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(54) **Title**: TETRAKIS(DIMETHOXYPHENYL)ADAMANTANE (TDA) AND ITS INCLUSION COMPLEXES

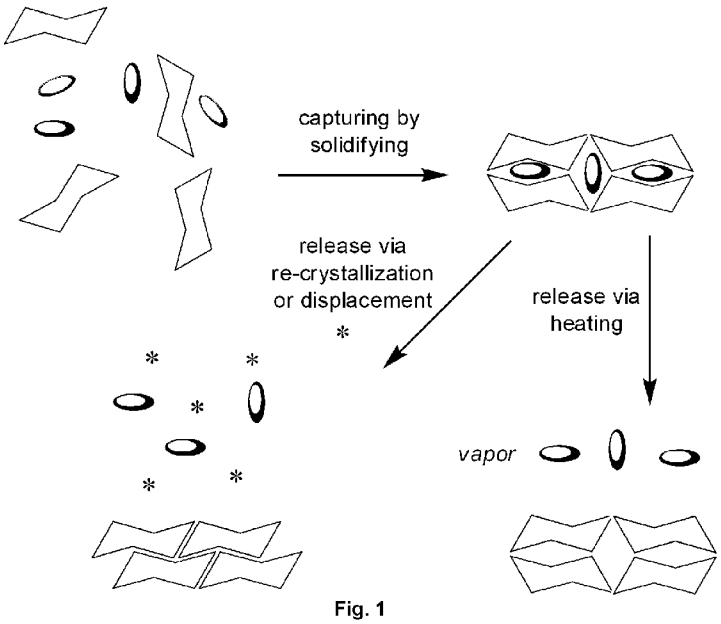

Fig. 1

(57) **Abstract**: Molecular storage materials for incorporating small molecules in solid matrices may find applications in structure elucidation, decontamination, and slow release of active ingredients. The syntheses of 1,3,5,7-tetrakis(2,4-dimethoxyphenyl)adamantane (TDA), 1,3,5,7-tetrakis(4-methoxyphenyl)adamantane, 1,3,5,7-tetrakis(4-methoxy-2-methylphenyl)adamantane, and 1,3,5,7-tetrakis(4-methoxy-2-ethylphenyl)adamantane are reported, together with details on their X-ray crystal structures. All four adamantanes crystallize readily. The octaether shows an unusual level of pseudopolymorphism in the solid state,and includes a wide range of different guest molecules in its crystal lattices. Thus far, 20 different inclusion complexes with guest molecules ranging from methanol or trifluorobenzene were characterized. Both nitromethane and benzene were taken up into inclusion materials and were shown to be released by one of three different processes.

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Description

Tetrakis(dimethoxyphenyl)adamantane (TDA) and its Inclusion Complexes

[0001] The invention is directed to tetraphenyladamantanes (TPA), inclusion compounds comprising tetraphenyladamantanes (TPA) as host molecule and the use of such inclusion complexes.

Technical Field

[0002] Developing molecular materials from organic molecules that have the ability to act as host for small molecule ligands is a challenge (J. D. Wuest, *Chem. Commun.***2005**, 5830). The uptake of guest molecules is usually facilitated by the formation of networks of the host molecules (W. Lu, D. Yuan, D. Zhao, C. Schilling, O. Plietzsch, T. Muller, S. Bräse, J. Guenther, J. Blümel, R. Krishna, Z. Li, and H.-C. Zhou, *Chem. Mater.***2010**, *22*, 5964 and H. Zhao, Z. Jin, H. Su, J. Zhang, X. Yao, H. Zhao and G. Zhu, *Chem. Commun.* **2013**, *49*, 2780).

[0003] Crystalline or amorphous organic materials reported in the literature that have the ability to incorporate guest molecules include organic cages (M. Mastalerz, *Chem. Eur. J.***2012**, *18*, 10082), porous aromatic frameworks (PAF; T. Ben, H. Ren, S. Ma, D. Cao, J. Lan, X. Jing, W. Wang, J. Xu, F. Deng, J. M. Simmons, S. Qiu, and G. Zhu, *Angew. Chem. Int. Ed.***2009**, *48* , 9457), but also porous polymer networks (PPN, D. Yuan , W. Lu , D. Zhao, and H.-C. Zhou, *Adv. Mat.***2011**, *23*, 3723) and porous organic frameworks (POF; A. P. Katsoulidis and M. G. Kanatzidis, *Chem. Mat.* **2011**, *23*, 1818).

[0004] Among the guest molecules that have been studied are gases, and the host molecules are often rigid, with aromatic and/or aliphatic rings in their structure (G. Zhang, and M. Mastalerz, *Chem. Soc. Rev.* **2014**, *43*, 1934)

[0005] Among the ring systems of hosts, the adamantane scaffold is prominent, because it combines rigidity with the ability to form diamondoid structures (V. R. Reichert and L. J. Mathias, *Macromolecules***1994**, *27*, 1030; V. R. Reichert and L. J. Mathias, *Macromolecules***1994**, **27**, 7015).

[0006] Branched adamantane derivatives are known to form molecular assemblies with an ability to act as hosts for small molecules (O. Ermer, *J. Am. Chem. Soc.***1988**, *110*, 3747; E. Galoppini and R. Gilardib, *Chem.*

*Commun.*1999, 173).

[0007] Further, covalent hybrids of oligonucleotides with tetrakis-(hydroxybiphenyl)adamantine (C. I. Schilling, O. Plietzsch, M. Nieger, T. Muller and S. Bräse, *Eur.J. Org. Chem.*2011, *9*, 1743; O. Plietzsch, C. I. Schilling, M. Tolev, M. Nieger, C. Richert, T. Muller, S. Bräse, *Org. Biomol. Chem.*2009, *7*, 4734) or tetrakis(triazolylphenyl)adamantane (A. Singh, M. Tolev, M. Meng, K. Klenin, O. Plietzsch, C. I. Schilling, T. Muller, M. Nieger, S. Bräse, W. Wenzel and C. Richert, *Angew. Chem. Int. Ed.*2011, *50*, 3227) have been reported.

[0008] Upon hybridization of short DNA arms of the sequence 5'-CG-3', such hybrids form nanoporous materials from aqueous buffers when treated with divalent cations. The materials thus generated take up salts and intercalators, suggesting that they are indeed porous (A. Singh, M. Tolev, C. I. Schilling, S. Bräse, H. Griesser and C. Richert, *J. Org. Chem.*2012, *77*, 2718; . Griesser, M. Tolev, A. Singh, T. Sabirov, C. Gerlach and C. Richert, *J. Org. Chem.*2012, 77, 2703; A. Schwenger, C. Gerlach, H. Griesser and C. Richert, *J. Org. Chem.*2014, *79*, 11558).

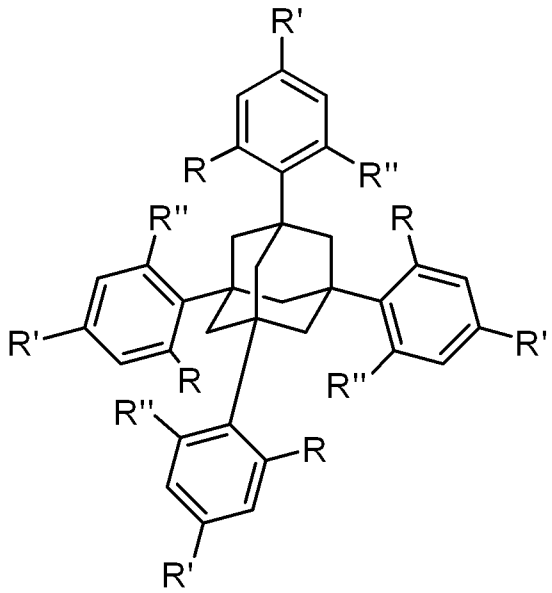
[0009] It would be beneficial to have access to tetrasubstituted adamatanes, which can be used as hosts for molecular storage of guest molecules when in the solid state.

Disclosure of Invention

[0010] It was found that some substituted tetraphenyladamantanes (TPAs), like 2,4 methoxy-substituted tetraphenyladamantanes can act as a host for small molecules (guests) by incorporating the guest compounds in their solid state. The ability of TPA to crystallize in different forms enables TPAs to act as host for a wide range of different guest molecules, which makes TPAs useful for molecular storage and release.

[0011] Surprisingly, the formation of inclusion complexes with TPAs is selective, as some molecules are easily included in its crystal structure while others, having a different chemical structure are not.

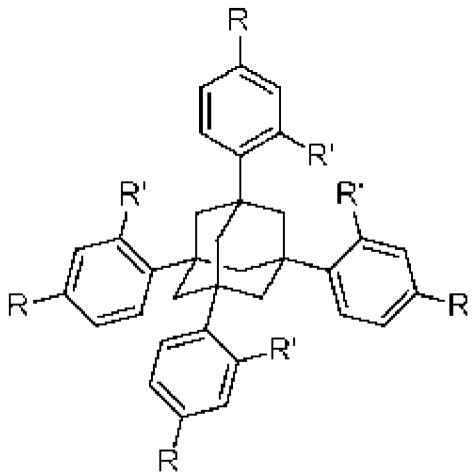
[0012] Object of the invention are tetraphenyladamantanes (TPA) according to formula I,



(Formula I),

[0013] wherein R, R', and R" are same or different residues selected from the group H, O-R1, S-R1, NHR1, NR1R2 or halogen with R1, R2 same or different substituted or unsubstituted, aliphatic or aromatic residues with 1 to 25 carbon atoms, alkyl residues with 1 to 25 carbon atoms, wherein at most one residue R, R', or R" stands for H.

[0014] In a preferred embodiment, the tetraphenyladamantanes (TPA) according to the invention have the formula II,



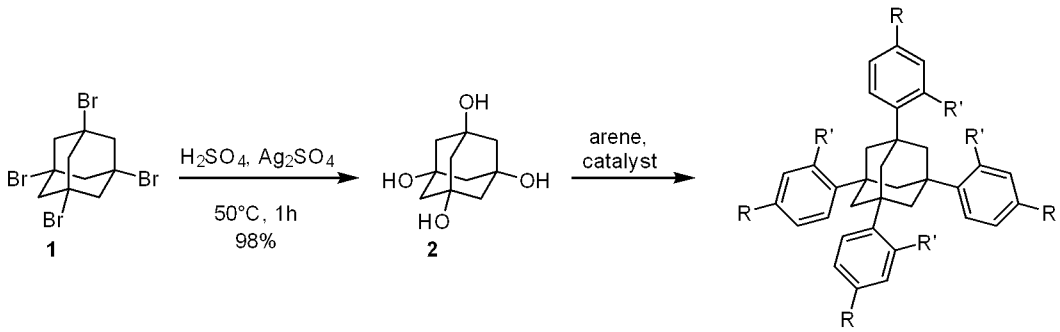
(Formula II)

[0015] wherein R and R' are same of different residues selected from the group O-R1, S-R1, NHR1, NR1R2 or halogen (F, Cl, Br, I) with R1, R2 same or

different substituted or unsubstituted, aliphatic or aromatic residues with 1 to 25 carbon atoms and alkyl residues with 1 to 25 carbon atoms. Preferrable, R, R' and/or R'' are methoxy groups.

[0016] The general synthesis of tetraphenyladamantanes according to the invention follows scheme 1 and is disclosed in more detail in the examples. The materials disclosed in this application are numbered according to table 1 and 2, wherein materials **4-6** are comparative examples not according to the invention.

[0017]



Scheme 1. Synthesis of tetrasubstituted adamatanes

Inclusion materials of tetraphenyladamantanes with a guest compound

[0018] Another object of the invention are inclusion materials comprising tetraphenyladamantanes as defined above as host compound and at least one substituted or unsubstituted, aliphatic, cycloaliphatic or aromatic organic guest compound. In a preferred embodiment, the organic guest compound does not contain carboxylic and/or amino groups. For example, the guest compound may be substituted with halogen (F, Cl, Br, I) or an hydroxyl group. Preferable, the guest molecules have a lower molecular weight than the host molecule.

[0019] Suitable organic guest compound are selected from the group consisting of acid chlorides, dichloromethane, chloroform, cyclohexane, n-hexane, ethanol, 2-propanol, 2-methyl-2-butanol, 2-butanol, acetonitrile, acetone, benzene, trifluorobenzene, nitrobenzene, nitromethane, pyridine, N,N-dimethylformamide, toluene, piperidine, styrene, 2,3,5-trimethylpyrazine, trimethylphosphate, anisole, N,N-dimethylaniline, dimethylsulfoxide, dioxane, morpholine, 1-vinylimidazole, pyrrolidine,

xylenes, tetrahydrofuran, fufural, di-tert-butylmethylphosphine, benzyl chloride and trimethylsilyl chloride.

[0020] Acid chlorides are for example benzoylchloride, acetylchloride, phosphoryl chloride, phosgene, thionyl chloride, sulfuryl chloride, methanesulfuryl chloride, and oxalyl chloride.

[0021] The term “inclusion material” refers to any solid material wherein the host compound absorbs or embeds a guest compound to form a macroscopic solid material. For example, the guest compound may be embedded in the crystalline lattice of the host compound. The embedded guest compound may form another crystalline lattice or may be in a disordered/amorphous state. Inclusion materials according to the invention may be overall crystalline, or only crystalline in view of the host compound.

[0022] The terms “inclusion material”, “inclusion complex”, ”inclusion compound”, or “pseudopolymorphism” are used as synonyms in this application. The term is not limited to single crystals of the material, but also to partially crystalline or microcrystalline solids or powders, as long as the host compound forms a molecular or crystalline lattice.

[0023] The term “forming an inclusion material” refers to the process of producing such materials, for example by providing an favorable environment for crystallization like cooling, evaporation of solvent, addition of precipitant, change in pH, or change in solvent composition.

[0024] In contrast to compounds 4-6, adamantane 3 with its four dimethoxyphenyl substituents shows a strong propensity to include guest molecules in its crystals. So far, a total of 20 different inclusion complexes have been found for this compound, as well as two crystal structures that do not show guest molecules, obtained when 3 was crystallized from acetic acid or aniline (entries No. 4 and 22 in table 1 and 2).

[0025] Some inclusion complexes of TDA like compound 3 were obtained by crystallizing the octaether from specific solvents. X-ray crystal structures were then solved. Fifteen of the structures of 3 were monoclinic, whereas eight were tricilinic, including two structures lacking small molecules as inclusion guests. The monoclinic structures showed inclusion of molecules as different as dichloromethane, cyclohexane, acetonitrile, nitrobenzene,

and acetone. In many cases, the guest molecules were well ordered (see entries 5-7, 10-11, 13-20 and 23 in table 1), whereas disordered guests were identified by X-ray crystallography in the materials obtained from crystallization in media such as CH_2Cl_2 or $CHCl_3$ with alcohols like ethanol, 2-propanol, or n-propanol as co-solvents (entries 8-9 and 12 in table 1).

[0026] For example, cyclohexane as guest compound was incorporated in solids of 3 at a molar ratio of 1:1 (entry 7 of table 1). In this case, a large volume of the unit cell and a large asymmetric unit were found. The crystallization with n-hexane (entry No. 6 in table 1) showed inclusion of the linear alkane at a ratio of 4:1 (3: n-hexane), and the crystal structure showed small unit cells. This demonstrates the degree of flexibility in the crystal packing of TDA and the molecular recognition of small molecules in materials formed. When a mixture of halogenated solvents like dichloromethane or chloroform with alcohols like ethanol or propanol was used, X-ray structures showed crystals including a mixture of two solvents.

[0027] The observation mentioned above show how avidly TDA takes up organic guest molecules, and its ability to form a promiscuous set of pockets for inclusion of guests.

Uptake and Release of guest compounds

[0028] The detection (Z. Takàts, I. Cotte-Rodriguez, N. Talaty, H. Chen, and R. G. Cooks, *Chem. Commun.***2005**, *15*, 1950; T. Naddo, Y. Che, W. Zhang, K. Balakrishnan, X. Yang, M. Yen, J. Zhao, J. S. Moore, and L. Zang, *J. Am. Chem. Soc.***2007**, *129*, 6978) and removal (J. D. Rodgersa, N. J Bunce, *Water Res.***2001**, *35*, 2101) of combustible compounds and explosives are important challenges that require molecular solutions. Some unstable compounds, such as acetylene, have to be stored in porous materials to render them safe for transport and use. For other compounds, such matrices are still lacking.

[0029] It is therefore important that the range of small molecules incorporated in the crystal lattices of TDA included aromatic compounds with electron-withdrawing substituents, for example trifluorobenzene and nitrobenzene. Nitroarenes are a class of compounds that includes several

explosives. Several small aliphatic nitro compounds are also explosives, including nitromethane (J. M. Schnorr, D. van der Zwaag, J. J. Walish, Y. Weizmann, T. M. Swager, *Adv. Funct. Mat.* **2013**, *23*, 5285).

[0030] Liquid nitromethane is also used as solvent (W. Hofman, L. Stefaniak, T. Urbanski, M. Witanowski, *J. Am. Chem. Soc.* **1964**, *86*, 554), making it a good example for uptake and release by compound **3**. Nitromethane is also known for its role in the production of rocket propellants, explosive materials (S. A. Koldunov, A. V. Ananin, V. A. Garanin, V. A. Sosikov and S. I. Torunov, *Central European Journal of Energetic Materials* **2009**, *6*, 1), and as additive for high performance fuel of automotive engines. We studied uptake of nitromethane into TDA crystals and avenues for its controlled release. Fig. 1 shows proposed regimes. As a first step, the uptake of nitromethane via crystallization of **3** was studied.

[0031] In order to identify conditions that allow the recovery of **3** after acting as storage material for a small molecule as guest, solvent were screened that have the potential to act as release agent for the guest compound. Therefore, mixtures of nitromethane and different solvents (1:1, *v/v)* were screened for the ability to induce crystallization of **3**, including methanol, ethanol, toluene, and 1,2-dichloroethane. After adding TDA, heating to obtain a clear solution, and cooling, samples were examined for crystals.

[0032] Larger volumes of toluene and 1,2-dichloroethane gave no solids. But, both methanol and ethanol induced crystallization. When the mother liquors and the crystals were examined by NMR, peak integrals indicated that methanol is a release agent for nitromethane.

[0033] Accordingly, another object of the invention is a process for depleting a target compound from a mixture comprising a target compound and at least one non-target compound by forming an inclusion material comprising of at least a part of the target compound as guest compound with tetraphenyladamantanes as defined above as host compound.

[0034] A first embodiment of this process can be characterized by steps a) to c) with a) providing the mixture as solution in a solvent or as liquid mixture, b) adding the host compound in solid form, suspension or as solution and c) forming an inclusion material comprising the host compound and at least a

part of the guest compound.

[0035] In a second embodiment of this process, in step a) a first inclusion material comprising tetraphenyladamantanes as defined above is provided as host compound and at least one substituted or unsubstituted, aliphatic, cycloaliphatic, or aromatic organic compound is provided as first guest compound, in step b) the mixture is provided as solution in a solvent or as liquid mixture to which c) the first inclusion material is added and d) the forming an second inclusion material comprising of the host compound and at least a part of the target compound is initiated.

[0036] Figure 2 shows ^{1}H-NMR spectra from solutions and materials of crystallization experiments with TDA and a mixture of MeOH and nitromethane, recorded in $CDCl_3$ (300 MHz). Figure 2a shows a spectrum of the mixture of the two solvents (1:1). Figure 2b shows a spectrum of the mother liquor of the crystallization experiment with TDA and the 1:1 (*v/v*) mixture of the two solvents. Figure 2c shows a solution generated by dissolving the crystalline material obtained from the crystallization in $CDCl_3$. Little nitromethane is found in the solid material of **3** formed under these conditions, making methanol suitable for the release of nitromethane as guest and recovery of the host (TDA).

[0037] Crystallization of ethanol led to the incorporation of both nitromethane and the alcohol at a ratio of approx. 2:1, but, as described above, methanol induced the crystallization of **3** in essentially guest-free form. Just 14 mol % of nitromethane were found in the sample (Figure 2). MeOH was not detectable in the NMR spectrum of the crystalline material dissolved in $CDCl_3$ (Figure 2c), and the loss of nitromethane in the mother liquor over the starting mixture confirmed the ability of MeOH to capture a large fraction of the explosive and to induce the crystallization of **3**.

[0038] Experiments were also performed with 1:1 mixtures of other solvents. A mixture of glacial acetic acid and toluene gave inclusion material containing 0.8 equiv of toluene and just traces of AcOH, confirming that TDA did not include the carboxylic acid. A mixture of acetic acid and cyclohexane showed predominant inclusion of C_6H_{12}, but mixtures of ethanol/benzene and methanol/benzene gave benzene as the only guest

molecule detectable. Up to 2.23 equivalents of benzene were taken up from the mixture with ethanol, as determined by NMR analysis of crystals obtained. The crystal structure of the material harvested from the mixture of ethanol and benzene is given as entry 23 in Table 1. The X-ray structure obtained with a mixture of MeOH/C_6H_6 was almost identical in its crystal details. Since benzene was taken up very selectively from a mixture, this suggests that alcoholic solutions of TDA can be used for decontaminating samples polluted with benzene.

[0039] A third embodiment of the process can be characterized in step a) providing a first inclusion material comprising tetraphenyladamantanes as defined above as host compound and at least one substituted or unsubstituted, aliphatic, cycloaliphatic,or aromatic organic compound as first guest compound, b) providing the mixture as solution in a solvent or as liquid mixture, c) adding the first inclusion material to the mixture and d) and initiate forming an second inclusion material comprising of the host compound and at least a part of the target compound.

[0040] In a forth embodiment, the guest compounds can be released from the inclusion material, by separating the inclusion material from the mixture and releasing at least a part of the target compound from the inclusion material by thermal treatment like keeping for at least 5 min at a temperature of at least 50°C or by exposure to air at 25 °C for at least 6 hours. In a variant of the invention, the guest compounds can be released from the inclusion material by applying reduced pressure like at most 100 mbar at 25 °C for at least 5 minutes.

[0041] In addition or in alternative, the inclusion material can be separated from the mixture and at least a part of the target compound is released from the inclusion material by dissolving inclusion material in an organic solvent

[0042] In another variant of the process, a release mechanism was established for inclusion materials containing benzene. This can be achieved by displacing benzene with chloroform at room temperature which occurs without loss of crystallinity. In one example, crystals obtained from a mixture of ethanol and benzene (1:1, *v/v*) were harvested, washed with water, and cyclohexane and immersed in chloroform. After 24 h, a crystal

was collected whose X-ray crystal structure showed a combination of well-ordered benzene and chloroform molecules together with crystal sites partially occupied by either of the two solvents in the unit cell. After an additional day of exposure to chloroform, a crystal harvested from the same sample showed two strongly disordered chloroform molecules only and no residual benzene. The displacement of the benzene as guest occurred without visible loss of crystallinity.

[0043] Accordingly, the process of the invention may further be characterized in separating a first inclusion material from the mixture and releasing at least a part of the target compound from the first inclusion material by forming a second inclusion material with a second guest compound displacing at least a part of the target compound.

[0044] Without being bound to the following theory, it is suggested that a combination of porosity of the lattice and conformational flexibility of TDA molecules in the solid state allows for the level of structural diversity found in its unit cells. The chloroform molecules may displace benzene guests without breaking down crystalline order. This is confirmed by the observation that the chloroform guests were less well ordered in the final structure than in the crystal structures obtained from chloroform as only a crystallization solvents. The fact that benzene can be released from inclusion complexes of **3** at room temperature without fully dissolving it show that TDA materials are capable of capture and release.

[0045] It was furthermore found that TDA is capable of capturing small molecules even from the case phase. It is another object of the invention to provide a process for depleting a target compound from a gaseous mixture comprising a target compound and at least one non-target compound by forming an inclusion material comprising tetraphenyladamantanes as disclosed as host compound and at least a part of the target compound as guest compound. The gaseous mixture can for example originate from industrial processes or air which is contaminated with toxic or hazardous gases, like phosgene, benzene or pyridine. The capability of TDA to absorb small molecules can be further enhanced by absorbing the tetraphenyladamantanes at or on a porous matrix like activated charcoal

or silica.

Industrial Applicability

[0046] On the level of possible applications, it is noteworthy that the uptake properties of TDA can be tuned by adding an inexpensive and largely harmless solvent, like an alcohol, and inducing recrystallization or by adding a second solvent as displacement compound to release a first guest compound included in the material. As shown by the example, suitable for displacement of a first guest compound without heating are organic solvents like a halogenated solvent. This shows that TDA can be used to absorb toxic or unstable small molecules that are later released by treating with another solvent, and the TDA being recovered for subsequent usage.

[0047] Thus, another object of the invention is the use of tetraphenyladamantanes (TDA) as defined above as host compound for forming inclusion materials with reactive, explosive, toxic, environmentally harmful or flammable guest compounds like nitromethane or benzene.

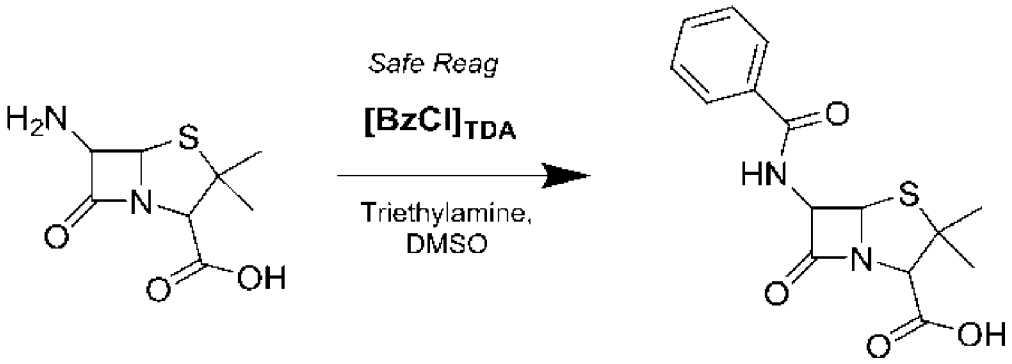
[0048] Therefore, TDA may become useful to safely ship small molecules in inclusion materials, and later releasing toxic or explosive small molecules, such as nitromethane in a number of different ways.

[0049] Another application of TDA and/or inclusion materials of TDA as disclosed is as carrier for a guest compound in chemical reactions between the guest compound and at least one reactive compound wherein the inclusion material and least one reactive compound are provided as mixture in an organic solvent. This process is especially advantageous for compounds which are in pure form or in solution unstable or hazardous, but can be incorporated as guest compound in the crystal lattice of TDA to provide an inclusion material. In form of the inclusion material, such unstable or hazardous compounds are stabilized and/or can be handled in a save and easy manner. When dissolved in organic solvent, the guest compound is released and can undergo a chemical reaction with another reactive compound. The product of the reaction of the guest compound of the inclusion material remains in solution while at least part of the tetraaryladamantane precipitates.

[0050] Fig.3 shows this schematically the proposed process: an inclusion material comprising TDA and a guest compound is provided to an organic solvent together with a reactive compound. The guest compound reacts with the reactive compound and forms a compound and the “free” TDA (without guest molecule) can be isolated or precipitated from the mixture.

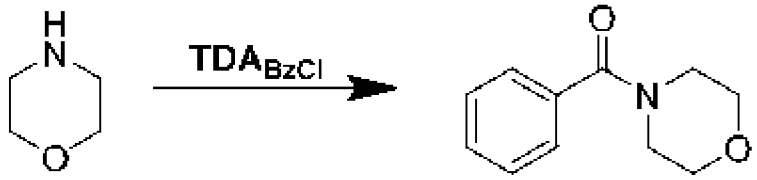
[0051] For example, by forming an inclusion material of an acid chloride and TDA, and exposing the inclusion material to 6- aminopenicillanic acid under basic conditions, penicilin can be obtained without the hazards of handling acid chlorides.

[0052]



[0053] In another example for the use of TDA as carrier for a guest compound, N-benzoylmorpholine can be obtained via an inclusion material comprising benzoylchloride.

[0054]



Examples

[0055] The general synthesis was performed according to Scheme 1.

[0056] NMR spectra were recorded on a Bruker *AVANCE 300* spectrometer. Chemical shifts (δ values) are in parts per million (ppm) relative to

tetramethylsilane (TMS, 0 ppm) as internal standard or residual solvent peaks; coupling constants (J) are given in Hertz (Hz). Mass spectra were obtained on a Varian MS MAT 311A spectrometer in EI mode. The following starting materials were synthesized according to literature procedures: 1,3,5,7-tetrabromoadamantane (**1**) (H. Stetter, C. Wulff, *Chem. Ber.***1960**, *93*, 1366) and 1,3,5,7-tetrahydroxyadamantane (**2**) (H. Stetter, M. Krause, *Liebigs Ann. Chem.***1968**, *717*, 60)

1,3,5,7-Tetrakis(2,4-dimethoxyphenyl)adamantane (3).

[0057] In a 10 mL flask combined with a Dean-Stark apparatus a mixture of 2 (20 mg, 0.1 mmol, 1 eq.), 1,3-dimethoxybenzene (1.5 mL) and *p* -toluenesulfonic acid (9.5 mg, 0.05 mmol, 0.5 eq.), , was heated to 140°C for 96 h. After the reaction, the solvent was evaporated in vacuo. Then, the crude product was co-evaporated methanol (4 x a 3-5 mL). The resulting residue was dissolved in CH_2Cl_2 (40 mL) washed with a saturated aqueous solution of $NaHCO_3$ (50 mL), HCl (50 mL, 2M) and H_2O (50 mL), dried over Na_2SO_4, filtered, and subsequently evaporated *in vacuo*. The resulting dark brown crude product was dissolved in CH_2Cl_2 and filtered through a short silica gel pad, by eluting first petroleum ether (200 mL) and then CH_2Cl_2 / petroleum ether (3:1, *v/v*, 300 mL). The second fraction was concentrated under reduced pressure. Purification *via* column chromatography (silica gel, petroleum ether / CH_2Cl_2 1:4, *v/v*) yielded 26 mg (0.04 mmol, 38%) of 1,3,5,7-tetrakis(2,4-dimethoxyphenyl)adamantane (**3**) as a white solid: R_f = 0.22 (petroleum ether / CH_2Cl_2, 1:3, *v/v*). ^1H NMR (300 MHz, $CDCl_3$): δ =7.28 (d, *J* = 8.4 Hz, 4H), 6.48-6.44 (m, 8H), 3.78 (s, 12H), 3.77 (s, 12H), 2.41 (s, 12H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 159.8, 158.8, 131.1, 127.2, 103.3, 99.7, 55.2, 55.0, 42.8, 39.0 ppm. MS (70 eV, EI) 680/681/682/683 (M^+); HRMS m/z calcd for $C_{42}H_{48}O_8$ 680.335, found 680.334.

1,3,5,7-Tetrakis(4-methoxyphenyl)adamantane (4).

[0058] In a 10 mL vial was placed 2 (50 mg, 0.25 mmol, 1 eq.), anisole (1 mL), andTfOH (11 µL, 0.12 mmol, 0.5 eq.),. After that the mixture was heated to 120°C for 20 h in a Dean–Stark apparatus. After aqueous work up as described for compound **3**, followed by a purification via column

chromatography (silica gel, petroleum ether / CH_2Cl_2 1:1, *v/v*) yielded 54 mg (0.096 mmol, 39%) of 1,3,5,7-tetrakis(4-methoxyphenyl)adamantane (**4**) as a colorless solid: R*f* = 0.28 (petroleum ether / CH_2Cl_2 1:1, *v/v*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 8.7 Hz, 8H), 6.88 (d, *J* = 9Hz, 8H), 3.84 (s, 12H), 2.80 (s, 12H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 157.7, 141.8, 126.0, 113.6, 55.2, 47.7, 38.6 ppm. MS (FAB, 3-NBA) 560, 561, 562 (M^+); HRMS m/z calcd for $C_{38}H_{40}O_4$ 560.293, found 560.293.

1,3,5,7-Tetrakis(4-methoxy-2-methylphenyl)adamantane (5).

[0059] A mixture of 2 (75 mg, 0.37 mmol, 1 eq.), 3-methylanisole (3 mL), and *p* -toluenesulfonic acid (35.6 mg, 0.18 mmol, 0.5 eq.) was heated to 130°C for 72 h in a Dean–Stark apparatus. After aqueous work up as as described above , the resulting dark brown crude product was treated in an ultrasonic bath with MeOH (10 mL), and the slurry was centrifuged. This purification step was repeated two times, and the title compound **5** was isolated as an off-white/gray solid, yield 94.7 mg (0.165 mmol, 41%): R*f* = 0.41 (petroleum ether / CH_2Cl_2, 2:1, *v/v*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 7.9 Hz, 4H), 6.76-6.70 (m, 8H), 3.77 (s, 12H), 2.45 (s, 12H), 2.32 (s, 12H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 158.7, 136.6, 135.5, 126.7, 120.8, 112.5, 54.9, 42.4, 39.2, 21.1 ppm. MS (70 eV, EI) 616/617/618/619 (M^+); HRMS m/z calcd for $C_{42}H_{48}O_4$ 616.355, found 616.356.

1,3,5,7-Tetrakis(4-methoxy-2-ethylphenyl)adamantane (6).

[0060] In a 10 mL vial was placed 2 (35 mg, 0.17 mmol, 1 eq.), and 3-ethylanisole (0.61 mL), and *p*-toluenesulfonic acid (16.6 mg, 0.09 mmol, 0.5 eq). Thereafter, the mixture was heated to120°C for 48 h in a Dean–Stark apparatus. After aqueous work up as described above , the resulting solid was treated with MeOH (5 mL) in an ultrasonic bath. After centrifugation, the supernatant was discarded. This washing step was repeated for two times. The title compound (**6**) was isolated in 34 mg (0.05 mmol, 30%) yield as a colorless solid: R*f* = 0.51 (petroleum ether / CH_2Cl_2, 2:1, *v/v*). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.30 (d, *J* = 7.8 Hz, 4H), 6.79-6.72 (m, 8H), 3.79 (s, 12H), 2.63 (q, *J* = 7.6 Hz, 8H,), 2.470 (s, 12H), 1.24 (t, *J* = 7.5 Hz, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8, 142.9, 135.7, 126.7,

119.4, 111.4, 54.9, 42.4, 39.3, 28.5, 15.3 ppm. MS (70 eV, EI) 672/673/674/675 (M^+); HRMS m/z calcd for $C_{46}H_{56}O_4$ 672.418, found 672.418.

Inclusion complex obtained by crystallization from a single solvent

[0061] To a sample of TDA (10-30 mg, 15-44 µmol) which was previously placed in a crystallizer vessel, 100-300 µL of a solvent as listed in Table 1 was added and heated until a homogeneous solution formed. The sample was cooled first slowly and then stored at 4 °C for 1-2 d to induce near-complete crystallization.

[0062] The sample was then centrifuged and the supernatant was removed. The crystals were washed twice with water (600 µL) and once with cyclohexane (600 µL), including centrifugation and discarding of the supernatant.

Analysis

[0063] Crystals were harvested and subjected to X-ray crystallography and NMR analysis by dissolving them in a deuterated solvent, like $CDCl_3$ (0.45 mL), and measuring ^{1}H-NMR spectra of the resulting solution.

[0064] Inclusion complex obtained by crystallization from mixture of solvents

[0065] A sample of TDA (10-30 mg, 15-44 µmol) was transferred into a crystallization vessel thereupon, 100-300 µL of a mixture of a solvents as listed in Table 1 (like benzene : EtOH or MeOH, 1:1, *v/v*) was added and then heated until a homogeneous solution formed. The sample was then cooled slowly and subsequently stored at 4 °C for 1-2 d to induce near-complete crystallization.

[0066] The vessel was then centrifuged and the supernatant was removed. The crystals formed were washed twice with water (600 µL) and once with cyclohexane (600 µL), including centrifugation and discarding of the supernatant.

Analysis

[0067] Crystals were harvested and subjected to X-ray crystallography and NMR analysis by dissolving them in a deuterated solvent, like $CDCl_3$ (0.45 mL), and measuring ^{1}H-NMR spectra of the resulting solution.

[0068] Table 1 and 2 show structural data for crystals of tetraaryladamantane

derivatives with or without guest molecules in the crystal lattice

[0069] Description of the Tables

[a] Number of molecules in a unit cell, asymmetric unit.

Vol: Volume of unit cell in [$Å^3$];

Den: Density in [Mg/m^3];

host : guest: Calculated Stoichiometry of (host/guest)

[0070]

Table 1

Entry	Compound	Crystal system	space group	Vol	Z[a]	Den
1	4	monoclinic	P 21/n	3009	4	1.238
2	5	tetragonal	I 41/a	3414	4	1,200
3	6	triclinic	P -1	1866	2	1.198
4	3	triclinic	P -1	3538	4	1.278
5	3	monoclinic	C 2/c	15932	16	1.312
6	3	monoclinic	P 21/n	7415	8	1.258
7	3	monoclinic	C 2/c	16380	16	1.241
8	3	monoclinic	P 21/n	7484	8	1.267
9	3	monoclinic	P 21/n	7542	8	1.258
10	3	monoclinic	P 21/n	7497	8	1.247
11	3	triclinic	P -1	7764	8	1.308
12	3	monoclinic	P 21/n	7513	8	1.276
13	3	monoclinic	P 21/c	7445	8	1.325
14	3	monoclinic	P 21/n	7650	8	1.259
15	3	monoclinic	P 21/n	7572	8	1.259
16	3	triclinic	P -1	2066	2	1.306
17	3	monoclinic	P 21/n	7511	8	1.279
18	3	monoclinic	P 21/n	7577	8	1.246
19	3	monoclinic	C 2/c	15704	16	1.304
20	3	monoclinic	C 2/c	15798	16	1.279
21	3	monoclinic	C 2/c	15800	16	1.230
22	3	triclinic	P -1	1746	2	1.295

Entry	Compound	Crystal system	space group	Vol	Z[a]	Den
23	3	triclinic	P -1	2015	2	1.250
24	3	triclinic	P -1	4087	4	1.324
25	3	triclinic	P -1	1985	2	1.288

[0071]

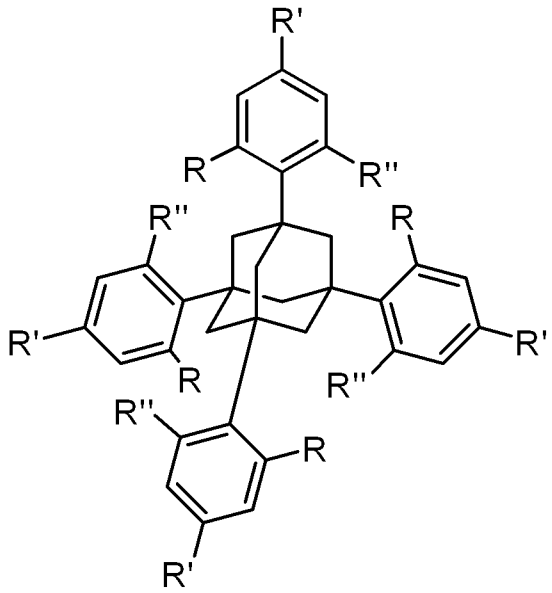
Table 2

Entry	Compound	Solvent(s)	guest	Host :guest
1	4	CH_2Cl_2/C_6H_{12}	-	-
2	5	CH_2Cl_2/C_6H_{12}	-	-
3	6	CH_2Cl_2/C_6H_{12}	-	-
4	3	acetic acid	-	-
5	3	CH_2Cl_2	CH_2Cl_2	4:5
6	3	CH_2Cl_2/C_6H_{14}	C_6H_{14}	4:1
7	3	CH_2Cl_2/C_6H_{12}	C_6H_{12}	1:1
8	3	CH_2Cl_2/EtOH	CH_2Cl_2 /EtOH	4:1:1
9	3	CH_2Cl_2/2-propanol	CH_2Cl_2/2-propanol	8:1:3
10	3	EtOH	EtOH	2:1
11	3	$CHCl_3$/n-propanol	$CHCl_3$/n-propanol	4:1:1
12	3	$CHCl_3$/EtOH	$CHCl_3$/EtOH	n.d.
13	3	nitrobenzene	nitrobenzene	2:1
14	3	2-methyl-2-butanol	2-methyl-2-butanol	2:1
15	3	2-butanol	2-butanol	2:1
16	3	trifluorobenzene	trifluorobenzene	1:1
17	3	CH_2Cl_2/n-propanol	CH_2Cl_2	2:1
18	3	$MeNO_2$/n-prop	n-propanol	2:1

Entry	Compound	Solvent(s)	guest	Host :guest
		anol		
19	**3**	nitromethane	nitromethane	2:3
20	**3**	acetone	acetone	8:11
21	**3**	acetonitrile	acetonitrile	1:1.25
22	**3**	aniline	-	-
23	**3**	EtOH/C_6H_6	benzene	1:1
24	**3**	+ $CHCl_3$	benzene/$CHCl_3$	8:3:7
25	**3**	+ $CHCl_3$	$CHCl_3$	4:3

Claims

1. Tetraphenyladamantanes according to formula I,



(Formula I),

2. wherein R, R', and R" are same or different residues selected from the group H, O-R1, S-R1, NHR1, NR1R2 or halogen with R1, R2 same or different substituted or unsubstituted, aliphatic or aromatic residues with 1 to 25 carbon atoms, alkyl residues with 1 to 25 carbon atoms, wherein at most one residue R, R', or R" stands for H.
3. Inclusion material comprising tetraphenyladamantanes according to claim 1 as host compound and at least one substituted or unsubstituted, aliphatic, cycloaliphatic or aromatic organic guest compound.
4. Inclusion material according to claim 2, characterized in that the organic guest compound is selected from the group consisting of acid chlorides, dichloromethane, chloroform, cyclohexane, n-hexane, ethanol, 2-propanol, 2-methyl-2-butanol, 2-butanol, acetonitrile, acetone, benzene, trifluorobenzene, nitrobenzene, nitromethane, pyridine, N,N-dimethylformamide, toluene, piperidine, styrene, 2,3,5-trimethylpyrazine, trimethylphosphate, anisole, N,N-dimethylaniline, dimethylsulfoxide, dioxane, morpholine, 1-vinylimidazole, pyrrolidine, xylenes, tetrahydrofuran, fufural, di-tert-butylmethylphosphine, benzyl chloride and trimethylsilyl chloride.

5. Process for depleting a target compound from a mixture comprising a target compound and at least one non-target compound by forming an inclusion material comprising tetraphenyladamantanes according to claim 1 as host compound and at least a part of the target compound as guest compound.
6. Process according to claim 4, characterized in the steps a) providing the mixture as solution in a solvent or as liquid mixture, b) adding the host compound in solid form, suspension or as solution and c) forming an inclusion material comprising the host compound and at least a part of the guest compound.
7. Process according to claim 4, characterized in the steps a) providing a first inclusion material comprising tetraphenyladamantanes according to claim 1 as host compound and at least one substituted or unsubstituted, aliphatic, cycloaliphatic,or aromatic organic compound as first guest compound, b) providing the mixture as solution in a solvent or as liquid mixture, c) adding the first inclusion material to the mixture and d) and initiate forming an second inclusion material comprising of the host compound and at least a part of the target compound.
8. Process according to any of the claims 4 to 6, characterized in separating the inclusion material from the mixture and releasing at least a part of the target compound from the inclusion material by thermal treatment or applying reduced pressure.
9. Process according to any of the claims 4 to 6, characterized in separating the inclusion material from the mixture and releasing at least a part of the target compound from inclusion material by dissolving inclusion material in an organic solvent
10. Process according to any of the claims 4 to 6, characterized in separating a first inclusion material from the mixture and releasing at least a part of the target compound from the first inclusion material by forming a second inclusion material with a second guest compound displacing at least a part of the target compound.
11. Process for depleting a target compound from a gaseous mixture comprising a target compound and at least one non-target compound by forming an inclusion material comprising tetraphenyladamantanes according to claim 1 as

host compound and at least a part of the target compound as guest compound.

12. Process according to claim 11, characterized in that the tetraphenyladamantanes are absorbed on a porous matrix.
13. Use of tetraphenyladamantanes according to formula I as host compound for forming inclusion materials with reactive, explosive, toxic, environmentally harmful or flammable guest compounds.
14. Use of inclusion material according to claims 2 or 3 as carrier for a guest compound in chemical reactions between the guest compound and at least one reactive compound wherein the inclusion material and at least one reactive compound are provided as mixture in an organic solvent.

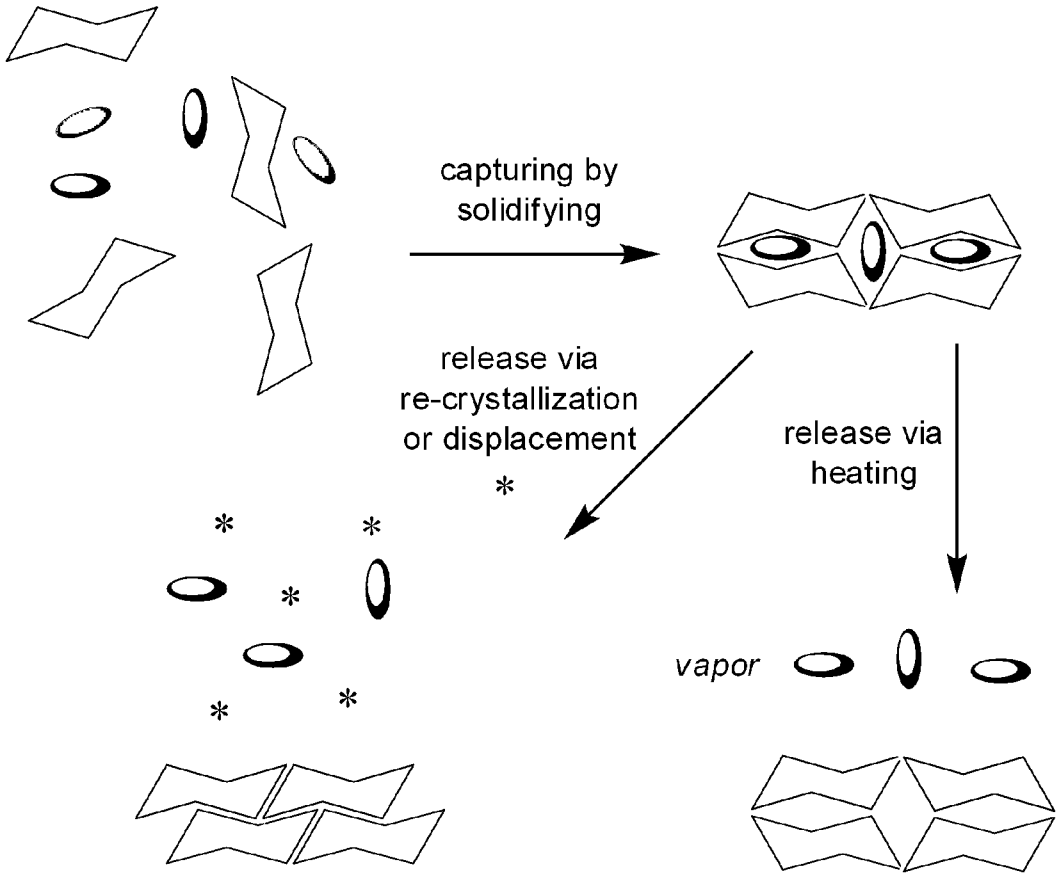

capturing by
solidifying
release via
re-crystallization
or displacement
release via
heating
vapor

Fig. 1

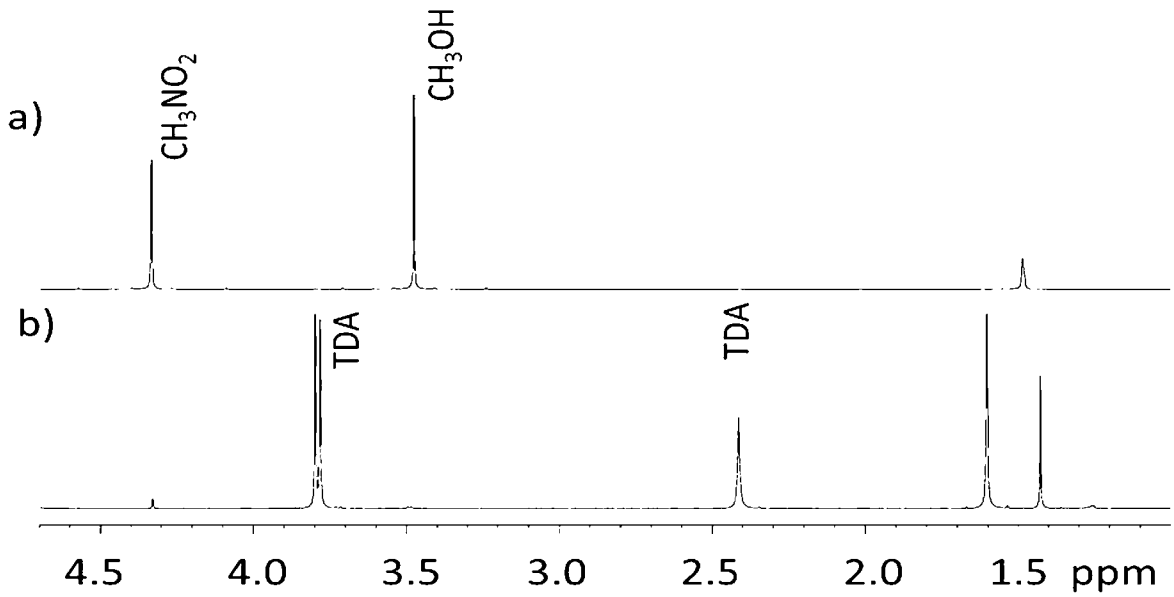

a)
CH_3NO_2
CH_3OH
b)
TDA
TDA
4.5
4.0
3.5
3.0
2.5
2.0
1.5 ppm

Fig. 2

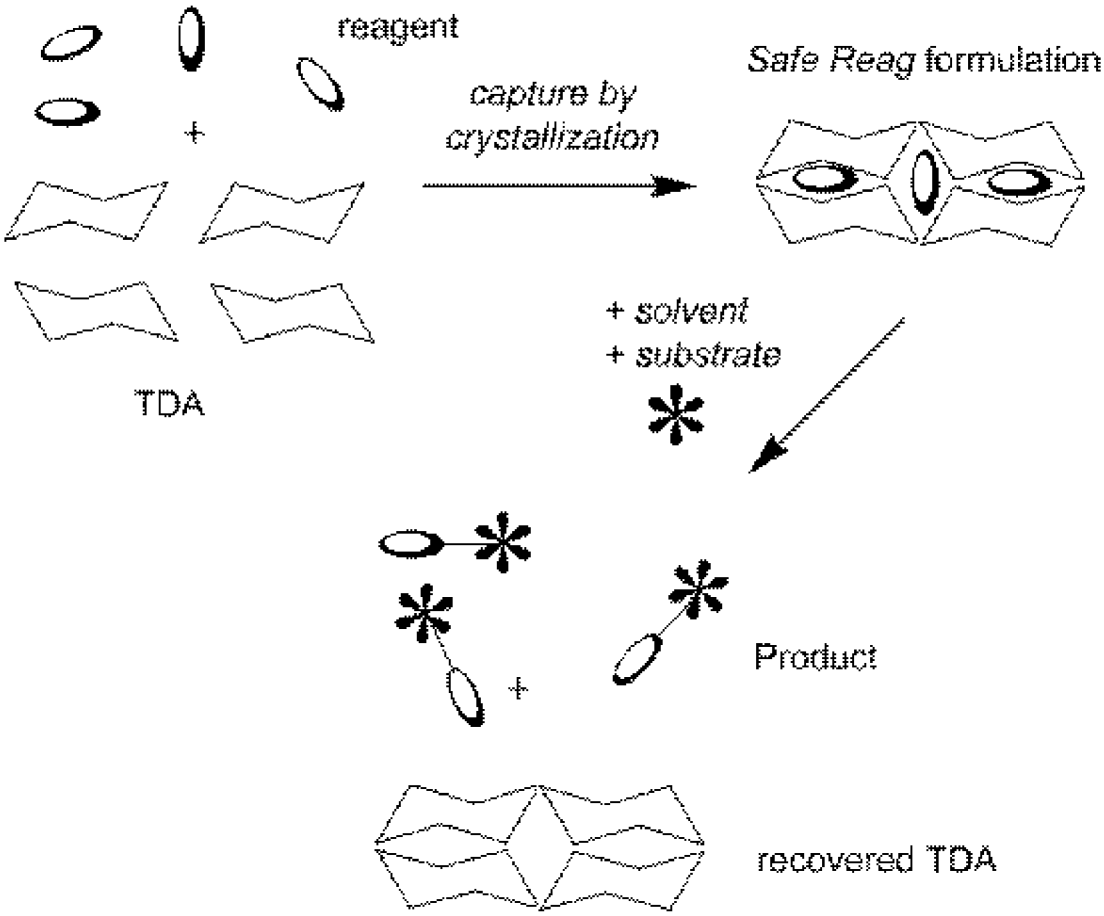

reagent
+
TDA
capture by
crystallization
Safe Reag formulation
+ solvent
+ substrate
+
Product
recovered TDA

Fig. 3

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/054833

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07C43/21 B01J20/22 C07C31/08 C07C31/10 C07C31/125
C07C205/02 C07C205/06 C07C211/46 C07C49/08 C07D499/12
C07C255/03 C07C9/15 C07C13/18 C07D295/192 C07C15/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07C C07D B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MASAHIDE TOMINAGA ET AL: "Self-Assembly of a Tetrapodal Adamantane with Carbazole Branches into Hollow Spherical Aggregates in Organic Media", ORGANIC LETTERS, vol. 16, no. 17, 5 September 2014 (2014-09-05), pages 4622-4625, XP055275606, US ISSN: 1523-7060, DOI: 10.1021/ol502116m the whole document	1-13

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[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 May 2016	24/06/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Kardinal, Siegmar

2

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MICHAEL MASTALERZ: "Permanent Porous Materials from Discrete Organic Molecules-Towards Ultra-High Surface Areas", CHEMISTRY - A EUROPEAN JOURNAL., vol. 18, no. 33, 13 August 2012 (2012-08-13), pages 10082-10091, XP055275000, WEINHEIM, DE ISSN: 0947-6539, DOI: 10.1002/chem.201201351 cited in the application the whole document -----	1-13
A	NADINE PANNIER ET AL: "RigidC3-Symmetric Scaffolds Based on Adamantane", EUROPEAN JOURNAL OF ORGANIC CHEMISTRY, vol. 2008, no. 7, 1 March 2008 (2008-03-01), pages 1278-1284, XP055274939, DE ISSN: 1434-193X, DOI: 10.1002/ejoc.200701003 page 1279; figure 1; compound 16 page 1281, right-hand column; compound 16 -----	1
X,P	ALEXANDER SCHWENGER ET AL: "Tetrakis(dimethoxyphenyl)adamantane (TDA) and Its Inclusion Complexes in the Crystalline State: A Versatile Carrier for Small Molecules", CHEMISTRY - A EUROPEAN JOURNAL., vol. 21, no. 24, 8 June 2015 (2015-06-08), pages 8781-8789, XP055274923, WEINHEIM, DE ISSN: 0947-6539, DOI: 10.1002/chem.201406568 the whole document -----	1-13

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