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N132**: (56 mg, 10% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (d, J=1.6Hz, 2H), 5.15-5.09 (m, 1H), 4.90-4.69 (m, 1H). 4.60-4.42 (m, 1H), 4.39-4.34 (m, 1H), 4.09-4.03 (m, 1H), 1.23 (s, 9H). LC t_r=2.86 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 ml/min with detection 254 nm, at 23° C). ES(pos)MS m/z 270 (M+Na calcd for $C_9H_{17}N_3O_5$ requires 270).

[00201] **(Z)-3-(2-hydroxyethyl)-3-methyl-1-((butyryloxy)methoxy)triaz-1-ene 2-oxide (N550-A)**



[00202] Chloromethyl butryate (1.0 g, 7.3 mmol) and **N006** (1.26 g, 8.0 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **N132**: (752 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (s, 2H), 3.80-3.78 (m, 2H), 3.52-3.50 (m, 2H), 3.11 (s, 3H), 2.36 (t, J=7.4 Hz, 2H), 1.70-1.67 (m, 2H), 0.96 (t, J=7.4 Hz, 3H). LC t_r=3.69 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 258 (M+Na calcd for $C_8H_{17}N_3O_5$ requires 258).

[00203] **Table 6. Ester-Capped Alcohol NONOates.**

NONOate Salt	Capping Reagent	NONOate #	NONOate Name
N001	Chloroethyl acetate	N351	(Z)-1-(1-acetoxyethoxy)-3-((S)-1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N001	Chloroethyl benzoate	N352	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((S)-1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N001	Chloroethyl isobutyrate	N353	(Z)-3-((S)-1-hydroxypropan-2-yl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N001	Chloroethyl pivalate	N354	(Z)-3-((S)-1-hydroxypropan-2-yl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N001	Chloroethyl propionate	N355	(Z)-3-((S)-1-hydroxypropan-2-yl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N001	Chloromethyl acetate	N356	(S,Z)-1-(acetoxymethoxy)-3-(1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N001	Chloromethyl benzoate	N357	(S,Z)-1-((benzoyloxy)methoxy)-3-(1-hydroxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N001	Chloromethyl	N358	(S,Z)-3-(1-hydroxypropan-2-yl)-1-

	isobutyrate		((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N001	Chloromethyl pivalate	N359	(S,Z)-3-(1-hydroxypropan-2-yl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N001	Chloromethyl propionate	N360	(S,Z)-3-(1-hydroxypropan-2-yl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N002	Chloroethyl acetate	N361	(Z)-1-(1-acetoxyethoxy)-3-((S)-1-hydroxy-3-methylbutan-2-yl)-3-methyltriaz-1-ene 2-oxide
N002	Chloroethyl benzoate	N362	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((S)-1-hydroxy-3-methylbutan-2-yl)-3-methyltriaz-1-ene 2-oxide
N002	Chloroethyl isobutyrate	N363	(Z)-3-((S)-1-hydroxy-3-methylbutan-2-yl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N002	Chloroethyl pivalate	N364	(Z)-3-((S)-1-hydroxy-3-methylbutan-2-yl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N002	Chloroethyl propionate	N365	(Z)-3-((S)-1-hydroxy-3-methylbutan-2-yl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N002	Chloromethyl isobutyrate	N366	(S,Z)-3-(1-hydroxy-3-methylbutan-2-yl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N002	Chloromethyl pivalate	N367	(S,Z)-3-(1-hydroxy-3-methylbutan-2-yl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N003	Chloroethyl acetate	N368	(Z)-2-(1-acetoxyethoxy)-1-((S)-2-(hydroxymethyl)azetidin-1-yl)diazene oxide
N003	Chloroethyl benzoate	N369	(Z)-2-(1-(benzoyloxy)ethoxy)-1-((S)-2-(hydroxymethyl)azetidin-1-yl)diazene oxide
N003	Chloroethyl isobutyrate	N370	(Z)-1-((S)-2-(hydroxymethyl)azetidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N003	Chloroethyl pivalate	N371	(Z)-1-((S)-2-(hydroxymethyl)azetidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N003	Chloroethyl propionate	N372	(Z)-1-((S)-2-(hydroxymethyl)azetidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
N003	Chloromethyl pivalate	N373	(S,Z)-1-(2-(hydroxymethyl)azetidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N004	Chloroethyl acetate	N374	(Z)-1-(1-acetoxyethoxy)-3-(2-hydroxyethyl)-3-ethyltriaz-1-ene 2-oxide
N004	Chloroethyl benzoate	N375	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(2-hydroxyethyl)-3-ethyltriaz-1-ene 2-oxide
N004	Chloroethyl isobutyrate	N376	(Z)-3-(2-hydroxyethyl)-1-(1-(isobutyryloxy)ethoxy)-3-ethyltriaz-1-ene 2-oxide
N004	Chloroethyl pivalate	N377	(Z)-3-(2-hydroxyethyl)-3-ethyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N004	Chloroethyl propionate	N378	(Z)-3-(2-hydroxyethyl)-3-ethyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N004	Chloromethyl acetate	N379	(Z)-1-(acetoxymethoxy)-3-(2-hydroxyethyl)-3-ethyltriaz-1-ene 2-oxide
N004	Chloromethyl benzoate	N380	(Z)-1-((benzoyloxy)methoxy)-3-(2-hydroxyethyl)-3-ethyltriaz-1-ene 2-oxide
N004	Chloromethyl isobutyrate	N381	(Z)-3-(2-hydroxyethyl)-1-((isobutyryloxy)methoxy)-3-ethyltriaz-1-ene 2-oxide
N004	Chloromethyl pivalate	N382	(Z)-3-(2-hydroxyethyl)-3-ethyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N004	Chloromethyl	N383	(Z)-3-(2-hydroxyethyl)-3-ethyl-1-

	propionate		((propionyloxy)methoxy)triaz-1-ene 2-oxide
N005	Chloroethyl acetate	N384	(Z)-1-(1-acetoxyethoxy)-3-(2-hydroxyethyl)-3-isopropyltriaz-1-ene 2-oxide
N005	Chloroethyl benzoate	N385	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(2-hydroxyethyl)-3-isopropyltriaz-1-ene 2-oxide
N005	Chloroethyl isobutyrate	N386	(Z)-3-(2-hydroxyethyl)-1-(1-(isobutyryloxy)ethoxy)-3-isopropyltriaz--1-ene 2-oxide
N005	Chloroethyl pivalate	N387	(Z)-3-(2-hydroxyethyl)-3-isopropyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N005	Chloroethyl propionate	N388	(Z)-3-(2-hydroxyethyl)-3-isopropyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N005	Chloromethyl acetate	N389	(Z)-1-(acetoxymethoxy)-3-(2-hydroxyethyl)-3-isopropyltriaz-1-ene 2-oxide
N005	Chloromethyl benzoate	N390	(Z)-1-((benzoyloxy)methoxy)-3-(2-hydroxyethyl)-3-isopropyltriaz-1-ene 2-oxide
N005	Chloromethyl isobutyrate	N391	(Z)-3-(2-hydroxyethyl)-1-((isobutyryloxy)methoxy)-3-isopropyltriaz--1-ene 2-oxide
N005	Chloromethyl pivalate	N392	(Z)-3-(2-hydroxyethyl)-3-isopropyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N005	Chloromethyl propionate	N393	(Z)-3-(2-hydroxyethyl)-3-isopropyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N006	Chloroethyl acetate	N394	(Z)-1-(1-acetoxyethoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide
N006	Chloroethyl benzoate	N395	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide
N006	Chloroethyl isobutyrate	N396	(Z)-3-(2-hydroxyethyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N006	Chloroethyl pivalate	N397	(Z)-3-(2-hydroxyethyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N006	Chloroethyl propionate	N398	(Z)-3-(2-hydroxyethyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N006	Chloromethyl acetate	N399	(Z)-1-(acetoxymethoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide
N006	Chloromethyl benzoate	N400	(Z)-1-((benzoyloxy)methoxy)-3-(2-hydroxyethyl)-3-methyltriaz-1-ene 2-oxide
N006	Chloromethyl isobutyrate	N401	(Z)-3-(2-hydroxyethyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N006	Chloromethyl pivalate	N402	(Z)-3-(2-hydroxyethyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N006	Chloromethyl propionate	N403	(Z)-3-(2-hydroxyethyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N007	Chloroethyl acetate	N404	(Z)-1-(1-acetoxyethoxy)-3-(tert-butyl)-3-(2-hydroxyethyl)triaz-1-ene 2-oxide
N007	Chloroethyl benzoate	N405	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(tert-butyl)-3-(2-hydroxyethyl)triaz-1-ene 2-oxide
N007	Chloroethyl isobutyrate	N406	(Z)-3-(tert-butyl)-3-(2-hydroxyethyl)-1-(1-(isobutyryloxy)ethoxy)triaz-1-ene 2-oxide
N007	Chloroethyl pivalate	N407	(Z)-3-(tert-butyl)-3-(2-hydroxyethyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N007	Chloroethyl	N408	(Z)-3-(tert-butyl)-3-(2-hydroxyethyl)-1-(1-

	propionate		(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N007	Chloromethyl acetate	N409	(Z)-1-(acetoxymethoxy)-3-(tert-butyl)-3-(2-hydroxyethyl)triaz-1-ene 2-oxide
N007	Chloromethyl benzoate	N410	(Z)-1-((benzoyloxy)methoxy)-3-(tert-butyl)-3-(2-hydroxyethyl)triaz-1-ene 2-oxide
N007	Chloromethyl isobutyrate	N411	(Z)-3-(tert-butyl)-3-(2-hydroxyethyl)-1-((isobutyryloxy)methoxy)triaz-1-ene 2-oxide
N007	Chloromethyl pivalate	N412	(Z)-3-(tert-butyl)-3-(2-hydroxyethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N007	Chloromethyl propionate	N413	(Z)-3-(tert-butyl)-3-(2-hydroxyethyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N008	Chloroethyl acetate	N414	(Z)-1-(1-acetoxyethoxy)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N008	Chloroethyl benzoate	N415	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N008	Chloroethyl isobutyrate	N416	(Z)-3-(1-hydroxy-2-methylpropan-2-yl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N008	Chloroethyl pivalate	N417	(Z)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N008	Chloroethyl propionate	N418	(Z)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N008	Chloromethyl acetate	N419	(Z)-1-(acetoxymethoxy)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N008	Chloromethyl benzoate	N420	(Z)-1-((benzoyloxy)methoxy)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N008	Chloromethyl isobutyrate	N421	(Z)-3-(1-hydroxy-2-methylpropan-2-yl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N008	Chloromethyl pivalate	N422	(Z)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N008	Chloromethyl propionate	N423	(Z)-3-(1-hydroxy-2-methylpropan-2-yl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N009	Chloroethyl acetate	N424	(Z)-1-(1-acetoxyethoxy)-3-(3-hydroxypropyl)-3-methyltriaz-1-ene 2-oxide
N009	Chloroethyl benzoate	N425	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(3-hydroxypropyl)-3-methyltriaz-1-ene 2-oxide
N009	Chloroethyl isobutyrate	N426	(Z)-3-(3-hydroxypropyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N009	Chloroethyl pivalate	N427	(Z)-3-(3-hydroxypropyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N009	Chloroethyl propionate	N428	(Z)-3-(3-hydroxypropyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N009	Chloromethyl acetate	N429	(Z)-1-(acetoxymethoxy)-3-(3-hydroxypropyl)-3-methyltriaz-1-ene 2-oxide
N009	Chloromethyl benzoate	N430	(Z)-1-((benzoyloxy)methoxy)-3-(3-hydroxypropyl)-3-methyltriaz-1-ene 2-oxide
N009	Chloromethyl isobutyrate	N431	(Z)-3-(3-hydroxypropyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N009	Chloromethyl pivalate	N432	(Z)-3-(3-hydroxypropyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N009	Chloromethyl	N433	(Z)-3-(3-hydroxypropyl)-3-methyl-1-

	propionate		((propionyloxy)methoxy)triaz-1-ene 2-oxide
N010	Chloroethyl acetate	N434	(Z)-1-(1-acetoxyethoxy)-3-(4-hydroxybutyl)-3-methyltriaz-1-ene 2-oxide
N010	Chloroethyl benzoate	N435	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(4-hydroxybutyl)-3-methyltriaz-1-ene 2-oxide
N010	Chloroethyl isobutyrate	N436	(Z)-3-(4-hydroxybutyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N010	Chloroethyl pivalate	N437	(Z)-3-(4-hydroxybutyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N010	Chloroethyl propionate	N438	(Z)-3-(4-hydroxybutyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N010	Chloromethyl acetate	N439	(Z)-1-(acetoxymethoxy)-3-(4-hydroxybutyl)-3-methyltriaz-1-ene 2-oxide
N010	Chloromethyl benzoate	N440	(Z)-1-((benzoyloxy)methoxy)-3-(4-hydroxybutyl)-3-methyltriaz-1-ene 2-oxide
N010	Chloromethyl isobutyrate	N441	(Z)-3-(4-hydroxybutyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N010	Chloromethyl pivalate	N442	(Z)-3-(4-hydroxybutyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N010	Chloromethyl propionate	N443	(Z)-3-(4-hydroxybutyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N011	Chloroethyl acetate	N444	(Z)-1-(1-acetoxyethoxy)-3-(5-hydroxypentyl)-3-methyltriaz-1-ene 2-oxide
N011	Chloroethyl benzoate	N445	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(5-hydroxypentyl)-3-methyltriaz-1-ene 2-oxide
N011	Chloroethyl isobutyrate	N446	(Z)-3-(5-hydroxypentyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N011	Chloroethyl pivalate	N447	(Z)-3-(5-hydroxypentyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N011	Chloromethyl isobutyrate	N448	(Z)-3-(5-hydroxypentyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N011	Chloromethyl pivalate	N449	(Z)-3-(5-hydroxypentyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N012	Chloroethyl acetate	N450	(Z)-1-(1-acetoxyethoxy)-3-(6-hydroxyhexyl)-3-methyltriaz-1-ene 2-oxide
N012	Chloroethyl benzoate	N451	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(6-hydroxyhexyl)-3-methyltriaz-1-ene 2-oxide
N012	Chloroethyl isobutyrate	N452	(Z)-3-(6-hydroxyhexyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N012	Chloroethyl pivalate	N453	(Z)-3-(6-hydroxyhexyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N012	Chloromethyl isobutyrate	N454	(Z)-3-(6-hydroxyhexyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N012	Chloromethyl pivalate	N455	(Z)-3-(6-hydroxyhexyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N013	Chloroethyl acetate	N456	(Z)-2-(1-acetoxyethoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide
N013	Chloroethyl benzoate	N457	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide
N013	Chloroethyl	N458	(Z)-1-(3-hydroxyazetidin-1-yl)-2-(1-

	isobutyrate		(isobutyryloxy)ethoxy)diazene oxide
N013	Chloroethyl pivalate	N459	(Z)-1-(3-hydroxyazetidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N013	Chloroethyl propionate	N460	(Z)-1-(3-hydroxyazetidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
N013	Chloromethyl acetate	N461	(Z)-2-(acetoxymethoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide
N013	Chloromethyl benzoate	N462	(Z)-2-((benzoyloxy)methoxy)-1-(3-hydroxyazetidin-1-yl)diazene oxide
N013	Chloromethyl isobutyrate	N463	(Z)-1-(3-hydroxyazetidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N013	Chloromethyl pivalate	N464	(Z)-1-(3-hydroxyazetidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N013	Chloromethyl propionate	N465	(Z)-1-(3-hydroxyazetidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
N014	Chloroethyl acetate	N466	(Z)-2-(1-acetoxyethoxy)-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide
N014	Chloroethyl benzoate	N467	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide
N014	Chloroethyl isobutyrate	N468	(Z)-1-(3-(hydroxymethyl)azetidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N014	Chloroethyl pivalate	N469	(Z)-1-(3-(hydroxymethyl)azetidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N014	Chloroethyl propionate	N470	(Z)-1-(3-(hydroxymethyl)azetidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
N014	Chloromethyl acetate	N471	(Z)-2-(acetoxymethoxy)-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide
N014	Chloromethyl benzoate	N472	(Z)-2-((benzoyloxy)methoxy)-1-(3-(hydroxymethyl)azetidin-1-yl)diazene oxide
N014	Chloromethyl isobutyrate	N473	(Z)-1-(3-(hydroxymethyl)azetidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N014	Chloromethyl pivalate	N474	(Z)-1-(3-(hydroxymethyl)azetidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N014	Chloromethyl propionate	N475	(Z)-1-(3-(hydroxymethyl)azetidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
N015	Chloroethyl acetate	N476	(Z)-1-(1-acetoxyethoxy)-3,3-bis(2-hydroxyethyl)triaz-1-ene 2-oxide
N015	Chloroethyl benzoate	N477	(Z)-1-(1-(benzoyloxy)ethoxy)-3,3-bis(2-hydroxyethyl)triaz-1-ene 2-oxide
N015	Chloroethyl isobutyrate	N478	(Z)-3,3-bis(2-hydroxyethyl)-1-(1-(isobutyryloxy)ethoxy)triaz-1-ene 2-oxide
N015	Chloroethyl pivalate	N479	(Z)-3,3-bis(2-hydroxyethyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N015	Chloroethyl propionate	N480	(Z)-3,3-bis(2-hydroxyethyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N015	Chloromethyl acetate	N481	(Z)-1-(acetoxymethoxy)-3,3-bis(2-hydroxyethyl)triaz-1-ene 2-oxide
N015	Chloromethyl benzoate	N482	(Z)-1-((benzoyloxy)methoxy)-3,3-bis(2-hydroxyethyl)triaz-1-ene 2-oxide
N015	Chloromethyl	N483	(Z)-3,3-bis(2-hydroxyethyl)-1-

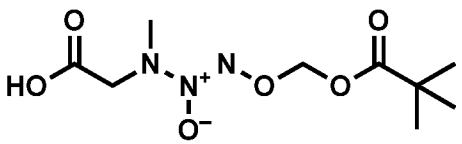
	isobutyrate		((isobutyryloxy)methoxy)triaz-1-ene 2-oxide
N015	Chloromethyl pivalate	N484	(Z)-3,3-bis(2-hydroxyethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N016	Chloroethyl acetate	N485	(Z)-2-(1-acetoxyethoxy)-1-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N016	Chloroethyl benzoate	N486	(Z)-2-(1-(benzoyloxy)ethoxy)-1-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N016	Chloroethyl isobutyrate	N487	(Z)-1-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N016	Chloroethyl pivalate	N488	(Z)-1-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N016	Chloroethyl propionate	N489	(Z)-1-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
N016	Chloromethyl acetate	N490	(S,Z)-2-(acetoxymethoxy)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N016	Chloromethyl benzoate	N491	(S,Z)-2-((benzoyloxy)methoxy)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N016	Chloromethyl isobutyrate	N492	(S,Z)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N016	Chloromethyl pivalate	N493	(S,Z)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N016	Chloromethyl propionate	N494	(S,Z)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
N017	Chloroethyl acetate	N495	(Z)-1-(1-acetoxyethoxy)-3-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide
N017	Chloroethyl benzoate	N496	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide
N017	Chloroethyl isobutyrate	N497	(Z)-3-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N017	Chloroethyl pivalate	N498	(Z)-3-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N017	Chloromethyl isobutyrate	N499	(Z)-3-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N017	Chloromethyl pivalate	N500	(Z)-3-((2S,3R)-1-hydroxy-3-methylpentan-2-yl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N018	Chloroethyl acetate	N501	(Z)-1-(1-acetoxyethoxy)-3-((S)-1-hydroxy-4-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide
N018	Chloroethyl benzoate	N502	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((S)-1-hydroxy-4-methylpentan-2-yl)-3-methyltriaz-1-ene 2-oxide
N018	Chloroethyl isobutyrate	N503	(Z)-3-((S)-1-hydroxy-4-methylpentan-2-yl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N018	Chloroethyl pivalate	N504	(Z)-3-((S)-1-hydroxy-4-methylpentan-2-yl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N018	Chloromethyl isobutyrate	N505	(S,Z)-3-(1-hydroxy-4-methylpentan-2-yl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N018	Chloromethyl pivalate	N506	(S,Z)-3-(1-hydroxy-4-methylpentan-2-yl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N019	Chloroethyl acetate	N507	(Z)-1-(1-acetoxyethoxy)-3-((S)-1-hydroxy-3-phenylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N019	Chloroethyl	N508	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((S)-1-hydroxy-3-

	benzoate		phenylpropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N019	Chloroethyl isobutyrate	N509	(Z)-3-((S)-1-hydroxy-3-phenylpropan-2-yl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N019	Chloroethyl pivalate	N510	(Z)-3-((S)-1-hydroxy-3-phenylpropan-2-yl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N019	Chloromethyl isobutyrate	N511	(S,Z)-3-(1-hydroxy-3-phenylpropan-2-yl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N019	Chloromethyl pivalate	N512	(S,Z)-3-(1-hydroxy-3-phenylpropan-2-yl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N020	Chloroethyl acetate	N513	(Z)-2-(1-acetoxyethoxy)-1-(3-hydroxypiperidin-1-yl)diazene oxide
N020	Chloroethyl benzoate	N514	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-hydroxypiperidin-1-yl)diazene oxide
N020	Chloroethyl isobutyrate	N515	(Z)-1-(3-hydroxypiperidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N020	Chloroethyl pivalate	N516	(Z)-1-(3-hydroxypiperidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N020	Chloromethyl isobutyrate	N517	(Z)-1-(3-hydroxypiperidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N020	Chloromethyl pivalate	N518	(Z)-1-(3-hydroxypiperidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N021	Chloroethyl acetate	N519	(Z)-2-(1-acetoxyethoxy)-1-(4-hydroxypiperidin-1-yl)diazene oxide
N021	Chloroethyl benzoate	N520	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(4-hydroxypiperidin-1-yl)diazene oxide
N021	Chloroethyl isobutyrate	N521	(Z)-1-(4-hydroxypiperidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N021	Chloroethyl pivalate	N522	(Z)-1-(4-hydroxypiperidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N021	Chloromethyl benzoate	N523	(Z)-2-((benzoyloxy)methoxy)-1-(4-hydroxypiperidin-1-yl)diazene oxide
N021	Chloromethyl isobutyrate	N524	(Z)-1-(4-hydroxypiperidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N021	Chloromethyl pivalate	N525	(Z)-1-(4-hydroxypiperidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N022	Chloroethyl acetate	N526	(Z)-2-(1-acetoxyethoxy)-1-(3-(hydroxymethyl)piperidin-1-yl)diazene oxide
N022	Chloroethyl benzoate	N527	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(hydroxymethyl)piperidin-1-yl)diazene oxide
N022	Chloroethyl isobutyrate	N528	(Z)-1-(3-(hydroxymethyl)piperidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N022	Chloroethyl pivalate	N529	(Z)-1-(3-(hydroxymethyl)piperidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N022	Chloromethyl isobutyrate	N530	(Z)-1-(3-(hydroxymethyl)piperidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N022	Chloromethyl pivalate	N531	(Z)-1-(3-(hydroxymethyl)piperidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N023	Chloroethyl acetate	N532	(Z)-2-(1-acetoxyethoxy)-1-(4-(hydroxymethyl)piperidin-1-yl)diazene oxide
N023	Chloroethyl	N533	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(4-

	benzoate		(hydroxymethyl)piperidin-1-yl)diazene oxide
N023	Chloroethyl isobutyrate	N534	(Z)-1-(4-(hydroxymethyl)piperidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N023	Chloroethyl pivalate	N535	(Z)-1-(4-(hydroxymethyl)piperidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N023	Chloroethyl propionate	N536	(Z)-1-(4-(hydroxymethyl)piperidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
N023	Chloromethyl isobutyrate	N537	(Z)-1-(4-(hydroxymethyl)piperidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N023	Chloromethyl pivalate	N538	(Z)-1-(4-(hydroxymethyl)piperidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N024	Chloroethyl acetate	N539	(Z)-2-(1-acetoxyethoxy)-1-(3-hydroxypyrrolidin-1-yl)diazene oxide
N024	Chloroethyl benzoate	N540	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-hydroxypyrrolidin-1-yl)diazene oxide
N024	Chloroethyl isobutyrate	N541	(Z)-1-(3-hydroxypyrrolidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N024	Chloroethyl pivalate	N542	(Z)-1-(3-hydroxypyrrolidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N024	Chloromethyl isobutyrate	N543	(Z)-1-(3-hydroxypyrrolidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N024	Chloromethyl pivalate	N544	(Z)-1-(3-hydroxypyrrolidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N024	Chloromethyl propionate	N545	(Z)-1-(3-hydroxypyrrolidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
N025	Chloroethyl acetate	N546	(Z)-2-(1-acetoxyethoxy)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N025	Chloroethyl benzoate	N547	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)diazene oxide
N025	Chloroethyl isobutyrate	N548	(Z)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N025	Chloroethyl pivalate	N549	(Z)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N025	Chloromethyl propionate	N550	(Z)-1-(3-(hydroxymethyl)pyrrolidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N006	Chloromethyl butyrate	N550-A	(Z)-3-(2-hydroxyethyl)-3-methyl-1-((butyryloxy)methoxy)triaz-1-ene 2-oxide

ESTER-CAPPED CARBOXYLIC ACID NONOATES

[00204] (Z)-3-(Carboxymethyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide (N602)



[00205] **N402** (200 mg, 0.80 mmol) was converted to the title compound by a procedure similar to that described in the synthesis of **N207**: (106 mg, 50% yield). ^{1}H NMR (400 MHz,

$CDCl_3$) δ 5.80 (s, 2H), 4.30 (s, 2H), 3.30 (s, 3H), 1.23 (s, 9H). LC t_r=2.99 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 ml/min with detection 254 nm, at 23° C). ES(pos)MS m/z 263 (M+Na calcd for $C_9H_{17}N_3O_6$ requires 286).

[00206] Table 7. Ester-Capped Carboxylic Acid NONOates.

Starting NONOate	NONOate #	NONOate Name
N351	N551	(Z)-1-(1-acetoxyethoxy)-3-((S)-1-carboxyethyl)-3-methyltriaz-1-ene 2-oxide
N352	N552	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((S)-1-carboxyethyl)-3-methyltriaz-1-ene 2-oxide
N353	N553	(Z)-3-((S)-1-carboxyethyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N354	N554	(Z)-3-((S)-1-carboxyethyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N355	N555	(Z)-3-((S)-1-carboxyethyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N356	N556	(S,Z)-1-(acetoxymethoxy)-3-(1-carboxyethyl)-3-methyltriaz-1-ene 2-oxide
N357	N557	(S,Z)-1-((benzoyloxy)methoxy)-3-(1-carboxyethyl)-3-methyltriaz-1-ene 2-oxide
N358	N558	(S,Z)-3-(1-carboxyethyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N359	N559	(S,Z)-3-(1-carboxyethyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N360	N560	(S,Z)-3-(1-carboxyethyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N361	N561	(Z)-1-(1-acetoxyethoxy)-3-((S)-1-carboxy-2-methylpropyl)-3-methyltriaz-1-ene 2-oxide
N362	N562	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((S)-1-carboxy-2-methylpropyl)-3-methyltriaz-1-ene 2-oxide
N363	N563	(Z)-3-((S)-1-carboxy-2-methylpropyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N364	N564	(Z)-3-((S)-1-carboxy-2-methylpropyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N365	N565	(Z)-3-((S)-1-carboxy-2-methylpropyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N366	N566	(S,Z)-3-(1-carboxy-2-methylpropyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N367	N567	(S,Z)-3-(1-carboxy-2-methylpropyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N368	N568	(Z)-2-(1-acetoxyethoxy)-1-((S)-2-carboxyazetidin-1-yl)diazene oxide
N369	N569	(Z)-2-(1-(benzoyloxy)ethoxy)-1-((S)-2-carboxyazetidin-1-yl)diazene oxide
N370	N570	(Z)-1-((S)-2-carboxyazetidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N371	N571	(Z)-1-((S)-2-carboxyazetidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N372	N572	(Z)-1-((S)-2-carboxyazetidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide

N373	N573	(S,Z)-1-(2-carboxyazetidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N374	N574	(Z)-1-(1-acetoxyethoxy)-3-(carboxymethyl)-3-ethyltriaz-1-ene 2-oxide
N375	N575	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(carboxymethyl)-3-ethyltriaz-1-ene 2-oxide
N376	N576	(Z)-3-(carboxymethyl)-3-ethyl-1-(1-(isobutyryloxy)ethoxy)triaz-1-ene 2-oxide
N377	N577	(Z)-3-(carboxymethyl)-3-ethyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N378	N578	(Z)-3-(carboxymethyl)-3-ethyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N379	N579	(Z)-1-(acetoxymethoxy)-3-(carboxymethyl)-3-ethyltriaz-1-ene 2-oxide
N380	N580	(Z)-1-((benzoyloxy)methoxy)-3-(carboxymethyl)-3-ethyltriaz-1-ene 2-oxide
N381	N581	(Z)-3-(carboxymethyl)-3-ethyl-1-((isobutyryloxy)methoxy)triaz-1-ene 2-oxide
N382	N582	(Z)-3-(carboxymethyl)-3-ethyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N383	N583	(Z)-3-(carboxymethyl)-3-ethyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N384	N584	(Z)-1-(1-acetoxyethoxy)-3-(carboxymethyl)-3-isopropyltriaz-1-ene 2-oxide
N385	N585	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(carboxymethyl)-3-isopropyltriaz-1-ene 2-oxide
N386	N586	(Z)-3-(carboxymethyl)-1-(1-(isobutyryloxy)ethoxy)-3-isopropyltriaz-1-ene 2-oxide
N387	N587	(Z)-3-(carboxymethyl)-3-isopropyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N388	N588	(Z)-3-(carboxymethyl)-3-isopropyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N389	N589	(Z)-1-(acetoxymethoxy)-3-(carboxymethyl)-3-isopropyltriaz-1-ene 2-oxide
N390	N590	(Z)-1-((benzoyloxy)methoxy)-3-(carboxymethyl)-3-isopropyltriaz-1-ene 2-oxide
N391	N591	(Z)-3-(carboxymethyl)-1-((isobutyryloxy)methoxy)-3-isopropyltriaz-1-ene 2-oxide
N392	N592	(Z)-3-(carboxymethyl)-3-isopropyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N393	N593	(Z)-3-(carboxymethyl)-3-isopropyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N394	N594	(Z)-1-(1-acetoxyethoxy)-3-(carboxymethyl)-3-methyltriaz-1-ene 2-oxide
N395	N595	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(carboxymethyl)-3-methyltriaz-1-ene 2-oxide
N396	N596	(Z)-3-(carboxymethyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N397	N597	(Z)-3-(carboxymethyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N398	N598	(Z)-3-(carboxymethyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N399	N599	(Z)-1-(acetoxymethoxy)-3-(carboxymethyl)-3-methyltriaz-1-ene 2-oxide
N400	N600	(Z)-1-((benzoyloxy)methoxy)-3-(carboxymethyl)-3-methyltriaz-1-ene 2-oxide
N401	N601	(Z)-3-(carboxymethyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-

		oxide
N402	N602	(Z)-3-(carboxymethyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N403	N603	(Z)-3-(carboxymethyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N404	N604	(Z)-1-(1-acetoxyethoxy)-3-(tert-butyl)-3-(carboxymethyl)triaz-1-ene 2-oxide
N405	N605	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(tert-butyl)-3-(carboxymethyl)triaz-1-ene 2-oxide
N406	N606	(Z)-3-(tert-butyl)-3-(carboxymethyl)-1-(1-(isobutyryloxy)ethoxy)triaz-1-ene 2-oxide
N407	N607	(Z)-3-(tert-butyl)-3-(carboxymethyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N408	N608	(Z)-3-(tert-butyl)-3-(carboxymethyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N409	N609	(Z)-1-(acetoxymethoxy)-3-(tert-butyl)-3-(carboxymethyl)triaz-1-ene 2-oxide
N410	N610	(Z)-1-((benzoyloxy)methoxy)-3-(tert-butyl)-3-(carboxymethyl)triaz-1-ene 2-oxide
N411	N611	(Z)-3-(tert-butyl)-3-(carboxymethyl)-1-((isobutyryloxy)methoxy)triaz-1-ene 2-oxide
N412	N612	(Z)-3-(tert-butyl)-3-(carboxymethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N413	N613	(Z)-3-(tert-butyl)-3-(carboxymethyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N414	N614	(Z)-1-(1-acetoxyethoxy)-3-(2-carboxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N415	N615	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(2-carboxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N416	N616	(Z)-3-(2-carboxypropan-2-yl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N417	N617	(Z)-3-(2-carboxypropan-2-yl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N418	N618	(Z)-3-(2-carboxypropan-2-yl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N419	N619	(Z)-1-(acetoxymethoxy)-3-(2-carboxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N420	N620	(Z)-1-((benzoyloxy)methoxy)-3-(2-carboxypropan-2-yl)-3-methyltriaz-1-ene 2-oxide
N421	N621	(Z)-3-(2-carboxypropan-2-yl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N422	N622	(Z)-3-(2-carboxypropan-2-yl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N423	N623	(Z)-3-(2-carboxypropan-2-yl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N424	N624	(Z)-1-(1-acetoxyethoxy)-3-(2-carboxyethyl)-3-methyltriaz-1-ene 2-oxide
N425	N625	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(2-carboxyethyl)-3-methyltriaz-1-ene 2-oxide
N426	N626	(Z)-3-(2-carboxyethyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide

N427	N627	(Z)-3-(2-carboxyethyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N428	N628	(Z)-3-(2-carboxyethyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N429	N629	(Z)-1-(acetoxymethoxy)-3-(2-carboxyethyl)-3-methyltriaz-1-ene 2-oxide
N430	N630	(Z)-1-((benzoyloxy)methoxy)-3-(2-carboxyethyl)-3-methyltriaz-1-ene 2-oxide
N431	N631	(Z)-3-(2-carboxyethyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N432	N632	(Z)-3-(2-carboxyethyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N433	N633	(Z)-3-(2-carboxyethyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N434	N634	(Z)-1-(1-acetoxyethoxy)-3-(3-carboxypropyl)-3-methyltriaz-1-ene 2-oxide
N435	N635	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(3-carboxypropyl)-3-methyltriaz-1-ene 2-oxide
N436	N636	(Z)-3-(3-carboxypropyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N437	N637	(Z)-3-(3-carboxypropyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N438	N638	(Z)-3-(3-carboxypropyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N439	N639	(Z)-1-(acetoxymethoxy)-3-(3-carboxypropyl)-3-methyltriaz-1-ene 2-oxide
N440	N640	(Z)-1-((benzoyloxy)methoxy)-3-(3-carboxypropyl)-3-methyltriaz-1-ene 2-oxide
N441	N641	(Z)-3-(3-carboxypropyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N442	N642	(Z)-3-(3-carboxypropyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N443	N643	(Z)-3-(3-carboxypropyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N444	N644	(Z)-1-(1-acetoxyethoxy)-3-(4-carboxybutyl)-3-methyltriaz-1-ene 2-oxide
N445	N645	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(4-carboxybutyl)-3-methyltriaz-1-ene 2-oxide
N446	N646	(Z)-3-(4-carboxybutyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N447	N647	(Z)-3-(4-carboxybutyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N448	N648	(Z)-3-(4-carboxybutyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N449	N649	(Z)-3-(4-carboxybutyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N450	N650	(Z)-1-(1-acetoxyethoxy)-3-(5-carboxypentyl)-3-methyltriaz-1-ene 2-oxide
N451	N651	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(5-carboxypentyl)-3-methyltriaz-1-ene 2-oxide
N452	N652	(Z)-3-(5-carboxypentyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N453	N653	(Z)-3-(5-carboxypentyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide

N454	N654	(Z)-3-(5-carboxypentyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N455	N655	(Z)-3-(5-carboxypentyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N466	N656	(Z)-2-(1-acetoxyethoxy)-1-(3-carboxyazetidin-1-yl)diazene oxide
N467	N657	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-carboxyazetidin-1-yl)diazene oxide
N468	N658	(Z)-1-(3-carboxyazetidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N469	N659	(Z)-1-(3-carboxyazetidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N470	N660	(Z)-1-(3-carboxyazetidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
N471	N661	(Z)-2-(acetoxymethoxy)-1-(3-carboxyazetidin-1-yl)diazene oxide
N472	N662	(Z)-2-((benzoyloxy)methoxy)-1-(3-carboxyazetidin-1-yl)diazene oxide
N473	N663	(Z)-1-(3-carboxyazetidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N474	N664	(Z)-1-(3-carboxyazetidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N475	N665	(Z)-1-(3-carboxyazetidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
N485	N666	(Z)-2-(1-acetoxyethoxy)-1-((S)-2-carboxypyrrolidin-1-yl)diazene oxide
N486	N667	(Z)-2-(1-(benzoyloxy)ethoxy)-1-((S)-2-carboxypyrrolidin-1-yl)diazene oxide
N487	N668	(Z)-1-((S)-2-carboxypyrrolidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N488	N669	(Z)-1-((S)-2-carboxypyrrolidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N489	N670	(Z)-1-((S)-2-carboxypyrrolidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
N490	N671	(S,Z)-2-(acetoxymethoxy)-1-(2-carboxypyrrolidin-1-yl)diazene oxide
N491	N672	(S,Z)-2-((benzoyloxy)methoxy)-1-(2-carboxypyrrolidin-1-yl)diazene oxide
N492	N673	(S,Z)-1-(2-carboxypyrrolidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N493	N674	(S,Z)-1-(2-carboxypyrrolidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N494	N675	(S,Z)-1-(2-carboxypyrrolidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
N495	N676	(Z)-1-(1-acetoxyethoxy)-3-((1S,2R)-1-carboxy-2-methylbutyl)-3-methyltriaz-1-ene 2-oxide
N496	N677	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((1S,2R)-1-carboxy-2-methylbutyl)-3-methyltriaz-1-ene 2-oxide
N497	N678	(Z)-3-((1S,2R)-1-carboxy-2-methylbutyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N498	N679	(Z)-3-((1S,2R)-1-carboxy-2-methylbutyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N499	N680	(Z)-3-((1S,2R)-1-carboxy-2-methylbutyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N500	N681	(Z)-3-((1S,2R)-1-carboxy-2-methylbutyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N501	N682	(Z)-1-(1-acetoxyethoxy)-3-((S)-1-carboxy-3-methylbutyl)-3-methyltriaz-1-ene 2-oxide

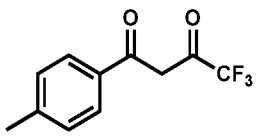
N502	N683	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((S)-1-carboxy-3-methylbutyl)-3-methyltriaz-1-ene 2-oxide
N503	N684	(Z)-3-((S)-1-carboxy-3-methylbutyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N504	N685	(Z)-3-((S)-1-carboxy-3-methylbutyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N505	N686	(S,Z)-3-(1-carboxy-3-methylbutyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N506	N687	(S,Z)-3-(1-carboxy-3-methylbutyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N507	N688	(Z)-1-(1-acetoxyethoxy)-3-((S)-1-carboxy-2-phenylethyl)-3-methyltriaz-1-ene 2-oxide
N508	N689	(Z)-1-(1-(benzoyloxy)ethoxy)-3-((S)-1-carboxy-2-phenylethyl)-3-methyltriaz-1-ene 2-oxide
N509	N690	(Z)-3-((S)-1-carboxy-2-phenylethyl)-1-(1-(isobutyryloxy)ethoxy)-3-methyltriaz-1-ene 2-oxide
N510	N691	(Z)-3-((S)-1-carboxy-2-phenylethyl)-3-methyl-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N511	N692	(S,Z)-3-(1-carboxy-2-phenylethyl)-1-((isobutyryloxy)methoxy)-3-methyltriaz-1-ene 2-oxide
N512	N693	(S,Z)-3-(1-carboxy-2-phenylethyl)-3-methyl-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N526	N694	(Z)-2-(1-acetoxyethoxy)-1-(3-carboxypiperidin-1-yl)diazene oxide
N527	N695	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-carboxypiperidin-1-yl)diazene oxide
N528	N696	(Z)-1-(3-carboxypiperidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N529	N697	(Z)-1-(3-carboxypiperidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N530	N698	(Z)-1-(3-carboxypiperidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N531	N699	(Z)-1-(3-carboxypiperidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N532	N700	(Z)-2-(1-acetoxyethoxy)-1-(4-carboxypiperidin-1-yl)diazene oxide
N533	N701	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(4-carboxypiperidin-1-yl)diazene oxide
N534	N702	(Z)-1-(4-carboxypiperidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N535	N703	(Z)-1-(4-carboxypiperidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N536	N704	(Z)-1-(4-carboxypiperidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
N537	N705	(Z)-1-(4-carboxypiperidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
N538	N706	(Z)-1-(4-carboxypiperidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide
N546	N707	(Z)-2-(1-acetoxyethoxy)-1-(3-carboxypyrrolidin-1-yl)diazene oxide
N547	N708	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-carboxypyrrolidin-1-yl)diazene oxide
N548	N709	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(1-(isobutyryloxy)ethoxy)diazene oxide
N549	N710	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide

N550	N711	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
	N712	(S,Z)-2-(acetoxymethoxy)-1-(2-carboxyazetidin-1-yl)diazene oxide
	N713	(S,Z)-2-((benzoyloxy)methoxy)-1-(2-carboxyazetidin-1-yl)diazene oxide
	N714	(S,Z)-1-(2-carboxyazetidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
	N715	(S,Z)-1-(2-carboxyazetidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
	N716	(Z)-3-(4-carboxybutyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
	N717	(Z)-1-(acetoxymethoxy)-3-(4-carboxybutyl)-3-methyltriaz-1-ene 2-oxide
	N718	(Z)-1-((benzoyloxy)methoxy)-3-(4-carboxybutyl)-3-methyltriaz-1-ene 2-oxide
	N719	(Z)-3-(4-carboxybutyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
	N720	(Z)-3-(5-carboxypentyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
	N721	(Z)-1-(acetoxymethoxy)-3-(5-carboxypentyl)-3-methyltriaz-1-ene 2-oxide
	N722	(Z)-1-((benzoyloxy)methoxy)-3-(5-carboxypentyl)-3-methyltriaz-1-ene 2-oxide
	N723	(Z)-3-(5-carboxypentyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
	N724	(Z)-3-((1S,2R)-1-carboxy-2-methylbutyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
	N725	(Z)-1-(acetoxymethoxy)-3-((1S,2R)-1-carboxy-2-methylbutyl)-3-methyltriaz-1-ene 2-oxide
	N726	(Z)-1-((benzoyloxy)methoxy)-3-((1S,2R)-1-carboxy-2-methylbutyl)-3-methyltriaz-1-ene 2-oxide
	N727	(Z)-3-((1S,2R)-1-carboxy-2-methylbutyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
	N728	(Z)-3-((S)-1-carboxy-3-methylbutyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
	N729	(S,Z)-1-(acetoxymethoxy)-3-(1-carboxy-3-methylbutyl)-3-methyltriaz-1-ene 2-oxide
	N730	(S,Z)-1-((benzoyloxy)methoxy)-3-(1-carboxy-3-methylbutyl)-3-methyltriaz-1-ene 2-oxide
	N731	(S,Z)-3-(1-carboxy-3-methylbutyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
	N732	(Z)-3-((S)-1-carboxy-2-phenylethyl)-3-methyl-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
	N733	(S,Z)-1-(acetoxymethoxy)-3-(1-carboxy-2-phenylethyl)-3-methyltriaz-1-ene 2-oxide
	N734	(S,Z)-1-((benzoyloxy)methoxy)-3-(1-carboxy-2-phenylethyl)-3-methyltriaz-1-ene 2-oxide
	N735	(S,Z)-3-(1-carboxy-2-phenylethyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
	N736	(S,Z)-1-(acetoxymethoxy)-3-(1-carboxy-2-methylpropyl)-3-methyltriaz-1-ene 2-oxide
	N737	(S,Z)-1-((benzoyloxy)methoxy)-3-(1-carboxy-2-methylpropyl)-3-methyltriaz-

		1-ene 2-oxide
	N738	(S,Z)-3-(1-carboxy-2-methylpropyl)-3-methyl-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
	N739	(Z)-1-(3-carboxypiperidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
	N740	(Z)-2-(acetoxymethoxy)-1-(3-carboxypiperidin-1-yl)diazene oxide
	N741	(Z)-2-((benzoyloxy)methoxy)-1-(3-carboxypiperidin-1-yl)diazene oxide
	N742	(Z)-1-(3-carboxypiperidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
	N743	(Z)-2-(acetoxymethoxy)-1-(4-carboxypiperidin-1-yl)diazene oxide
	N744	(Z)-2-((benzoyloxy)methoxy)-1-(4-carboxypiperidin-1-yl)diazene oxide
	N745	(Z)-1-(4-carboxypiperidin-1-yl)-2-((propionyloxy)methoxy)diazene oxide
	N746	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-(1-(propionyloxy)ethoxy)diazene oxide
	N747	(Z)-2-(acetoxymethoxy)-1-(3-carboxypyrrolidin-1-yl)diazene oxide
	N748	(Z)-2-((benzoyloxy)methoxy)-1-(3-carboxypyrrolidin-1-yl)diazene oxide
	N749	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-((isobutyryloxy)methoxy)diazene oxide
	N750	(Z)-1-(3-carboxypyrrolidin-1-yl)-2-((pivaloyloxy)methoxy)diazene oxide

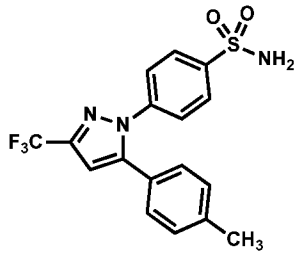
CARBAMATE-LINKED CELECOXIB - DIIMIDE-CAPPED NONOATE

[00207] 4,4,4-Trifluoro-1-(p-tolyl)butane-1,3-dione (C01)



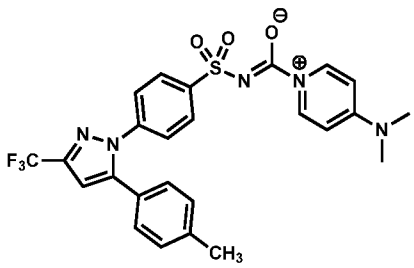
[00208] 25% sodium methoxide in methanol (51.3 ml, 223.5 mmol) and ethyl trifluoroacetate (24.4 ml, 204.9 mmol) were dissolved in 110 mL methyl tert-butyl ether under N2, at room temperature. 4'-methyl acetophenone (25.0 ml, 186.3 mmol) was added and stirred at room temperature overnight. The reaction was washed with 3M HCl and dried over magnesium sulfate. The solution was then evaporated and the resulting oil dried under vacuum overnight. The resulting light orange crystalline solid was washed with cold isooctane and dried under vacuum to yield an off white crystalline solid (37.3 g, 87% yield). LC t_r=3.49 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23 ^{o}C).

[00209] 4-(5-(p-Tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (C02)



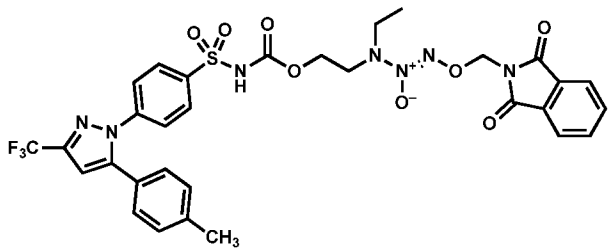
[00210] **C01** (23.55 g, 102.3 mmol) was refluxed with 4-sulphonamidophenyl hydrazine·HCl (23.95 g, 127.9 mmol) in 700 mL ethanol overnight. The reaction was evaporated, dissolved in 700 mL ethyl acetate, washed with water and brine, dried over magnesium sulfate and evaporated to ~100 mL ethyl acetate. The product was crystalized by the addition of ~ 400 mL isooctane. After 15 minutes, the white crystalline solid was broken up, washed with isooctane and dried under vacuum (35.15 g, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94-7.91 (m, 2H), 7.51-7.49 (m, 2H), 7.21-7.20 (m, 2H), 7.15-7.13 (m, 2H), 6.77 (s, 1H), 2.41 (s, 3H). LC t_r=4.27 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(neg)MS m/z 380 (M-H calcd for $C_{17}H_{14}F_3N_3O_2S$ requires 380).

[00211] **(Z)-4-(Dimethylamino)-N-((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)pyridin-1-ium-1-carbimidate (C03)**



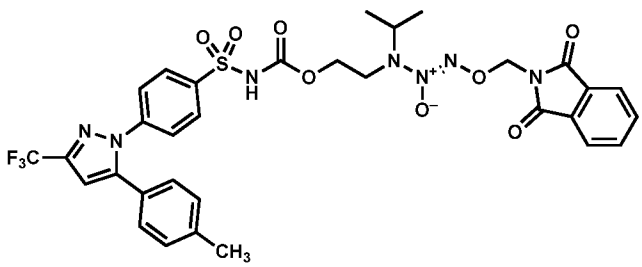
[00212] **C02** (5.0 g, 13.11 mmol) was dissolved in 20 mL acetonitrile. 4-Dimethylamino pyridine (3.30 g, 27.01 mmol) was added, followed by diphenyl carbonate (2.95 g, 13.77 mmol) and stirred at room temperature for 10 minutes. The resulting white precipitate was filtered, washed with ethyl ether and dried under vacuum (6.77 g, 98% yield). ^{1}H NMR (400 MHz, d-DMSO) δ 8.23-8.20 (m, 2H), 7.82-7.78 (m, 2H), 7.39-7.36 (m, 2H), 7.29-7.25 (m, 2H), 7.09-7.04 (m, 1H), 6.99-6.96 (m, 2H), 6.91-6.88 (m, 2H), 3.18 (s, 6H), 2.31 (s, 3H). LC t_r=4.93 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 502 (M+H calcd for $C_{25}H_{22}F_3N_5O_3S$ requires 502), ES(neg)MS m/z 500 (M-H calcd for $C_{25}H_{22}F_3N_5O_3S$ requires 500).

[00213] **(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-ethyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide (8)**



[00214] **C03** (100 mg, 0.19 mmol) was suspended in 1.0 mL acetonitrile and **N033** (70 mg, 0.23 mmol) was added and the reaction was heated at 50 °C overnight, becoming homogeneous. The mixture was evaporated, dissolved in ethyl acetate, washed with potassium hydrogensulfate solution, brine, dried over magnesium sulfate, and evaporated. The product was chromatographed, eluting with 50% ethyl acetate/hexanes to yield desired product (17 mg, 13% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.97 (m, 2H), 7.84-7.77 (m, 4H), 7.52-7.49 (m, 2H), 7.22-7.13 (m, 4H), 6.76 (s, 1H), 5.80-5.77 (m, 2H), 4.20-4.17 (m, 2H), 3.37-3.33 (m, 2H), 3.19 (q, J=7.1 Hz, 2H), 2.41 (s, 3H), 1.06 (t, J=7.1 Hz, 3H). LC t_r=4.86 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 695 (M+Na calcd for $C_{31}H_{28}F_3N_7O_8S$ requires 695), ES(neg)MS m/z 671 (M-H calcd for $C_{31}H_{28}F_3N_7O_8S$ requires 671).

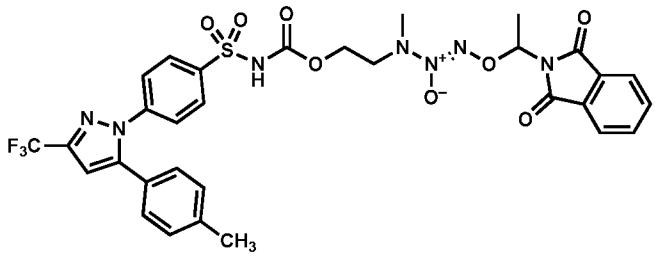
[00215] **(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-isopropyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide (10)**



[00216] **C03** (100 mg, 0.19 mmol) and **N035** (74 mg, 0.23 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (18 mg, 13% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.07 (m, 2H), 7.99-7.81 (m, 4H), 7.54-7.51 (m, 2H), 7.21-7.13 (m, 4H), 6.75 (s, 1H), 5.79 (s, 2H), 4.17 (t, J=4.8 Hz, 2H), 3.75-3.71 (m, 1H), 3.31 (t, J=4.8

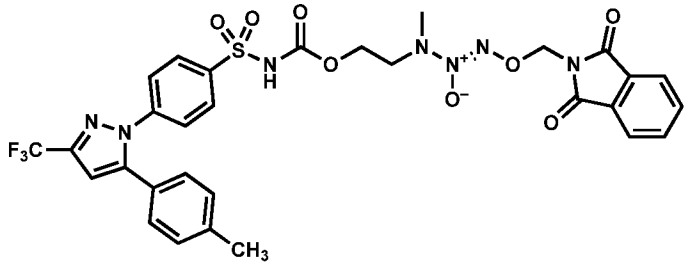
Hz, 2H), 2.41 (s, 3H), 1.07 (d, J=6.5 Hz, 6H). LC t_r=4.93 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 752 (M+Na calcd for $C_{32}H_{30}F_3N_7O_8S$ requires 752), ES(neg)MS m/z 728 (M-H calcd for $C_{32}H_{30}F_3N_7O_8S$ requires 728).

[00217] (Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide (11)



[00218] **C03** (100 mg, 0.19 mmol) and **N036** (71 mg, 0.23 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (86 mg, 63% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.05 (m, 2H), 7.92-7.90 (m, 2H), 7.80-7.78 (m, 2H), 7.52-7.49 (m, 2H), 7.27-7.13 (m, 4H), 6.76 (s, 1H), 6.26 (q, J=6.6 Hz, 1H), 4.25-4.20 (m, 1H), 4.02-3.96 (m, 1H), 3.65-3.58 (m, 1H), 3.32-3.36 (m, 1H), 2.88 (s, 3H), 2.40 (s, 3H), 2.00 (d, J=6.6 Hz, 3H). LC t_r=4.87 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 738 (M+Na calcd for $C_{31}H_{28}F_3N_7O_8S$ requires 738), ES(neg)MS m/z 714 (M-H calcd for $C_{31}H_{28}F_3N_7O_8S$ requires 714).

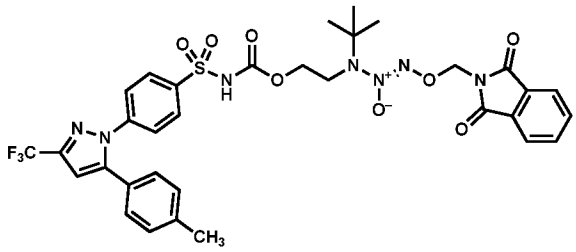
[00219] (Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide (12)



[00220] **C03** (100 mg, 0.19 mmol) was suspended in 1.0 mL acetonitrile and **N037** (62 mg, 0.21 mmol) was added and the reaction was heated at 50 °C overnight, becoming homogeneous. The mixture was evaporated, dissolved in ethyl acetate, washed with potassium

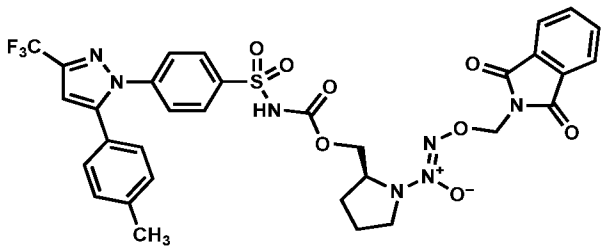
hydrogensulfate solution, brine, dried over magnesium sulfate, and evaporated. The product was chromatographed, eluting with 50% ethyl acetate/hexanes to yield desired product (15 mg, 11% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-7.96 (m, 5H), 7.83-7.81 (m, 2H), 7.51-7.49 (m, 2H), 7.21-7.13 (m, 4H), 6.75 (s, 1H), 5.75 (s, 2H), 4.21-4.18 (m, 2H), 3.58-3.54 (m, 2H), 2.99 (s, 3H), 2.40 (s, 3H). LC t_r=4.76 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 724 (M+Na calcd for $C_{30}H_{26}F_3N_7O_8S$ requires 724), ES(neg)MS m/z 700 (M-H calcd for $C_{30}H_{26}F_3N_7O_8S$ requires 700).

[00221] (Z)-3-(tert-Butyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide (14)



[00222] **C03** (100 mg, 0.19 mmol) and **N039** (77.4 mg, 0.23 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (15 mg, 11% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.07 (m, 2H), 8.00-7.98 (m, 2H), 7.84-7.82 (m, 2H), 7.53-7.51 (m, 2H), 7.21-7.13 (m, 4H), 6.75 (s, 1H), 5.82 (s, 2H), 4.11 (t, J=4.8 Hz, 2H), 3.30 (t, J=4.8 Hz, 2H), 2.41 (s, 3H), 1.16 (s, 9H). LC t_r=5.04 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 766 (M+Na calcd for $C_{33}H_{32}F_3N_7O_8S$ requires 766), ES(neg)MS m/z 742 (M-H calcd for $C_{33}H_{32}F_3N_7O_8S$ requires 742).

[00223] (S,Z)-2-((1,3-Dioxoisoindolin-2-yl)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide (32)



[00224] **C03** (138 mg, 0.26 mmol) and **N057** (100 mg, 0.31 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (127 mg, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94-7.86 (m, 4H), 7.74-7.71 (m, 2H), 7.35-7.31 (m, 2H), 7.16-7.08 (m, 4H), 6.71 (s, 1H), 5.70 (s, 2H), 4.22-4.16 (br m, 1H), 4.08-3.95 (br m, 1H), 3.53-3.43 (m, 2H), 2.35 (s, 3H), 1.96-1.80 (br m, 3H), 1.70-1.63 (br m, 2H). LC t_r=4.82 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 750 (M+Na calcd for $C_{32}H_{28}F_3N_7O_8S$ requires 750), ES(neg)MS m/z 726 (M-H calcd for $C_{32}H_{28}F_3N_7O_8S$ requires 726).

[00225] **Table 8. Carbamate-Linked Celecoxib - Diimide-Capped NONOate.**

Starting NONOate	Compound #	Compound Name
N026	1	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((S)-1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)propan-2-yl)triaz-1-ene 2-oxide
N027	2	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)propan-2-yl)triaz-1-ene 2-oxide
N028	3	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((S)-3-methyl-1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)butan-2-yl)triaz-1-ene 2-oxide
N029	4	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(3-methyl-1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)butan-2-yl)triaz-1-ene 2-oxide
N030	5	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N031	6	(S,Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N032	7	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-ethyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
N033	8	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-ethyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
N034	9	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-isopropyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
N035	10	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-isopropyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
N036	11	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide

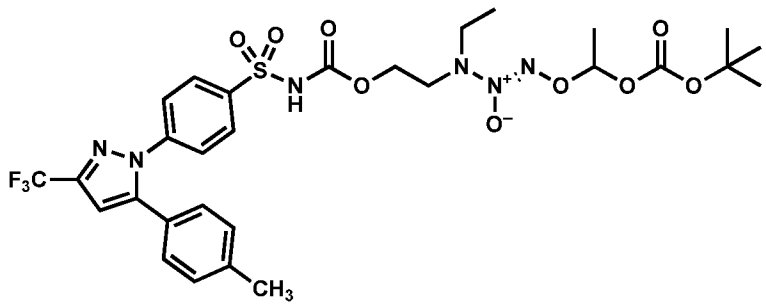
N037	12	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
N038	13	(Z)-3-(tert-butyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
N039	14	(Z)-3-(tert-butyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
N040	15	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-methyl-1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)propan-2-yl)triaz-1-ene 2-oxide
N041	16	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(2-methyl-1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)propan-2-yl)triaz-1-ene 2-oxide
N042	17	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)propyl)triaz-1-ene 2-oxide
N043	18	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)propyl)triaz-1-ene 2-oxide
N044	19	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)butyl)triaz-1-ene 2-oxide
N045	20	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)butyl)triaz-1-ene 2-oxide
N046	21	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(5-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pentyl)triaz-1-ene 2-oxide
N047	22	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(5-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pentyl)triaz-1-ene 2-oxide
N048	23	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(6-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)hexyl)triaz-1-ene 2-oxide
N049	24	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(6-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)hexyl)triaz-1-ene 2-oxide
N050	25	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N051	26	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N052	27	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N053	28	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-

		yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N054	29	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(2-hydroxyethyl)-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide
N055	30	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(6-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)hexyl)triaz-1-ene 2-oxide
N056	31	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N057	32	(S,Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N058	33	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((2S,3R)-3-methyl-1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pentan-2-yl)triaz-1-ene 2-oxide
N059	34	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((2S,3R)-3-methyl-1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pentan-2-yl)triaz-1-ene 2-oxide
N060	35	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((S)-4-methyl-1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pentan-2-yl)triaz-1-ene 2-oxide
N061	36	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(4-methyl-1-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pentan-2-yl)triaz-1-ene 2-oxide
N062	37	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((S)-1-phenyl-3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)propan-2-yl)triaz-1-ene 2-oxide
N063	38	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(1-phenyl-3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)propan-2-yl)triaz-1-ene 2-oxide
N064	39	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N065	40	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N066	41	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N067	42	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N068	43	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N069	44	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N070	45	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(4-(((((4-(5-(p-tolyl)-3-

		(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N071	46	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N072	47	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
N073	48	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
N074	49	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N075	50	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide

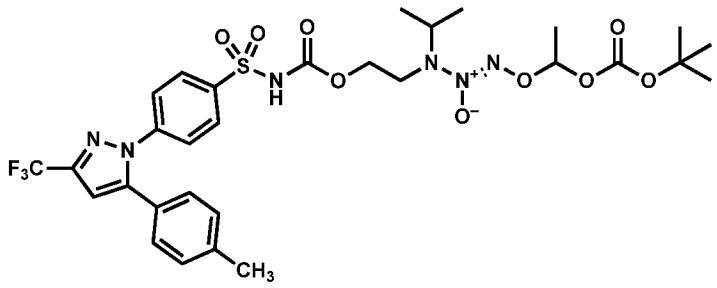
CARBAMATE-LINKED CELECOXIB - CARBONATE-CAPPED NONOATE

[00226] (Z)-5-Ethyl-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide (89)



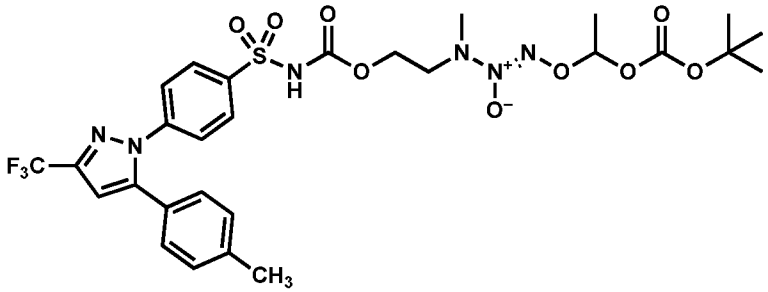
[00227] **C03** (100 mg, 0.19 mmol) and **N129** (67 mg, 0.23 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (21 mg, 16% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.03 (m, 2H), 7.52-7.50 (m, 2H), 7.21-7.13 (m, 4H), 6.75 (s, 1H), 6.41 (q, J= 5.6 Hz, 1H), 4.31-4.18 (m, 2H), 3.42-3.34 (m, 2H), 3.31-3.15 (m, 2H), 2.40 (s, 3H), 1.62 (d, J=5.6 Hz, 3H), 1.49 (s, 9H), 1.07 (t, J=7.1 Hz, 3H). LC t_r=5.15 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 723 (M+Na calcd for $C_{29}H_{35}F_3N_6O_9S$ requires 723), ES(neg)MS m/z 699 (M-H calcd for $C_{29}H_{35}F_3N_6O_9S$ requires 699).

[00228] (Z)-5-Isopropyl-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide (91)



[00229] **C03** (100 mg, 0.19 mmol) and **N131** (71 mg, 0.23 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (58 mg, 43% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.50-7.48 (m, 2H), 7.21-7.12 (m, 4H), 6.75 (s, 1H), 6.42 (q, J=5.6 Hz, 1H), 4.27-4.10 (m, 2H), 3.76-3.70 (m, 1H), 3.33 (t, J=5.2 Hz, 2H), 3.21 (q, J=7.3 Hz, 1H), 2.40 (s, 3H), 1.64 (d, J=5.6 Hz, 3H), 1.49 (s, 9H), 1.09 (dd, J=6.5, 1.9 Hz, 6H). LC t_r=5.25 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 737 (M+Na calcd for $C_{30}H_{37}F_3N_6O_9S$ requires 737), ES(neg)MS m/z 713 (M-H calcd for $C_{30}H_{37}F_3N_6O_9S$ requires 713).

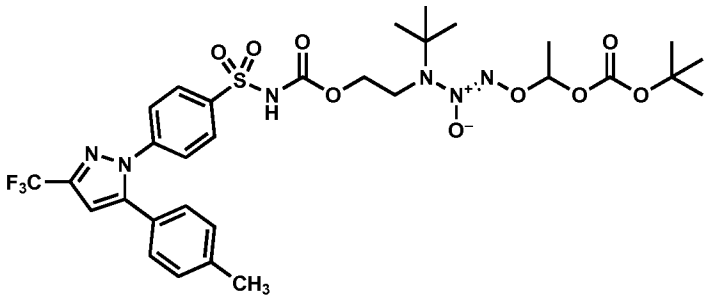
[00230] (Z)-5,9,13,13-Tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide (93)



[00231] **C03** (100 mg, 0.19 mmol) and **N133** (59 mg, 0.21 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (21 mg, 16% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.53-7.50 (m, 2H), 7.21-7.13 (m, 4H), 6.75 (s, 1H), 6.41 (q, J=5.6 Hz, 1H), 4.33-4.20 (m, 2H), 3.62-3.58 (m, 2H), 3.02 (s, 3H), 2.40 (s, 3H), 1.62 (d, J=5.6 Hz, 3H), 1.50 (s, 9H). LC t_r=5.07 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS

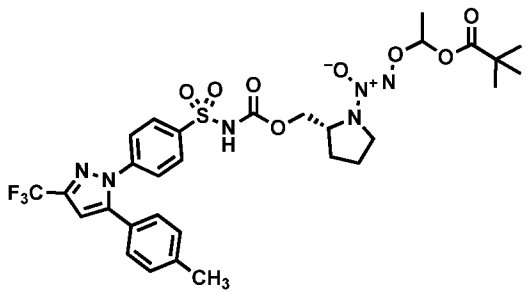
m/z 709 (M+Na calcd for $C_{28}H_{33}F_3N_6O_9S$ requires 709), ES(neg)MS m/z 685 (M-H calcd for $C_{28}H_{33}F_3N_6O_9S$ requires 685).

[00232] (Z)-5-(tert-Butyl)-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide (95)



[00233] **C03** (100 mg, 0.19 mmol) and **N135** (74 mg, 0.23 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (51 mg, 37% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.51-7.48 (m, 2H), 7.21-7.12 (m, 4H), 6.75 (s, 1H), 6.45 (dq, J=20.5, 5.6 Hz, 1H), 4.25-4.20 (m, 1H), 4.06-4.00 (m, 1H), 3.33-3.28 (m, 2H), 2.40 (s, 3H), 1.65 (dd, J=5.6, 3.7 Hz, 3H), 1.49 (s, 9H), 1.18 (s, 9H). LC t_r=5.36 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 751 (M+Na calcd for $C_{31}H_{39}F_3N_6O_9S$ requires 751), ES(neg)MS m/z 727 (M-H calcd for $C_{31}H_{39}F_3N_6O_9S$ requires 727).

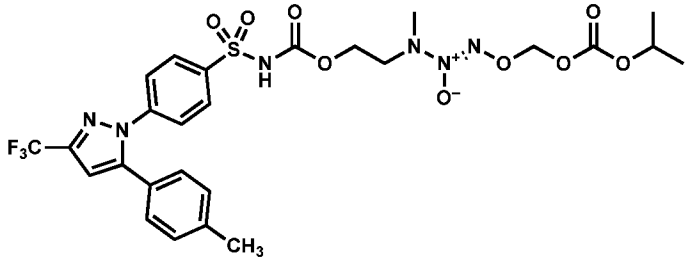
[00234] (Z)-2-(1-((tert-Butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide (126)



[00235] **C03** (100 mg, 0.19 mmol) and **N166** (70 mg, 0.23 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (71.8 mg, 53% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-7.97 (m, 2H), 7.47-7.42 (m, 2H), 7.11-7.11 (m, 4H), 6.74 (s, 1H), 6.40-6.34 (s, 1H), 4.29-4.11 (m, 2H), 2.39 (s, 3H), 2.03-1.67 (br m, 6H), 1.60 (dd,

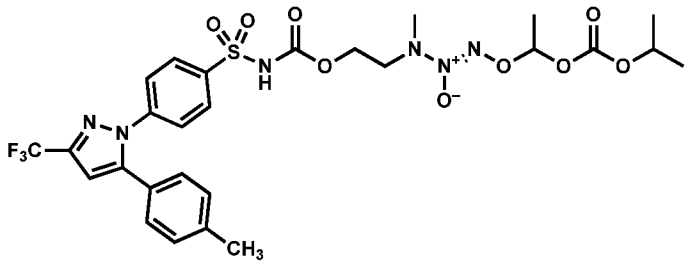
J=5.6, 1.7 Hz, 3H), 1.49 (d, J=5.6 Hz, 9H). LC t_r=5.14 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 735 (M+Na calcd for $C_{30}H_{35}F_3N_6O_9S$ requires 735), ES(neg)MS m/z 711 (M-H calcd for $C_{30}H_{35}F_3N_6O_9S$ requires 711).

[00236] (Z)-5,13-Dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide (150-A)



[00237] **C03** (50 mg, 0.09 mmol) and **N190-A** (26 mg, 0.10 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (14 mg, 23% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.04 (m, 2H), 7.54-7.52 (m, 2H), 7.22-7.12 (m, 4H), 6.77 (s, 1H), 5.78 (s, 1H), 4.99-4.92 (m, 1H), 4.30-4.25 (m, 2H), 3.67-3.60 (m, 2H), 3.06 (s, 3H), 2.41 (s, 3H), 1.30 (dd, J=6.0, 2.8 Hz, 6H). LC t_r=4.96 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 681 (M+Na calcd for $C_{26}H_{29}F_3N_6O_9S$ requires 681), ES(neg)MS m/z 657 (M-H calcd for $C_{26}H_{29}F_3N_6O_9S$ requires 657).

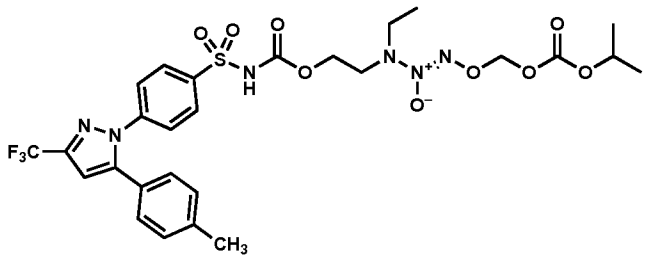
[00238] (Z)-5,9,13-Trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide (150-B)



[00239] **C03** (100 mg, 0.19 mmol) and **N190-B** (50 mg, 0.19 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (17 mg, 13% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.03 (m, 2H), 7.53-7.49 (m, 2H), 7.21-7.12 (m, 4H), 6.76 (s,

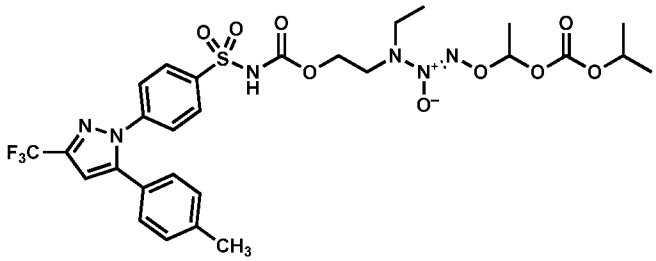
1H), 6.42 (d, J=5.6 Hz, 1H), 4.97-4.91 (m, 1H), 4.33-4.21 (m, 2H), 3.66-3.50 (m, 2H), 3.01 (s, 3H), 2.41 (s, 3H), 1.64 (d, J=5.6 Hz, 3H), 1.32 (dd, J=6.2, 5.4 Hz, 6H). LC t_r=4.62 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 695 (M+Na calcd for $C_{27}H_{31}F_3N_6O_9S$ requires 695).

[00240] (Z)-5-Ethyl-13-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide (150-C)



[00241] **C03** (100 mg, 0.19 mmol) and **N190-C** (61 mg, 0.23 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (19 mg, 15% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.05 (m, 2H), 7.54-7.51 (m, 2H), 7.22-7.13 (m, 4H), 6.76 (s, 1H), 5.80 (s, 2H), 5.00-4.90 (m, 1H), 4.28-4.23 (m, 2H), 4.26-4.21 (m, 2H), 3.28 (q, J=7.1 Hz, 2H), 2.41 (s, 3H), 1.33 (dd, J=6.2, 4.6 Hz, 6H), 1.14 (dt, J=25.9, 7.1 Hz, 6H). LC t_r=5.03 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 695 (M+Na calcd for $C_{27}H_{31}F_3N_6O_9S$ requires 695), ES(neg)MS m/z 671 (M-H calcd for $C_{27}H_{31}F_3N_6O_9S$ requires 671).

[00242] (Z)-5-Ethyl-9,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide (150-D)



[00243] **C03** (100 mg, 0.19 mmol) and **N190-D** (47 mg, 0.21 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (19 mg, 15% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.05 (m, 2H), 7.53-7.51 (m, 2H), 7.22-7.13 (m, 4H), 6.76 (s,

1H), 6.47 (dq, J= 23.5, 5.6 Hz, 2H), 5.00-4.90 (m, 1H), 4.31-4.17 (m, 2H), 3.46-3.33 (m, 2H), 3.30-3.13 (m, 2H), 2.40 (s, 3H), 1.65 (d, J=5.6 Hz, 3H), 1.31 (dd, J=13.8, 6.2 Hz, 6H). LC t_r=5.08 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 709 (M+Na calcd for $C_{28}H_{33}F_3N_6O_9S$ requires 709), ES(neg)MS m/z 685 (M-H calcd for $C_{28}H_{33}F_3N_6O_9S$ requires 685).

[00244] Table 9. Carbamate-Linked Celecoxib - Carbonate-Capped NONOate.

Starting NONOate	Compound #	Compound Name
N116	76	(4S,Z)-4,5,9-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N117	77	(4S,Z)-4,5,9,13-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N121	78	(4S,Z)-4,5,9,13,13-pentamethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N122	79	(S,Z)-4,5,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N126	80	(S,Z)-4,5,13,13-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N127	81	(4S,Z)-4-isopropyl-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N128	82	(4S,Z)-4-isopropyl-5,9,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N129	83	(4S,Z)-4-isopropyl-5,9,13,13-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N130	84	(S,Z)-4-isopropyl-5,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N131	85	(S,Z)-4-isopropyl-5,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N132	86	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N133	87	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N134	88	(Z)-5-ethyl-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-

		oxide
N135	89	(Z)-5-ethyl-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N136	90	(Z)-5-isopropyl-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N137	91	(Z)-5-isopropyl-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N138	92	(Z)-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N139	93	(Z)-5,9,13,13-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N140	94	(Z)-5-(tert-butyl)-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N141	95	(Z)-5-(tert-butyl)-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N143	96	(Z)-4,4,5,9-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N144	97	(Z)-4,4,5,9,13,13-hexamethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N148	98	(Z)-6,10-dimethyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,9,11,13-tetraoxa-6,7,8-triazapentadec-7-ene 7-oxide
N149	99	(Z)-6,10,14,14-tetramethyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,9,11,13-tetraoxa-6,7,8-triazapentadec-7-ene 7-oxide
N150	100	(Z)-7,11-dimethyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12,14-tetraoxa-7,8,9-triazahexadec-8-ene 8-oxide
N151	101	(Z)-7,11,15-trimethyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12,14-tetraoxa-7,8,9-triazahexadec-8-ene 8-oxide
N155	102	(Z)-7,11,15,15-tetramethyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12,14-tetraoxa-7,8,9-triazahexadec-8-ene 8-oxide
N156	103	(Z)-8,12-dimethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13,15-tetraoxa-8,9,10-triazaheptadec-9-ene 9-oxide
N160	104	(Z)-8,12,16-trimethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13,15-tetraoxa-8,9,10-triazaheptadec-9-ene 9-oxide
N161	105	(Z)-8,12,16,16-tetramethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13,15-tetraoxa-8,9,10-triazaheptadec-9-ene 9-oxide
N164	106	(Z)-8,16-dimethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13,15-tetraoxa-8,9,10-triazaheptadec-9-ene 9-oxide

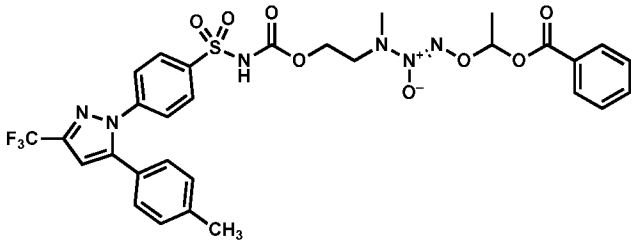
N165	107	(Z)-8,16,16-trimethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13,15-tetraoxa-8,9,10-triazaheptadec-9-ene 9-oxide
N169	108	(Z)-9,13-dimethyl-1,15-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,12,14,16-tetraoxa-9,10,11-triazaoctadec-10-ene 10-oxide
N170	109	(Z)-9,13,17,17-tetramethyl-1,15-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,12,14,16-tetraoxa-9,10,11-triazaoctadec-10-ene 10-oxide
N171	110	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N172	111	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N173	112	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N174	113	(Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N175	114	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N176	115	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N177	116	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N178	117	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N179	118	(Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N180	119	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N181	120	(Z)-5-(2-hydroxyethyl)-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N182	121	(Z)-5-(2-hydroxyethyl)-9,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N185	122	(Z)-5-(2-hydroxyethyl)-9,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N186	123	(Z)-5-(2-hydroxyethyl)-13,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-

		triazatetradec-6-ene 6-oxide
N188	124	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N189	125	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N190	126	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
	127	(S,Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
	128	(S,Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
	129	(4S,Z)-4-((R)-sec-butyl)-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
	130	(S,Z)-4-((R)-sec-butyl)-5,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
	131	(4S,Z)-4-isobutyl-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
	132	(S,Z)-4-isobutyl-5,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
	133	(4S,Z)-4-benzyl-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
	134	(S,Z)-4-benzyl-5,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
	135	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
	136	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
	137	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
	138	(Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
	139	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
	140	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-

		(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
	141	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
	142	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
	143	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
	144	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
	145	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
	146	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
	147	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
	148	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
	149	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
	150	(Z)-2-((isobutyryloxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N190-A	150-A	(Z)-5,13-Dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N190-B	150-B	(Z)-5,9,13-Trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N190-C	150-C	(Z)-5-Ethyl-13-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide
N190-D	150-D	(Z)-5-Ethyl-9,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide

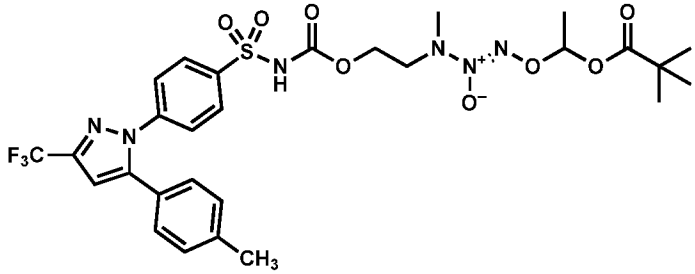
CARBAMATE-LINKED CELECOXIB - ESTER-CAPPED NONOATE

[00245] (Z)-3,7-Dimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide (195)



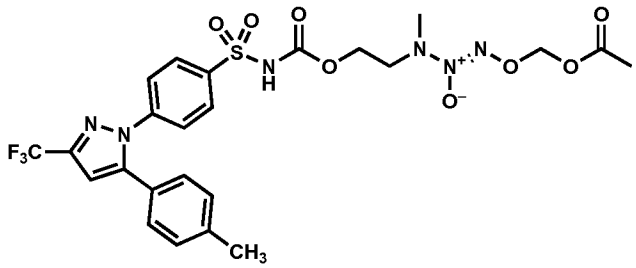
[00246] **C03** (50 mg, 0.09 mmol) and **N395** (27 mg, 0.09 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (14 mg, 22% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.03 (m, 4H), 7.64-7.60 (m, 1H), 7.52-7.48 (m, 4H), 7.22-7.12 (m, 4H), 6.83 (q, J=5.6 Hz, 1H), 6.76 (s, 1H), 4.22-4.20 (m, 2H), 3.54-3.52 (m, 2H), 2.97 (s, 3H), 2.41 (s, 3H), 1.75 (d, J=5.6 Hz, 3H). LC t_r=5.04 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 713 (M+Na calcd for $C_{30}H_{29}F_3N_6O_8S$ requires 713), ES(neg)MS m/z 689 (M-H calcd for $C_{30}H_{29}F_3N_6O_8S$ requires 689).

[00247] **(Z)-5,9,12,12-Tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide (197)**



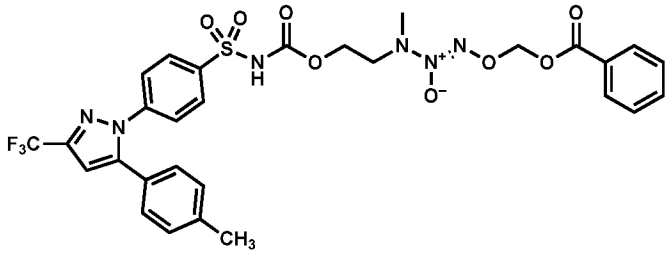
[00248] **C03** (100 mg, 0.19 mmol) and **N397** (60 mg, 0.23 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (19 mg, 15% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.04 (m, 2H), 7.53-7.51 (m, 2H), 7.22-7.13 (m, 4H), 6.76 (s, 1H), 6.57 (dq, J= 18.8, 5.6 Hz, 1H), 4.27-4.23 (m, 2H), 3.56-3.54 (m, 2H), 3.00 (s, 3H), 2.41 (s, 3H), 1.61 (dd, J=5.6, 5.0 Hz, 3H), 1.22 (d, J=6.4 Hz, 9H). LC t_r=5.11 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 693 (M+Na calcd for $C_{28}H_{33}F_3N_6O_8S$ requires 693), ES(neg)MS m/z 669 (M-H calcd for $C_{28}H_{33}F_3N_6O_8S$ requires 669).

[00249] **(Z)-5-Methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide (199)**



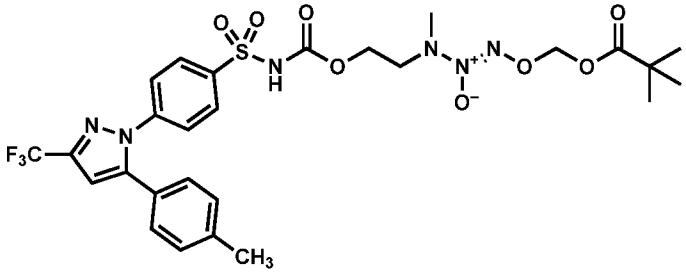
[00250] **C03** (100 mg, 0.19 mmol) and **N399** (39.2 mg, 0.19 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (16 mg, 14% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.54-7.51 (m, 2H), 7.22-7.13 (m, 4H), 6.76 (s, 1H), 5.78 (s, 2H), 4.29-4.26 (m, 2H), 3.63-3.60 (m, 2H), 3.05 (s, 3H), 2.41 (s, 3H), 2.15 (s, 3H). LC t_r=4.68 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 637 (M+Na calcd for $C_{24}H_{25}F_3N_6O_8S$ requires 637), ES(neg)MS m/z 613 (M-H calcd for $C_{24}H_{25}F_3N_6O_8S$ requires 613).

[00251] **(Z)-7-Methyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide (200)**



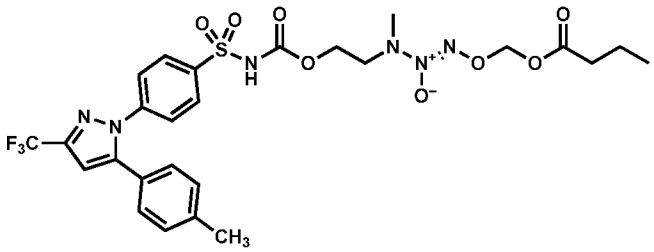
[00252] **C03** (40 mg, 0.07 mmol) was suspended in 0.5 mL acetonitrile. **N400** (20.0 mg, 0.084 mmol) was added and the reaction heated at 50 °C overnight. The reaction became homogeneous. The reaction was evaporated and dissolved in ethyl acetate, which was washed with potassium hydrogensulfate solution and brine, dried over magnesium sulfate and evaporated. The product was chromatographed, eluting with 50% ethyl acetate/hexanes to yield a residue (8 mg, 16% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-8.01 (m, 2H), 7.96-7.93 (m, 2H), 7.58-7.54 (m, 1H), 7.42.-7.38 (m, 2H), 7.33-7.31 (m, 2H), 7.10 (dd, J=19.9, 8.1 Hz, 4H), 6.71 (s, 1H), 5.98 (s, 2H), 4.12 (t, J=5.0 Hz, 2H), 3.56 (t, J=5.1 Hz, 2H), 2.99 (s, 3H), 2.34 (s, 3H). LC t_r=4.41 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 699 (M+Na calcd for $C_{29}H_{27}F_3N_6O_8S$ requires 699), ES(neg)MS m/z 675 (M-H calcd for $C_{29}H_{27}F_3N_6O_8S$ requires 675).

[00253] (Z)-5,12,12-Trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide (202)



[00254] **C03** (100 mg, 0.19 mmol) and **N402** (47 mg, 0.19 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (30 mg, 24% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.54-7.51 (m, 2H), 7.22-7.13 (m, 4H), 6.76 (s, 1H), 5.79 (s, 2H), 4.27-4.25 (m, 2H), 3.60-3.58 (m, 2H), 3.03 (s, 3H), 2.41 (s, 3H), 1.22 (s, 9H). LC t_r=5.11 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 679 (M+Na calcd for $C_{27}H_{31}F_3N_6O_8S$ requires 679), ES(neg)MS m/z 655 (M-H calcd for $C_{27}H_{31}F_3N_6O_8S$ requires 655).

[00255] (Z)-5-Methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatetradec-6-ene 6-oxide (350-A)



[00256] **C03** (100 mg, 0.19 mmol) and **N550-A** (45 mg, 0.19 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **8**: (20 mg, 16% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.54-7.51 (m, 2H), 7.22-7.13 (m, 4H), 6.76 (s, 1H), 5.79 (s, 2H), 4.29-4.26 (m, 2H), 3.66-3.60 (m, 2H), 3.05 (s, 3H), 2.41 (s, 3H), 2.38 (t, J=7.4 Hz, 2H), 1.73-1.64 (m, 2H), 0.96 (t, J=7.4 Hz, 3H). LC t_r=4.98 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 665 (M+Na calcd for $C_{26}H_{29}F_3N_6O_8S$ requires 665), ES(neg)MS m/z 641 (M-H calcd for $C_{26}H_{29}F_3N_6O_8S$ requires 641).

[00257] Table 10. Carbamate-Linked Celecoxib - Ester-Capped NONOate.

Starting NONOate	Compound #	Compound Name

N351	151	(4S,Z)-4,5,9-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N352	152	(8S,Z)-3,7,8-trimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N353	153	(4S,Z)-4,5,9,12-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N354	154	(4S,Z)-4,5,9,12,12-pentamethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N355	155	(4S,Z)-4,5,9-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N356	156	(S,Z)-4,5-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N357	157	(S,Z)-7,8-dimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N358	158	(S,Z)-4,5,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N359	159	(S,Z)-4,5,12,12-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N360	160	(S,Z)-4,5-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N361	161	(4S,Z)-4-isopropyl-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N362	162	(8S,Z)-8-isopropyl-3,7-dimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N363	163	(4S,Z)-4-isopropyl-5,9,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N364	164	(4S,Z)-4-isopropyl-5,9,12,12-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N365	165	(4S,Z)-4-isopropyl-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N366	166	(S,Z)-4-isopropyl-5,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N367	167	(S,Z)-4-isopropyl-5,12,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N368	168	(Z)-2-(1-acetoxyethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N369	169	(Z)-2-(1-(benzoyloxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-

		1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N370	170	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N371	171	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N372	172	(Z)-2-(1-(propionyloxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N373	173	(S,Z)-2-((pivaloyloxy)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N374	174	(Z)-5-ethyl-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N375	175	(Z)-7-ethyl-3-methyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N376	176	(Z)-5-ethyl-9,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N377	177	(Z)-5-ethyl-9,12,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N378	178	(Z)-5-ethyl-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N379	179	(Z)-5-ethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N380	180	(Z)-7-ethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N381	181	(Z)-5-ethyl-12-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N382	182	(Z)-5-ethyl-12,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N383	183	(Z)-5-ethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N384	184	(Z)-5-isopropyl-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N385	185	(Z)-7-isopropyl-3-methyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N386	186	(Z)-5-isopropyl-9,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N387	187	(Z)-5-isopropyl-9,12,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N388	188	(Z)-5-isopropyl-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide

N389	189	(Z)-5-isopropyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N390	190	(Z)-7-isopropyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N391	191	(Z)-5-isopropyl-12-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N392	192	(Z)-5-isopropyl-12,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N393	193	(Z)-5-isopropyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N394	194	(Z)-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N395	195	(Z)-3,7-dimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N396	196	(Z)-5,9,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N397	197	(Z)-5,9,12,12-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N398	198	(Z)-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N399	199	(Z)-5-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N400	200	(Z)-7-methyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N401	201	(Z)-5,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N402	202	(Z)-5,12,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N403	203	(Z)-5-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N404	204	(Z)-5-(tert-butyl)-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N405	205	(Z)-7-(tert-butyl)-3-methyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N406	206	(Z)-5-(tert-butyl)-9,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N407	207	(Z)-5-(tert-butyl)-9,12,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N408	208	(Z)-5-(tert-butyl)-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N409	209	(Z)-5-(tert-butyl)-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide

N410	210	(Z)-7-(tert-butyl)-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N411	211	(Z)-5-(tert-butyl)-12-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N412	212	(Z)-5-(tert-butyl)-12,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N413	213	(Z)-5-(tert-butyl)-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N414	214	(Z)-4,4,5,9-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N415	215	(Z)-3,7,8,8-tetramethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N416	216	(Z)-4,4,5,9,12-pentamethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N417	217	(Z)-4,4,5,9,12,12-hexamethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N418	218	(Z)-4,4,5,9-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N419	219	(Z)-4,4,5-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N420	220	(Z)-7,8,8-trimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N421	221	(Z)-4,4,5,12-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N422	222	(Z)-4,4,5,12,12-pentamethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N423	223	(Z)-4,4,5-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N424	224	(Z)-6,10-dimethyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,9,11-trioxa-6,7,8-triazatridec-7-ene 7-oxide
N425	225	(Z)-3,7-dimethyl-1,12-dioxo-1-phenyl-12-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,11-trioxa-5,6,7-triazadodec-5-ene 6-oxide
N426	226	(Z)-6,10,13-trimethyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,9,11-trioxa-6,7,8-triazatetradec-7-ene 7-oxide
N427	227	(Z)-6,10,13,13-tetramethyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,9,11-trioxa-6,7,8-triazatetradec-7-ene 7-oxide
N428	228	(Z)-6,10-dimethyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,9,11-trioxa-6,7,8-triazatetradec-7-ene 7-oxide
N429	229	(Z)-6-methyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-

		yl)phenylsulfonamido)-2,9,11-trioxa-6,7,8-triazatridec-7-ene 7-oxide
N430	230	(Z)-7-methyl-1,12-dioxo-1-phenyl-12-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,11-trioxa-5,6,7-triazadodec-5-ene 6-oxide
N431	231	(Z)-6,13-dimethyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,9,11-trioxa-6,7,8-triazatetradec-7-ene 7-oxide
N432	232	(Z)-6,13,13-trimethyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,9,11-trioxa-6,7,8-triazatetradec-7-ene 7-oxide
N433	233	(Z)-6-methyl-1,12-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,9,11-trioxa-6,7,8-triazatetradec-7-ene 7-oxide
N434	234	(Z)-7,11-dimethyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12-trioxa-7,8,9-triazatetradec-8-ene 8-oxide
N435	235	(Z)-3,7-dimethyl-1,13-dioxo-1-phenyl-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,12-trioxa-5,6,7-triazatridec-5-ene 6-oxide
N436	236	(Z)-7,11,14-trimethyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12-trioxa-7,8,9-triazapentadec-8-ene 8-oxide
N437	237	(Z)-7,11,14,14-tetramethyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12-trioxa-7,8,9-triazapentadec-8-ene 8-oxide
N438	238	(Z)-7,11-dimethyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12-trioxa-7,8,9-triazapentadec-8-ene 8-oxide
N439	239	(Z)-7-methyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12-trioxa-7,8,9-triazatetradec-8-ene 8-oxide
N440	240	(Z)-7-methyl-1,13-dioxo-1-phenyl-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,12-trioxa-5,6,7-triazatridec-5-ene 6-oxide
N441	241	(Z)-7,14-dimethyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12-trioxa-7,8,9-triazapentadec-8-ene 8-oxide
N442	242	(Z)-7,14,14-trimethyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12-trioxa-7,8,9-triazapentadec-8-ene 8-oxide
N443	243	(Z)-7-methyl-1,13-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,10,12-trioxa-7,8,9-triazapentadec-8-ene 8-oxide
N444	244	(Z)-8,12-dimethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13-trioxa-8,9,10-triazapentadec-9-ene 9-oxide
N445	245	(Z)-3,7-dimethyl-1,14-dioxo-1-phenyl-14-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,13-trioxa-5,6,7-triazatetradec-5-ene 6-oxide
N446	246	(Z)-8,12,15-trimethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13-trioxa-8,9,10-triazahexadec-9-ene 9-oxide
N447	247	(Z)-8,12,15,15-tetramethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13-trioxa-8,9,10-triazahexadec-9-ene 9-oxide
N448	248	(Z)-8,15-dimethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13-trioxa-8,9,10-triazahexadec-9-ene 9-oxide
N449	249	(Z)-8,15,15-trimethyl-1,14-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,11,13-trioxa-8,9,10-triazahexadec-9-ene 9-oxide

N450	250	(Z)-9,13-dimethyl-1,15-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,12,14-trioxa-9,10,11-triazahexadec-10-ene 10-oxide
N451	251	(Z)-3,7-dimethyl-1,15-dioxo-1-phenyl-15-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,14-trioxa-5,6,7-triazapentadec-5-ene 6-oxide
N452	252	(Z)-9,13,16-trimethyl-1,15-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,12,14-trioxa-9,10,11-triazaheptadec-10-ene 10-oxide
N453	253	(Z)-9,13,16,16-tetramethyl-1,15-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,12,14-trioxa-9,10,11-triazaheptadec-10-ene 10-oxide
N454	254	(Z)-9,16-dimethyl-1,15-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,12,14-trioxa-9,10,11-triazaheptadec-10-ene 10-oxide
N455	255	(Z)-9,16,16-trimethyl-1,15-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,12,14-trioxa-9,10,11-triazaheptadec-10-ene 10-oxide
N456	256	(Z)-2-(1-acetoxyethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N457	257	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N458	258	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N459	259	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N460	260	(Z)-2-(1-(propionyloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N461	261	(Z)-2-(acetoxymethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N462	262	(Z)-2-((benzoyloxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N463	263	(Z)-2-((isobutyryloxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N464	264	(Z)-2-((pivaloyloxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N465	265	(Z)-2-((propionyloxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)azetidin-1-yl)diazene oxide
N466	266	(Z)-2-(1-acetoxyethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N467	267	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N468	268	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N469	269	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide

N470	270	(Z)-2-(1-(propionyloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N471	271	(Z)-2-(acetoxymethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N472	272	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N473	273	(Z)-2-((isobutyryloxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N474	274	(Z)-2-((pivaloyloxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N475	275	(Z)-2-((propionyloxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N476	276	(Z)-5-(2-hydroxyethyl)-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N477	277	(Z)-7-(2-hydroxyethyl)-3-methyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N478	278	(Z)-5-(2-hydroxyethyl)-9,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N479	279	(Z)-5-(2-hydroxyethyl)-9,12,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N480	280	(Z)-5-(2-hydroxyethyl)-9-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N481	281	(Z)-5-(2-hydroxyethyl)-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N482	282	(Z)-7-(2-hydroxyethyl)-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N483	283	(Z)-5-(2-hydroxyethyl)-12-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N484	284	(Z)-5-(2-hydroxyethyl)-12,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N485	285	(Z)-2-(1-acetoxyethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N486	286	(Z)-2-(1-(benzoyloxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide

N487	287	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N488	288	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N489	289	(Z)-2-(1-(propionyloxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N490	290	(S,Z)-2-(acetoxymethoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N491	291	(S,Z)-2-((benzoyloxy)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N492	292	(S,Z)-2-((isobutyryloxy)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N493	293	(S,Z)-2-((pivaloyloxy)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N494	294	(S,Z)-2-((propionyloxy)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N495	295	(4S,Z)-4-((R)-sec-butyl)-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N496	296	(8S,Z)-8-((R)-sec-butyl)-3,7-dimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N497	297	(4S,Z)-4-((R)-sec-butyl)-5,9,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N498	298	(4S,Z)-4-((R)-sec-butyl)-5,9,12,12-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N499	299	(S,Z)-4-((R)-sec-butyl)-5,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N500	300	(S,Z)-4-((R)-sec-butyl)-5,12,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N501	301	(4S,Z)-4-isobutyl-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N502	302	(8S,Z)-8-isobutyl-3,7-dimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N503	303	(4S,Z)-4-isobutyl-5,9,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-

		triazatridec-6-ene 6-oxide
N504	304	(4S,Z)-4-isobutyl-5,9,12,12-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N505	305	(S,Z)-4-isobutyl-5,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N506	306	(S,Z)-4-isobutyl-5,12,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N507	307	(4S,Z)-4-benzyl-5,9-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide
N508	308	(8S,Z)-8-benzyl-3,7-dimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide
N509	309	(4S,Z)-4-benzyl-5,9,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N510	310	(4S,Z)-4-benzyl-5,9,12,12-tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N511	311	(S,Z)-4-benzyl-5,12-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N512	312	(S,Z)-4-benzyl-5,12,12-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide
N513	313	(Z)-2-(1-acetoxyethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N514	314	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N515	315	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N516	316	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N517	317	(Z)-2-((isobutyryloxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N518	318	(Z)-2-((pivaloyloxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N519	319	(Z)-2-(1-acetoxyethoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N520	320	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N521	321	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N522	322	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N523	323	(Z)-2-((benzoyloxy)methoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide

N524	324	(Z)-2-((isobutyryloxy)methoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N525	325	(Z)-2-((pivaloyloxy)methoxy)-1-(4-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)piperidin-1-yl)diazene oxide
N526	326	(Z)-2-(1-acetoxyethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N527	327	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N528	328	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N529	329	(Z)-2-((pivaloyloxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N530	330	(Z)-2-((isobutyryloxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N531	331	(Z)-2-((pivaloyloxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N532	332	(Z)-2-(1-acetoxyethoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N533	333	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N534	334	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N535	335	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N536	336	(Z)-2-(1-(propionyloxy)ethoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N537	337	(Z)-2-((isobutyryloxy)methoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N538	338	(Z)-2-((pivaloyloxy)methoxy)-1-(4-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)piperidin-1-yl)diazene oxide
N539	339	(Z)-2-(1-acetoxyethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
N540	340	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
N541	341	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
N542	342	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-

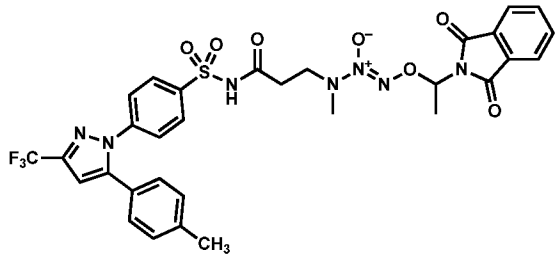
		pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
N543	343	(Z)-2-((isobutyryloxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
N544	344	(Z)-2-((pivaloyloxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
N545	345	(Z)-2-((propionyloxy)methoxy)-1-(3-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)pyrrolidin-1-yl)diazene oxide
N546	346	(Z)-2-(1-acetoxyethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N547	347	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N548	348	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N549	349	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N550	350	(Z)-2-((pivaloyloxy)methoxy)-1-(3-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N550-A	350-A	(Z)-5-Methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatetradec-6-ene 6-oxide

AMIDE-LINKED CELECOXIB - DIIMIDE-CAPPED NONOATE

[00258] 4-(5-(p-Tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide sodium salt (C04)

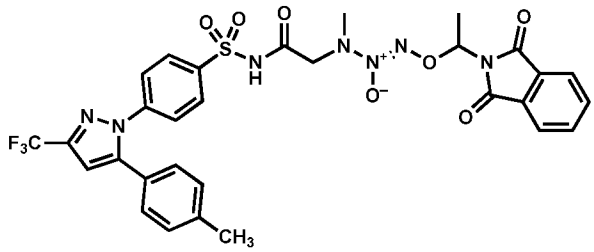
[00259] **C02** (5.0 g, 13.11 mmol) was dissolved in 120 mL ethanol, then 40 mL of water was added. Aqueous sodium hydroxide (0.49 M NaOH, 29.83 mL, 13.11 mmol) was added and stirred at room temperature for 5 minutes. The product was azeotroped with 25 mL acetonitrile and 25 mL ethanol. The resulting sodium salt of celecoxib (**2**) was dried under vacuum to yield a white solid (5.32 g, quantitative yield). Comparing starting material to product by thin layer chromatography confirmed the formation of the desired sodium salt.

[00260] (Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide (355)



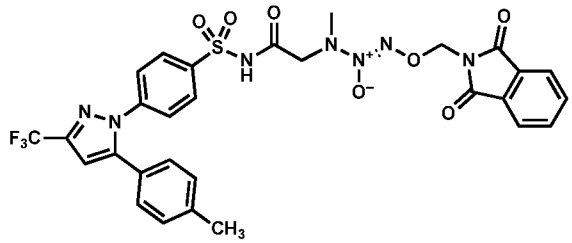
[00261] **C04** (0.182 g, 0.45 mmol) and **N080** (69 mg, 0.21 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **372** below (24 mg, 16% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.02 (m, 2H), 7.96-7.92 (m, 2H), 7.82-7.78 (m, 2H), 7.50-7.44 (m, 2H), 7.20-7.12 (m, 4H), 6.75 (s, 1H), 6.28 (q, J=6.6 Hz, 1H), 3.51-3.45 (m, 2H), 3.24-3.19 (m, 2H), 2.91 (s, 3H), 2.40 (s, 3H), 2.04 (d, J=6.6 Hz, 3H). LC t_r=4.85 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 722 (M+Na calcd for $C_{31}H_{28}F_3N_7O_7S$ requires 722), ES(neg)MS m/z 698 (M-H calcd for $C_{31}H_{28}F_3N_7O_7S$ requires 698).

[00262] **(Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide (371)**



[00263] **C04** (0.413 g, 1.02 mmol) and **N096** (0.150 g, 0.47 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **372** below (13 mg, 10% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.81 (m, 4H), 7.71-7.68 (m, 2H), 7.31-7.28 (m, 2H), 7.16-7.08 (m, 4H), 6.72 (s, 1H), 6.18 (q, J=6.6 Hz, 1H), 4.03-3.93 (m, 2H), 3.02 (s, 3H), 2.35 (s, 3H), 1.90 (d, J=5.6 Hz, 3H). LC t_r=4.82 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 708 (M+Na calcd for $C_{30}H_{26}F_3N_7O_7S$ requires 708), ES(neg)MS m/z 684 (M-H calcd for $C_{30}H_{26}F_3N_7O_7S$ requires 684).

[00264] **(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide (372)**



[00265] **N097** (0.150 g, 0.49 mmol) and benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (**PyBOP**) (306 mg, 0.59 mmol) were added to a suspension of **C04** (0.432 g, 1.07 mmol) in methylene chloride (1.5 mL). The resulting mixture was stirred at room temperature overnight. The methylene chloride was removed under reduced pressure and the residue was taken up in ethyl acetate. The organic layer was washed with water, brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was chromatographed to yield the product as a film (43.8 mg, 13% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.06 (m, 2H), 7.98-7.95 (m, 2H), 7.84-7.82 (m, 2H), 7.54-7.51 (m, 2H), 7.20-7.14 (m, 4H), 6.75 (s, 1H), 5.64 (s, 2H), 3.95 (s, 2H), 3.21 (s, 3H), 2.41 (s, 3H). LC t_r=4.66 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 694 (M+Na calcd for $C_{29}H_{24}F_3N_7O_7S$ requires 694), ES(neg)MS m/z 670 (M-H calcd for $C_{29}H_{24}F_3N_7O_7S$ requires 670).

[00266] **Table 11. Amide-Linked Celecoxib - Diimide-Capped NONOate.**

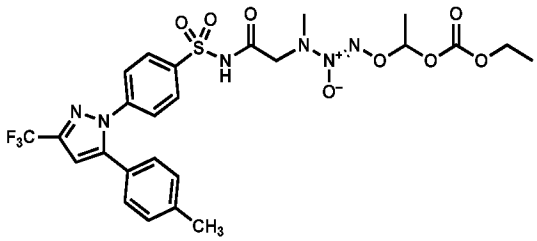
Starting NONOate	Compound #	Compound Name
N076	351	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N077	352	(S,Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N078	353	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N079	354	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N080	355	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide
N081	356	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide
N082	357	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)triaz-1-

		ene 2-oxide
N083	358	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)triaz-1-ene 2-oxide
N084	359	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)triaz-1-ene 2-oxide
N085	360	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)triaz-1-ene 2-oxide
N086	361	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)triaz-1-ene 2-oxide
N087	362	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)triaz-1-ene 2-oxide
N088	363	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N089	364	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N090	365	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N091	366	(S,Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N092	367	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N093	368	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N094	369	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N095	370	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N096	371	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N097	372	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N098	373	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((S)-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N099	374	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(1-oxo-1-(4-(5-(p-

		tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N100	375	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N101	376	(Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N102	377	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((S)-4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N103	378	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N104	379	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((S)-1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N105	380	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N106	381	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((S)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)triaz-1-ene 2-oxide
N107	382	(S,Z)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)triaz-1-ene 2-oxide
N108	383	(Z)-3-(tert-butyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N109	384	(Z)-3-(tert-butyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N110	385	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N111	386	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N112	387	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N113	388	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N114	389	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N115	390	(Z)-2-((1,3-dioxoisoindolin-2-yl)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide

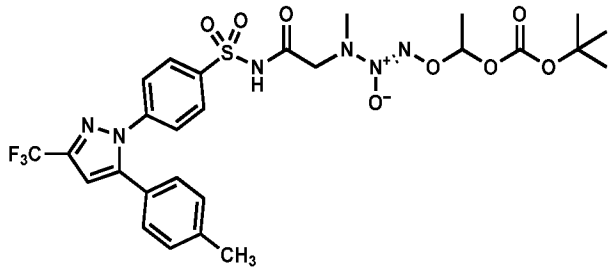
AMIDE-LINKED CELECOXIB - CARBONATE-CAPPED NONOATE

[00267] **(Z)-3,7-Dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (407)**



[00268] **C02** (126 mg, 0.33 mmol) and **N207** (108 mg, 0.41 mmol) were dissolved in 2.5 mL methylene chloride. Dicyclohexylcarbodiimide (85 mg, 0.41 mmol) and 4-dimethylamino pyridine (10 mg, 0.08 mmol) were added and stirred at room temperature overnight. The reaction underwent only partial conversion to product. The reaction mixture was evaporated and dissolved in ethyl acetate. The organic layer was washed with sat. potassium hydrogensulfate solution and brine, dried over magnesium sulfate and evaporated. The product was chromatographed using 35% ethyl acetate/hexanes to obtain a colorless oil (15 mg, 7% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-8.02 (m, 2H), 7.48-7.46 (m, 2H), 7.20-7.11 (m, 4H), 6.75 (s, 1H), 6.40 (dq, J=41.5, 5.6 Hz, 1H), 4.29-4.19 (m, 2H), 4.04 (d, J=6.3 Hz, 2H), 3.18 (d, J=2.8 Hz, 3H), 2.86 (d, J=4.9 Hz, 1H), 2.39 (s, 3H), 1.62 (dd, J=29.5, 5.6 Hz, 3H), 1.32 (tt, J=13.9, 7.2 Hz, 3H). LC t_r=4.84 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(neg)MS m/z 627 (M-H calcd for $C_{25}H_{27}F_3N_6O_8S$ requires 627).

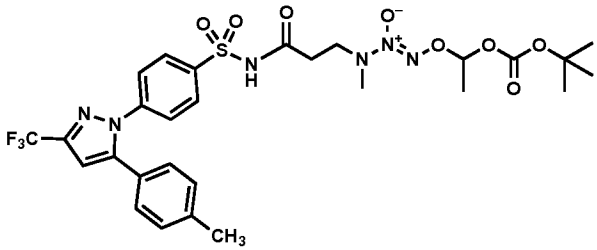
[00269] **(Z)-3,7,11,11-Tetramethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (408)**



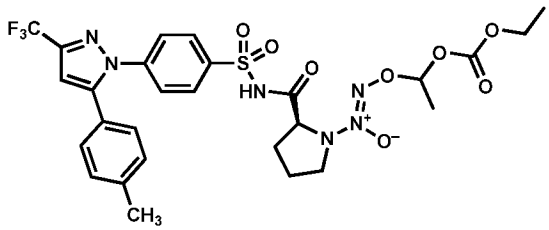
[00270] **C03** (200 mg, 0.38 mmol) was suspended in 4 mL acetonitrile. **N208** (111 mg, 0.38 mmol) was added and the reaction was stirred at 50 °C overnight. The reaction was

evaporated and dissolved in ethyl acetate. The organic layer was washed with potassium hydrogensulfate solution and brine, dried over magnesium sulfate, then evaporated. The product was chromatographed using 35% ethyl acetate/hexanes to yield a film (19 mg, 8% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.03 (m, 2H), 7.50-7.47 (m, 2H), 7.21-7.12 (m, 4H), 6.75 (s, 1H), 6.34 (q, J=5.6 Hz, 1H), 4.00-3.98 (m, 2H), 3.17 (s, 3H), 2.40 (s, 3H), 1.58 (d, J=5.6 Hz, 3H), 1.51 (s, 9H). LC t_r=5.04 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 679 (M+Na calcd for $C_{27}H_{31}F_3N_6O_8S$ requires 679), ES(neg)MS m/z 655 (M-H calcd for $C_{27}H_{31}F_3N_6O_8S$ requires 655).

[00271] (Z)-2,2,6,10-Tetramethyl-4,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide (414)



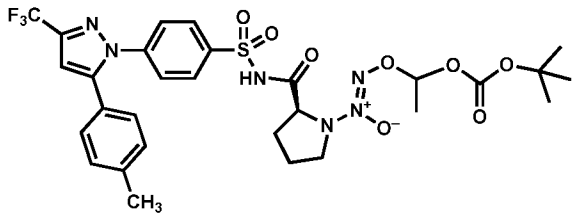
[00272] (Z)-2-(1-((Ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide (430)



[00273] **C02** (100 mg, 0.26 mmol) and **N230** (96.1 mg, 0.33 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **407**, step 3: (97 mg, 57% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.01 (m, 2H), 7.48-7.45 (m, 2H), 7.18-7.08 (m, 4H), 6.72 (s, 1H), 6.38 (dq, J=11.2, 5.6 Hz, 1H), 4.39 (ddd, J=25.1, 9.6, 2.9 Hz, 1H), 4.22 (qt, J=7.1, 2.1 Hz, 2H), 3.73-3.45 (m, 2H), 2.37 (s, 3H), 2.34-2.27 (m, 1H), 2.12-1.88 (m, 4H), 1.61 (dd, J=5.4, 5.0 Hz, 3H), 1.31 (dt, J=3.0, 7.2 Hz, 3H). LC t_r=4.90 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS

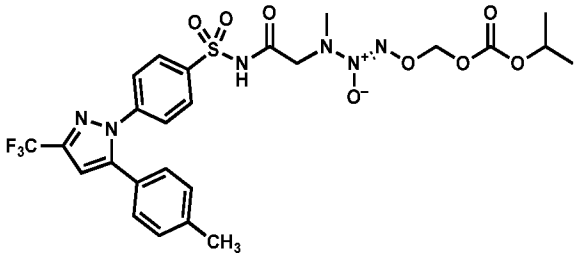
m/z 677 (M+Na calcd for $C_{27}H_{29}F_3N_6O_8S$ requires 677), ES(neg)MS m/z 653 (M-H calcd for $C_{27}H_{29}F_3N_6O_8S$ requires 653).

[00274] (Z)-2-(1-((tert-Butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide (432)



[00275] **C04** (167 mg, 0.41 mmol) and **N232** (60 mg, 0.19 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **372** (29 mg, 22% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10-8.06 (m, 2H), 7.53-7.50 (m, 2H), 7.21-7.12 (m, 4H), 6.76 (s, 1H), 6.43-6.36 (m, 1H), 4.48-4.38 (m, 1H), 3.76-3.51 (m, 2H), 2.41 (s, 3H), 2.16-1.90 (m, 4H), 1.69 (dd, J=5.6, 4.4 Hz, 3H), 1.52 (d, J=2.9 Hz, 9H). LC t_r=5.11 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 705 (M+Na calcd for $C_{29}H_{33}F_3N_6O_8S$ requires 705), ES(neg)MS m/z 681 (M-H calcd for $C_{29}H_{33}F_3N_6O_8S$ requires 681).

[00276] (Z)-3,11-Dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide (503)



[00277] **C02** (100 mg, 0.26 mmol) and **N303** (88 mg, 0.33 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **407**, step 3: (23 mg, 14% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.52-7.50 (m, 2H), 7.21-7.12 (m, 4H), 6.75 (s, 1H), 5.71 (s, 2H), 4.95-4.91 (m, 1H), 4.04 (s, 2H), 3.22 (s, 3H), 2.40 (s, 3H), 1.32 (d, J=6.2 Hz, 6H). LC t_r=4.91 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 651 (M+Na calcd for

$C_{25}H_{27}F_3N_6O_8S$ requires 651), ES(neg)MS m/z 627 (M-H calcd for $C_{25}H_{27}F_3N_6O_8S$ requires 627).

[00278] Table 12. Amide-Linked Celecoxib - Carbonate-Capped NONOate.

Starting NONOate	Compound #	Compound Name
N191	391	(2S,Z)-2,3,7-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N192	392	(2S,Z)-2,3,7,11-tetramethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N193	393	(2S,Z)-2,3,7,11,11-pentamethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N194	394	(S,Z)-2,3,11-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N195	395	(S,Z)-2,3,11,11-tetramethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N196	396	(11S,Z)-6,10,12-trimethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N197	397	(11S,Z)-2,6,10,12-tetramethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N198	398	(11S,12R,Z)-2,2,6,10,12-pentamethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N199	399	(S,Z)-2,10,12-trimethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N200	400	(S,Z)-2,2,10,12-tetramethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N201	401	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N202	402	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N203	403	(Z)-3-ethyl-7-methyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N204	404	(Z)-3-ethyl-7,11,11-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N205	405	(Z)-3-isopropyl-7-methyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N206	406	(Z)-3-isopropyl-7,11,11-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N207	407	(Z)-3,7-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-

		yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N208	408	(Z)-3,7,11,11-tetramethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N209	409	(Z)-3-(tert-butyl)-7-methyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N210	410	(11S,Z)-2,2,6,10,13-pentamethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N211	411	(Z)-2,2,3,7-tetramethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N212	412	(Z)-2,2,3,7,11,11-hexamethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N213	413	(Z)-6,10-dimethyl-4,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N214	414	(Z)-2,2,6,10-tetramethyl-4,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N215	415	(Z)-6,10-dimethyl-4,14-dioxo-14-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N216	416	(Z)-2,6,10-trimethyl-4,14-dioxo-14-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N217	417	(Z)-2,2,6,10-tetramethyl-4,14-dioxo-14-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N218	418	(Z)-6,10-dimethyl-4,15-dioxo-15-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N219	419	(Z)-2,6,10-trimethyl-4,15-dioxo-15-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N220	420	(Z)-2,2,6,10-tetramethyl-4,15-dioxo-15-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N221	421	(Z)-2,10-dimethyl-4,15-dioxo-15-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N222	422	(Z)-2,2,10-trimethyl-4,15-dioxo-15-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N223	423	(Z)-6,10-dimethyl-4,16-dioxo-16-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazahexadec-8-ene 9-oxide
N224	424	(Z)-2,2,6,10-tetramethyl-4,16-dioxo-16-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazahexadec-8-ene 9-oxide
N225	425	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide

N226	426	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N227	427	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N228	428	(Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N229	429	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N230	430	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N231	431	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N232	432	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N233	433	(S,Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N234	434	(S,Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N235	435	(11S,12R,Z)-6,10,12-trimethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N236	436	(11S,12R,Z)-2,10,12-trimethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N237	437	(11S,Z)-6,10,13-trimethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N238	438	(S,Z)-2,10,13-trimethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N239	439	(2S,Z)-2-benzyl-3,7-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N240	440	(S,Z)-2-benzyl-3,11-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N241	441	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N242	442	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-

		yl)diazene oxide
N243	443	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N244	444	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N245	445	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N246	446	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N247	447	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N248	448	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N249	449	(Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N250	450	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N251	451	(Z)-2-(1-((methoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N252	452	(S,Z)-2-(((ethoxycarbonyl)oxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N253	453	(S,Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N254	454	(S,Z)-2-(((methoxycarbonyl)oxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N255	455	(S,Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N256	456	(Z)-2,2,3,7,11-pentamethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N257	457	(Z)-5,9,10,10-tetramethyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N258	458	(Z)-2,2,3-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N259	459	(Z)-2,2,3,11-tetramethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N260	460	(Z)-9,10,10-trimethyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-

		pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N261	461	(Z)-2,2,3,11,11-pentamethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N262	462	(Z)-2,6,10-trimethyl-4,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N263	463	(Z)-5,9-dimethyl-3,12-dioxo-12-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazadodec-7-ene 8-oxide
N264	464	(Z)-10-methyl-4,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N265	465	(Z)-2,10-dimethyl-4,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N266	466	(Z)-9-methyl-3,12-dioxo-12-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazadodec-7-ene 8-oxide
N267	467	(Z)-2,2,10-trimethyl-4,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N268	468	(Z)-5,9-dimethyl-3,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
N269	469	(Z)-10-methyl-4,14-dioxo-14-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N270	470	(Z)-2,10-dimethyl-4,14-dioxo-14-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N271	471	(Z)-9-methyl-3,13-dioxo-13-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
N272	472	(Z)-2,2,10-trimethyl-4,14-dioxo-14-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N273	473	(Z)-5,9-dimethyl-3,14-dioxo-14-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazatetradec-7-ene 8-oxide
N274	474	(Z)-10-methyl-4,15-dioxo-15-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazapentadec-8-ene 9-oxide
N275	475	(Z)-9-methyl-3,14-dioxo-14-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazatetradec-7-ene 8-oxide
N276	476	(Z)-2,6,10-trimethyl-4,16-dioxo-16-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazahexadec-8-ene 9-oxide
N277	477	(Z)-5,9-dimethyl-3,15-dioxo-15-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazapentadec-7-ene 8-oxide
N278	478	(Z)-10-methyl-4,16-dioxo-16-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazahexadec-8-ene 9-oxide
N279	479	(Z)-2,10-dimethyl-4,16-dioxo-16-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazahexadec-8-ene 9-oxide
N280	480	(Z)-9-methyl-3,15-dioxo-15-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazapentadec-7-ene 8-oxide
N281	481	(Z)-2,2,10-trimethyl-4,16-dioxo-16-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7-trioxa-8,9,10-triazahexadec-8-ene 9-oxide
N282	482	(Z)-2-(1-((methoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-

		(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N283	483	(Z)-2-(((ethoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N284	484	(Z)-2-(((methoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N285	485	(Z)-2-(1-((methoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N286	486	(S,Z)-2-(((ethoxycarbonyl)oxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N287	487	(S,Z)-2-(((methoxycarbonyl)oxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N288	488	(Z)-3-ethyl-7,11-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N289	489	(Z)-9-ethyl-5-methyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N290	490	(Z)-3-ethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N291	491	(Z)-3-ethyl-11-methyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N292	492	(Z)-9-ethyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N293	493	(Z)-3-ethyl-11,11-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N294	494	(Z)-3-isopropyl-7,11-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N295	495	(Z)-9-isopropyl-5-methyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N296	496	(Z)-3-isopropyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N297	497	(Z)-3-isopropyl-11-methyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N298	498	(Z)-9-isopropyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N299	499	(Z)-3-isopropyl-11,11-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N300	500	(Z)-3,7,11-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N301	501	(Z)-5,9-dimethyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N302	502	(Z)-3-methyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide

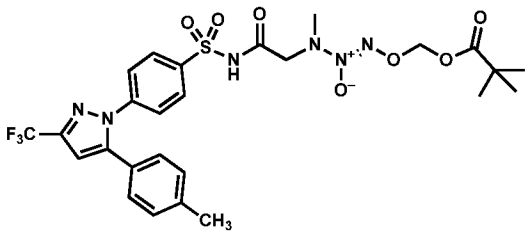
N303	503	(Z)-3,11-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N304	504	(Z)-9-methyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N305	505	(Z)-3,11,11-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N306	506	(10S,Z)-5,9,10-trimethyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N307	507	(S,Z)-2,3-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N308	508	(S,Z)-9,10-dimethyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N309	509	(11S,12R,Z)-2,6,10,12-tetramethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N310	510	(10S,11R,Z)-5,9,11-trimethyl-3-oxo-10-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
N311	511	(11S,12R,Z)-10,12-dimethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N312	512	(10S,11R,Z)-9,11-dimethyl-3-oxo-10-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
N313	513	(11S,12R,Z)-2,2,10,12-tetramethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N314	514	(11S,Z)-2,6,10,13-tetramethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N315	515	(10S,Z)-5,9,12-trimethyl-3-oxo-10-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
N316	516	(S,Z)-10,13-dimethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N317	517	(S,Z)-9,12-dimethyl-3-oxo-10-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-2,4,6-trioxa-7,8,9-triazatridec-7-ene 8-oxide
N318	518	(S,Z)-2,2,10,13-tetramethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatetradec-8-ene 9-oxide
N319	519	(2S,Z)-2-benzyl-3,7,11-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N320	520	(10S,Z)-10-benzyl-5,9-dimethyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N321	521	(2S,Z)-2-benzyl-3,7,11,11-tetramethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide

N322	522	(S,Z)-2-benzyl-3-methyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N323	523	(S,Z)-10-benzyl-9-methyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N324	524	(S,Z)-2-benzyl-3,11,11-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N325	525	(10S,Z)-5,9,11-trimethyl-3-oxo-10-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-2,4,6-trioxa-7,8,9-triazadodec-7-ene 8-oxide
N326	526	(11S,Z)-2,2,6,10,12-pentamethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N327	527	(S,Z)-10,12-dimethyl-4-oxo-11-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-3,5,7-trioxa-8,9,10-triazatridec-8-ene 9-oxide
N328	528	(S,Z)-9,11-dimethyl-3-oxo-10-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)-2,4,6-trioxa-7,8,9-triazadodec-7-ene 8-oxide
N329	529	(Z)-3-(tert-butyl)-7,11-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N330	530	(Z)-9-(tert-butyl)-5-methyl-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N331	531	(Z)-3-(tert-butyl)-7,11,11-trimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N332	532	(Z)-3-(tert-butyl)-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N333	533	(Z)-3-(tert-butyl)-11-methyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N334	534	(Z)-9-(tert-butyl)-3,11-dioxo-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,6-trioxa-7,8,9-triazaundec-7-ene 8-oxide
N335	535	(Z)-3-(tert-butyl)-11,11-dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide
N336	536	(Z)-2-(1-((methoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N337	537	(Z)-2-(((ethoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N338	538	(Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N339	539	(Z)-2-(((methoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide

N340	540	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N341	541	(Z)-2-(1-((methoxycarbonyl)oxy)ethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N342	542	(Z)-2-(((ethoxycarbonyl)oxy)methoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N343	543	(Z)-2-(((isopropoxycarbonyl)oxy)methoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N344	544	(Z)-2-(((methoxycarbonyl)oxy)methoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N345	545	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N346	546	(Z)-2-(1-((methoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N347	547	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N348	548	(Z)-2-(((ethoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N349	549	(Z)-2-(((methoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N350	550	(Z)-2-(((tert-butoxycarbonyl)oxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide

AMIDE-LINKED CELECOXIB - ESTER-CAPPED NONOATE

[00279] (Z)-3-Methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide (602)



[00280] **C04** (307 mg, 0.76 mmol) and **N602** (91 mg, 0.35 mmol) were converted to the title compound by a procedure similar to that described in the synthesis of **372** to afford desired

product (40 mg, 18% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.51-7.49 (m, 2H), 7.21-7.19 (m, 2H), 7.14-7.12 (m, 2H), 6.75 (s, 1H), 5.73 (s, 2H), 4.00 (s, 2H), 3.19 (s, 3H), 2.40 (s, 3H), 1.23 (s, 9H). LC t_r=4.95 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 626 (M+H calcd for $C_{26}H_{29}F_3N_6O_7S$ requires 627).

[00281] Table 13. Amide-Linked Celecoxib - Ester-Capped NONOate.

Starting NONOate	Compound #	Compound Name
N551	551	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-((S)-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N552	552	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-((S)-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N553	553	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-((S)-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N554	554	(Z)-3-methyl-3-((S)-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N555	555	(Z)-3-methyl-3-((S)-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N556	556	(S,Z)-1-(acetoxymethoxy)-3-methyl-3-(1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N557	557	(S,Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N558	558	(S,Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N559	559	(S,Z)-3-methyl-3-(1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N560	560	(S,Z)-3-methyl-3-(1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N561	561	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-((S)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)triaz-1-ene 2-oxide
N562	562	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-((S)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)triaz-1-ene 2-oxide
N563	563	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-((S)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-

		yl)triaz-1-ene 2-oxide
N564	564	(Z)-3-methyl-3-((S)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N565	565	(Z)-3-methyl-3-((S)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N566	566	(S,Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)triaz-1-ene 2-oxide
N567	567	(S,Z)-3-methyl-3-(3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N568	568	(Z)-2-(1-acetoxyethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N569	569	(Z)-2-(1-(benzoyloxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N570	570	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N571	571	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N572	572	(Z)-2-(1-(propionyloxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N573	573	(S,Z)-2-((pivaloyloxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N574	574	(Z)-1-(1-acetoxyethoxy)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N575	575	(Z)-1-(1-(benzoyloxy)ethoxy)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N576	576	(Z)-3-ethyl-1-(1-(isobutyryloxy)ethoxy)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N577	577	(Z)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N578	578	(Z)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N579	579	(Z)-1-(acetoxymethoxy)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N580	580	(Z)-1-((benzoyloxy)methoxy)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N581	581	(Z)-3-ethyl-1-((isobutyryloxy)methoxy)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N582	582	(Z)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N583	583	(Z)-3-ethyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-

		yl)phenylsulfonamido)ethyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N584	584	(Z)-1-(1-acetoxyethoxy)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N585	585	(Z)-1-(1-(benzoyloxy)ethoxy)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N586	586	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N587	587	(Z)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N588	588	(Z)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N589	589	(Z)-1-(acetoxymethoxy)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N590	590	(Z)-1-((benzoyloxy)methoxy)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N591	591	(Z)-1-((isobutyryloxy)methoxy)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N592	592	(Z)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N593	593	(Z)-3-isopropyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N594	594	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N595	595	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N596	596	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N597	597	(Z)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N598	598	(Z)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N599	599	(Z)-1-(acetoxymethoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N600	600	(Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N601	601	(Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N602	602	(Z)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-

		yl)phenylsulfonamido)ethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N603	603	(Z)-3-methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N604	604	(Z)-1-(1-acetoxyethoxy)-3-(tert-butyl)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N605	605	(Z)-1-(1-(benzoyloxy)ethoxy)-3-(tert-butyl)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N606	606	(Z)-3-(tert-butyl)-1-(1-(isobutyryloxy)ethoxy)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N607	607	(Z)-3-(tert-butyl)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N608	608	(Z)-3-(tert-butyl)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N609	609	(Z)-1-(acetoxymethoxy)-3-(tert-butyl)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N610	610	(Z)-1-((benzoyloxy)methoxy)-3-(tert-butyl)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N611	611	(Z)-3-(tert-butyl)-1-((isobutyryloxy)methoxy)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)triaz-1-ene 2-oxide
N612	612	(Z)-3-(tert-butyl)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N613	613	(Z)-3-(tert-butyl)-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N614	614	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N615	615	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N616	616	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N617	617	(Z)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N618	618	(Z)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N619	619	(Z)-1-(acetoxymethoxy)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N620	620	(Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide

N621	621	(Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N622	622	(Z)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N623	623	(Z)-3-methyl-3-(2-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N624	624	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide
N625	625	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide
N626	626	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide
N627	627	(Z)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N628	628	(Z)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N629	629	(Z)-1-(acetoxymethoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide
N630	630	(Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide
N631	631	(Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide
N632	632	(Z)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N633	633	(Z)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N634	634	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)triaz-1-ene 2-oxide
N635	635	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)triaz-1-ene 2-oxide
N636	636	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)triaz-1-ene 2-oxide
N637	637	(Z)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N638	638	(Z)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N639	639	(Z)-1-(acetoxymethoxy)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)triaz-1-ene 2-

		oxide
N640	640	(Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)triaz-1-ene 2-oxide
N641	641	(Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)triaz-1-ene 2-oxide
N642	642	(Z)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N643	643	(Z)-3-methyl-3-(4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N644	644	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)triaz-1-ene 2-oxide
N645	645	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)triaz-1-ene 2-oxide
N646	646	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)triaz-1-ene 2-oxide
N647	647	(Z)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N648	648	(Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)triaz-1-ene 2-oxide
N649	649	(Z)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N650	650	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)triaz-1-ene 2-oxide
N651	651	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)triaz-1-ene 2-oxide
N652	652	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)triaz-1-ene 2-oxide
N653	653	(Z)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N654	654	(Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)triaz-1-ene 2-oxide
N655	655	(Z)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N656	656	(Z)-2-(1-acetoxyethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N657	657	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N658	658	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N659	659	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-

		pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N660	660	(Z)-2-(1-(propionyloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N661	661	(Z)-2-(acetoxymethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N662	662	(Z)-2-((benzoyloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N663	663	(Z)-2-((isobutyryloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N664	664	(Z)-2-((pivaloyloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N665	665	(Z)-2-((propionyloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N666	666	(Z)-2-(1-acetoxyethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N667	667	(Z)-2-(1-(benzoyloxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N668	668	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N669	669	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N670	670	(Z)-2-(1-(propionyloxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N671	671	(S,Z)-2-(acetoxymethoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N672	672	(S,Z)-2-((benzoyloxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N673	673	(S,Z)-2-((isobutyryloxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N674	674	(S,Z)-2-((pivaloyloxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N675	675	(S,Z)-2-((propionyloxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N676	676	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N677	677	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N678	678	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N679	679	(Z)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N680	680	(Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N681	681	(Z)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)-1-

		((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N682	682	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-((S)-4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N683	683	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-((S)-4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N684	684	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-((S)-4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N685	685	(Z)-3-methyl-3-((S)-4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N686	686	(S,Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N687	687	(S,Z)-3-methyl-3-(4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N688	688	(Z)-1-(1-acetoxyethoxy)-3-methyl-3-((S)-1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N689	689	(Z)-1-(1-(benzoyloxy)ethoxy)-3-methyl-3-((S)-1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N690	690	(Z)-1-(1-(isobutyryloxy)ethoxy)-3-methyl-3-((S)-1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N691	691	(Z)-3-methyl-3-((S)-1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-(1-(pivaloyloxy)ethoxy)triaz-1-ene 2-oxide
N692	692	(S,Z)-1-((isobutyryloxy)methoxy)-3-methyl-3-(1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N693	693	(S,Z)-3-methyl-3-(1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide
N694	694	(Z)-2-(1-acetoxyethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N695	695	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N696	696	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N697	697	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N698	698	(Z)-2-((isobutyryloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N699	699	(Z)-2-((pivaloyloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N700	700	(Z)-2-(1-acetoxyethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-

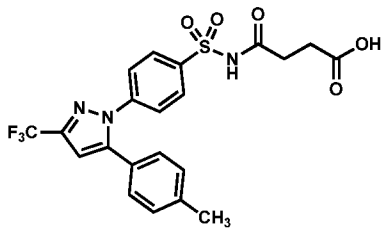
		pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N701	701	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N702	702	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N703	703	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N704	704	(Z)-2-(1-(propionyloxy)ethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N705	705	(Z)-2-((isobutyryloxy)methoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N706	706	(Z)-2-((pivaloyloxy)methoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N707	707	(Z)-2-(1-acetoxyethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N708	708	(Z)-2-(1-(benzoyloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N709	709	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N710	710	(Z)-2-(1-(pivaloyloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N711	711	(Z)-2-((propionyloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N712	712	(S,Z)-2-(acetoxymethoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N713	713	(S,Z)-2-((benzoyloxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N714	714	(S,Z)-2-((isobutyryloxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N715	715	(S,Z)-2-((propionyloxy)methoxy)-1-(2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)azetidin-1-yl)diazene oxide
N716	716	(Z)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N717	717	(Z)-1-(acetoxymethoxy)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)triaz-1-ene 2-oxide
N718	718	(Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)triaz-1-ene 2-oxide
N719	719	(Z)-3-methyl-3-(5-oxo-5-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N720	720	(Z)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N721	721	(Z)-1-(acetoxymethoxy)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)triaz-1-ene 2-oxide
N722	722	(Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)hexyl)triaz-1-ene 2-oxide
N723	723	(Z)-3-methyl-3-(6-oxo-6-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-

		yl)phenylsulfonamido)hexyl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N724	724	(Z)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N725	725	(Z)-1-(acetoxymethoxy)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N726	726	(Z)-1-((benzoyloxy)methoxy)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N727	727	(Z)-3-methyl-3-((2S,3R)-3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N728	728	(Z)-3-methyl-3-((S)-4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N729	729	(S,Z)-1-(acetoxymethoxy)-3-methyl-3-(4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N730	730	(S,Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)triaz-1-ene 2-oxide
N731	731	(S,Z)-3-methyl-3-(4-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)pentan-2-yl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N732	732	(Z)-3-methyl-3-((S)-1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-(1-(propionyloxy)ethoxy)triaz-1-ene 2-oxide
N733	733	(S,Z)-1-(acetoxymethoxy)-3-methyl-3-(1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N734	734	(S,Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)triaz-1-ene 2-oxide
N735	735	(S,Z)-3-methyl-3-(1-oxo-3-phenyl-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propan-2-yl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N736	736	(S,Z)-1-(acetoxymethoxy)-3-methyl-3-(3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)triaz-1-ene 2-oxide
N737	737	(S,Z)-1-((benzoyloxy)methoxy)-3-methyl-3-(3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)triaz-1-ene 2-oxide
N738	738	(S,Z)-3-methyl-3-(3-methyl-1-oxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butan-2-yl)-1-((propionyloxy)methoxy)triaz-1-ene 2-oxide
N739	739	(Z)-2-(1-(propionyloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N740	740	(Z)-2-(acetoxymethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide

N741	741	(Z)-2-((benzoyloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N742	742	(Z)-2-((propionyloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N743	743	(Z)-2-(acetoxymethoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N744	744	(Z)-2-((benzoyloxy)methoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N745	745	(Z)-2-((propionyloxy)methoxy)-1-(4-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)piperidin-1-yl)diazene oxide
N746	746	(Z)-2-(1-(propionyloxy)ethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N747	747	(Z)-2-(acetoxymethoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N748	748	(Z)-2-((benzoyloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N749	749	(Z)-2-((isobutyryloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide
N750	750	(Z)-2-((pivaloyloxy)methoxy)-1-(3-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide

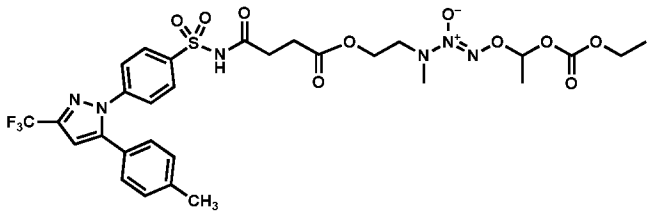
AMIDE-LINKED CELECOXIB - SUCCINAMIDE LINKER

[00282] (Z)-4-Oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoic acid (C05)



[00283] **C02** (250 mg, 0.66 mmol) was dissolved in 1 mL toluene. Succinic anhydride (329 mg, 3.28 mmol) and pyridine (80 ul, 0.99 mmol) were added and refluxed overnight. The rxn was washed with NH_4Cl solution, dried over magnesium sulfate and evaporated. The product was chromatographed using 50% ethyl acetate/hexanes to yield a colorless oil (100 mg, 31% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.93-7,89 (m, 2H), 7.48-7.42 (m, 2H), 7.20-7.07 (m, 4H), 6.79 (s, 1H), 2.73-2.68 (m, 2H), 2.58-2.52 (m, 2H), 2.39 (s, 3H). LC t_r=4.35 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(neg)MS m/z 480 (M-H calcd for $C_{21}H_{18}F_3N_3O_5S$ requires 480).

[00284] (Z)-6,10-Dimethyl-4,14,17-trioxo-17-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7,13-tetraoxa-8,9,10-triazaheptadec-8-ene 9-oxide (764)



[00285] **C05** (97 mg, 0.20 mmol) and **N132** (63 mg, 0.25 mmol) were dissolved in 2.5 ml methylene chloride. Dicyclohexylcarbodiimide (52 mg, 0.25 mmol) and 4-dimethylamino pyridine (10 mg, 0.08 mmol) were added and stirred at room temperature overnight. The reaction underwent only partial conversion to product. The reaction mixture was evaporated and dissolved in ethyl acetate. The organic layer was washed with saturated potassium hydrogen sulfate solution and brine, dried over magnesium sulfate and evaporated. The product was chromatographed using 35% ethyl acetate/hexanes to obtain a colorless oil (15.5 mg, 11% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.01 (m, 2H), 7.47-7.43 (m, 2H), 7.19-7.10 (m, 4H), 6.74 (s, 1H), 6.40 (q, J=5.6 Hz, 1H), 4.27-4.20 (m, 4H), 3.71-3.53 (m, 2H), 3.06 (s, 3H), 2.61-2.51 (m, 4H), 2.38 (s, 3H), 1.64 (d, J=5.6 Hz, 3H), 1.32 (t, J=7.1 Hz, 3H). LC t_r=4.85 minutes (C-18 column, 5 to 95% acetonitrile/water over 6 minutes at 1.7 mL/min with detection 254 nm, at 23° C). ES(pos)MS m/z 737 (M+Na calcd for $C_{29}H_{33}F_3N_6O_{10}S$ requires 737), ES(neg)MS m/z 713 (M-H calcd for $C_{29}H_{33}F_3N_6O_{10}S$ requires 713).

[00286] Table 14. Amide-Linked Celecoxib - Succinamide Linker.

Starting NONOate	Compound #	Compound Name
N001	751	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-((S)-1-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)propan-2-yl)triaz-1-ene 2-oxide
N003	752	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N004	753	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-ethyl-3-(2-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)ethyl)triaz-1-ene 2-oxide
N005	754	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-isopropyl-3-(2-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)ethyl)triaz-1-ene 2-oxide
N006	755	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-

		yl)phenylsulfonamido)butanoyl)oxy)ethyl)triaz-1-ene 2-oxide
N007	756	(Z)-3-(tert-butyl)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-(2-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)ethyl)triaz-1-ene 2-oxide
N008	757	(Z)-1-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-methyl-1-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)propan-2-yl)triaz-1-ene 2-oxide
N013	758	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)azetidin-1-yl)diazene oxide
N014	759	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-(3-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N016	760	(Z)-2-(1-(1,3-dioxoisoindolin-2-yl)ethoxy)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N116	761	(11S,Z)-6,10,11-trimethyl-4,14,17-trioxo-17-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7,13-tetraoxa-8,9,10-triazaheptadec-8-ene 9-oxide
N126	762	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N127	763	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N132	764	(Z)-6,10-dimethyl-4,14,17-trioxo-17-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7,13-tetraoxa-8,9,10-triazaheptadec-8-ene 9-oxide
N133	765	(Z)-2,2,6,10-tetramethyl-4,14,17-trioxo-17-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7,13-tetraoxa-8,9,10-triazaheptadec-8-ene 9-oxide
N134	766	(Z)-10-(tert-butyl)-6-methyl-4,14,17-trioxo-17-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7,13-tetraoxa-8,9,10-triazaheptadec-8-ene 9-oxide
N136	767	(Z)-6,10,11,11-tetramethyl-4,14,17-trioxo-17-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7,13-tetraoxa-8,9,10-triazaheptadec-8-ene 9-oxide
N150	768	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)azetidin-1-yl)diazene oxide
N151	769	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(3-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)azetidin-1-yl)diazene oxide
N152	770	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)azetidin-1-yl)diazene oxide
N155	771	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-(3-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N156	772	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-(3-(((4-oxo-4-(4-(5-(p-tolyl)-3-

		(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N157	773	(Z)-2-(1-((tert-butoxycarbonyl)oxy)ethoxy)-1-(3-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N164	774	(Z)-2-(1-((ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N165	775	(Z)-2-(1-((isopropoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N353	776	(10S,Z)-2,5,9,10-tetramethyl-3,13,16-trioxo-16-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-4,6,12-trioxa-7,8,9-triazahexadec-7-ene 8-oxide
N370	777	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)diazene oxide
N371	778	(Z)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N396	779	(Z)-2,5,9-trimethyl-3,13,16-trioxo-16-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-4,6,12-trioxa-7,8,9-triazahexadec-7-ene 8-oxide
N397	780	(Z)-2,2,5,9-tetramethyl-3,13,16-trioxo-16-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-4,6,12-trioxa-7,8,9-triazahexadec-7-ene 8-oxide
N458	781	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-(3-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)azetidin-1-yl)diazene oxide
N459	782	(Z)-1-(3-((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)azetidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N469	783	(Z)-1-(3-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)azetidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide
N487	784	(Z)-2-(1-(isobutyryloxy)ethoxy)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide
N488	785	(Z)-1-((S)-2-(((4-oxo-4-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)butanoyl)oxy)methyl)pyrrolidin-1-yl)-2-(1-(pivaloyloxy)ethoxy)diazene oxide

D. Definitions

[00287] The terms “substituent”, “radical”, “group”, “moiety” and “fragment” may be used interchangeably.

[00288] If a substituent is described as being “optionally substituted,” the substituent may be either (1) not substituted or (2) substituted on a substitutable position. If a substitutable

position is not substituted, the default substituent is H.

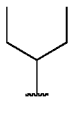
[00289] Singular forms "a" and "an" may include plural reference unless the context clearly dictates otherwise.

[00290] The number of carbon atoms in a substituent can be indicated by the prefix "C_{A-B}" where A is the minimum and B is the maximum number of carbon atoms in the substituent.

[00291] The term "hydrido" denotes a single -H atom (H) and may be used interchangeably with the symbol "H". Hydrido may be attached, for example, to an oxygen atom to form a "hydroxy" radical (i.e., –OH), or two hydrido radicals may be attached to a carbon atom to form a "methylene" ($–CH_2–$) radical.

[00292] The terms "hydroxyl" and "hydroxy" may be used interchangeably.

[00293] The term "halo" refers to fluoro (–F), chloro (–Cl), bromo (–Br), or iodo (–I).

[00294] The term "alkyl" denotes a linear or branched acyclic alkyl radical containing from 1 to about 15 carbon atoms. In some embodiments, alkyl is a C_{1-10}alkyl, C_{1-7}alkyl, C_{1-6}alkyl or C_{1-5}alkyl radical. Examples of alkyl include, but are not limited to, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentan-3-yl (i.e., ) and the like.

[00295] The term "alkylcarbonyl" denotes an alkyl radical attached to carbonyl.

[00296] The term "hydroxyalkyl" embraces a radical wherein any one or more of an alkyl carbon is substituted with a hydroxyl radical as defined above, for example, monohydroxyalkyl, dihydroxyalkyl and trihydroxyalkyl. More specific examples of hydroxyalkyl include hydroxymethyl, hydroxyethyl and hydroxypropyl.

[00297] Hydroxyalkyl may be substituted with, for example, alkyl, hydroxyalkyl, hydroxyalkoxy, hydroxyalkoxyalkyl, amino, aminoalkyl, aryl, aralkyl, and heterocyclyl. Further non-limiting examples include hydroxyalkyl substituted with methyl, isobutyl, benzyl, isopropyl, benzyl and *sec*-butyl.

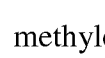
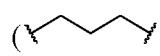
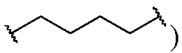
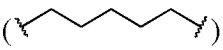
[00298] The term "hydroxyalkoxy" denotes a hydroxy radical attached to an alkoxy radical.

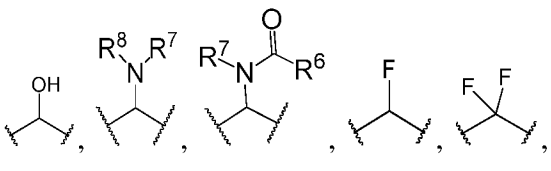
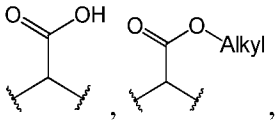
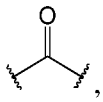
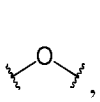
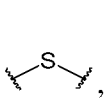
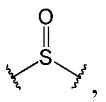
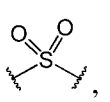
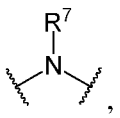
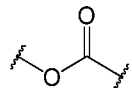
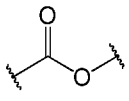
[00299] The term "hydroxyalkoxyalkyl" denotes a hydroxyalkoxy radical attached to an alkyl radical. Non-limiting examples include hydroxyethyl-O-ethyl and hydroxylmethyl-O-ethyl.

[00300] Hydroxyalkoxyalkyl may, for example, be substituted with alkyl, hydroxyalkyl, hydroxyalkoxy, hydroxyalkoxyalkyl, amino, aminoalkyl, aryl, aralkyl, and heterocyclyl. Further

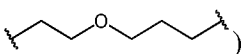
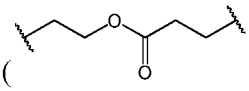
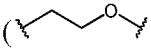
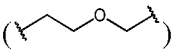
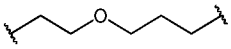
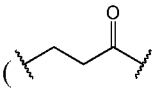
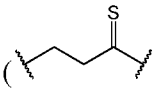
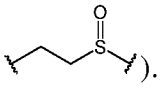
non-limiting examples include hydroxyalkoxyalkyl substituted with methyl, isobutyl, benzyl, isopropyl and *sec*-butyl. More specific non-limiting examples of substituted hydroxyalkoxyalkyl include hydroxyethyl-O-ethyl substituted with methyl, isobutyl, benzyl, isopropyl and *sec*-butyl.

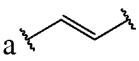
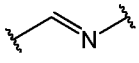
[00301] The term "haloalkyl" embraces an alkyl radical wherein any one or more of the alkyl carbon atoms is substituted with halo as defined above. For example, monohaloalkyl, dihaloalkyl and trihaloalkyl. A monohaloalkyl radical, for one example, may have either a bromo, chloro or a fluoro atom within the radical. A dihalo radical may have two of the same halo radicals or a combination of different halo radicals. A trihaloalkyl radical may have three of the same halo radicals or a combination of different halo radicals. Non-limiting examples of haloalkyl include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, trifluoroethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, iodomethyl, diiodomethyl and triiodomethyl.

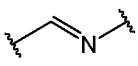
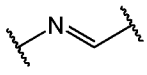
[00302] The term "alkylene" denotes a linear or branched alkyl radical containing from 2 to about 15 carbon atoms and having two or more attachment points for covalent bonds. The terms "alkylene" and "alkylenyl" may be used interchangeably. Non-limiting examples of alkylene radicals include methylene, ethylene (), propylene (), butylene () and pentylene ().

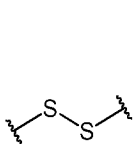
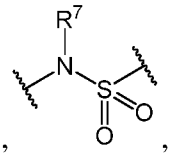
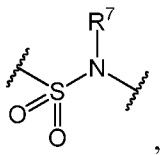
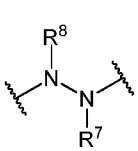
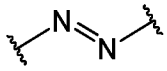
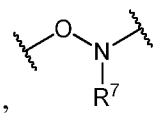
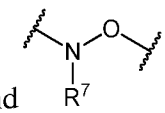
[00303] One or more substitutable carbons in an alkylene radical may be replaced with, for example,–CH(R^6)–, –CH(R^6)-O–, -C(R^6)$_2$-,  ,  , ,  ,  ,  ,  ,  ,  ,  or  ; where R^6 may be, for example, R^6 is independently selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, (e.g., heteroaryl, more specifically phthalimido) aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 may be taken together with R^2, R^7 or R^8 to form a cyclic ring; R^7 may be, for example, H, alkyl, hydroxyalkyl, aryl, heterocyclyl, alkylcarbonyl,

arylcarbonyl, heterocyclylcarbonyl, carboxyalkylcarbonyl, alkyloxycarbonylalkylcarbonyl, alkylsulfonyl, arylsulfonyl and heteroarylsulfonyl, or R^7 may be taken together with R^2, R^6 or R^8 to form a cyclic ring; and R^8 may be, for example, H, alkyl, hydroxyalkyl, aryl, heterocyclyl, alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, carboxyalkylcarbonyl, alkyloxycarbonylalkylcarbonyl, alkylsulfonyl, arylsulfonyl and heteroarylsulfonyl, or R^8 may be taken together with R^2, R^6 or R^7 to form a cyclic ring.

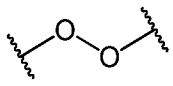
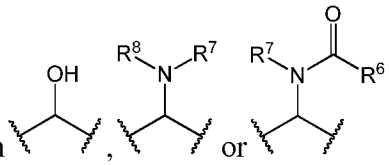
[00304] Examples of substituted alkylene include, ethyleneoxypropylene (), ethyleneoxycarbonylethylene (), ethyleneoxy (), ethyleneoxymethylene () ethyleneoxypropylene (), ethylenecarbonyl (), ethylenethiocarbonyl () and ethylenethionyl ().

[00305] One or more adjacent substitutable carbons in an alkylene radical may be replaced with a  ,  or a  radical.

[00306] When one or more substitutable carbons in alkylene are substituted, and the resulting radical has multiple orientations (e.g.,  vs ), both orientations are embraced by the display of a single orientation.

[00307] If two adjacent carbons in an alkylene radical are replaced with heteroatoms, only suitable combinations are embraced. Non-limiting examples of suitable combinations, where two or more adjacent carbon atoms are replaced with O, N or S include:  ,  ,  ,  ,  ,  and  ; where R^7 and R^8 are defined as above.

[00308] Unsuitable combinations are synthetically unstable combinations and are not

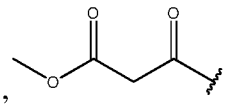
embraced by the current invention. Examples of unsuitable combinations include  and geminal heteroatom combinations with  ; where R^6, R^7 and R^8 are defined as above.

[00309] The term "alkoxy" is RO– where R is alkyl as defined above. Non-limiting examples of alkoxy radicals include methoxy, ethoxy and propoxy. The terms "alkyloxy" and "alkoxy" and "alkyl-O-" may be used interchangeably.

[00310] The term "alkoxyalkyl" refers to an alkoxy moiety substituted with an alkyl radical. Examples of alkoxyalkyl radicals include methoxymethyl, methoxyethyl, methoxypropyl and ethoxyethyl.

[00311] The term "alkoxycarbonyl" refers to an alkoxy radical substituted with carbonyl. Non-limiting examples include methoxycarbonyl and ethoxycarbonyl.

[00312] The term "alkoxycarbonylalkyl" refers to an alkoxycarbonyl radical substituted with alkyl.

[00313] The term "alkyloxycarbonylalkylcarbonyl" refers to alkoxycarbonylalkyl radical substituted with carbonyl (e.g., ).

[00314] The term "alkenyl" refers to an unsaturated, acyclic hydrocarbon radical with at least one double bond. Such alkenyl radicals contain from 2 to about 15 carbon atoms.

[00315] The term "alkynyl" refers to an unsaturated, acyclic hydrocarbon radical with at least one triple bond. Such alkynyl radicals containing from 2 to about 15 carbon atoms. A non-limiting example is propargyl.

[00316] The term "cyano" denotes a carbon radical having three of four covalent bonds shared by a single nitrogen atom.

[00317] The term "carbonyl" denotes a carbon radical having two of four covalent bonds shared with a single oxygen atom.

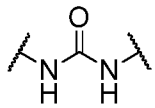
[00318] The term "alkylcarbonyl" denotes an alkyl radical attached to a carbonyl radical.

[00319] The term "carbonylalkyl" denotes a carbonyl radical attached to an alkyl radical.

[00320] The term "carbonylalkylcarbonyl" denotes a carbonylalkyl radical attached to a

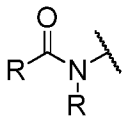
carbonyl radical.

[00321] The term "thiocarbonyl" denotes a carbon radical having two of four covalent bonds shared with a single sulfur atom, i.e.,  .

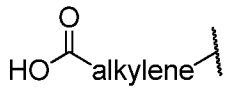
[00322] The term "ureido" denotes  and may be used interchangeably with carbamido.

[00323] The term "acyl", is  where R may be, for example, H, alkyl, nitrooxyalkyl, aryl and aralkyl. More specific examples of acyl include formyl, acetyl, benzoyl, nitrooxymethylcarbonyl and nitrooxyethylcarbonyl.

[00324] Collectively, the term "O-cap" embraces both ester and carbonate moieties.

[00325] The term "acylamino" is  , where R may be, for example, H, alkyl, nitrooxyalkyl, aryl and aralkyl. A more specific example of acylamino is acetylamino.

[00326] The term "carboxy" embraces a hydroxy radical attached to one of two unshared bonds in a carbonyl radical.

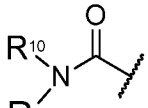
[00327] The term "carboxyalkyl" embraces a carboxy radical attached to an alkyl radical (e.g., ). Non-limiting examples of carboxyalkyl include carboxymethylene and carboxyethylene. The terms "carboxyalkyl" and "hydroxycarbonylalkyl" may be used interchangeably.

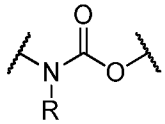
[00328] The term "carboxyalkylcarbonyl" denotes a carboxyalkyl radical attached to a carbonyl radical.

[00329] The term "thiocarboxy" embraces a hydroxyl radical, as defined above, attached to one of two unshared bonds in a thiocarbonyl radical.

[00330] The term "thiocarboxyalkyl" embraces a thiocarboxy radical, as defined above, attached to an alkyl radical. Non-limiting examples include thiocarboxymethylene and thiocarboxyethylene.

[00331] The term "amido" embraces an amino radical attached to a parent molecular

scaffold through carbonyl (e.g.,  , where R^{10} and R^{11} may be, H, alkyl or aralkyl or R^{10} may be taken together with R^{11} to form heterocyclyl, wherein at least one heteroatom is an amido nitrogen). The terms "amido" and "carboxamido" may be used interchangeably. Examples of amido radicals include monoalkylaminocarbonyl, dialkylaminocarbonyl. More specific examples of amido radicals include *N*-methylamino carbonyl and *N,N*-dimethylaminocarbonyl.

[00332] The term "carbamate" is  , where R may be, for example, H, alkyl or acyl.

[00333] The term "cyclic ring" embraces any aromatic or non-aromatic cyclized carbon radical (e.g., aryl and cycloalkyl respectively) which may contain one or more ring heteroatoms (e.g., heteroaryl and heterocyclyl).

[00334] The term "cycloalkyl" embraces any monocyclic, bicyclic or tricyclic cyclized carbon radical of 3 to about 15 carbon atoms that is fully or partially saturated. Cycloalkyl may be attached to an aryl, cycloalkyl or a heterocyclyl radical in a fused or pendant manner.

[00335] Cycloalkyl may be substituted with alkyl, alkoxy, carboxyalkyl, hydroxyalkyl, amino, acylamino, amido, alkylamino, nitrooxyalkyl, nitrooxy, carbonyl, acyl, aralkyl, aryl, heterocyclyl or cycloalkyl.

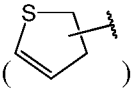
[00336] The term "aryl" refers to any monocyclic, bicyclic or tricyclic cyclized carbon radical, wherein at least one ring is aromatic. An aromatic radical may be attached to a non-aromatic cycloalkyl or heterocyclyl radical in a fused or pendant manner. Examples of aryl radicals include, but are not limited to, phenyl and naphthyl.

[00337] The term "arylcarbonyl" denotes an aryl radical attached to a carbonyl radical. The terms "aroyl" and "arylcarbonyl" may be used interchangeably. Examples of arylcarbonyl include benzoyl and toluoyl.

[00338] The term "aralkyl" embraces aryl attached to an alkyl radical and may be used interchangeably with arylalkyl. Examples of aralkyl include benzyl, diphenylmethyl, triphenylmethyl, phenylethyl and diphenylethyl. The terms "benzyl" and "phenylmethyl" may be used interchangeably.

[00339] The term "heterocyclyl" refers to any monocyclic, bicyclic or tricyclic ring

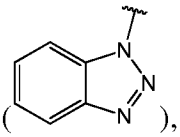
system having from 5 to about 15 ring members selected from carbon, nitrogen, sulfur and oxygen, wherein at least one ring member is a heteroatom. Heterocyclyl embraces a fully saturated, partially saturated and fully unsaturated radical (e.g., heteroaryl). Heterocyclyl may be fused or attached in a pendant manner to another heterocyclyl, aryl or cycloalkyl radical.

[00340] Heterocyclyl embraces combinations of different heteroatoms within the same cyclized ring system. When nitrogen is a ring member, heterocyclyl may be attached to the parent molecular scaffold through a ring nitrogen. Non-limiting examples of fully saturated five and six-membered heterocyclyl include: pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl, tetrahydrofuranyl, morpholinyl and thiazolidinyl. Examples of partially saturated heterocyclyl include dihydrothiophenyl (), dihydropyranyl, dihydrofuranyl and dihydrothiazolyl.

[00341] Heterocyclyl may be substituted, for example, with alkyl, alkoxy, carboxyalkyl, hydroxyalkyl, amino, acylamino, amido, alkylamino, nitrooxyalkyl, nitrooxy, carbonyl, acyl, aralkyl, aryl, heterocyclyl or cycloalkyl. Non-limiting examples include, five-membered heterocyclyl substituted with hydroxyalkyl, alkoxyalkyl, acyl, carbonyl or alkylaminocarbonyl. More specifically, pyrrolidinyl may be substituted with hydroxyalkyl, alkoxyalkyl, acyl, carbonyl or alkylaminocarbonyl. Substituted and un-substituted 5-membered heterocyclyl may be fused or attached in a pendant manner to an additional heterocyclyl, aryl or cycloalkyl radical. For example, pyrrolidinyl-2,5-dione may be fused to phenyl giving isoindolinyl,1,3-dione (also termed "phthalimido").

[00342] Six-membered heterocyclyl may be substituted with, for example, hydroxyalkyl, alkoxyalkyl, acyl, carbonyl or alkylaminocarbonyl. More specifically, piperidinyl, piperazinyl and morpholinyl may be substituted with hydroxyalkyl, alkoxyalkyl, acyl, carbonyl or alkylaminocarbonyl. Substituted and un-substituted 6-membered heterocyclyl may be fused or attached in a pendant manner to an additional heterocyclyl, aryl or cycloalkyl radical.

[00343] The term "heteroaryl" refers to an aromatic heterocyclyl radical. Heteroaryl may be fused or attached in a pendant manner to another heterocyclyl, aryl or cycloalkyl radical. Heteroaryl embraces combinations of different heteroatoms within the same cyclized radical. When nitrogen is a ring member, heteroaryl may be attached to the parent molecular scaffold through a ring nitrogen. Non-limiting examples of heteroaryl include pyridyl, thienyl, furanyl, pyrimidyl, imidazolyl, pyrazolyl, thiazolyl, thiadiazolyl, isothiazolyl, oxazolyl, isoxazoyl,

pyrrolyl, pyridazinyl, pyrazinyl, quinolinyl, isoquinolinyl, benzofuranyl, benzothienyl, indolyl, benzothiazolyl, benzooxazolyl, benzimidazolyl, isoindolyl, benzotriazolyl (), purinyl and thianaphthenyl. The term "heteroaryl" is also understood to include the N-oxide derivative of any nitrogen containing heteroaryl.

[00344] The term "alkylamino" embraces an alkyl radical attached to a molecular scaffold through an amino radical (e.g., alkyl-NH-scaffold). Specific non-limiting examples of alkylamino include *N,N*-dimethylamino-scaffold and *N*-methylamino-scaffold.

[00345] The term "aminoalkyl" embraces an amino radical attached to a molecular scaffold through an alkyl radical (e.g., NH_2-alkyl-scaffold).

[00346] The term "aralkoxy" embraces an arylalkyl radical attached through an oxygen atom to the parent molecular scaffold. The terms "arylalkoxy" and "aralkoxy" may be used interchangeably.

[00347] The term "aryloxy" is RO-, where R is aryl.

[00348] The term "arylthio" is RS–, where R is aryl.

[00349] The term "alkylthio" is RS-, where R is alkyl (e.g., alkyl-S-scaffold).

[00350] The term "thiolalkyl" is HSR-, where R is alkyl (e.g., HS-alkyl-scaffold).

[00351] The term "aryloxyalkyl" embraces an aryloxy radical attached to an alkyl radical.

[00352] The term "sulfonyl" is $-SO_2-$.

[00353] The term "alkylsulfonyl" embraces an alkyl radical attached to a sulfonyl radical, where alkyl is defined as above.

[00354] The term "arylsulfonyl" embraces an aryl radical attached to a sulfonyl radical.

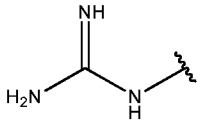
[00355] The term "heteroarylsulfonyl" embraces a heteroaryl radical attached to a sulfonyl radical.

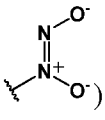
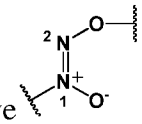
[00356] The term "alkylsulfonylalkyl", embraces an alkylsulfonyl radical attached to an alkyl radical, where alkyl is defined as above.

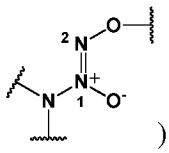
[00357] The term "haloalkylsulfonyl" embraces a haloalkyl radical attached to a sulfonyl radical, where haloalkyl is defined as above.

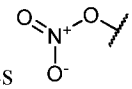
[00358] The term "sulfonamide" denotes sulfonyl attached to an amino radical. For example: NH_2SO_2- and $-NHSO_2-$. Sulfonamide may be used interchangeably with sulfamyl,

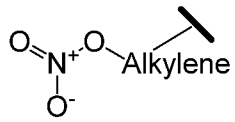
sulfonamido and aminosulfonyl.

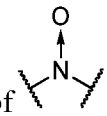
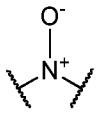
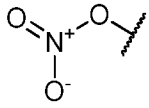
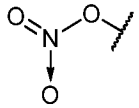
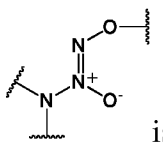
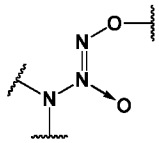
[00359] The term "guanidino" denotes  and may be used interchangeably with guanido.

[00360] The term "diazeniumdiolate" denotes an anion containing N=N linkage ("diazen") which has a formal positive charge ("ium") and which bridges two negatively charged oxygen atoms ("diolate") (e.g., ). Diazeniumdiolate can act as a linker by forming a bond through N=N–O to give  . This bonding configuration is denoted as "diazen-1-ium-1,2-diolate."

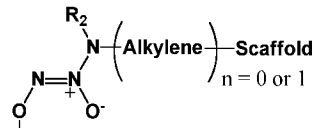
[00361] When diazeniumdiolate is attached to nitrogen at position "1", the resulting radical is termed "NONOate" (e.g., ). Species-compounds containing NONOate in the chemical formula, are denoted as "NONOates."

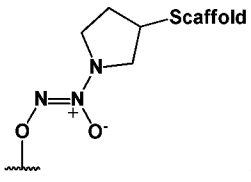
[00362] The term "nitrooxy" denotes  .

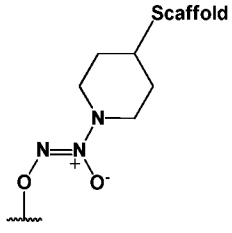
[00363] The term "nitrooxyalkyl" denotes nitrooxy substituted with alkyl (e.g., ).

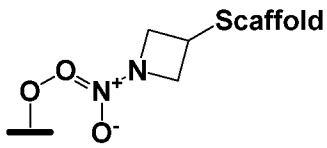
[00364] Structural display of  is equivalent to  . For example,  is equivalent to  ; and  is equivalent to  .

[00365] The term "nitrogen-bound" denotes NONOate bound to a parent molecular



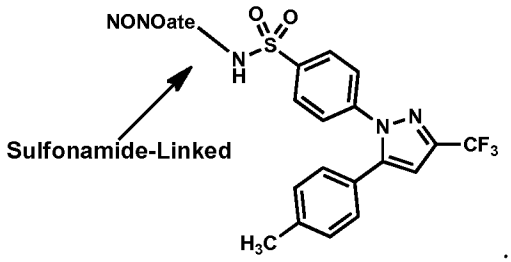
scaffold through nitrogen. For example; , where R^2 may be, for example, H, alkyl, aryl, heterocyclyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, carboxyalkyl and hydroxyalkyl, or R^2 may be taken together with R^6, R^7 or R^8 (as defined above) to form a cyclic ring. More specific examples include R^2 taken together with R^6 to form five or six-membered heterocyclyl. Non-limiting examples of five or six-membered heterocyclyl formed when R^2 is taken together with R^6 include, 

and 

and 

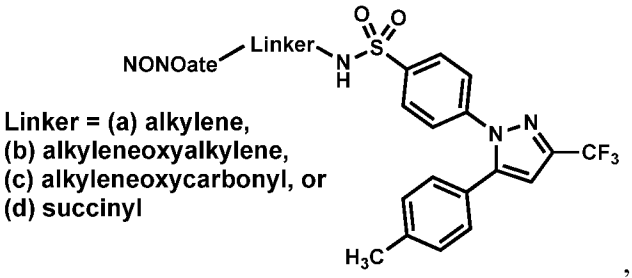
.

[00366] The term "sulfonamide-linked-coxib" refers to the position where a radical is attached to coxib (e.g., celecoxib). For example, when a NONOate radical is attached to celecoxib through sulfonamide nitrogen, it is termed "NONOate-sulfonamide-linked-coxib":



.

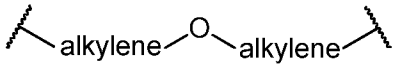
[00367] If a linking radical is present which links NONOate to sulfonamide nitrogen, the linking radical may be indicated with the appropriate prefix, for example:



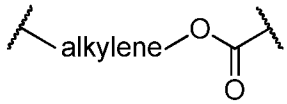
,

where (a) is NONOate-alkylene-sulfonamide-linked coxib, (b) is NONOate-

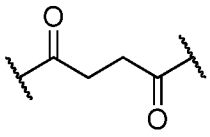
alkyleneoxyalkylene-sulfonamide-linked coxib, (c) is NONOate-alkyleneoxycarbonyl-sulfonamide-linked coxib, and (d) is NONOate-succinyl-sulfonamide-linked coxib.

[00368] The term "alkyleneoxyalkylene" is 

, where alkylene is defined as above.

[00369] The term "alkyleneoxycarbonyl" is 

, where alkylene is defined as above.

[00370] The term "succinyl" denotes 

.

[00371] The term "imine" denotes a compound containing the structure >C=N–.

[00372] The term "coxib" characterizes any member of a class of nonsteroidal anti-inflammatory drugs that causes fewer gastrointestinal side effects by selective inhibition of prostaglandin formation. The terms "coxib" and "selective COX-2 inhibitor" may be used interchangeably.

[00373] The term "pharmaceutically-acceptable" means suitable for use in pharmaceutical preparations, generally considered as safe for such use, officially approved by a regulatory agency of a national or state government for such use, or being listed in the U. S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, and more particularly in humans.

[00374] The term "pharmaceutically-acceptable salt" refers to a salt which may enhance desired pharmacological activity or may enhance stability of a compound. Examples of pharmaceutically-acceptable salts include acid addition salts formed with inorganic or organic acids, metal salts and amine salts. Examples of acid addition salts formed with inorganic acids include salts with hydrochloric acid, hydrobromic acid, hydriodic acid, sulfuric acid, nitric acid and phosphoric acid. Examples of acid addition salts formed with organic acids include acetic acid, propionic acid, hexanoic acid, heptanoic acid, cyclopentanepropionic acid, glycolic acid, pyruvic acid, lactic acid, citric acid, malonic acid, succinic acid, malic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, o-(4-hydroxy-benzoyl)-benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, 1,2-ethanedisulfonic acid, 2-

hydroxyethane-sulfonic acid, benzenesulfonic acid, p-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, p-toluenesulfonic acid, camphorsulfonic acid, 4-methyl-bicyclo[2.2.2]oct-2-ene1-carboxylic acid, glucoheptonic acid, 4,4'-methylenebis(3-hydroxy-2-naphthoic) acid, 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, lauryl sulfuric acid, gluconic acid, glutamic acid, hydroxynaphthoic acids, salicylic acid, stearic acid and muconic acid. Examples of metal salts include salts with sodium, potassium, calcium, magnesium, aluminum, iron, and zinc ions. Examples of amine salts include salts with ammonia and organic nitrogenous bases (e.g., cytosine, thymine, uracil and guanine).

[00375] The term "therapeutically-effective amount" refers to an amount of a compound that, when administered to a subject for treating a disease, is sufficient to effect treatment for the disease. "Therapeutically effective amount" can vary depending on the compound, the disease and its severity, the age, the weight, etc. of the subject to be treated.

[00376] The term "solvate" denotes a molecular or ionic complex of molecules or ions of solvent with those of a compound of the present invention. The term "solvate" embraces the term "hydrate".

[00377] The term "hydrate" denotes a compound of the present invention containing water combined in the molecular form.

[00378] Some of the compounds described contain one or more stereocenters and are meant to include R, S and mixtures of R and S forms for each stereocenter present.

[00379] The term "NO-releasing" means releasing, liberating or generating nitric oxide (NO).

[00380] Additional Suitable Protecting Groups:

Acetyl (Ac)
Acylals
Benzoyl (Bz)
Benzyl (Bn, Bnl)
Benzyl esters
Carbamate
Carbobenzyloxy (Cbz)
Dimethoxytrityl, [bis-(4-methoxyphenyl)phenylmethyl] (DMT)
Dithianes
Ethoxyethyl ethers (EE)
Methoxymethyl ether (MOM)
Methoxytrityl [(4-methoxyphenyl)diphenylmethyl], (MMT)

Methyl Ethers
Methyl (Me)
Methyl esters
Methylthiomethyl ether
Orthoesters
Oxazoline
Pivaloyl (Piv)
Phthalimido
p-Methoxybenzyl carbonyl (Moz or MeOZ)
p-Methoxybenzyl (PMB)
Propargyl alcohols
Silyl groups (e.g., trimethylsilyl (TMS), *tert*-butyldimethylsilyl (TBDMS), tri-*iso*-propylsilyloxymethyl (TOM) and triisopropylsilyl (TIPS))
Silyl esters
tert-Butyl esters
tert-Butyloxycarbonyl (BOC or tBOC)
Tetrahydropyranyl (THP)
Tosyl (Ts or Tos)
Trimethylsilylethoxymethyl (SEM)
Trityl (triphenylmethyl, Tr)
β-Methoxyethoxymethyl ether (MEM)
(4-nitrophenyl)sulfonyl or (4-nitrophenyl)(dioxido)-lambda(6)-sulfanyl) (Nosyl)
2-cyanoethyl
2-nitrophenylsulfenyl (Nps)
3,4-Dimethoxybenzyl (DMPM)
9-Fluorenylmethyloxycarbonyl (FMOC)

[00381] List of abbreviations:

ACN	acetonitrile
Boc	tert-butyloxycarbonyl
DCC	Dicyclohexylcarbodiimide
DCI	dicyclohexylcarbodiimide
DCM	dichloromethane or methylenechloride
DIPEA	diisopropylethylamine
DMAP	4-dimethylaminopyridine or *N,N*-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide
eq.	equivalents
EtOAC	ethyl acetate
EtOH	ethanol
Fmoc	fluorenylmethyloxycarbonyl chloride

HPLC	high performance liquid chromatography
hr	hour
hrs	hours
K_2CO_3	potassium carbonate
LC/MS	liquid chromatography mass spectrometry
LC/MS/MS	liquid chromatography tandem mass spectrometry
MeOH	methanol
$MgSO_4$	magnesium sulfate
min.	minute(s)
mL	milliliter
mmol	millimole
$Na_2S_2O_3$	sodium thiosulfate
Na_2SO_4	sodium sulfate
NaH	sodium hydride
$NaHCO_3$	sodium bicarbonate
NaI	sodium Iodide
$NaIO_4$	sodium periodate
$NaOCH_3$	sodium methoxide
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
NMR	nuclear magnetic resonance
NO	nitric oxide
psi	pounds per square inch
PyBOP	benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate
$RuCl_3$	ruthenium trichloride hydrate
TEA	triethylamine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TSA	p-toluenesulfonic acid

E. Method of Treatment

[00382] A compound of Formula (I), as used herein, is meant to include a pharmaceutically acceptable salt, or solvate of a compound or salt, of Formula (I).

[00383] The present invention further provides methods for treating a disease condition in a subject having or susceptible to having such a disease condition, by administering to the subject a therapeutically-effective amount of one or more compounds as described in Formula (I). In one embodiment, the treatment is preventative treatment. In another embodiment, the treatment is palliative treatment. In another embodiment, the treatment is restorative treatment.

In another embodiment, the subject is a mammal. In yet another embodiment, the subject is a human.

1. Conditions

[00384] The conditions that can be treated in accordance with the present invention include, but are not limited to, autoimmune disorders, chronic inflammatory disorders, acute inflammatory disorders, auto-inflammatory disorders, pain, cancer, neoplasia, lung cancer, colorectal cancer and the like.

[00385] In some embodiments, methods described herein are used to treat or prevent a disease condition comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I), wherein the condition is selected from the group consisting of non-small cell lung cancer, skin cancer, liver cancer, colorectal cancer (and FAP), squamous cell cancer, bladder cancer, breast cancer, biliary tract cancer, cervical cancer, prostate cancer, small cell lung cancer, ovarian cancer, pancreatic cancer, gastrointestinal cancer and CNS cancer.

[00386] In some embodiments, methods described herein are used to treat a disease condition comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I), wherein the condition is selected from the group consisting of actinic keratosis, cystic fibrosis and acne.

[00387] In some embodiments, methods described herein are used for healing wounds by administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I).

[00388] In some embodiments, methods described herein are used to treat a disease condition comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I), wherein the condition is non-small cell lung cancer

[00389] In some embodiments the methods described herein are used to treat patients with disorders arising from dysregulated enzymes and/or inflammatory mediator production, stability, secretion and posttranslational processing. Examples of inflammatory mediators that may be dysregulated include nitric oxide, prostaglandins and leukotrienes. Examples of enzymes include cyclo-oxygenase and nitric oxide synthase.

[00390] In some embodiments, the methods described herein are used to treat a patient in need thereof suffering from an autoimmune disorder, chronic and/or acute inflammatory disorder

and/or auto-inflammatory disorder. Examples of disorders include, but are not limited to arthritis, rheumatoid arthritis, osteoarthritis, juvenile arthritis, psoriatic arthritis.

[00391] In some embodiments, the methods described herein can be used to treat a patient in need thereof and suffering from neoplasia. Examples of these conditions include but are not limited to the following:

acral lentiginous melanoma	fibrolamellar carcinoma	neuroepithelial adenocarcinoma nodular melanoma
actinic keratoses	focal nodular hyperplasia	oat cell carcinoma
adenocarcinoma	gastrinoma	oligodendroglial
adenoid cycstic carcinoma	germ cell tumors	osteosarcoma
adenomas	glioblastoma	pancreatic cancer
adenosarcoma	glucagonoma	papillary serous adenocarcinoma
adenosquamous carcinoma	hemangiblastomas	pineal cell
astrocytic tumors	hemangioendothelioma	pituitary tumors
bartholin gland carcinoma	hemangiomas	plasmacytoma
basal cell carcinoma	hepatic adenoma	pseudosarcoma
bronchial gland carcinomas	hepatic adenomatosis	pulmonary blastoma
capillary	hepatocellular carcinoma	renal cell carcinoma
carcinoids	insulinoma	retinoblastoma
carcinoma	intaepithelial neoplasia	rhabdomyosarcoma
carcinosarcoma	interepithelial squamous cell neoplasia	sarcoma
cavernous	invasive squamous cell carcinoma	serous carcinoma
cholangiocarcinoma	large cell carcinoma	small cell carcinoma
chondosarcoma	leiomyosarcoma	soft tissue carcinomas
Choroid plexus papilloma/carcinoma	lentigo maligna melanomas	somatostatin-secreting tumor
clear cell carcinoma	malignant melanoma	squamous carcinoma
cystadenoma	malignant mesothelial tumors	squamous cell carcinoma
endodermal sinus tumor	medulloblastoma	submesothelial
endometrial hyperplasia	medulloepithelioma	superficial spreading melanoma
endometrial stromal sarcoma	melanoma	undifferentiatied carcinoma
endometrioid adenocarcinoma	meningeal	uveal melanoma
ependymal	mesothelial	verrucous carcinoma
epitheloid	metastatic carcinoma	vipoma
Ewing's sarcoma	mucoepidermoid carcinoma	well differentiated carcinoma
familial adenomatous polyposis (FAP)	neuroblastoma	Wilm's tumor

[00392] The term patient refers to both humans and non-human animals with the abovementioned conditions. Non-human animals could be companion animals such as, but not limited to canine and feline species.

2. Subjects

[00393] Suitable subjects to be treated according to the present invention include mammalian subjects. Mammals according to the present invention include, but are not limited to, human, canine, feline, bovine, caprine, equine, ovine, porcine, rodents, lagomorphs, primates, and the like, and encompass mammals in utero. Subjects may be of either gender and at any stage of development.

3. Administration and Dosing

[00394] A compound of the present invention may be administered in the form of prodrug in a therapeutically effective amount.

[00395] The compounds of the present invention can be administered by any suitable route in the form of a pharmaceutical composition adapted to such a route, and in a dose effective for the treatment intended. Therapeutically effective doses of the compounds of the present invention required to prevent or arrest the progress of, or to treat the medical condition, are readily ascertained by one of ordinary skill in the art using preclinical and clinical approaches familiar to the medicinal arts.

[00396] For convenience the compounds of the present invention can be administered in a unit dosage form. If desired, multiple doses per day of the unit dosage form can be used to increase the total daily dose. The unit dosage form, for example, may be a tablet or capsule containing about 0.01, 0.05, 0.1, 0.5, 1, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 125, 150, 175, 200, 250 or 500 mg of the compound of the present invention. In one embodiment, the unit dosage form contains from about 0.01 mg to about 500 mg of the compound of the present invention. In another embodiment, the unit dosage form contains from about 0.02 to about 400 mg of the compound of the present invention. In another embodiment, the unit dosage form contains from about 0.05 mg to about 250 mg of the compound of the present invention. In another embodiment, the unit dosage form contains from about 0.1 mg to about 200 mg of the compound of the present invention. In another embodiment, the unit dosage form contains from about 0.5 mg to about 150 mg of the compound of the present invention. In

another embodiment, the unit dosage form contains from about 1.0 mg to about 100 mg of the compound of the present invention.

[00397] The dosage regimen for the compounds and/or compositions containing the compounds is based on a variety of factors, including the type, age, weight, sex and medical condition of the patient; the severity of the condition; the route of administration; and the activity of the particular compound employed. Thus the dosage regimen may vary based on the specific situation. Dosage levels from about 0.001 mg to about 100 mg of the compound of the present invention per kilogram of body weight per day are useful in the treatment of the above-indicated conditions. In one embodiment, the total daily dose of the compound of the present invention (administered in single or divided doses) is typically from about 0.001 mg/kg to about 20 mg/kg (i.e., mg compound/kg body weight). In another embodiment, the total daily dose of the compound of the present invention is from about 0.005 mg/kg to about 10 mg/kg. In another embodiment, the total daily dose is from about 0.005 mg/kg to about 5 mg/kg. In another embodiment, the total daily dose is from about 0.01 mg/kg to about 1 mg/kg. In another embodiment, the total daily dose is from about 0.8 mg/kg to about 15 mg/kg. In another embodiment, the total daily dose is from about 0.2 mg/kg to about 4 mg/kg. These dosages are based on an average human subject having a weight of about 65 kg to about 75 kg. A physician will readily be able to determine doses for subjects whose weight falls outside of this range, such as infants. The administration of the compound of the present invention can be repeated a plurality of times in a day (typically no greater than 4 times) to achieve the desired daily dose.

[00398] The present invention further comprises use of a compound of the present invention as a medicament (such as a unit dosage tablet or unit dosage capsule).

[00399] In another embodiment, the present invention comprises the use of a compound of the present invention for the manufacture of a medicament (such as a unit dosage tablet or unit dosage capsule) to treat one or more of the conditions previously identified in the above sections discussing methods of treatment. In one embodiment, the condition is cancer. In another embodiment the condition is an inflammatory condition.

F. Pharmaceutical Compositions

[00400] For treatment of the conditions referred to above, the compounds described herein can be administered as follows:

1. Oral Administration

[00401] The compounds of the present invention may be administered orally, including by swallowing, so that the compound enters the gastrointestinal tract, or absorbed into the blood stream directly from the mouth (e.g., buccal or sublingual administration).

[00402] Suitable compositions for oral administration include solid formulations such as tablets, lozenges, pills, cachets, and hard and soft capsules, which can contain liquids, gels, or powders.

[00403] Compositions for oral administration may be formulated as immediate or modified release, including delayed or sustained release, optionally with enteric coating.

[00404] Liquid formulations can include solutions, syrups and suspensions, which can be used in soft or hard capsules. Such formulations may include a pharmaceutically acceptable carrier, for example, water, ethanol, polyethylene glycol, cellulose, or an oil. The formulation may also include one or more emulsifying agents and/or suspending agents.

[00405] In a tablet dosage form the amount of drug present may be from about 0.05% to about 95% by weight, more typically from about 2% to about 50% by weight of the dosage form. In addition, tablets may contain a disintegrant, comprising from about 0.5% to about 35% by weight, more typically from about 2% to about 25% of the dosage form. Examples of disintegrants include methyl cellulose, sodium or calcium carboxymethyl cellulose, croscarmellose sodium, polyvinylpyrrolidone, hydroxypropyl cellulose, starch and the like.

[00406] Suitable lubricants, for use in a tablet, may be present in amounts from about 0.1% to about 5% by weight, and include calcium, zinc or magnesium stearate, sodium stearyl fumarate and the like.

[00407] Suitable binders, for use in a tablet, include gelatin, polyethylene glycol, sugars, gums, starch, hydroxypropyl cellulose and the like. Suitable diluents, for use in a tablet, include mannitol, xylitol, lactose, dextrose, sucrose, sorbitol and starch.

[00408] Suitable surface active agents and glidants, for use in a tablet, may be present in amounts from about 0.1% to about 3% by weight, and include polysorbate 80, sodium dodecyl sulfate, talc and silicon dioxide.

[00409] In another embodiment, a pharmaceutical composition comprises a therapeutically effective amount of a compound of Formula (I) or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

2. Parenteral Administration

[00410] Compounds of the present invention may be administered directly into the blood stream, muscle, or internal organs. Suitable means for parenteral administration include intravenous, intra-muscular, subcutaneous intraarterial, intraperitoneal, intrathecal, intracranial, and the like. Suitable devices for parenteral administration include injectors (including needle and needle-free injectors) and infusion methods.

[00411] Compositions for parenteral administration may be formulated as immediate or modified release, including delayed or sustained release.

[00412] Most parenteral formulations are aqueous solutions containing excipients, including salts, buffering agents and carbohydrates.

[00413] Parenteral formulations may also be prepared in a dehydrated form (e.g., by lyophilization) or as sterile non-aqueous solutions. These formulations can be used with a suitable vehicle, such as sterile water. Solubility-enhancing agents may also be used in preparation of parenteral solutions.

3. Topical Administration

[00414] Compounds of the present invention may be administered topically to the skin or transdermally. Formulations for this topical administration can include lotions, solutions, creams, gels, hydrogels, ointments, foams, implants, patches and the like. Pharmaceutically acceptable carriers for topical administration formulations can include water, alcohol, mineral oil, glycerin, polyethylene glycol and the like. Topical administration can also be performed by electroporation, iontophoresis, phonophoresis and the like.

[00415] Compositions for topical administration may be formulated as immediate or modified release, including delayed or sustained release.

4. Rectal Administration

[00416] Suppositories for rectal administration of the compounds of the present invention can be prepared by mixing the active agent with a suitable non-irritating excipient such as cocoa butter, synthetic mono-, di-, or triglycerides, fatty acids, or polyethylene glycols which are solid at ordinary temperatures but liquid at the rectal temperature, and which will therefore melt in the rectum and release the drug.

[00417] Other carrier materials and modes of administration known in the pharmaceutical art may also be used. Pharmaceutical compositions of the invention may be prepared by any of the well-known techniques of pharmacy, such as effective formulation and administration

procedures. The above considerations in regard to effective formulations and administration procedures are well known in the art and are described in standard textbooks. Formulation of drugs is discussed in, for example, Hoover, John E., Remington's Pharmaceutical Sciences, Mack Publishing Co., Easton, Pa., 1975; Liberman, et al., Eds., Pharmaceutical Dosage Forms, Marcel Decker, New York, N.Y., 1980; and Kibbe, et al., Eds., Handbook of Pharmaceutical Excipients (3rd Ed.), American Pharmaceutical Association, Washington, 1999.

G. Combinations and Combination Therapy

[00418] The compounds of the present invention can be used, alone or in combination with other pharmaceutically active compounds, to treat conditions such as those previously described above. The compound(s) of the present invention and other pharmaceutically active compound(s) can be administered simultaneously (either in the same dosage form or in separate dosage forms) or sequentially. Accordingly, in one embodiment, the present invention comprises methods for treating a condition by administering to the subject a therapeutically-effective amount of one or more compounds of the present invention and one or more additional pharmaceutically active compounds.

[00419] In another embodiment, there is provided a pharmaceutical composition comprising one or more compounds of the present invention, one or more additional pharmaceutically active compounds, and a pharmaceutically acceptable carrier.

[00420] In another embodiment, the one or more additional pharmaceutically active compounds is selected from the group consisting of anti-inflammatory drugs, cytostatic drugs, anti-proliferative agents and angiogenesis inhibitors.

[00421] In another embodiment, the one or more additional pharmaceutically active compounds are selected from the group consisting of anti-cancer drugs and anti-inflammatory drugs.

[00422] NO-releasing coxib conjugates described herein are also optionally used in combination with other therapeutic reagents that are selected for their therapeutic value for the condition to be treated. In general, the compounds described herein and, in embodiments where combinational therapy is employed, other agents do not have to be administered in the same pharmaceutical composition and, because of different physical and chemical characteristics, are optionally administered by different routes. The initial administration is generally made according to established protocols and then, based upon the observed effects, the dosage, modes

of administration and times of administration subsequently modified. In certain instances, it is appropriate to administer an NO-releasing coxib conjugate, as described herein, in combination with another therapeutic agent or NO-releasing coxib conjugate. By way of example only, the therapeutic effectiveness of an NO-releasing coxib conjugate is enhanced by administration of another therapeutic agent (which also includes a therapeutic regimen) that also has therapeutic benefit. Regardless of the disease, disorder or condition being treated, the overall benefit experienced by the patient is either simply additive of the two therapeutic agents or the patient experiences an enhanced benefit.

[00423] Therapeutically effective dosages vary when the drugs are used in treatment combinations. Methods for experimentally determining therapeutically effective dosages of drugs and other agents for use in combination treatment regimens are documented methodologies. Combination treatment further includes periodic treatments that start and stop at various times to assist with the clinical management of the patient. In any case, the multiple therapeutic agents (one of which is an NO-releasing coxib conjugate as described herein) are administered in any order, or even simultaneously. If simultaneously, the multiple therapeutic agents are optionally provided in a single, unified form, or in multiple forms (by way of example only, either as a single pill or as two separate pills).

[00424] In some embodiments, one of the therapeutic agents is given in multiple doses, or both are given as multiple doses. If not simultaneous, the timing between the multiple doses optionally varies from more than zero weeks to less than twelve weeks.

[00425] In addition, the combination methods, compositions and formulations are not to be limited to the use of only two agents, the use of multiple therapeutic combinations are also envisioned. It is understood that the dosage regimen to treat, prevent, or ameliorate the condition(s) for which relief is sought, is optionally modified in accordance with a variety of factors. These factors include the disorder from which the subject suffers, as well as the age, weight, sex, diet, and medical condition of the subject. Thus, the dosage regimen actually employed varies widely, in some embodiments, and therefore deviates from the dosage regimens set forth herein.

[00426] The pharmaceutical agents which make up the combination therapy disclosed herein are optionally a combined dosage form or in separate dosage forms intended for substantially simultaneous administration. The pharmaceutical agents that make up the

combination therapy are optionally also administered sequentially, with either agent being administered by a regimen calling for two-step administration. The two-step administration regimen optionally calls for sequential administration of the active agents or spaced-apart administration of the separate active agents. The time period between the multiple administration steps ranges from a few minutes to several hours, depending upon the properties of each pharmaceutical agent, such as potency, solubility, bioavailability, plasma half-life and kinetic profile of the pharmaceutical agent.

[00427] In another embodiment, an NO-releasing coxib conjugate is optionally used in combination with procedures that provide additional benefit to the patient. An NO-releasing coxib conjugate and any additional therapies are optionally administered before, during or after the occurrence of a disease or condition, and the timing of administering the composition containing an NO-releasing coxib conjugate varies in some embodiments. Thus, for example, an NO-releasing coxib conjugate is used as a prophylactic and is administered continuously to subjects with a propensity to develop conditions or diseases in order to prevent the occurrence of the disease or condition. An NO-releasing coxib conjugate is optionally administered to a subject during or as soon as possible after the onset of the symptoms. While embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that in some embodiments of the invention various alternatives to the embodiments described herein are employed in practicing the invention.

[00428] An NO-releasing coxib conjugate can be used in combination with anti-cancer drugs, including but not limited to the following classes: alkylating agents, anti-metabolites, plant alkaloids and terpenoids, topoisomerase inhibitors, cytotoxic antibiotics, angiogenesis inhibitors and tyrosine kinase inhibitors.

[00429] For use in cancer and neoplastic diseases an NO-releasing coxib conjugate may be optimally used together with one or more of the following non-limiting examples of anti-cancer agents. A first example, alkylating agents, includes but is not limited to cisplatin (PLATIN), carboplatin (PARAPLATIN), streptozocin (ZANOSAR), busulfan (MYLERAN) and cyclophosphamide (ENDOXAN). A second example, anti-metabolites, includes but is not limited to mercaptopurine (PURINETHOL), thioguanine, pentostatin (NIPENT), cytosine

arabinoside (ARA-C) and methotrexate (RHEUMATREX). A third example, plant alkaloids and terpenoids, includes but is not limited to vincristine (ONCOVIN), vinblastine and paclitaxel (TAXOL). A fourth example, topoisomerase inhibitors, includes but is not limited to irinotecan (CAMPTOSAR), topotecan (HYCAMTIN) and etoposide (EPOSIN). A fifth example, cytotoxic antibiotics, includes but is not limited to actinomycin D (COSMEGEN), doxorubicin (ADRIAMYCIN), bleomycin (BLENOXANE) and mitomycin (MITOSOL). A sixth example, angiogenesis inhibitors, includes but is not limited to sunitinib (SUTENT) and bevacizumab (AVASTIN). A seventh example, tyrosine kinase inhibitors, includes but is not limited to imatinib (GLEEVEC), erlotinib (TARCEVA), lapatininb (TYKERB) and axitinib (INLYTA).

[00430] Where a subject is suffering from or at risk of suffering from an inflammatory condition, an NO-releasing coxib conjugate described herein is optionally used together with one or more agents or methods for treating an inflammatory condition in any combination. Therapeutic agents/treatments for treating an autoimmune and/or inflammatory condition include, but are not limited to any of the following examples. A first example, corticosteroids, includes but is not limited to cortisone, dexamethasone, and methylprednisolone. A second example, nonsteroidal anti-inflammatory drugs (NSAID's), includes but is not limited to ibuprofen, naproxen, acetaminophen, aspirin, fenoprofen (NALFON), flurbiprofen (ANSAID), ketoprofen, oxaprozin (DAYPRO), diclofenac sodium (VOLTAREN), diclofenac potassium (CATAFLAM), etodolac (LODINE), indomethacin (INDOCIN), ketorolac (TORADOL), sulindac (CLINORIL), tolmetin (TOLECTIN), meclofenamate (MECLOMEN), mefenamic acid (PONSTEL), nabumetone (RELAFEN) and piroxicam (FELDENE). A third example, immunosuppressants, includes but is not limited to methotrexate (RHEUMATREX), leflunomide (ARAVA), azathioprine (IMURAN), cyclosporine (NEORAL, SANDIMMUNE), tacrolimus and cyclophosphamide (CYTOXAN). A fourth example, CD20 blockers, includes but is not limited to rituximab (RITUXAN). A fifth example, Tumor Necrosis Factor (TNF) blockers, includes but is not limited to etanercept (ENBREL), infliximab (REMICADE) and adalimumab (HUMIRA). A sixth example, interleukin-1 receptor antagonists, includes but is not limited to anakinra (KINERET). A seventh example, interleukin-6 inhibitors, includes but is not limited to tocilizumab (ACTEMRA). An eighth example, interleukin-17 inhibitors, includes but is not limited to AIN457. A ninth example, Janus kinase inhibitors, includes but is not limited to tasocitinib. A tenth example, syk inhibitors, includes but is not limited to fostamatinib.

H. Kits

[00431] The present invention further comprises kits that are suitable for use in performing the methods of treatment or prevention described above. In one embodiment, the kit contains a first dosage form comprising one or more of the compounds of the present invention and a container for the dosage, in quantities sufficient to carry out the methods of the present invention.

I. Biological Assays

[00432] Compound Metabolism in Plasma: The present invention includes compounds that are enzymatically activated *in vivo* to produce coxibs. Compounds are analyzed, after incubation in plasma, for the rate of disappearance of the compound species and appearance of coxib and/or intermediate compounds.

[00433] Compounds are incubated with rat plasma at 37°C and extracted at various time points (T =30 min, 1h, 2h, 4h, and 8h). Extracts are analyzed using HPLC-UV/ELSD (evaporative light scattering detector) for the presence of starting compound, coxib, and intermediate compounds.

Compound Testing in the Air Pouch Assay of Acute Inflammation Measuring PGE2 Levels in Exudate in Rats

[00434] Animals: Sprague-Dawley rats (Charles River Laboratories., R #3234, PO #738990, male, 160-180g) were received, individually examined, and housed in cages of five rats each. The rats were ear notched for identification purposes.

[00435] Compounds and dosing solutions: The vehicle was prepared by dissolving 40 g (2-hydroxypropyl)-β-cyclodextrin (HP-β-CD, Sigma, Cat. 332593, lot MKBJ5858V) in 160 mL sterile saline for injection, USP (Hospira, lot 26-801-FW) making a 25% solution which was filter sterilized (0.2 μm, Nalgene, Cat. 151-4020, lot 1095610). A 1% carrageenan solution was prepared by dissolving g λ-carrageenan (Fluka, Cat. 22049, lot 1318338) in hot 60 mL sterile saline for injection, USP. This solution was stored at 4-8^{O}C. Test compounds were dissolved in DMSO (Fisher Scientific, Cat. D128-500, lot 874999) to make 75 mM stocks. 0.25mL of compound DMSO stocks were mixed with 12.5 mL of HP-β-CD solution at 50^{O}C (maximum DMSO concentation was 2% of the final volume of vehicle,). Final concentration of all test compounds was 1.5 mM and compounds were dosed within 2 hours of preparation at 0.01mmol/kg (12 nmol of test compound per rat).

[00436] Day 0 - Air pouch initiation: The rats were anesthetized in a biological cabinet, the nape of the neck was cleansed with 70% isopropanol (Butler Schein Animal Health, Cat. 002498, lot 29EMS07104547) followed by 1% povidone-iodine solution (Ricca Chemical Co., Cat. 3955-16, lot 2205469). Twenty mL of sterile (0.22 μm, Millipore, Cat. SLGP033RS, lot R2KA55925, exp 08/2015) air was injected subcutaneously (SC) using a 23G x 1½ inch needle fixed to a 20 mL syringe. The rats were returned to routine housing. No adverse reactions were observed.

[00437] Day 3 - Air pouch maintance: The rats were anesthetized in a biological cabinet, the nape of the neck was cleansed with 70% isopropanol followed by 1% povidone-iodine solution. Ten mL of sterile air was injected SC using a 23G x 1½ inch needle fixed to a 20 mL syringe. The rats were returned to routine housing in clean cages. No adverse reactions were observed.

[00438] Day 6 - Compound administration and carrageenan insult: At commencement of the study, each rat was weighed and sorted into treatment groups of 5 rats/group based upon average weight. Each rat was dosed orally via gavage at 6.809 mL/kg (1.6 mL/235 g) with their respective test material/vehicle. Two hours after test material/vehicle administration, the rats were injected with 1.0 mL of the room temperature 1% carrageenan saline solution into the air pouch. Four hours after carrageenan injection, the rats were anesthetized and 5 mL of the exudate buffer was injected into the air pouch. The pouch was gently massaged, the exudate immediately removed, and exudate volume recorded. The exudate was collected in a serum separator tube on an ice bath. The exudates were centrifuged (refrigerated) and an aliquot of the supernatant was stored in a labeled Eppendorf tube at -80^{O}C.

[00439] Termination of Study: Animals were euthanized via CO_2 asphyxiation at the completion of the in-life portion of this study and carcasses were disposed of according to standard protocols.

[00440] Data analysis: The exudate samples were thawed to room temperature and assayed by ELISA for PGE_2 (R&D Systems, Cat. KGE004B, lot 307711). Statistical significance of treatments on mean exudate volumes are determined by comparison of means for treatment groups with vehicle group. Mean cytokine concentrations and standard deviations are determined for each group. Statistical significance of treatments on cytokine concentrations are determined

for each compound group compared to vehicle group. Statistical significance (p-value) was calculated vs control groups by Student's t-Test.

[00441] PGE_2 Measurements: Oral administration of 6.809 ml/kg of vehicle two hours prior to intra-pouch challenge with 1% carrageenan resulted in a collected exudate volume of 5.7 ml and 4358 pg/ml PGE_2 in the exudate. Pretreatment with orally administered 0.01 mmol/kg celecoxib (positive control) resulted in a significant 19% reduction in collected exudate volume and an 80% reduction in exudate PGE_2 release. Pretreatment with orally administered 0.01 mmol/kg **N402** (negative control), or test compound **202** (carbamate-linked celecoxib) did not show any effect on the carrageenan-induced increase in exudate volume or PGE_2 release. Oral pretreatment with 0.01 mmol/kg of test compound **602** (amide-linked celecoxib) resulted in a significant 20% reduction in collected exudate volume and a 56% reduction in exudate PGE_2 releas, similar to that observed with celecoxib.

	Treatment	Volume (mL)	PGE_2 (pg/mL)
Mean	Vehicle	5.7	4357.7
SD		0.2	1122.0
Mean	Negative Control **N402**	5.4	3782.4
SD		0.3	2096.2
p-value		0.14	0.60
Mean	Positive Control Celecoxib	4.6	907.1
SD		0.3	258.4
p-value		0.0002	0.0002
Mean	Test Compound **202**	5.6	4959.1
SD		0.1	1672.3
p-value		0.27	0.52
Mean	Test Compound **602**	4.5	1915.2
SD		0.3	1139.6
p-value		0.0001	0.009

NO Release in Plasma:

[00442] Prodrugs were dissolved into DMSO to make 3 mM stocks and stored at -20 deg C. Solutions of 5% rat serum (Sigma Cat. # S7648) or 15% human serum (Bioreclaimation, Cat. # HMSRM) where made in PBS (% v/v). In a 96-well plate, 3 μL of DMSO in 127 μL PBS were placed in blank wells and 3 μL of DMSO in 127 μL of diluted serum were placed in wells for reference standards. Test wells were charged with 127 μL of diluted serum followed by 3 μL of 3 mM compound DMSO stocks tested in quadruplicate. Plates were incubated at 37 °C for 90

minutes, removed from the incubator, and placed on ice. Reference wells were diluted with 150 μL of sodium nitrite stock solutions in PBS. Remaining wells were diluted with 150 μL of PBS and then every well received 20 μL of Griess Reagent (Promega Cat. # G2930). Wells were mixed, the plates were incubated for 30 minutes at room temperature, and then absorbance was measured at 562 nm using a microplate reader. Reference standards final concentrations were 100, 33.3, 11.1, 3.7, 1.23, and 0.41 μM nitrite and final test concentrations for all compounds was 30 μM. The average DMSO blank readings were subtracted from test readings and a standard curve was generated from the reference standard wells. Nitrite levels were determined, and percent release of nitric oxide was calculated, relative to theoretical maximum (60 μM), for each compound.

Compound	NO Release (5% Rat Serum)	NO Release (5% Human Serum)
8	13%	28%
10	12%	22%
11	7%	24%
12	11%	24%
14	4%	8%
89	33%	<2%
91	40%	<2%
93	28%	<2%
95	17%	<2%
150-A	55%	<2%
150-B	71%	<2%
150-C	58%	<2%
150-D	47%	<2%
195	32%	12%
197	57%	<2%
199	64%	15%
200	69%	ND
202	72%	<2%
350-A	66%	17%
355	6%	18%
371	2%	17%
372	6%	30%
407	37%	6%
408	13%	<2%
414	14%	<2%
430	52%	9%
503	57%	<2%
764	68%	8%

[00443] Plasma & Microsomal Stability: The present invention includes compounds that are enzymatically activated *in vivo* to produce coxibs. Compounds are analyzed, after incubation in plasma or liver microsomes, for the rate of disappearance of the compound species.

[00444] Compounds (1 μM) will be incubated, in triplicate, in rat plasma or liver microsomes at 37°C and analyzed by LC/MS/MS (T = 0, 10, 20, 30, 45 and 60 min). Reaction is quenched by acetonitrile. Analysis used will be standard reverse phase HPLC and API 4000 triple quadrupole mass spectrometry. Elimination rate constant, *in vitro* half-life and intrinsic clearance are calculated from results. Plasma results using LC/MS/MS will also verify results using HPLC-UV/ELSD.

[00445] Selectivity: Evaluation of COX-1 & COX-2 Activity *In Vitro*: The compounds of the present invention are coxib conjugates, therefore they will be evaluated for selective COX-1 or COX-2 inhibition. Assays for COX-1 and COX-2 activity in vitro are described in US 5,760,068.

[00446] Preparation of recombinant COX-1 and COX-2:

(1) A fragment containing the coding region of either human or murine COX-1 or COX-2 is cloned into a BamH1 site of a baculovirus transfer vector to generate transfer vectors for COX-I and COX-II.

(2) Recombinant baculoviruses are isolated by transfecting baculovirus transfer vector DNA into SF9 insect cells.

(3) Recombinant viruses are purified and high titer stocks of virus are prepared.

(4) SF9 insect cells are infected with the recombinant baculovirus stock. After 72 hours the cells are centrifuged and the cell pellet homogenized. The homogenate is centrifuged and the supernatant is assayed for COX activity.

[00447] Assay for COX-1 and COX-2 activity:

(1) COX activity is assayed as PGE_2 formed/μg protein/time using an ELISA to detect the prostaglandin formed.

(2) Insect cell membranes containing the appropriate COX enzyme are incubated in buffer containing arachidonic acid.

(3) Compounds are pre-incubated with the enzyme for 10-20 minutes prior to the addition of arachidonic acid.

(4) Reaction between the arachidonic acid and the enzyme is stopped after ten minutes, and the PGE_2 formed is measured by standard ELISA technology.

[00448] Assessment of Anti-Cancer Activity of Test Compounds by MTT Based Cell Proliferation Assay: Anti-tumor growth potential of test compounds are evaluated in vitro using various human tumor cells, available from the American Type Culture Collection (ATCC), such as A549 lung tumor cells, DU145 prostate tumor cells, HT29 colon cancer cells, MIA PaCa-2 pancreatic cancer cells, MCF-7 (ER^+) breast tumor cells and BEAS-2B cells (immortalized normal lung epithelial cells) as control [Hida, et al., Clin. Cancer Res. 6, 2006-2011 (2000)]. Test compound effect on cell proliferation will be determined using the MTT based cell proliferation assay. MTT based cell proliferation assays are described in US 8,143,237.

[00449] MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] incorporation based cell proliferation assay is performed using the MTT cell proliferation assay kit (Roche Applied Sciences, Germany). The assay is carried out according to the instruction provided by the vendor. Briefly, equal numbers of cells are plated in 96-well flat-bottomed plates and are incubated with test compounds at various concentrations for a period of three days. Vehicle control culture wells receive an equal volume of vehicle solution. Thereafter, 0.5 mg/ml of MTT reagent is added to each well and the microplate is incubated further for 4 hours at 37° C in presence of 5% CO_2. Cells are then solubilized by adding solubilizing solution and allowed to incubate at 37° C overnight. After complete solubilization of the formazan crystals, the absorbance is read at 540 nm in a microplate reader (BioRad, USA). The results (mean optical density (OD) ± standard dethroughtion (SD)) obtained from quadruplicate wells are used to calculate the inhibition of cell proliferation (50% of inhibitory concentration, IC_{50}) of the test compounds.

[00450] Suppression of Lung Cancer Cell Migration: Efficacy testing will be done to evaluate test compound suppression of lung cancer cell migration, a model of metastasis. Methods to evaluate lung cancer cell migration are described in Park, et al. Mol. Med. Reports 3, 1007-1013 (2010).

[00451] Cell Culture: Human lung cancer cells A549 are obtained from American Type Culture Collection (ATCC, Manassas, VA). Cells are incubated in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) and penicillin/streptomycin (GibcoBRL, Grand Island, NY, USA).

[00452] Monolayer Wound Healing Assay: Cell proliferation in confluent A549 monolayers is blocked by a 30 minute pre-incubation in the presence of mitomycin C (3 μg/ml). Test compounds, in cell culture buffer, are added to confluent monolayers 30 minutes before wound induction. A549 monolayers are subsequently scratched with a pipette tip. Wound areas are evaluated with phase contrast microscopy on an inverted microscope. Images of the same areas are obtained at intervals from zero to 96 hours. Cell migration rate through wound healing is evaluated from the images using Paint.Net v.3.10 software. Cell migration is expressed as the fold change in the migration area, relative to untreated control cells at the same time period.

[00453] Compound Formulations for Intravenous (IV), Oral Gavage (PO) or Intraperitoneal (IP) Administration: Compounds will be formulated for administration using 25% hydroxypropyl-beta-cyclodextrin-PBS buffer (HBCD-PBS) at 1 mg/ml. HBCD-PBS is the preferred formulation media for compound administration. Additional formulation vehicles may also be used, including 2% Tween 80 in saline, and 20% polyethylene glycol (PEG-300) in 0.9% sodium chloride in water.

[00454] Determination of Maximum Tolerated Dose (MTD) of Test Compounds in Rats: In order to estimate the doses of test compounds for use in efficacy testing in animal models of cancer, it will be determined at what doses adverse events occur. Methods to determine MTD in rats are described in Rao, et al., Mol. Cancer Ther. 5, 1530-1538 (2006).

[00455] In order to determine doses for efficacy studies, the maximum tolerated dose (MTD) is determined. Male F344 rats are fed various concentrations of test compounds for six weeks. MTD is determined based on the highest dose that causes a 10% loss in body weight without mortality or signs of toxicity. Body weights are recorded twice weekly. Animals are examined daily for signs of toxicity. At termination, animals are euthanized and organs dissected and examined.

[00456] Compound Metabolism (PK) in Rats: The pharmacokinetics (PK) of compounds will be tested by single dose IV administration to Sprague Dawley rats.

[00457] For each test compound, three (3) Sprague Dawley (CD® IGS) male rats are used. Animals are weighed and dosed individually by body weight on the day of treatment. Compounds are administered intravenously (IV), through surgically placed jugular catheters, at 10 mg/kg using 10 ml/kg volume per animal. Animals found in severe distress or a moribund condition are euthanized. Peripheral blood collections are done primarily through venipuncture

of the tail or saphenous veins at various times (T = 15min, 30min, 1h, 2h, 4h, 8h, and 24h). Whole blood samples are collected in an EDTA microtainer, processed to plasma by centrifugation, and the plasma frozen at -80°C. Bioanalysis is done using LC/MS/MS methods using standard reverse phase HPLC and API 4000 triple quadrupole mass spectrometry. The amount of compound present will be used to calculate PK parameters C_{max}, T_{max} and AUC.

[00458] Compound Effects on Blood Pressure: Since COX-2 inhibitors have been shown to have adverse effects on blood pressure *in vivo*, the effect of the present compounds will be evaluated for blood pressure effects in spontaneously hypertensive rats (SHR).

[00459] Thirty-two male, spontaneously hypertensive rats (SHR), 12-weeks old (four groups of eight) will be used in this study. Initially, mean arterial blood pressure (MAP) is measured through tail-cuff daily, throughout the study. Animals undergo 2 days of blood pressure training and 1 day of baseline blood pressure measurements. Animals are weighed and dosed individually by body weight on the day of treatment. Compounds are administered orally (PO) or by intraperitoneal (IP) injection once on Day 1 at 10 mg/kg using 10 ml/kg volume per animal. Blood pressures are monitored for 6 days post-dose. A total of 7 time points are measured: Day 0 for baseline and Days 1, 2, 3, 4, 5, and 6 of the study. Animals found in severe distress or in a moribund condition will be euthanized. Celecoxib is the positive control tested in these studies.

[00460] Anti-inflammatory Efficacy: Rat Carrageenan Foot Pad Edema: The compounds of the present invention are conjugates of coxibs, therefore they will be evaluated for efficacy *in vivo* in a model of inflammation. Methods to determine efficacy in rat carrageenan foot pad edema are described in US 5,760,068.

[00461] Male Sprague Dawley rats are selected for equal average body weight per group. After fasting, with free access to water sixteen hours prior to test, animals are dosed orally (1 mL) with test compounds in a vehicle containing 0.5% methylcellulose and 0.025% surfactant. The control group is dosed with vehicle alone.

[00462] One hour after dosing, a subplantar injection of 0.1 mL of 1% solution of carrageenan/sterile 0.9% saline is administered in one foot, to all animals. The volume of the injected foot is measured using a displacement plethysmometer. Foot volume is measured again three hours after carrageenan injection. The three hour foot volume measurement is compared between treated and control groups; the percent inhibition of edema is calculated.

[00463] Anti-inflammatory Efficacy: Rat Carrageenan-Induced Analgesia Test: The compounds of the present invention are conjugates of coxibs, therefore they will be evaluated for efficacy *in vivo* in a model of inflammatory analgesia. Methods to determine efficacy in rat carrageenan-induced analgesia test are described in US 5,760,068.

[00464] Male Sprague Dawley rats are selected for equal average body weight per group. After fasting, with free access to water sixteen hours prior to test, animals are dosed orally (1 mL) with test compounds in vehicle containing 0.5% methylcellulose and 0.025% surfactant. Control groups are dosed with vehicle alone.

[00465] One hour after dosing, a subplantar injection of 0.1 mL of 1% solution of carrageenan/sterile 0.9% saline is administered in one foot, to all animals. Three hours after carrageenan injection, rats are placed in a plexiglass container with a high intensity lamp under the floor. After twenty minutes, thermal stimulation is begun on either the injected or the uninjected foot. Foot withdrawal is determined by a photoelectric cell. The time until foot withdrawal is measured and compared between treated and control groups. The percent inhibition of the hyperalgesic foot withdrawal is calculated.

[00466] Tumor Growth Inhibition in Xenograft Mouse Model of NSCLC: Efficacy testing will be done in animal models of cancer tumors. Methods to determine tumor growth inhibition in xenograft mouse models of NSCLC are described in Williams, et al., Clin. Cancer Res. 7, 724-733 (2001)

[00467] Female HRLN nu/nu mice are injected subcutaneously with 1 x 10^7 MV-522 cells in 0.1 ml of phosphate-buffered saline. Treatment is initiated when tumors measure 5x5 mm. Mice are weighed and tumors measured by calipers twice weekly. Animals are euthanized and tumors harvested and measured after 67 days or when animal dies. Drug efficacy is measured based on animal survival and tumor growth.

[00468] Tumor Growth Inhibition in Xenograft Mouse Model of Colon Cancer: Efficacy testing will be done in animal models of cancer tumors. Methods to determine tumor growth inhibition in xenograft mouse models of colon cancer are described in Carie, et al., J. Drug Delivery 2011, 1-9 (Article ID 869027).

[00469] Female HRLN nu/nu mice are injected subcutaneously with 5 x 10^7 HT-29 cells in 0.1 ml of phosphate-buffered saline. Treatment is initiated when tumors measure 5x5mm. Mice are weighed and tumors measured by calipers twice weekly. Animals are euthanized and

tumors harvested and measured after 67 days or when animal dies. Drug efficacy is measured based on animal survival and tumor growth.

[00470] Growth Inhibition of Gallbladder Adenocarcinoma in Transgenic Mice: Efficacy testing will be done in animal models of cancer tumors. Gallbladder adenocarcinoma in transgenic mice is described in Kiguchi, et al., Mol. Cancer Ther. 6, 1709-1717 (2007).

[00471] Homozygous BK5.ErbB-2 transgenic mice, that overexpress rat ErbB-2, and nontransgenic littermates receive a control AIN76A diet or an experimental diet containing the test compound for one month. The transgenic mice develop adenocarcinoma of the gallbladder with a 90% incidence. Ultrasound image analysis and histologic evaluation are used to determine compound effects on gall bladder tumor reversion to a milder phenotype and inhibition of tumor progression.

[00472] Inhibition of Colon Cancer in Azomethane-Treated Rats: Efficacy testing will be done in animal models of cancer tumors. Colon cancer in azomethane-treated rats is described in Rao, et al., Mol. Cancer Ther. 5, 1530-1538 (2006).

[00473] Male F344 rats (Charles River Breeding Laboratories) are given test compounds blended into the diet. Efficacy of test compounds is determined following initiation of azoxymethane-induced colon cancer. Rats are randomly distributed by weight into various groups and housed in cages. Azomethane treated animals are injected subcutaneous (s.c.), twice weekly, at 15 mg/kg body weight. Vehicle-treated groups are injected with normal saline. Rats are placed on control diet or diets containing test compounds, two weeks after the second injection of azomethane or saline. Body weights are measured every two weeks until termination, 52 weeks after the last azoxymethane treatment. Organs are dissected and examined using a dissecting microscope.

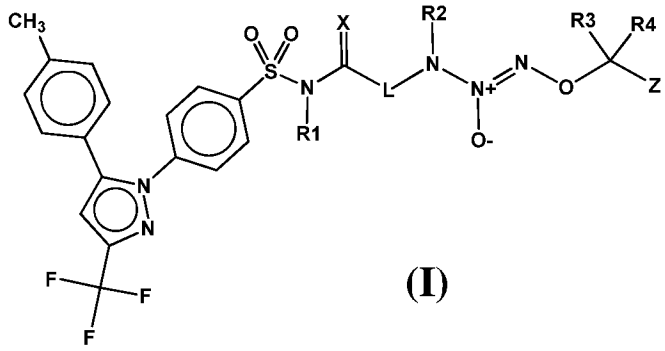
[00474] Colon tumors with a diameter of >0.4 cm are fixed in 10% neutral buffered formalin for histopathologic evaluation. Test compounds are evaluated for effect on colonocyte proliferation. Proliferating cell nuclear antigen (PCNA) expression is determined by immunohistochemistry. Paraffin-embedded colons are sectioned and mounted on slides. PCNA antibody (PharMingen, San Diego, CA), at a 1:200 dilution, is added for 1 hour. Sections are washed, then incubated with secondary anti-rabbit IgG (30 minutes). Following washing, avidin biotin-complex reagent (Vector Laboratories, Burlingame, CA) is added. Sections are washed

and 3,3″-diaminobenzidine is added and sections are counterstained with hematoxylin. Proliferation index is calculated based on the number of positive cells (brown nucleus) per crypt.

[00475] All mentioned documents are incorporated by reference as if herein written. When introducing elements of the present invention or the exemplary embodiment(s) thereof, the articles "a," "an," "the" and "said" are intended to mean that there are one or more of the elements. The terms "comprising," "including" and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements. Although this invention has been described with respect to specific embodiments, the details of these embodiments are not to be construed as limitations.

WHAT IS CLAIMED IS:

1. A compound, or pharmaceutically acceptable salt, or solvate of a compound or salt, of Formula (I):



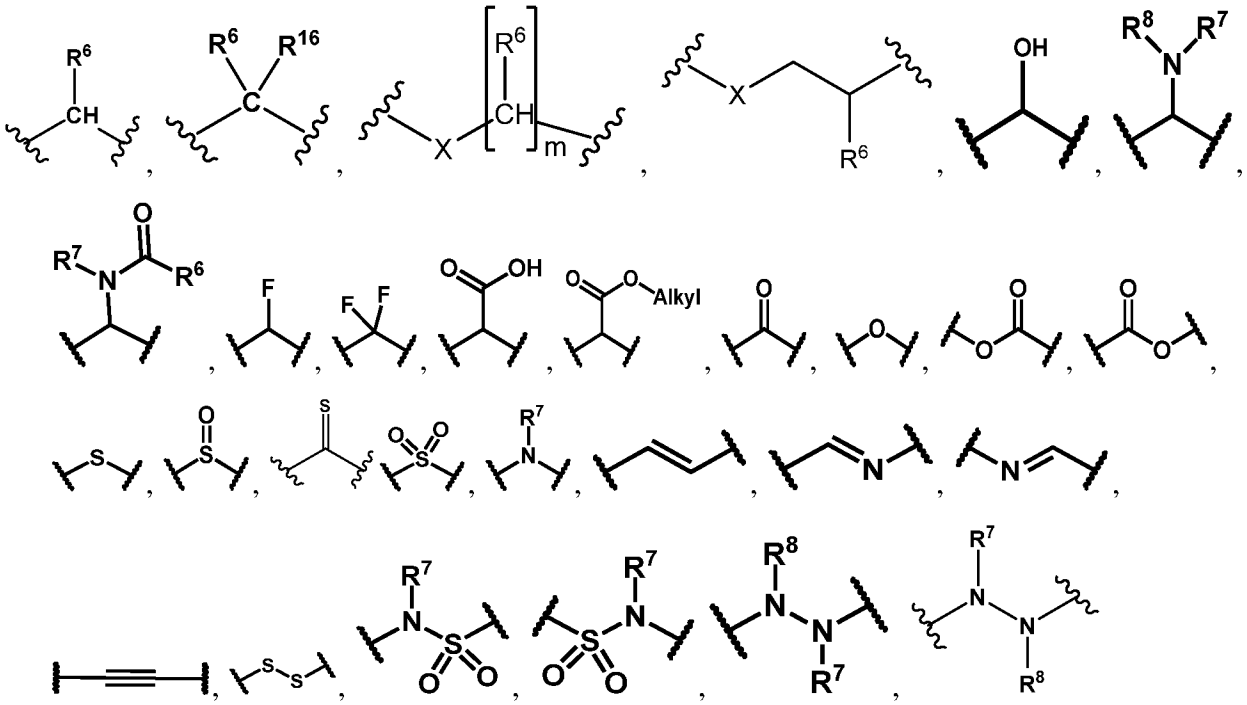
(I)

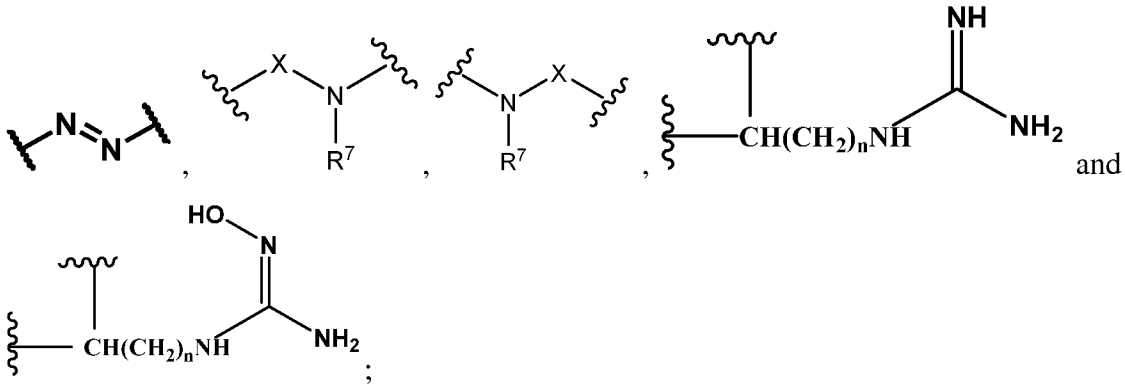
wherein:

R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-;

X is O or S;

–L– is C_{1-15} alkylene, wherein one or more $–CH_2–$ radicals are optionally replaced with a radical selected from the group consisting of:



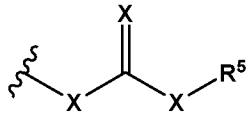


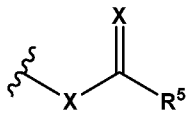
n is 0, 1, 2, 3 or 4;

m is 1, 2, 3, 4, 5 or 6;

R^2 is selected from the group consisting of H, alkyl, aryl, heterocyclyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, carboxyalkyl and hydroxyalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl, or R^3 is taken together with R^4 to form a carbocyclic ring having 3 to 7 ring atoms including optionally one or more O, N, or S atoms as ring atoms;

Z is selected from the group consisting of phthalimido, succinimido, 

and 

, wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl;

R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl;

each of R^6 and R^{16} is independently selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or each of R^6 and R^{16} is independently taken together with R^2, R^7 or R^8 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and

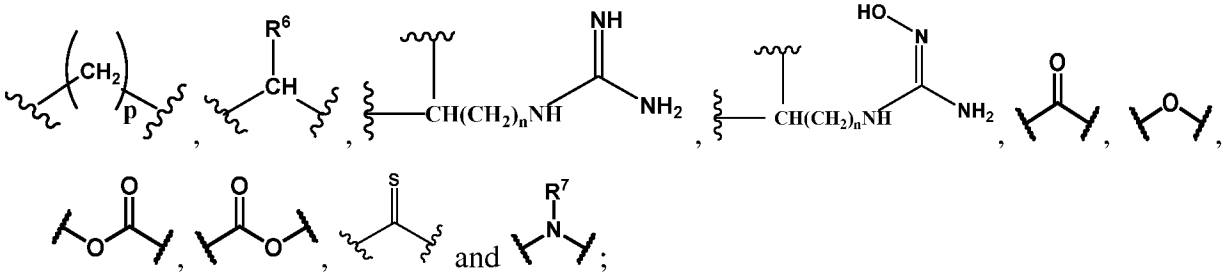
each of R^7 and R^8 is independently selected from the group consisting of H, alkyl, hydroxyalkyl, aryl, heterocyclyl, alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, carboxyalkylcarbonyl, alkyloxycarbonylalkylcarbonyl, alkylsulfonyl, arylsulfonyl and heteroarylsulfonyl, or R^7 is taken together with R^2, R^6 or R^8 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms.

2. Compound of Claim 1, wherein:

R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-;

X is O or S;

–L– is one or more radicals selected from the group consisting of:



and

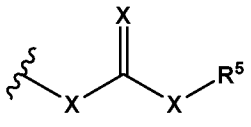
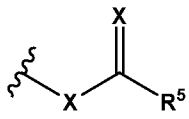
;

p is 0, 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

R^2 is selected from the group consisting of H, alkyl, aryl, heterocyclyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, carboxyalkyl and hydroxyalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is selected from the group consisting of phthalimido, succinimido,  and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl and heteroaryl;

R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl;

R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 is taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and

R^7 is selected from the group consisting of H, alkyl, hydroxyalkyl, aryl, heterocyclyl, alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, carboxyalkylcarbonyl, alkyloxycarbonylalkylcarbonyl, alkylsulfonyl, arylsulfonyl and heteroarylsulfonyl, or R^7 is

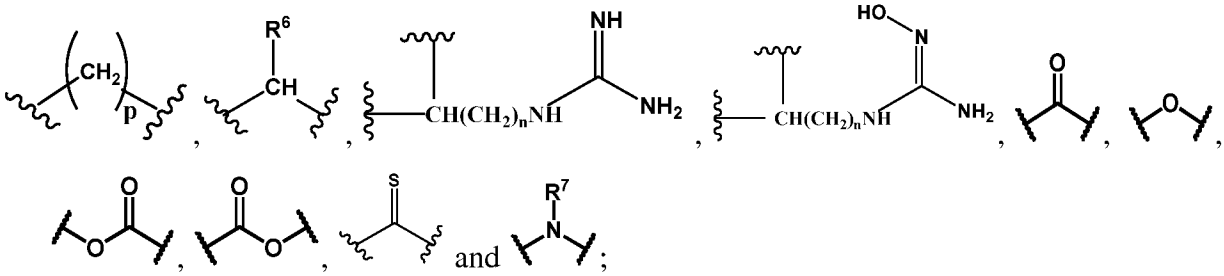
taken together with R^2 or R^6 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms.

3. Compound of Claim 2, wherein:

R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-;

X is O;

–L– is one or more radicals selected from the group consisting of:



p is 0, 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

R^2 is selected from the group consisting of H, alkyl and cycloalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is phthalimido or succinimido, wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl or heteroaryl;

R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 is taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and

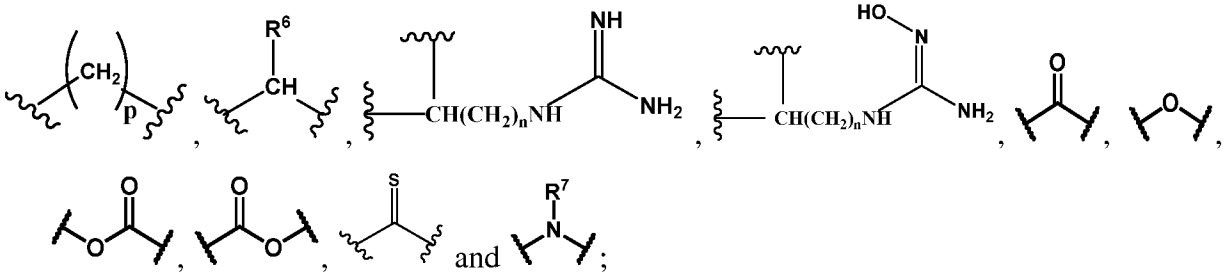
R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl.

4. Compound of Claim 2, wherein:

R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-;

X is O;

–L– is one or more radicals selected from the group consisting of:

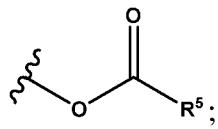


p is 0, 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

R2 is selected from the group consisting of H, alkyl and cycloalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is  ;

R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl;

R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH– , or R^6 is taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and

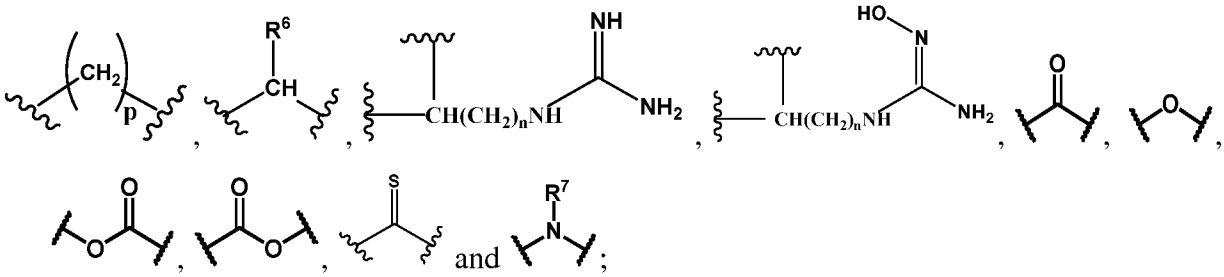
R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl.

5. Compound of Claim 2, wherein:

R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-;

X is O;

–L– is one or more radicals selected from the group consisting of:

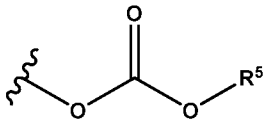


p is 0, 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

R^2 is selected from the group consisting of H, alkyl and cycloalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is  ;

R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl;

R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 is taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and

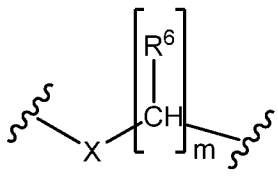
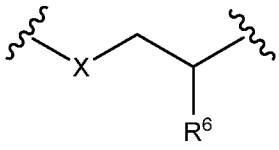
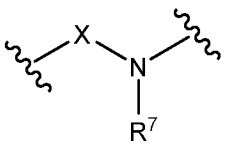
R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl.

6. Compound of Claim 1, wherein:

R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-;

X is O or S;

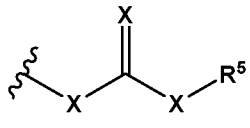
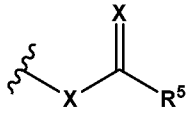
–L– is one or more radicals selected from the group consisting of:

 ,  and  ;

m is 1, 2, 3, 4, 5 or 6;

R^2 is selected from the group consisting of H, alkyl, aryl, heterocyclyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, carboxyalkyl and hydroxyalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is selected from the group consisting of phthalimido, succinimido,  and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl or heteroaryl;

R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl;

R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 is taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and

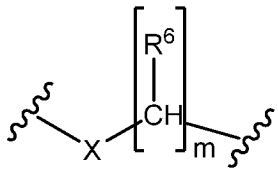
R^7 is selected from the group consisting of H, alkyl, hydroxyalkyl, aryl, heterocyclyl, alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, carboxyalkylcarbonyl, alkyloxycarbonylalkylcarbonyl, alkylsulfonyl, arylsulfonyl and heteroarylsulfonyl, or R^7 is taken together with R^2 or R^6 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms.

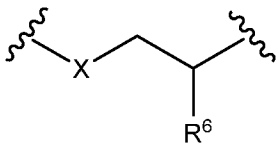
7. Compound of Claim 6, wherein:

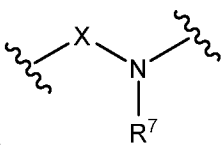
R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-;

X is O or S;

–L– is one or more radicals selected from the group consisting of:



,


, and


;

m is 1, 2, 3, 4, 5 or 6;

R^2 is selected from the group consisting of H, alkyl and cycloalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is phthalimido or succinimido, wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl or heteroaryl;

R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 is taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and

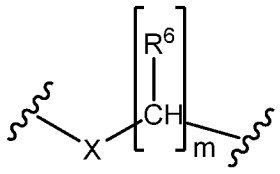
R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl.

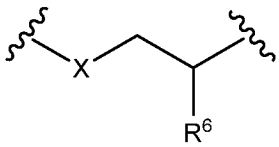
8. Compound of Claim 6, wherein:

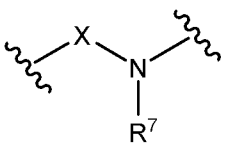
R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-;

X is O or S;

–L– is one or more radicals selected from the group consisting of:



, 

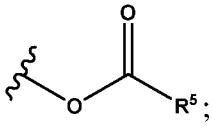
, and 

;

m is 1, 2, 3, 4, 5 or 6;

R^2 is selected from the group consisting of H, alkyl and cycloalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is 

;

R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl;

R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 is taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and

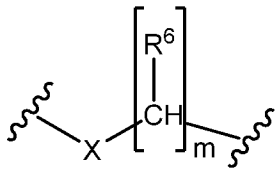
R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl.

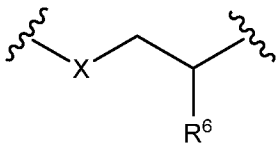
9. Compound of Claim 6, wherein:

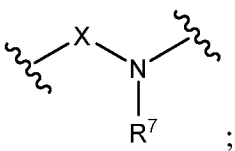
R^1 is selected from the group consisting of H, OH, alkyl and alkyl-O-;

X is O or S;

–L– is one or more radicals selected from the group consisting of:



, 

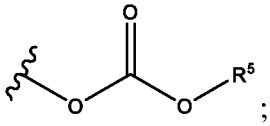
, 

;

m is 1, 2, 3, 4, 5 or 6;

R^2 is selected from the group consisting of H, alkyl and cycloalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

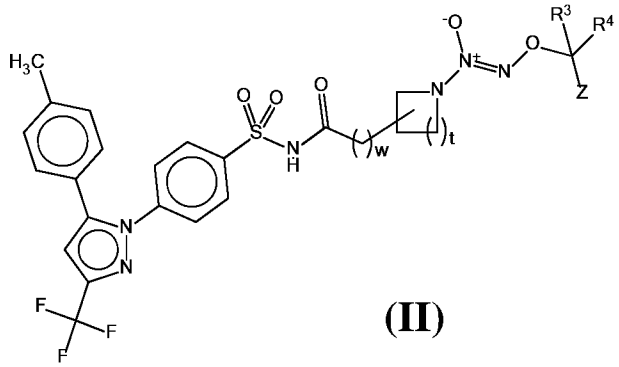
Z is  ;

R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl;

R^6 is selected from the group consisting of H, alkyl, hydroxy, aminoalkyl, acylamino, amido, carboxy, carboxyalkyl, hydroxyalkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, alkyl-O–, alkyl-S– and alkyl-NH–, or R^6 is taken together with R^2 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms; and

R^7 is selected from the group consisting of H, alkyl, aryl, alkylcarbonyl and arylcarbonyl, or R^7 is taken together with R^2 or R^6 to form a nitrogen-containing heterocyclyl ring having 3, 4, 5 or 6 ring-carbon atoms.

10. Compound of Claim 2, of Formula (II)



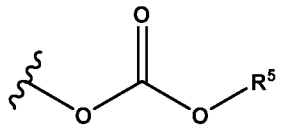
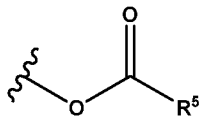
(II)

wherein:

w is 0, 1 or 2;

t is 1, 2, 3 or 4;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is selected from the group consisting of phthalimido, succinimido,  and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl or heteroaryl; and

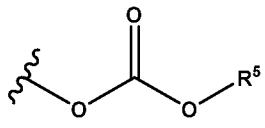
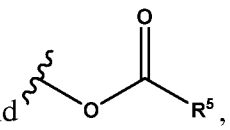
R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl.

11. Compound of Claim 10, wherein:

w is 0, 1 or 2;

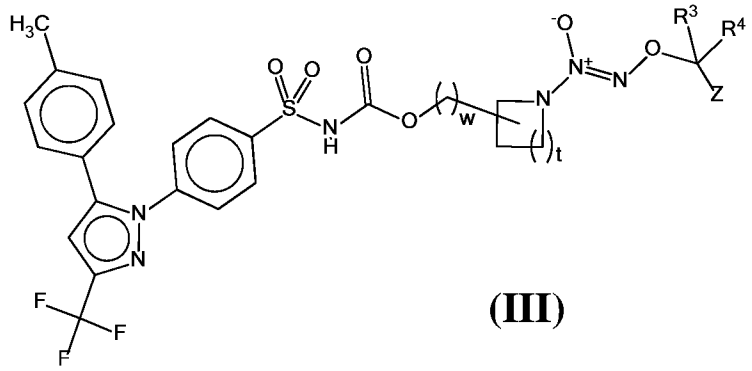
t is 1 or 2;

each of R^3 and R^4 is independently selected from the group consisting of H and alkyl;

Z is selected from the group consisting of phthalimido,  and  , wherein phthalimido is optionally substituted by halo, alkyl or alkyl-O; and

R^5 is selected from the group consisting of alkyl, phenyl and benzyl.

12. Compound of Claim 6, of Formula (III)



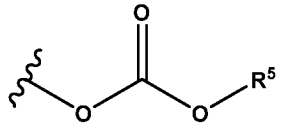
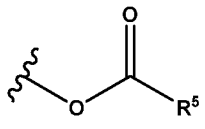
(III)

wherein:

w is 0, 1 or 2;

t is 1, 2, 3 or 4;

each of R^3 and R^4 is independently selected from the group consisting of H and alkyl;

Z is selected from the group consisting of phthalimido, succinimido,  and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl or heteroaryl; and

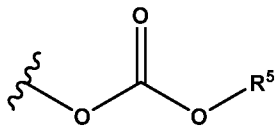
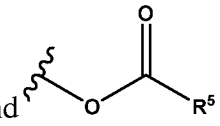
R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl.

13. Compound of Claim 12, wherein:

w is 0, 1, or 2;

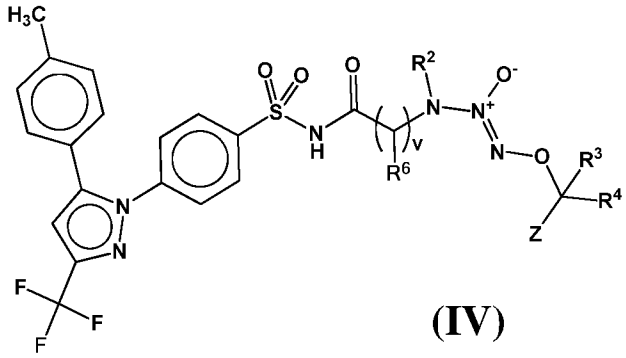
t is 1 or 2;

each of R^3 and R^4 is independently selected from the group consisting of H and alkyl;

Z is selected from the group consisting of phthalimido,  and  , wherein phthalimido is optionally substituted by halo, alkyl or alkyl-O; and

R^5 is selected from the group consisting of alkyl, phenyl and benzyl.

14. Compound of Claim 2, of Formula (IV)



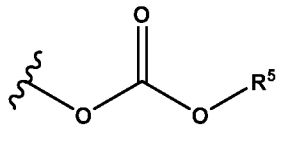
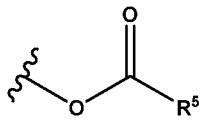
(IV)

wherein:

v is 1, 2, 3 or 4;

R^2 is selected from the group consisting of H, alkyl and cycloalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is selected from the group consisting of phthalimido, succinimido,  and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl or heteroaryl;

R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; and

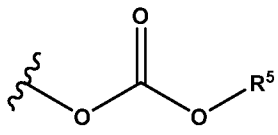
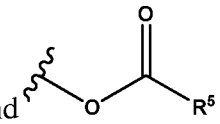
R^6 is selected from the group consisting of H, alkyl and aralkyl.

15. Compound of Claim 14, wherein:

v is 1 or 2;

R^2 is selected from the group consisting of alkyl and cycloalkyl;

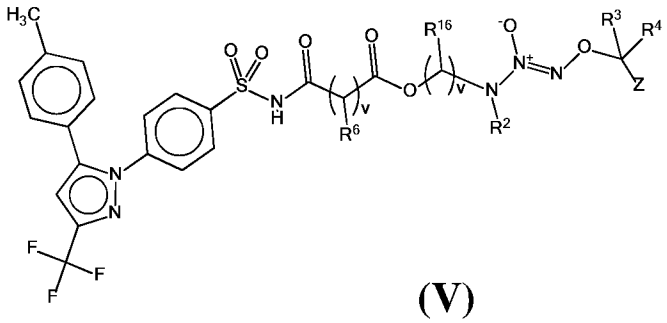
each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is selected from the group consisting of phthalimido,  and  , wherein phthalimido is optionally substituted by halo, alkyl or alkyl-O; and

R^5 is selected from the group consisting of alkyl, phenyl and benzyl; and

R^6 is selected from the group consisting of H, alkyl and aralkyl.

16. Compound of Claim 2, of Formula (V)



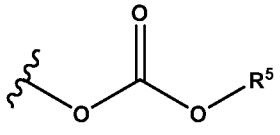
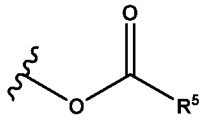
(V)

wherein:

v is 1, 2, 3 or 4;

R^2 is selected from the group consisting of H, alkyl and cycloalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is selected from the group consisting of phthalimido, succinimido,  and  , wherein phthalimido or succinimido is optionally substituted by halo, alkyl, alkyl-O, aryl or heteroaryl;

R^5 is selected from the group consisting of alkyl, aryl, heterocyclyl and aralkyl; and

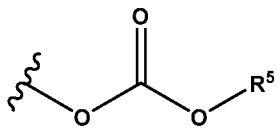
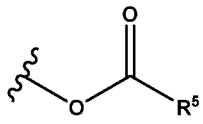
each of R^6 and R^{16} is independently selected from the group consisting of H, alkyl and aralkyl.

17. Compound of Claim 16, wherein:

v is 1 or 2;

R^2 is selected from the group consisting of alkyl and cycloalkyl;

each of R^3 and R^4 is independently selected from the group consisting of H, alkyl, aryl and heterocyclyl;

Z is selected from the group consisting of phthalimido,  and  , wherein phthalimido is optionally substituted by halo, alkyl or alkyl-O;

R^5 is selected from the group consisting of alkyl, phenyl and benzyl; and

each of R^6 and R^{16} is independently selected from the group consisting of H and alkyl.

18. Compound of Claim 7, which is selected from the group consisting of:

(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-methyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide;

(Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide;

(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-ethyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide;

(Z)-1-((1,3-Dioxoisoindolin-2-yl)methoxy)-3-isopropyl-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide; and

(Z)-3-(tert-Butyl)-1-((1,3-dioxoisoindolin-2-yl)methoxy)-3-(2-((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)ethyl)triaz-1-ene 2-oxide.

19. Compound of Claim 15, wherein the compound is (Z)-1-(1-(1,3-Dioxoisoindolin-2-yl)ethoxy)-3-methyl-3-(3-oxo-3-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)propyl)triaz-1-ene 2-oxide.

20. Compound of Claim 9, which is selected from the group consisting of:

(Z)-5-Ethyl-13-methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide;

(Z)-5-Ethyl-9,13-dimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide;

(Z)-5,9,13,13-Tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide;

(Z)-5-Ethyl-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide;

(Z)-5-Isopropyl-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide; and

(Z)-5-(tert-Butyl)-9,13,13-trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10,12-tetraoxa-5,6,7-triazatetradec-6-ene 6-oxide.

21. Compound of Claim 17, wherein the compound is (Z)-6,10-Dimethyl-4,14,17-trioxo-17-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-3,5,7,13-tetraoxa-8,9,10-triazaheptadec-8-ene 9-oxide.

22. Compound of Claim 5, which is selected from the group consisting of:

(Z)-3,7-Dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide;
(Z)-3,11-Dimethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide; and
(Z)-3,7,11,11-Tetramethyl-1,9-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-6,8,10-trioxa-3,4,5-triazadodec-4-ene 4-oxide.

23. Compound of Claim 8, which is selected from the group consisting of:
(Z)-5-Methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazadodec-6-ene 6-oxide;
(Z)-5-Methyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatetradec-6-ene 6-oxide;
(Z)-7-Methyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide;
(Z)-3,7-Dimethyl-1,11-dioxo-1-phenyl-11-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,4,10-trioxa-5,6,7-triazaundec-5-ene 6-oxide;
(Z)-5,12,12-Trimethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide; and
(Z)-5,9,12,12-Tetramethyl-1,11-dioxo-1-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)-2,8,10-trioxa-5,6,7-triazatridec-6-ene 6-oxide.

24. Compound of Claim 15, wherein the compound is (Z)-3-Methyl-3-(2-oxo-2-(4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenylsulfonamido)ethyl)-1-((pivaloyloxy)methoxy)triaz-1-ene 2-oxide.

25. Compound of Claim 13, which is selected from the group consisting of:
(S,Z)-2-((1,3-Dioxoisoindolin-2-yl)methoxy)-1-(2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide; and
(Z)-2-(1-((tert-Butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)oxy)methyl)pyrrolidin-1-yl)diazene oxide.

26. Compound of Claim 11, which is selected from the group consisting of:

(Z)-2-(1-((Ethoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide; and

(Z)-2-(1-((tert-Butoxycarbonyl)oxy)ethoxy)-1-((S)-2-(((4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)sulfonyl)carbamoyl)pyrrolidin-1-yl)diazene oxide.