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Notice of Entitlement

We, MONSANTO COMPANY, a Corporation organised and existing under the laws of the State of Delaware, United States of America, having its principal place of business at 800 North Lindbergh Boulevard, St. Louis, State of Missouri 63167, United States of America, being the Applicant and Nominated person in respect of Application No. 29695/95, state the following:

The actual inventors of the invention of Application No. 29695/95 are Bruce Cameron Hamper and Kindrick Lee Leschinsky.

The basic application listed on the PCT Request form, namely, United States Serial No. 08/277,725, was filed in the names of the said actual inventors.

The said basic application listed in the declaration under Article 8 of the PCT was the first application made in a Convention country in respect of the invention.

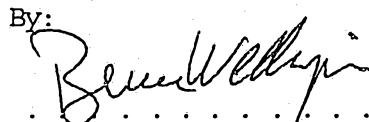
We have entitlement from the actual inventors, as well as from the applicants of the basic application, by assignment.

Our address for service is care of E. F. WELLINGTON & CO., Patent Attorneys, 312 St. Kilda Road, Melbourne, Southbank, Victoria, 3006.

DATED this 15th day of January 1997

For and on behalf of
MONSANTO COMPANY,

By:



BRUCE S. WELLINGTON
Patent Attorney for Applicant/
Nominated Person

To: The Commissioner of Patents,
Commonwealth of Australia

C/BA/5049/3

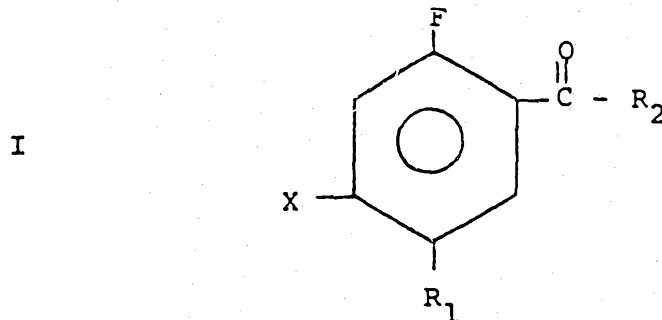


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- (57) Claim

1. Compounds according to Formula I



wherein

X is ~~H or~~ halogen;

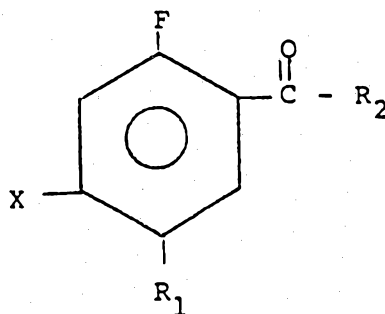
R₁ is C₁₋₆ alkyl optionally substituted with halogen or alkoxy or alkoxyalkyl having up to 6 carbon atoms and

R₂ is H, OH, C₂₋₆ alkyl or C₁₋₆ haloalkyl or -CH₂COR₃, wherein R₃ is C₁₋₆ haloalkyl.

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20. Use of compounds according to Formula I



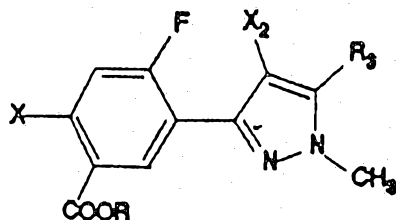
wherein

X is halogen;

R₁ is C₁₋₆ alkyl optionally substituted with halogen or alkoxy or alkoxyalkyl having up to 6 C atoms, and

R₂ is H, OH, C₁₋₆ alkyl or C₁₋₆ haloalkyl or -CH₂COR₃, wherein R₃ is C₁₋₆ haloalkyl,

for the preparation of compounds of Formula VII



VII

wherein R₁, R₃ and X are as defined above, X₂ is halogen and
10 R is C₁₋₆ or substituted alkyl.

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AOJP DATE 28/03/96 PCT NUMBER PCT/US95/08720



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(21) International Application Number: PCT/US95/08720 (22) International Filing Date: 14 July 1995 (14.07.95) (30) Priority Data: 08/277,725 20 July 1994 (20.07.94) US (71) Applicant: MONSANTO COMPANY [US/US]; 800 North Lindbergh Boulevard, St. Louis, MO 63167 (US). (72) Inventors: HAMPER, Bruce, Cameron; 132 Wildwood Lane, Kirkwood, MO 63122 (US). LESCHINSKY, Kindrick, Lee; 811 Palm Bay Drive, Ellisville, MO 63011 (US). (74) Agent: BOLDING, James, Clifton; Monsanto Company, 800 North Lindbergh Boulevard, St. Louis, MO 63167 (US).			(81) Designated States: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG). Published <i>With international search report.</i> 68 1976
(54) Title: BENZOYL DERIVATIVES AND SYNTHESIS THEREOF			
(57) Abstract The present invention relates to novel 4-halo-2-fluoro-5-alkylbenzoyl compounds and their methods of manufacture. These compounds are useful for the preparation of agricultural chemicals and medicines, particularly as intermediates for an active class of aryl-haloalkylpyrazole and aryl-alkylsulfonylpyrazole herbicides.			

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BENZOYL DERIVATIVES AND SYNTHESIS THEREOFFIELD OF THE INVENTION

The present invention relates to novel benzoyl derivatives and their methods of manufacture. These compounds are useful for the preparation of agricultural chemicals and medicines and particularly, as intermediates for an active class of arylhaloalkylpyrazole and aryl alkylsulfonylpyrazole herbicides.

BACKGROUND OF THE INVENTION

10 In recent years it has been found that one class of active herbicides are the substituted phenylpyrazoles, the phenyl and pyrazole moieties of which contain a variety of substituents.

Methods of manufacturing these phenylpyrazoles commonly involve chemical conversions of one or more radicals substituted on the phenyl and/or pyrazole moieties, e.g., by halogenation, esterification, etc. It is also known to prepare these compounds from substituted acetophenones by interaction with various compounds, including various esters which contribute the desired substituent radical to the 5-position of the pyrazole radical via cyclization of an intermediate phenyl diketone. For example, various halo- and/or alkyl-substituted acetophenones have been reacted with (halo)acetic acid esters to produce the corresponding phenyl diketone which is cyclized with hydrazine to yield phenylpyrazoles substituted in the 5-position of the pyrazole radical with (halo)alkyl groups.

It has recently been disclosed that certain 3-substituted aryl-5-substituted pyrazoles are particularly useful for broadspectrum control of a variety of weeds at very low application rates in a number of economically important crops. The aryl group is typically the phenyl radical substituted with halogen, alkyl, alkoxy and ester groups, which substituents are also commonly found on the pyrazole moiety. Particularly effective within this class of compounds are esters of

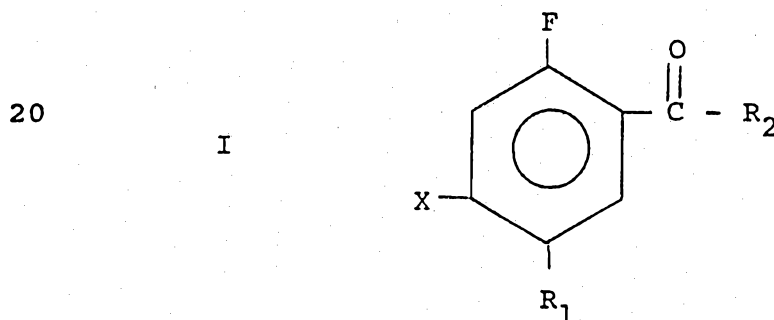
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2-chloro-5-(4-halo-1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl)-4-fluorobenzoic acid. These particular compounds are most readily available from 2-fluoro-5-alkylacetophenones and their derivatives. The literature, however, does not provide methods of preparation of these intermediates or related compounds that could provide the desired pyrazolylbenzoic acids. Thus, there is a need in the art for the discovery of novel intermediates and for efficient methods for the preparation of these substituted arylpyrazole compounds.

The present invention describes intermediates useful for production of compounds within this new class of herbicides.

SUMMARY OF THE INVENTION

The present invention relates to a class of benzoyl derivatives of Formula I and synthesis methods therefor:



wherein X is H or a halogen atom, R_1 is a C_{1-6} alkyl group optionally substituted with halogen or alkoxy or alkoxyalkyl having up to 6 carbon atoms; and R_2 is C_{2-6} alkyl or C_{1-6} haloalkyl or H, OH or $-CH_2COR_3$; wherein R_3 is a C_{1-6} haloalkyl group.

A preferred subgenus of the benzoyl compounds in this invention are those according to Formula I wherein:

35

X is Cl or Br;
 R_1 is methyl and
 R_2 is H, OH, halogen, methyl or $-CH_2COR_3$
 wherein R_3 is CF_3 , CF_2Cl or CF_2H .

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The most preferred species herein are those according to Formula I wherein X is chloro, R_1 is CH_3 and R_2 is $-CH_2COCF_3$.

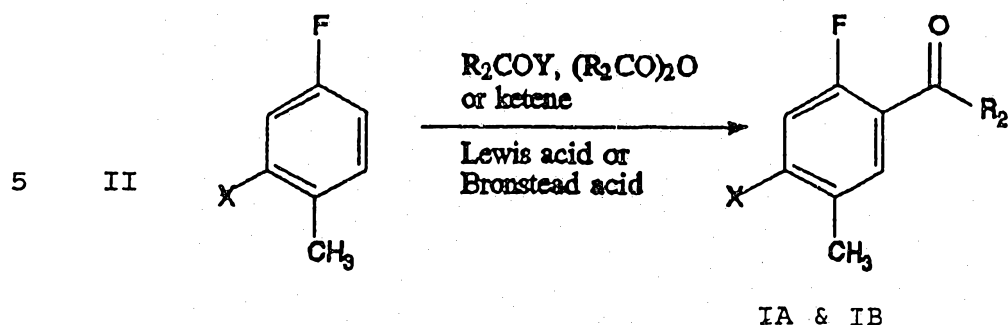
As readily apparent to those skilled in the art, when R_2 in Formula I is hydrogen, the resulting compound (Formula IA below) is a substituted benzaldehyde; when R_2 is methyl (Formula IB below), the compound is a substituted acetophenone and when R_2 is the $-CH_2COR_3$ radical, the resulting compound is a substituted phenyldiketone (Formula ID below). All of these compounds have the substituted benzoyl radical as a common structural feature, hence, for simplicity and convenience herein all of these compounds will be referred to collectively as benzoyl derivatives.

To applicants' knowledge all of the substituted benzoyl derivatives herein are novel compounds, except the 4-chloro-2-fluoro-5-methyl acetophenone compounds, which is known in the art as an intermediate to make substituted phenyl ketoesters wherein the radical analogous to R_3 in the above Formula I is an alkoxy radical, but not a haloalkyl radical as herein. Moreover, said substituted phenylketoesters when cyclized with hydrazine yield substituted phenylpyrazolones wherein the pyrazole moiety is substituted on the carbon atoms only with $O \rightleftharpoons OH$ moieties. (Japanese LOP Application (KOKAI) No. 3-72460.)

DETAILED DESCRIPTION OF THE INVENTION

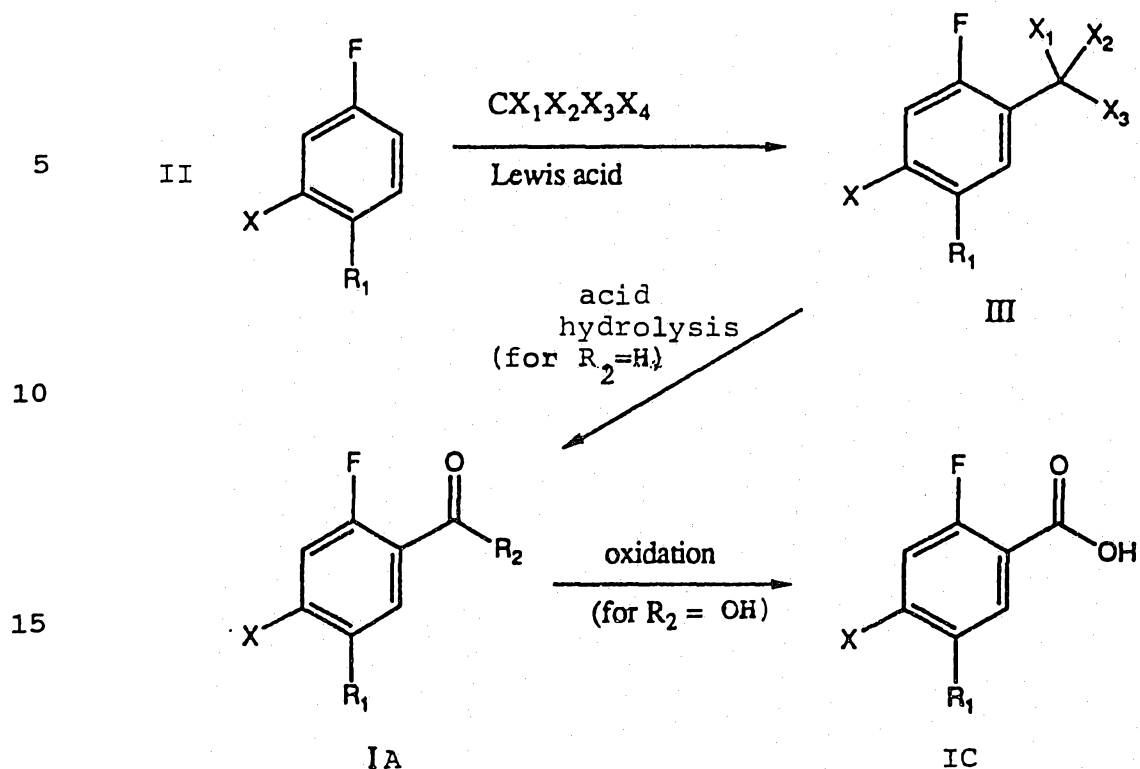
Compounds of Formula I wherein R_1 is a methyl group and X is H or a halogen and R_2 is H (Formula IA) or methyl (Formula IB) are prepared from 2-substituted-4-fluorotoluenes of Formula II, which are known in the art.

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The 2-substituted-4-fluorotoluenes of Formula II can be acylated by either an acyl halide (R_2COY wherein Y is a halogen atom), an anhydride or a ketene ($(R_2CO)_2O$) in the presence of a Lewis acid or Bronstead acid at a temperature in the range of -50°C to 200°C , preferably 0°C to 100°C . The amount of acylating agent, an acyl halide, anhydride or ketene, can range from just greater than one molar equivalent to an excess, preferably from 1 to 2 molar equivalents relative to the fluorotoluene. The acylating catalyst may be a Lewis acid, such as $AlCl_3$, $TiCl_4$, BF_3 , $SnCl_4$ or $FeCl_3$ or a Bronstead acid such as polyphosphoric acid, HF, CF_3COOH , H_2SO_4 , etc. The amount of catalyst can be from less than 0.1 mole % to excesses greater than 100 mole % relative to the fluorotoluene. Any inert solvent may be used in this reaction that does not markedly hinder the reaction from proceeding or the reaction may be carried out neat. Preferred solvents include, but are not limited to, nitrobenzene, carbon disulfide organic acids or halogenated hydrocarbons. The reaction pressure is usually from 1 to 60 kg/cm^2 , preferably from 1 to 10 kg/cm^2 . The reaction period may be chosen from the range of a few minutes to several weeks depending on the amounts of reagents, reaction temperature, etc.

Compounds according to Formula I wherein R_2 is the hydroxy (OH) radical, i.e., benzoic acids according to Formula IC below, can be prepared, e.g., by the direct oxidation of the corresponding benzaldehyde or by a two-step procedure described below wherein R_2 is OH or H.



20 The compounds of Formula III above are prepared by alkylation of 2-substituted-4-fluoro-1-alkylbenzenes of Formula II with an alkylating agent $CX_1X_2X_3X_4$ in the presence of a Lewis acid. For the alkylating agent, X_1 and X_2 are independently halogens, 25 X_3 is a halogen or hydrogen and X_4 is a halogen or (substituted)alkoxy substituent. Typical and preferred alkylating agents include, but are not limited to, 1,1-dichloromethyl methyl ether, carbon tetrachloride and carbon tetrabromide. The alkylating catalyst may be a 30 Lewis acid, such as $AlCl_3$, $TiCl_4$, BF_3 , $SnCl_4$ or $FeCl_3$ or a Bronstead acid such as polyphosphoric acid, HF , CF_3COOH , H_2SO_4 , etc. The amount of catalyst can be from less than 0.1 mole % to excesses greater than 100 mole % relative to the fluorobenzene. Any inert solvent may be 35 used in this reaction that does not markedly hinder the reaction from proceeding or the reaction may be carried out neat. Preferred solvents include, but are not

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limited to, nitrobenzene, carbon disulfide organic acids or halogenated hydrocarbons. The reaction pressure is usually from ambient pressure to 60 kg/cm², preferably from 0.5 to 10 kg/cm². The reaction period may be

5 chosen from the range of a few minutes to several weeks depending on the amounts of reagents, reaction temperature, etc. Products are obtained by treatment of the reaction mixture with water and isolation of the product by standard methods. Often, the intermediate of Formula

10 III is not isolated, but directly converted to the benzaldehyde compounds of Formula IA by acid hydrolysis, then if desired to benzoic acids by oxidation. Overall yields can be greatly improved by treatment of the crude product from the alkylation step with mineral acids,

15 such as conc. H₂SO₄ or HCl to convert any geminal dichlorides or trichlorides to aldehydes and carboxylic acids, respectively. Isolation of compounds of Formula IA and IC can then be carried out in the usual manner.

As mentioned above, while benzoic acids of

20 Formula IC can be obtained by a 2-step route from alkylation of the substituted toluene substrate with compounds such as carbon tetrachloride followed by hydrolysis, it is also possible to convert the Formula IA benzaldehydes directly to the benzoic acids of

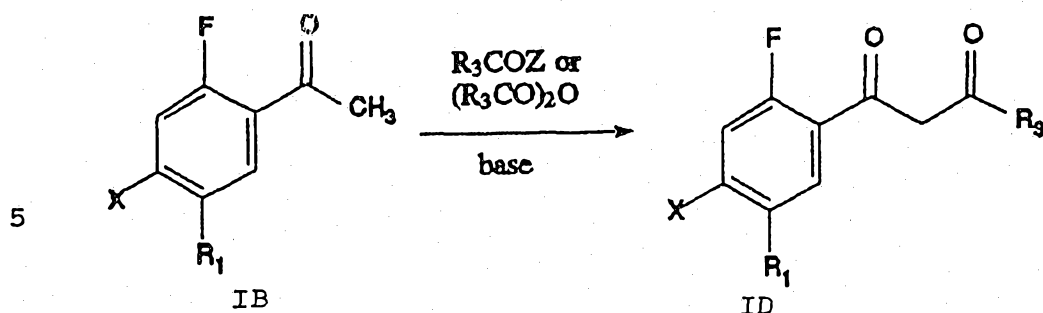
25 Formula IC by oxidation. Preferred oxidants include, but are not limited to, chromium oxide, chromium oxide in sulfuric acid, potassium permanganate, potassium dichromate, etc. Reaction temperature is in the range of -78°C to the boiling point of the reaction mixture,

30 preferably 0°C to 100°C. The reaction period may be chosen from the range of a few minutes to several weeks depending on the amounts of reagents, reaction temperature, etc.

Compounds of Formula ID are prepared from com-

35 pounds of Formula IB by reaction with R₃COZ wherein Z is a C₁₋₆ alkoxy or C₆₋₈ aryloxy group or a halogen atom or by reaction with anhydride (R₃CO)₂O, where in both formulae, R₃ is C₁₋₆ haloalkyl.

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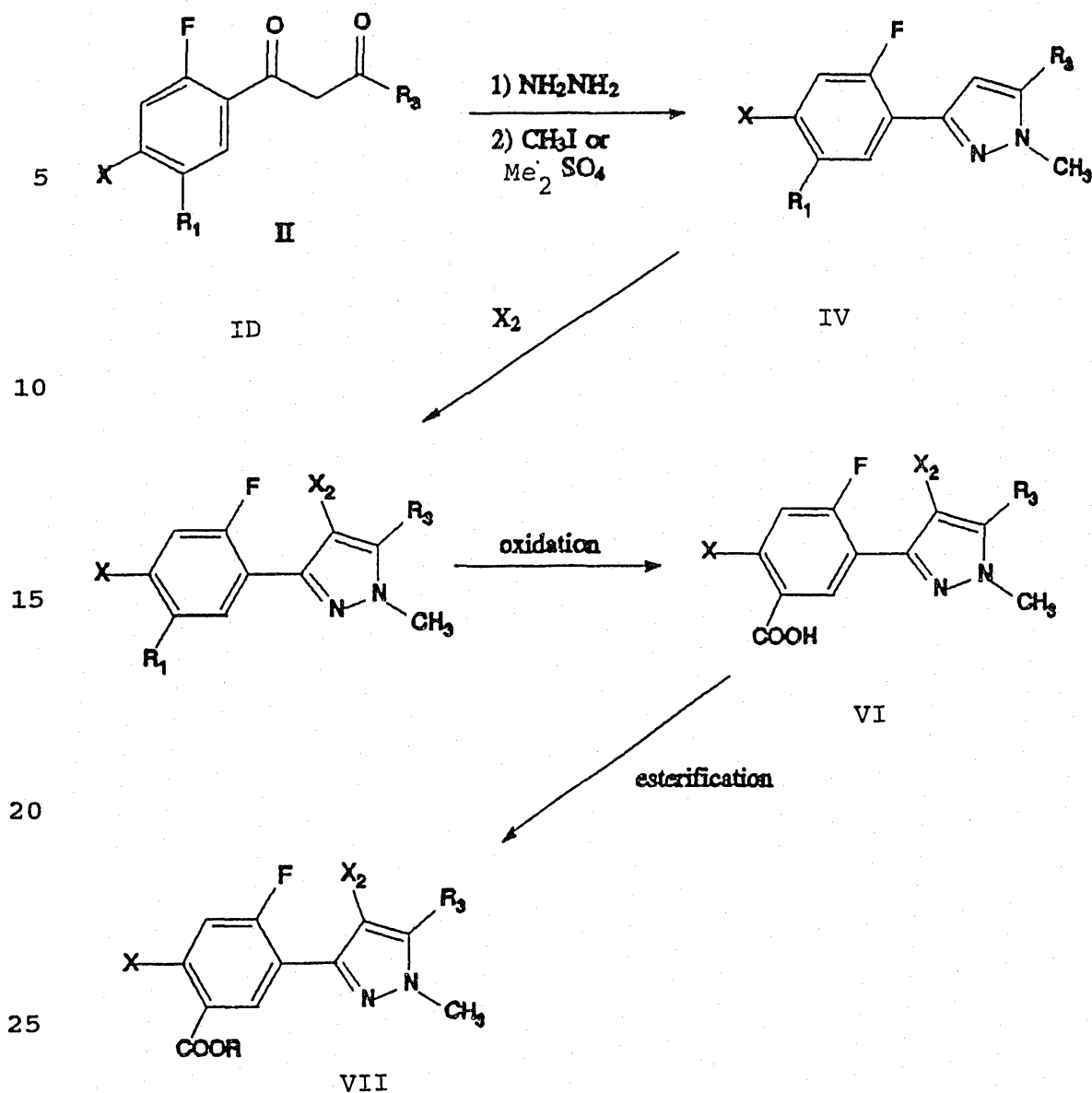


Thus, diketones of Formula ID can be prepared
 10 by treatment of 2-fluoro-4-(H or halogen)-5-alkylaceto-
 phenones with an ester, an anhydride or an acid halide
 in the presence of a base. Any suitable solvent or
 mixture of solvents can be employed; the preferred
 solvents are anhydrous ether, alcohols, dimethylsul-
 15 foxide, toluene, benzene, etc. The reaction is carried
 out in the presence of a base such as an alkali
 alkoxide, alkali amide or alkali hydride with the alkali
 alkoxides such as sodium methoxide being preferred.
 Reaction temperature is in the range of -100°C to 200°C ,
 20 preferably -78°C to the reflux temperature of the
 solvent. The reaction period may be chosen from the
 range of a few minutes to several weeks depending on the
 amounts of reagents, reaction temperature, etc.

Compounds of Formula ID are meant to include
 25 all possible tautomers, such as enols and all possible
 salts wherein the cation is an alkali metal or other
 suitable organic or inorganic cationic species.

The compounds of Formula ID can be converted
 to pyrazolylbenzoyl esters useful as synthetic herbi-
 30 cides by the following reactions.

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In the above formulae, R_1 , R_3 and X are as previously defined for Formula I, X_2 is a halogen atom and R is a C_{1-6} alkyl or substituted alkyl group, preferably those having C_{1-4} carbon atoms.

The following examples describe specific working embodiments for the preparation of representative compounds according to this invention.

Examples 1-5 exemplify preparation of representative substituted phenyldiketones.

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EXAMPLE 1

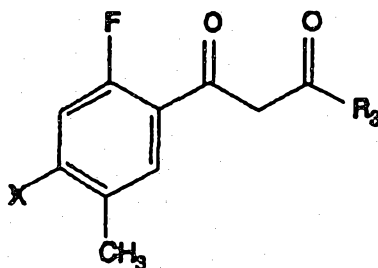
Preparation of 1-(4-Chloro-2-fluoro-5-methylphenyl)-4,4,4-trifluoro-1,3-butanedione

- A solution of 25.0 g of 1-(4-chloro-2-fluoro-5-methylphenyl)ethanone (see Example 6) and 23.9 ml of ethyl trifluoroacetate in 50 ml of ether was prepared in a 500 ml flask equipped with a magnetic stirrer. The solution was cooled in an ice water bath and 31.4 ml of 25% sodium methoxide in methanol was added slowly such that the temperature did not exceed 10°C. The cooling bath was removed and the clear orange solution was allowed to stir at ambient temperature overnight. The reaction was poured onto ice with 100 ml of 10% HCl, and extracted with diethyl ether. The organic layer was washed with 5% HCl, dried with MgSO₄, filtered and concd in vacuo. The residue was dissolved in 200 ml of warm hexanes, dried, filtered and chilled. The resulting solid was filtered and air dried to afford 24.0 g (63% yield) of 1-(4-chloro-2-fluoro-5-methylphenyl)-4,4,4-trifluoro-1,3-butanedione as an off-white solid: mp 59-60°C;
- ¹H NMR (CDCl₃) δ 14.9 (s, very broad, 1H), 7.78 (d, J=7 Hz, 1H), 7.14 (d, J=11 Hz, 1H), 6.60 (s, 1H), 2.33 (s, 3H).
- Anal. Calc. for C₁₁H₇O₂F₄Cl₁: C, 46.75; H, 2.50.
Found: C, 46.80; H, 2.49.

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Following substantially the same general procedure described in Example 1, the compounds of Examples 2-5 were prepared; these compounds are identified in Table 1, together with available physical properties.

TABLE 1



EXAMPLE No.	X	R ₃	mp/Physical Properties
2	F	CF ₃	38.5-40.0°C
3	Br	CF ₃	68-69°C
4	Cl	CF ₂ Cl	orange solid ¹
5	Cl	CF ₂ H	53-54°C

¹ NMR (CDCl₃) δ 7.74 (d, J=8 Hz, 1H), 7.10 (d, J=11 Hz, 1H), 6.54 (s, 1H), 2.29 (s, 3H).

In Examples 6-10 below are described the preparation of representative 2-fluoro-4-(H or halo)-5-methylphenyl ketone compounds according to Formula I in which R₂ is an alkyl radical, i.e., compounds according to Formula IB.

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EXAMPLE 6

Preparation of 1-(4-Chloro-2-fluoro-5-methylphenyl)ethanone.

A slurry of 22.9 g of 2-chloro-4-fluorotoluene
5 and 45.8 g of aluminum trichloride was prepared in a 500
ml, mechanically stirred flask and treated with 18.7 g
of acetyl chloride. An easily stirred slurry formed as
the reaction temperature rose to 40-50°C. Slow, steady
gas evolution began. When this gas evolution ceased,
10 the reaction was complete. The reaction mixture was
treated with 100 ml of methylene chloride and the liquid
decanted into an addition funnel. Ice was added to the
residual solid until reaction ceased, ice water was
added and the liquid from the addition funnel was added
15 dropwise with cooling such that the temperature did not
exceed 15°C. The organic layer was collected and washed
with water, dried with MgSO_4 , filtered and concd in
vacuo. The residue was bulb-to-bulb distilled (bp =
60°C @ 0.5-0.05 mm) to afford 28.0 g (95%) of 1-(4-
20 chloro-2-fluoro-5-methylphenyl)ethanone as a colorless
oil (melts near room temperature): $\eta_{D23.0}$ 1.5317; ^1H NMR
(CDCl_3) δ 7.60 (d, J=8 Hz, 1H), 7.01 (d, J=14 Hz, 1H),
2.47-2.49 (m, 3H), 2.22 (s, 3H).

Anal. Calc. for $\text{C}_9\text{H}_8\text{O}_1\text{F}_1\text{Cl}_1$: C, 57.93; H, 4.32.

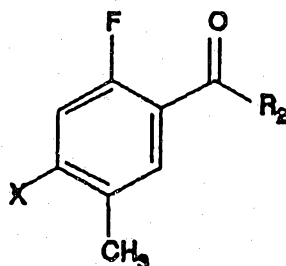
25 Found: C, 57.78; H, 4.27.

Following the same procedure described in Example
6, the compounds listed in Table 2 were also prepared
and identified.

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TABLE 2



EXAMPLE	X	R ₂	mp/refractive index
7	H	CH ₃	$\eta_D = 1.5063 @ 23^\circ\text{C}^1$
8	F	CH ₃	$\eta_D = 1.4905 @ 25^\circ\text{C}$
9	Br	CH ₃	$\eta_D = 1.5523 @ 23^\circ\text{C}$
10	Cl	CH ₂ CH ₃	34.5°C

1. Example 7 was obtained as a mixture of two isomers, i.e., 2-fluoro-5-methylacetophenone and 5-fluoro-2-methylacetophenone in a ratio of 85:15, the 2-fluoro isomer being the major product.

EXAMPLE 11

This example describes the preparation of compounds according to Formula I wherein R₂ is hydrogen; these are the 2-fluoro-4-chlorobenzaldehydes of Formula IA; in this example the prepared compound was 4-chloro-2-fluoro-5-methylbenzaldehyde.

To a stirred solution of 25 g (0.17 mole) of 2-chloro-4-fluorotoluene in 200 mL of methylene chloride was added 39 mL (0.35 mole) of titanium tetrachloride followed by the dropwise addition of 1,1-dichloromethyl methyl ether. The solution was kept at 0°C for 4 hours, subsequently poured onto ice and extracted with ethyl acetate. The combined extracts were washed twice with brine, dried with MgSO₄ and concd. in vacuo. The

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resultant oil was diluted with 200 mL of sulfuric acid and stirred overnight at room temperature. This hydrolysis reaction mixture was poured onto ice, extracted with ethyl acetate, the combined extracts washed with sodium bicarbonate solution, dried with MgSO_4 and concd. to give 17.0g (57%) of a white solid: mp 69°C - 70°C ; ^1H NMR (CDCl_3) δ 2.41 (s, 3H), 7.24 (d, 1H), 7.75 (d, 1H), 10.31 (s, 1H).
Anal. Calcd for $\text{C}_8\text{H}_6\text{O}_1\text{F}_1\text{Cl}_1$: C, 55.68; H, 3.50
Found: C, 55.77; H, 3.51.

EXAMPLE 12

This example exemplifies the preparation of Formula I compounds wherein R_2 is OH; these are, of course, the intermediate substituted benzoic acid compounds of Formula IC.

This example describes the preparation of 4-chloro-2-fluoro-5-methylbenzoic acid by the direct oxidation of the corresponding precursor benzaldehyde.

To a solution of 219 g (1.3 mole) of 4-chloro-2-fluoro-5-methylbenzaldehyde (see Example 11) in 2 L of acetone cooled to 0°C was added 487 mL (1.3 mole) of freshly prepared Jones' reagent dropwise; this reagent is a well-known oxidizing agent comprising a solution of chromic acid in H_2SO_4 , 2.67M. After addition was complete, the mixture was allowed to warm to room temperature and stirred for three hours. The mixture was added to 2L of saturated brine, extracted twice with ethyl acetate and the combined extracts washed with 5% aq. HCl, dried with MgSO_4 and concd. to afford 147 g (60%) of a white solid: mp 172°C - 173°C ; ^1H NMR (d^6 -DMSO) δ 2.32 (s, 3H), 7.49 (d, 1H, $J = 10$ Hz), 7.83 (d, 1H, $J = 8$ Hz), 13.35 (brs, 1H); ^{19}F NMR (d^6 -DMSO) δ -111.8 (m, 1F).

The novel benzoyl derivatives of the present invention are useful as intermediates for the preparation or manufacture of agricultural chemicals and

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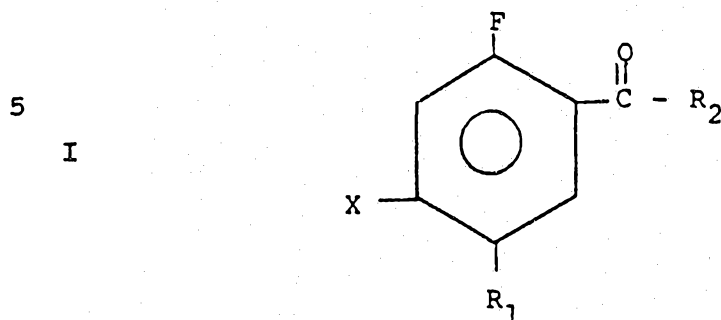
medicines, particularly the substituted phenylpyrazole
type herbicides. These intermediates allow direct
introduction of a 5'-alkyl substituent on the phenyl
ring of the phenylpyrazole which can be converted to
5 pyrazolylbenzoic acids and esters thereof.

As will be appreciated by those skilled in the
art, various modifications of the invention described
herein may be made without departing from the spirit and
scope thereof.

10

~~THE~~ CLAIMS

1. Compounds according to Formula I



wherein

X is ~~H or~~ halogen;

R₁ is C₁₋₆ alkyl optionally substituted with halogen or alkoxy or alkoxyalkyl having up to 6 carbon atoms and

R₂ is H, OH, C₂₋₆ alkyl or C₁₋₆ haloalkyl or -CH₂COR₃, wherein R₃ is C₁₋₆ haloalkyl.

2. Compounds according to Claim 1 wherein X is chloro and R₁ is methyl.

3. Compounds according to Claim 2 wherein R₂ is hydrogen.

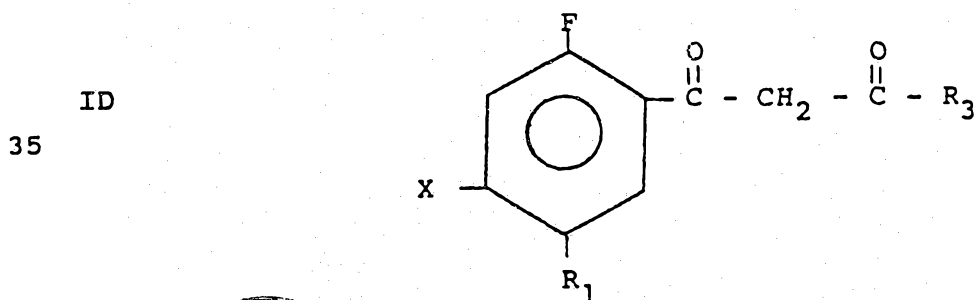
4. Compound according to Claim 2 wherein R₂ is OH.

5. Compounds according to Claim 2 wherein R₂ is C₂₋₆ alkyl or C₁₋₆ haloalkyl.

6. Compounds according to Claim 2 wherein R₂ is -CH₂COR₃ and R₃ is C₁₋₆ haloalkyl.

7. Compounds according to Claim 6 wherein R₃ is -CF₃.

8. Process for preparing compounds according to Formula ID

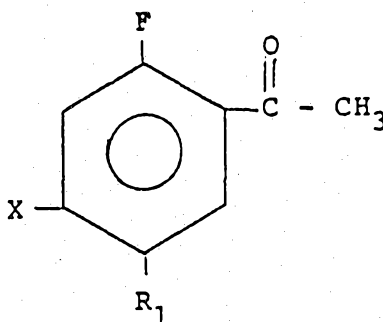


AMENDED SHEET.



which comprises acylating a compound according to Formula IB

5 IB



10

wherein

X is ~~H or~~ halogen;

R₁ is C₁₋₆ alkyl and

R₃ is C₁₋₆ haloalkyl,

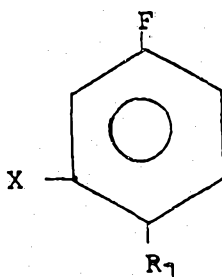
15 with an ester, ketene or acetyl halide or anhydride in an inert solvent in the presence of a strong base and after workup recovering said compound according to Formula ID.

20 9. Process according to Claim 8 wherein X is chloro, R₁ is methyl and R₃ is -CF₃.

10. Process according to Claim 9 wherein said compound of Formula ID is 1-(4-chloro-2-fluoro-5-methylphenyl)-4,4,4-trifluoro-1,3-butanedione.

25 11. Process according to Claim 8 wherein said compounds according to Formula IB are prepared by reacting a compound according to Formula II

30 II



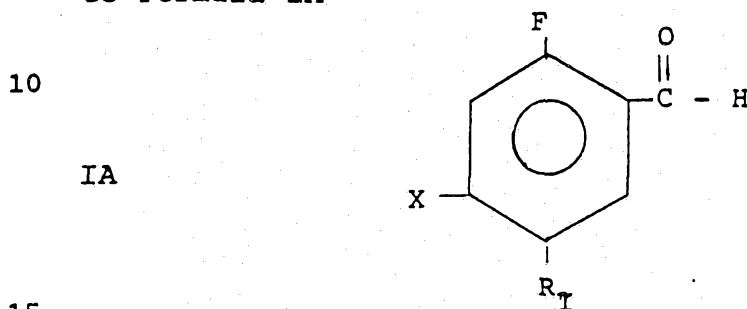
wherein X and R₁ are as previously defined, with an acylation agent in the presence of an acylation catalyst in an inert solvent.



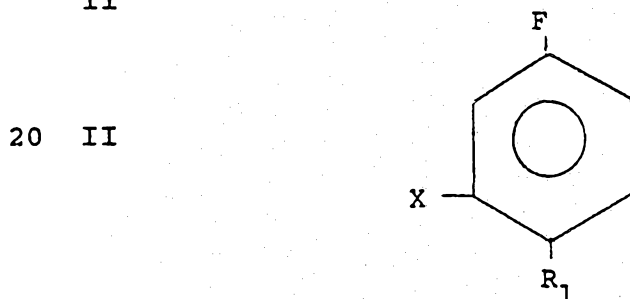
12. Process according to Claim 11 wherein said acylation agent is an ester, acetyl halide or anhydride or ketene and said acylation catalyst is a Lewis or Bronstead Acid.

5 13. Process according to Claim 12 wherein said Lewis Acid is a metal halide.

14. Process for preparing compounds according to Formula IA



which comprises reacting a compound according to Formula II



wherein X and R_I are as previously defined, with an alkylating agent in the presence of an alkylating catalyst.

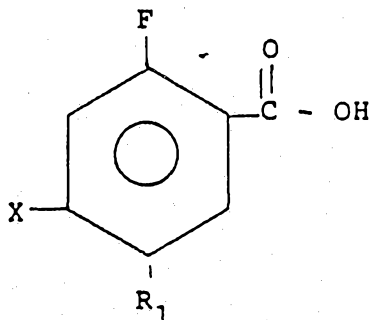
15. Process according to Claim 14 wherein said alkylating agent is a halo C₁₋₄ alkyl C₁₋₄ alkyl ether and said catalyst is a Lewis or Bronstead Acid.

30 16. Process according to Claim 14 wherein X is chloro, R_I is methyl, said alkylating agent is dichloromethyl methyl ether and said catalyst is a metal halide.



17. Process for preparing compounds according to Formula IC

5 IC

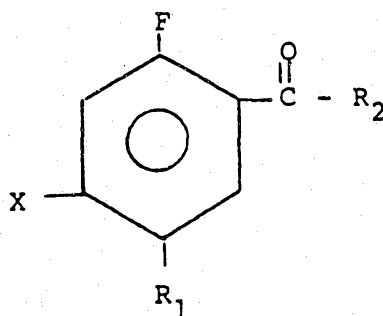


10 wherein X and R₁ are as previously defined, which comprises reacting a compound according to Formula IA as previously defined with an oxidizing agent in an inert solvent.

15 18. Process according to Claim 17 wherein X is chloro, R₁ is methyl and said oxidizing agent is Jones' reagent.

19. Process according to Claim 18 wherein said compound of Formula IC is 4-chloro-2-fluoro-5-methylbenzoic acid.

20. Use of compounds according to Formula I



wherein

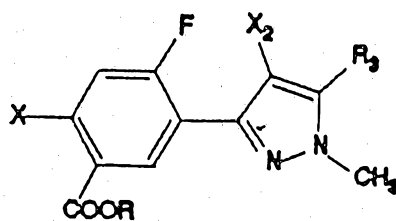
X is halogen;

5 R₁ is C₁₋₆ alkyl optionally substituted with halogen or alkoxy or alkoxyalkyl having up to 6 C atoms, and

R₂ is H, OH, C₁₋₆ alkyl or C₁₋₆ haloalkyl or -CH₂COR₃, wherein R₃ is C₁₋₆ haloalkyl,

for the preparation of compounds of Formula VII

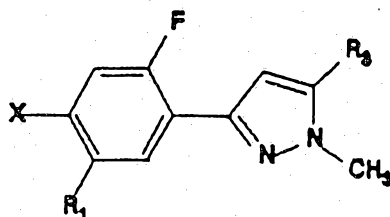




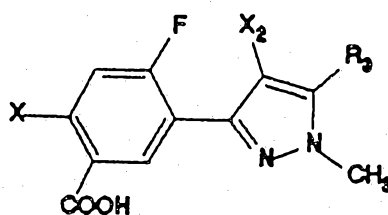
VII

wherein R_1 , R_3 and X are as defined above, X_2 is halogen and
 10 R is C_{1-6} or substituted alkyl.

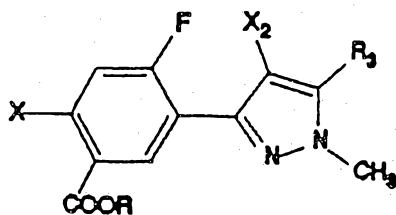
21. Use according to Claim 20, wherein a compound of Formula ID is converted into a compound of Formula IV



in the presence of NH_2NH_2 and CH_3I or Me_2SO_4 , further halogenated, then oxidised to form a compound of Formula VI



and esterified into VII



wherein, in the above formulae R , R_1 , R_3 and X being defined as in Claim 20.



INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 95/08720

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07C49/80 C07C49/807 C07C47/55 C07C63/70 C07C45/45
C07C45/46 C07C45/51 C07C51/21

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)

IPC 6 C07C

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 practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JOURNAL OF THE CHEMICAL SOCIETY, 1953 LETCHWORTH GB, pages 386-388, NG.PH. BUU-HOI ET AL. 'Friedel-Crafts Reactions with m- and p-Fluorotoluene' see page 388 ---	1,5, 11-13
X	J. INDIAN CHEM. SOC., vol. 61, no. 7, 1984 CALCUTTA, pages 644-646, R.S. SHARMA ET AL. 'Synthesis and Antifungal Activity of Aryloxyacetyl Hydrazones of Fluoro Aralkyl/Diaryl Ketones' see page 644 - page 645 --- -/--	1,5

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

10 October 1995

Date of mailing of the international search report

17. 10. 95

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 95/08720

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J. INDIAN CHEM. SOC., vol. 54, no. 7, 1977 CALCUTTA, pages 705-708, M.S. SHINGARE ET AL. 'Synthesis of Some Sulfonamide Derivatives' see page 705 ---	1,5,11
X	PHARMAZIE, vol. 36, no. 5, 1981 BERLIN DE, pages 331-332, V.N. PATHAK ET AL. 'Synthesis and Biological Activities of Some New 2-Arylamino-4-Fluoroarylthiazoles' see the whole document ---	1,5
X	INDIAN JOURNAL OF CHEMISTRY, vol. 10, no. 5, 1972 NEW DELHI, pages 485-488, K.C. JOSHI ET AL. 'Synthesis of Some New Fluorinated beta-Diketones & Their Copper Chelates' see page 485 - page 486 ---	1,6-8
X	EP,A,0 116 323 (BAYER AG) 22 August 1984 see example 5 ---	1,3,14
X	JOURNAL OF ORGANIC CHEMISTRY, vol. 22, 1957 EASTON US, pages 1715-1716, H. GILMAN ET AL. 'Metalation of Aryl Fluorides in Tetrahydrofuran' see page 1716 ---	1,4
A	FR,A,1 330 953 (J.R. GEIGY S.A.) 20 May 1963 see page 2; claims -----	1,2,5

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 95/08720

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FR-A-1330953	16-12-63	NONE	