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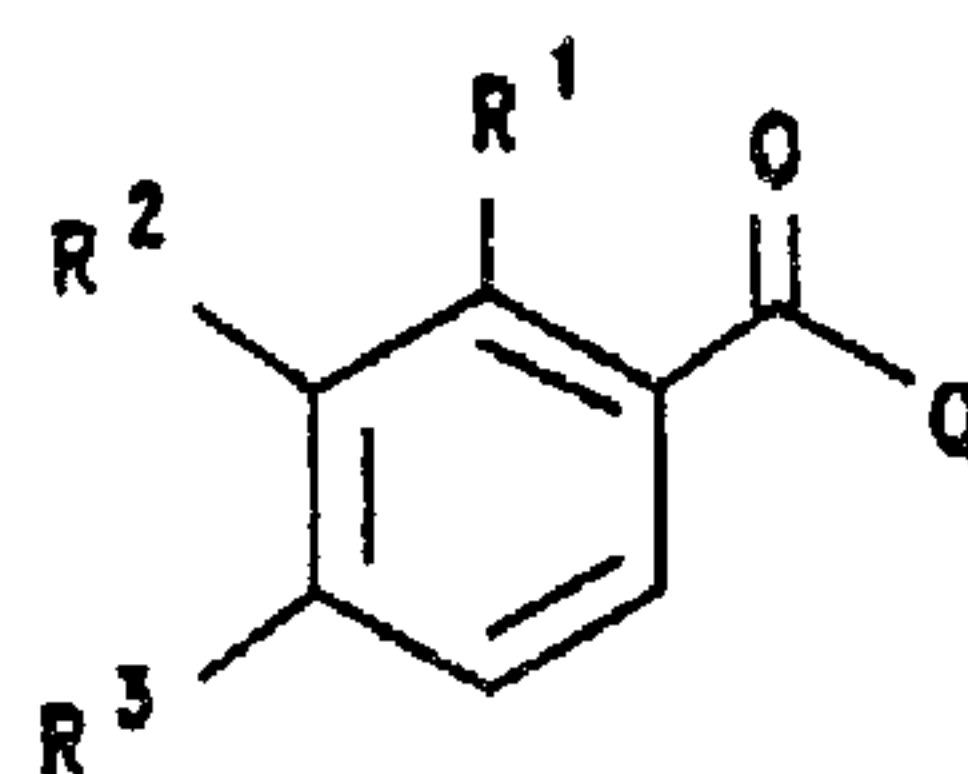
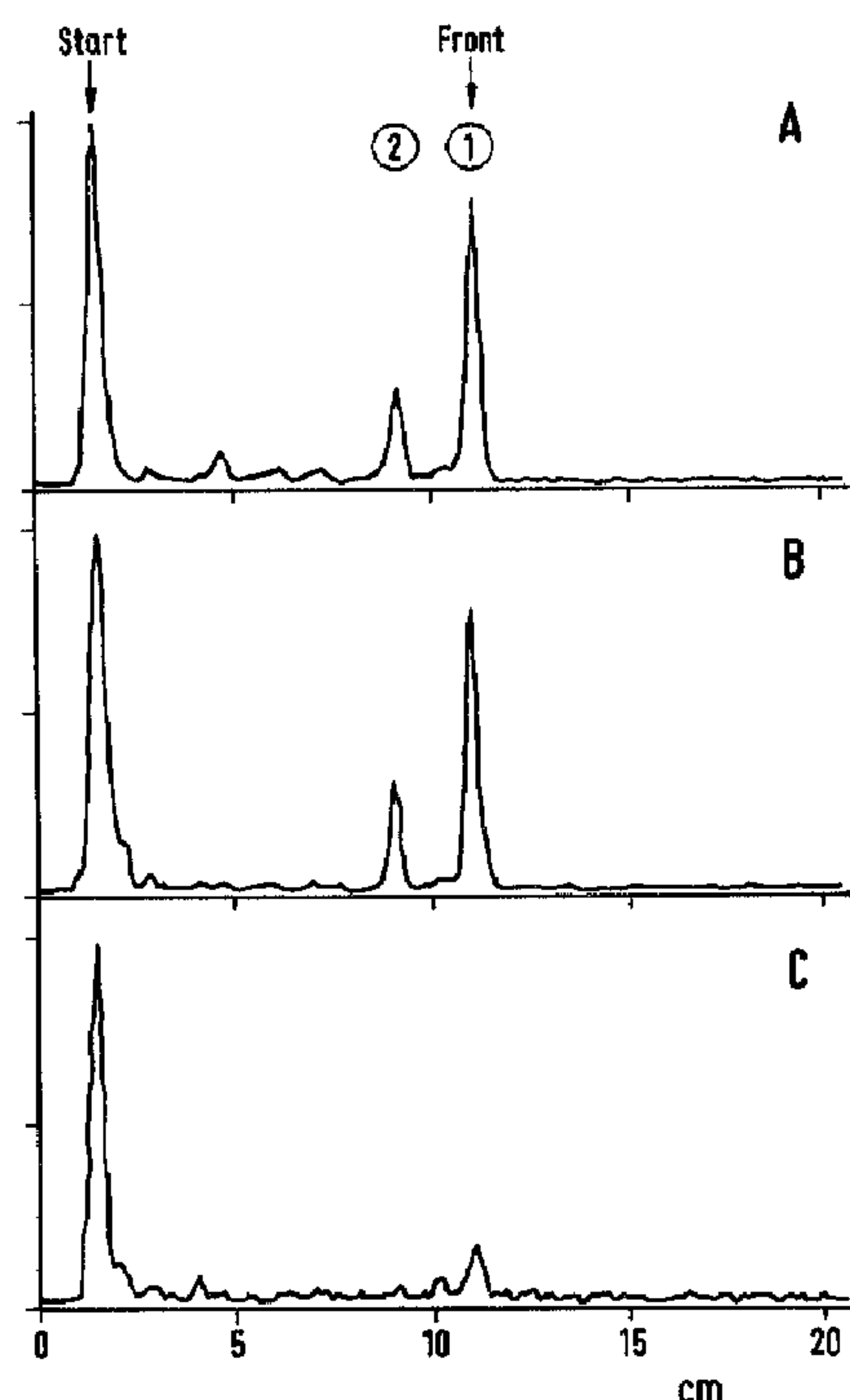
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(54) Titre : INHIBITEURS DE L'HYDROXYPHENYLPYRUVATE DIOXYGENASE ET METHODE D'IDENTIFICATION D'INHIBITEURS

(54) Title: INHIBITORS OF HYDROXYPHENYLPYRUVATE DIOXYGENASE AND AN ASSAY FOR IDENTIFICATION OF INHIBITORS



(I)

(57) Abrégé/Abstract:

Detection method for identifying inhibitors There are described a method for enriching the anabolic p-hydroxyphenylpyruvate dioxygenases from plant tissues and a method by means of which the enzymatic activity of the enzyme can be measured in a simple manner without complete purification of the enzyme being necessary. The invention furthermore describes an assay system for identifying inhibitors of p-hydroxyphenylpyruvate dioxy-genase from plants, in which an enriched HPPD from plants is incubated with a test substrate to be examined and the enzymatic activity of the enzyme is determined in comparison with the activity of the uninhibited enzyme. The invention furthermore describes the novel herbicidal active substances of the formula (I) (see formula I) which were found using the assay method according to the invention.

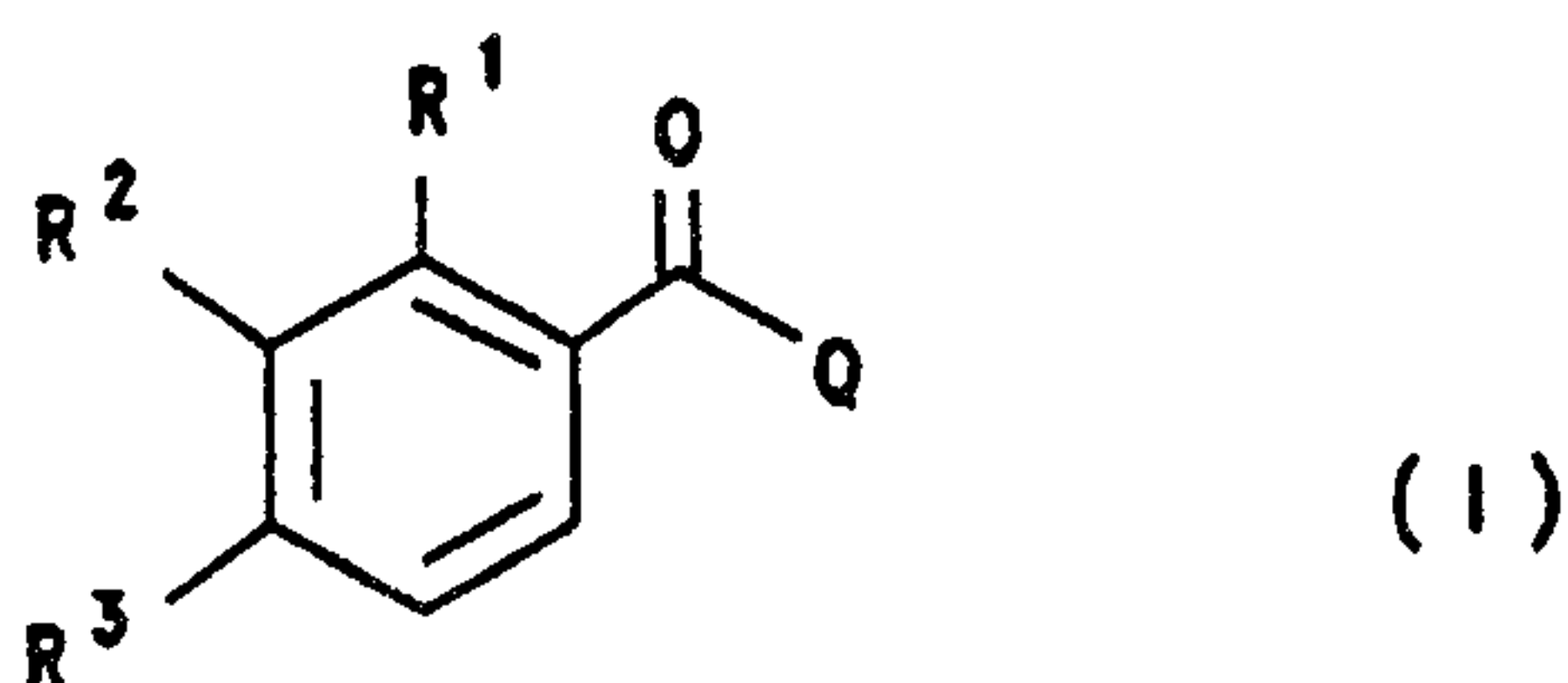
Abstract of the disclosure

Detection method for identifying inhibitors

There are described a method for enriching the anabolic p-hydroxyphenylpyruvate dioxygenases from plant tissues and a method by means of which the enzymatic activity of the enzyme can be measured in a simple manner without complete purification of the enzyme being necessary.

The invention furthermore describes an assay system for identifying inhibitors of p-hydroxyphenylpyruvate dioxygenase from plants, in which an enriched HPPD from plants is incubated with a test substrate to be examined and the enzymatic activity of the enzyme is determined in comparison with the activity of the uninhibited enzyme.

The invention furthermore describes the novel herbicidal active substances of the formula (I)



which were found using the assay method according to the invention.

Description

Inhibitors of hydroxyphenylpyruvate dioxygenase and an assay for identification of inhibitors

5 p-Hydroxyphenylpyruvate dioxygenase (HPPD; p-hydroxy-phenylpyruvate: oxygen oxidoreductase, EC 1.13.11.27) in plant tissues is an enzyme central to the biosynthesis of the quinoid compounds derived from the amino acid tyrosine, such as plastoquinones or tocopherols. During the biosynthesis of quinone, tyrosine is first trans-aminated by a transaminase to give p-hydroxyphenylpyruvate, which is then decarboxylated and hydroxylated by the enzyme HPPD in a complex sequence. The product of this reaction is homogentisic acid. These first two steps of quinone biosynthesis can analogously also be detected in animal tissues and microorganisms. While, in plants, the homogentisic acid formed can be reacted to give plastoquinones and tocopherols, however, it is an intermediate in the catabolism of the amino acid tyrosine in animals and microorganisms. Plastoquinones and tocopherols are essential structures for plants. Inhibitors of the biosynthesis of plastoquinones and tocopherols should therefore be potential herbicides.

25 Catabolic p-hydroxyphenylpyruvate dioxygenases have previously been purified and characterized from animal tissues (Lindstedt, S. and Odelhög, B. (1987) Meth. Enzymol. 142, 139-142) and microorganisms (Lindstedt, S. and Odelhög, B. (1987) Meth. Enzymol. 142, 143-148). (Anabolic) p-hydroxyphenylpyruvate dioxygenases from plants, in contrast, have been described in the literature (Fiedler, E., Soll, J. and Schultz, G. (1982) Planta 30 155, 511-515), but no method for enriching the enzyme has been described to date.

Specifically, there has been no information to date in the literature on simple methods of measuring the plant

enzyme which, of course, are indispensable for purification of the enzyme and detecting inhibitors of the enzyme.

The method described by Fiedler et al. is relatively complicated and does not allow the quantitative assays to
5 be carried out which are required for identifying potential herbicides.

What follows describes a method for enriching the anabolic p-hydroxyphenylpyruvate dioxygenases from plant tissues and a method by means of which the enzymatic
10 activity of the enzyme can be measured in a simple manner without complete purification of the enzyme being necessary.

The invention therefore relates to:

A method for enriching an anabolic p-hydroxyphenylpyruvate dioxygenase from plant cells, which comprises
15 isolating the enzyme directly from a buffer in which the cells were homogenized.

The invention furthermore relates to an assay system for identifying inhibitors of p-hydroxyphenylpyruvate dioxygenase from plants, which comprises incubating an
20 enriched HPPD from plants with a test substrate to be examined and determining the enzymatic activity of the enzyme in comparison with the activity of the uninhibited enzyme.

25 In particular, the invention relates to a method in which the plant tissue or cells are homogenized in extraction buffer, the extract is filtered, the supernatant is subjected to fractional ammonium sulfate precipitation, and the precipitate formed is redissolved.

30 Suitable extraction buffers are the extraction buffers conventionally used for plant cells, in particular the extraction buffer which is composed as follows:

20 mM phosphate buffer pH 7.0;
0.14 M KCl;
0.1 mg/ml glutathione and
1% of insoluble polyvinylpyrrolidone.

5 Suitable test substrates are all compounds which are
potential HPPD inhibitors. These potential inhibitors are
preferably structurally similar to the natural substrate
of HPPD. However, other substances which do not bind in
the active center of the enzyme, but which inhibit the
10 enzyme in a different manner, can also be used.

The enzymatic activity can be determined by means of the
methods known from the literature (see Bergmeyer, H.U.,
Methoden der enzymatischen Analyse [Methods in enzymatic
analysis], Volumes 1 and 2, Verlag Chemie, Weinheim,
15 (1974) and Suelter, C.H., Experimentelle Enzymologie:
Grundlagen für die Laborpraxis [Experimental Enzymology:
Fundamentals of Laboratory Practice], Fischer Stuttgart
(1990)).

A modified form of the method for measuring catabolic
20 HPPDs from human liver has been described by Lindblad
(Lindblad, B. (1971) Clin. Chim. Acta 34, 113-121). End-
point measurements are used in this case for detecting
 ^{14}C -CO₂, which is liberated from ^{14}C -p-hydroxyphenyl-
pyruvate by the enzymatic activity of HPPD. If HPPD
25 inhibitors are present in the reaction batch, the enzyme
reaction and hence the liberation of CO₂ are suppressed.
This assay method allows inhibitors of the enzyme to be
found.

It is preferred to carry out the assay in such a way that
30 the enzymatic activity of the HPPD is started up after
preincubation of the enriched HPPD with the potential
inhibitor by adding the radiolabeled ^{14}C -p-hydroxyphenyl-
pyruvate, stopping the reaction after a suitable incuba-
tion time, and measuring the enzymatic activity indirec-
35 tly via the radioactivity which has been liberated.

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It is self-evident that the assay according to the invention can also be carried out with the purified enzyme. The enzyme can be further enriched in a manner known per se by means of chromatography on anion exchangers, such as, for example, Q-Sepharose, by Pharmacia, followed by gel permeation chromatography, such as, for example, Superdex 200, by Pharmacia, but this is not necessary for carrying out the assay.

Surprisingly, a new class of HPPD inhibitors has now also been identified using this assay system. They are herbicides from the group of the 2-benzoylcyclohexane-1,3-diones. This is surprising since an entirely different mechanism of action is suggested in the literature for this compounds class on the basis of its herbicidal symptoms (they lead to bleaching of the plants). It is assumed that, analogously to other bleaching herbicides, they inhibit phytoene desaturase (Soeda, T. and Uchida, T. (1987) Pestic. Biochem. Physiol. 29, 35-42; Mayonada, D.J., Hatzios, K.K., Orcutt, D.M. and Wilson, H.P. (1989) Pestic. Biochem. Physiol. 35, 138-145). It was possible to demonstrate that this compounds class, while not inhibiting phytoene desaturase, does inhibit HPPD; under the assay conditions, 4.5×10^{-8} M 2-(2-chloro-4-methanesulfonylbenzoyl)-1,3-cyclohexanedione (SC-0051, a typical representative of this class of herbicides) showed a 50% inhibition on the anabolic plant HPPD from maize (which corresponds to the IC50 value). Bleaching herbicides which have a different structure do not, in contrast, inhibit HPPD, but inhibit the enzyme phytoene desaturase.

However, the method according to the invention allows not only the activity of known herbicides to be demonstrated at the molecular level, but also novel,

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previously unknown herbicidal active substances which inhibit HPPD to be identified.

According to another aspect of the present invention, there is provided a method for inhibiting plant growth by inhibiting p-hydroxyphenylpyruvate dioxygenase of a plant which comprises: i) identifying an inhibitor of p-hydroxyphenylpyruvate dioxygenase of the plant by an assay for identifying inhibitors of anabolic p-hydroxyphenylpyruvate dioxygenase from plants, said assay comprising the steps of: a) incubating an isolated p-hydroxyphenylpyruvate dioxygenase from the plant with a potential inhibitor and, b) after a suitable substrate reaction time, determining the enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant with the potential inhibitor in comparison with the enzymatic activity of p-hydroxyphenylpyruvate dioxygenase from the plant which has not been so incubated with the potential inhibitor, whereby a decrease in enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant incubated with the potential inhibitor identifies that the potential inhibitor is an inhibitor of the plant p-hydroxyphenylpyruvate dioxygenase; and ii) applying to the plant the identified inhibitor of the p-hydroxyphenylpyruvate dioxygenase of the plant.

According to still another aspect of the present invention, there is provided a method for inhibiting plant growth by inhibiting p-hydroxyphenylpyruvate dioxygenase of a plant which comprises: applying an inhibitor of p-hydroxyphenylpyruvate dioxygenase to the plant, wherein the inhibitor is identified by an assay for identifying inhibitors of anabolic p-hydroxyphenylpyruvate dioxygenase from plants, which assay comprises: a) incubating an isolated p-hydroxyphenylpyruvate dioxygenase from a plant

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with a potential inhibitor and, b) after a suitable substrate reaction time, determining the enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from a plant incubated with the potential inhibitor in comparison with
5 the enzymatic activity of p-hydroxyphenylpyruvate dioxygenase from a plant which has not been so incubated with the potential inhibitor, whereby a decrease in enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from a plant incubated with the potential
10 inhibitor indicates that the potential inhibitor is an inhibitor of a plant p-hydroxyphenylpyruvate dioxygenase.

According to yet another aspect of the present invention, there is provided a method for inhibiting undesired plants by inhibiting p-hydroxyphenylpyruvate
15 dioxygenase of undesired plants and thereby having a herbicidal effect on the undesired plants which comprises:
i) identifying an inhibitor of p-hydroxyphenylpyruvate dioxygenase of the plants by an assay for identifying inhibitors of anabolic p-hydroxyphenylpyruvate dioxygenase
20 from plants, said assay comprising the steps of: a)
incubating an isolated p-hydroxyphenylpyruvate dioxygenase from a plant with a potential inhibitor and, b) after a suitable substrate reaction time, determining the enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the
25 plant incubated with the potential inhibitor in comparison with the enzymatic activity of p-hydroxyphenylpyruvate dioxygenase from a plant which has not been so incubated with the potential inhibitor, whereby a decrease in enzymatic activity of the p-hydroxyphenylpyruvate
30 dioxygenase from the plant incubated with the potential inhibitor identifies that the potential inhibitor is an inhibitor of the plant p-hydroxyphenylpyruvate dioxygenase;
and ii) applying to the plants or areas in which they grow a

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herbicidally effective amount of the identified inhibitor of the p-hydroxyphenylpyruvate dioxygenase of the plant.

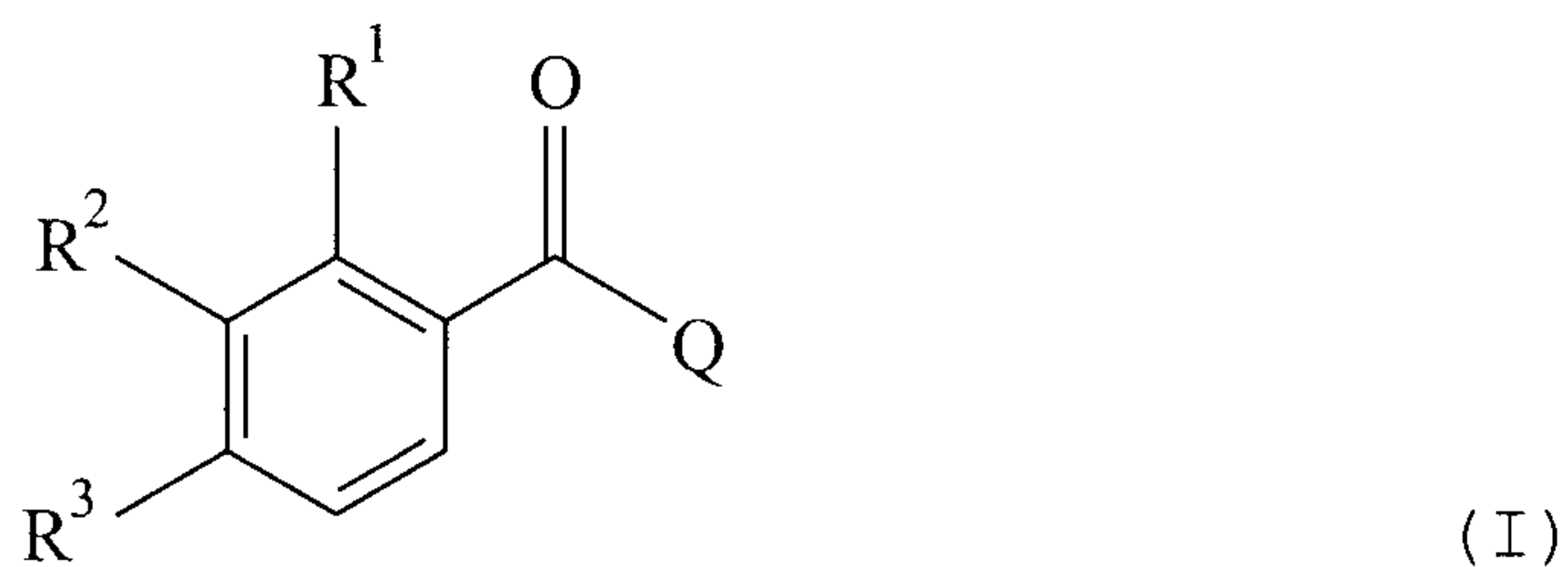
According to a further aspect of the present invention, there is provided a method for inhibiting
5 undesired plants by inhibiting p-hydroxyphenylpyruvate dioxygenase of undesired plants and thereby having a herbicidal effect on the undesired plants which comprises: applying a herbicidally effective amount of inhibitor of p-hydroxyphenylpyruvate dioxygenase to the plants or areas
10 in which they grow, wherein the inhibitor is identified by an assay for identifying inhibitors of anabolic p-hydroxyphenylpyruvate dioxygenase from plants, which assay comprises: a) incubating an isolated p-hydroxyphenylpyruvate dioxygenase from a plant with a
15 potential inhibitor and b) after a suitable substrate reaction time, determining the enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant incubated with the potential inhibitor in comparison with the enzymatic activity of p-hydroxyphenylpyruvate dioxygenase
20 from a plant which has not been so incubated with the potential inhibitor, whereby a decrease in enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant incubated with the potential inhibitor indicates that the potential inhibitor is an inhibitor of plant
25 p-hydroxyphenylpyruvate dioxygenase.

The invention therefore also relates to the novel herbicidal active substances found by the assay method according to the invention.

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The invention therefore also provides a compound of the formula (I)



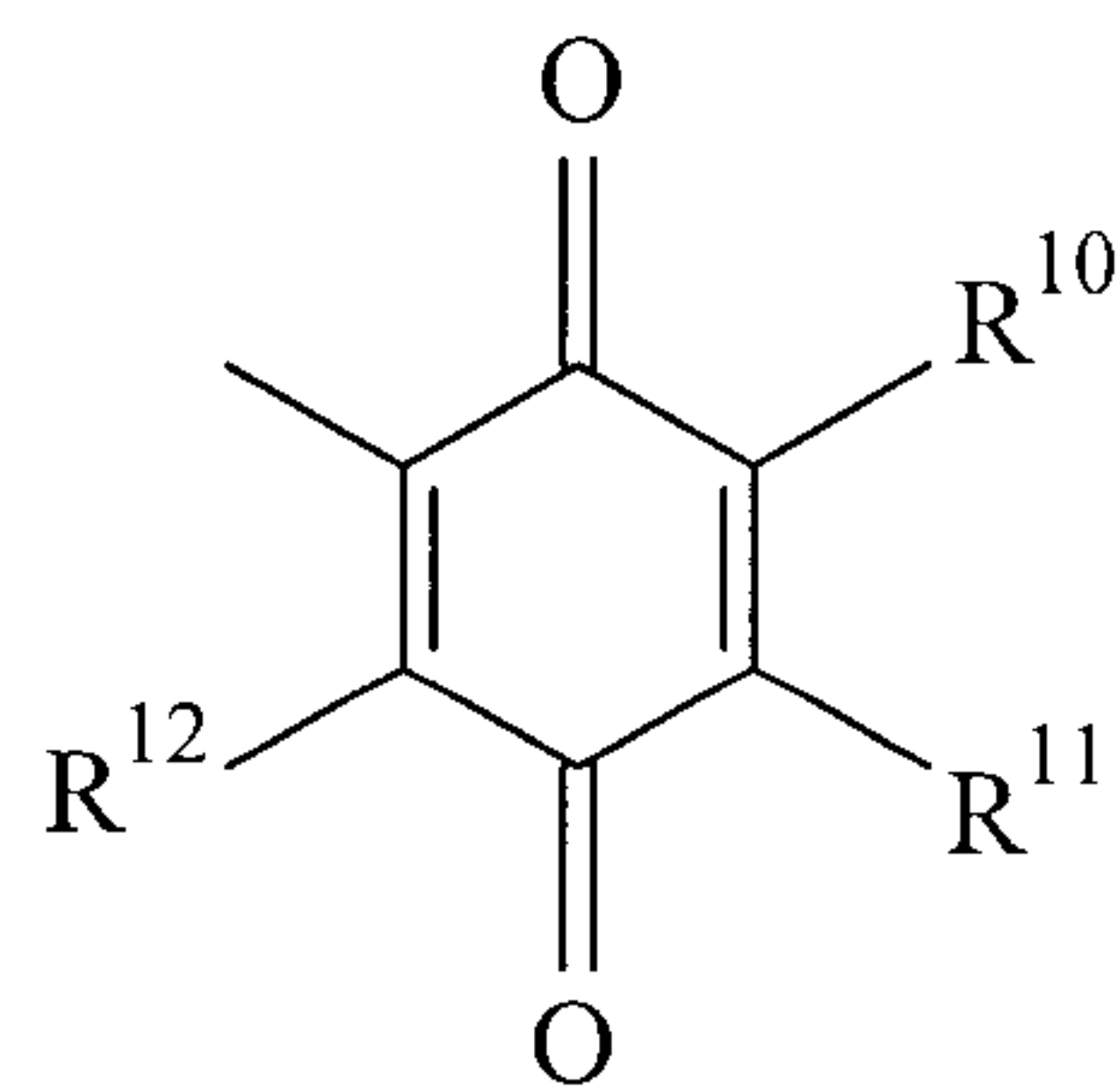
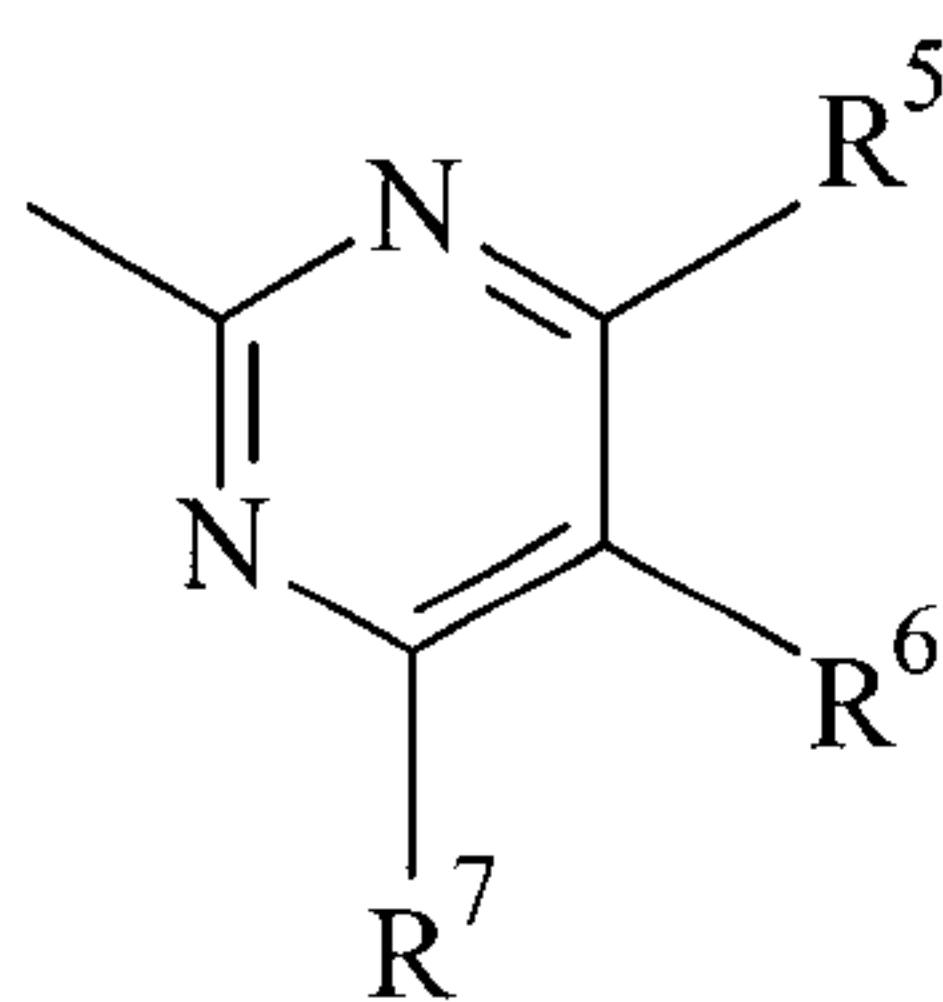
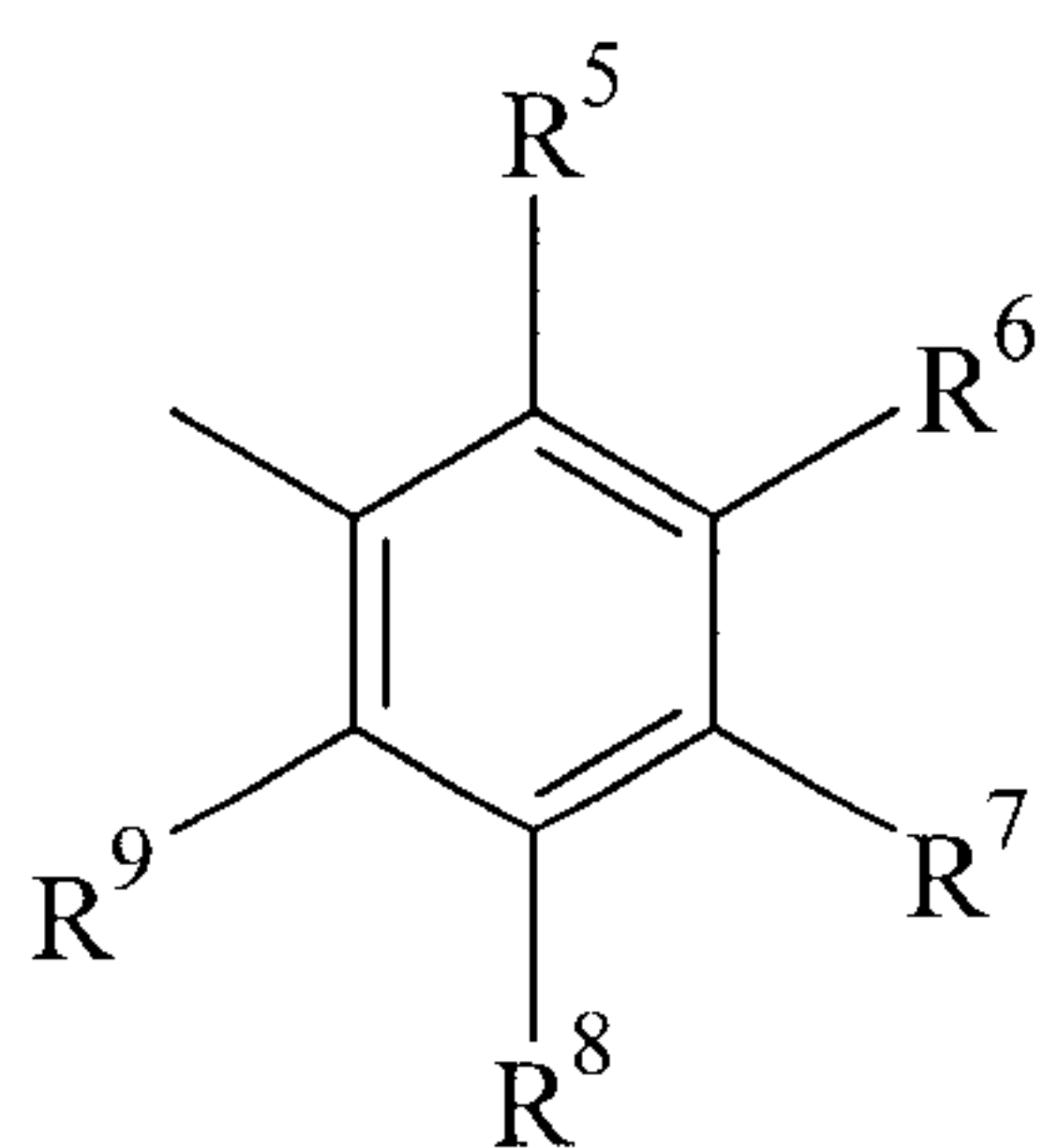
in which

R^1 is H, a halogen, OH, an alkoxy, CN, NO₂ or a
5 haloalkyl,

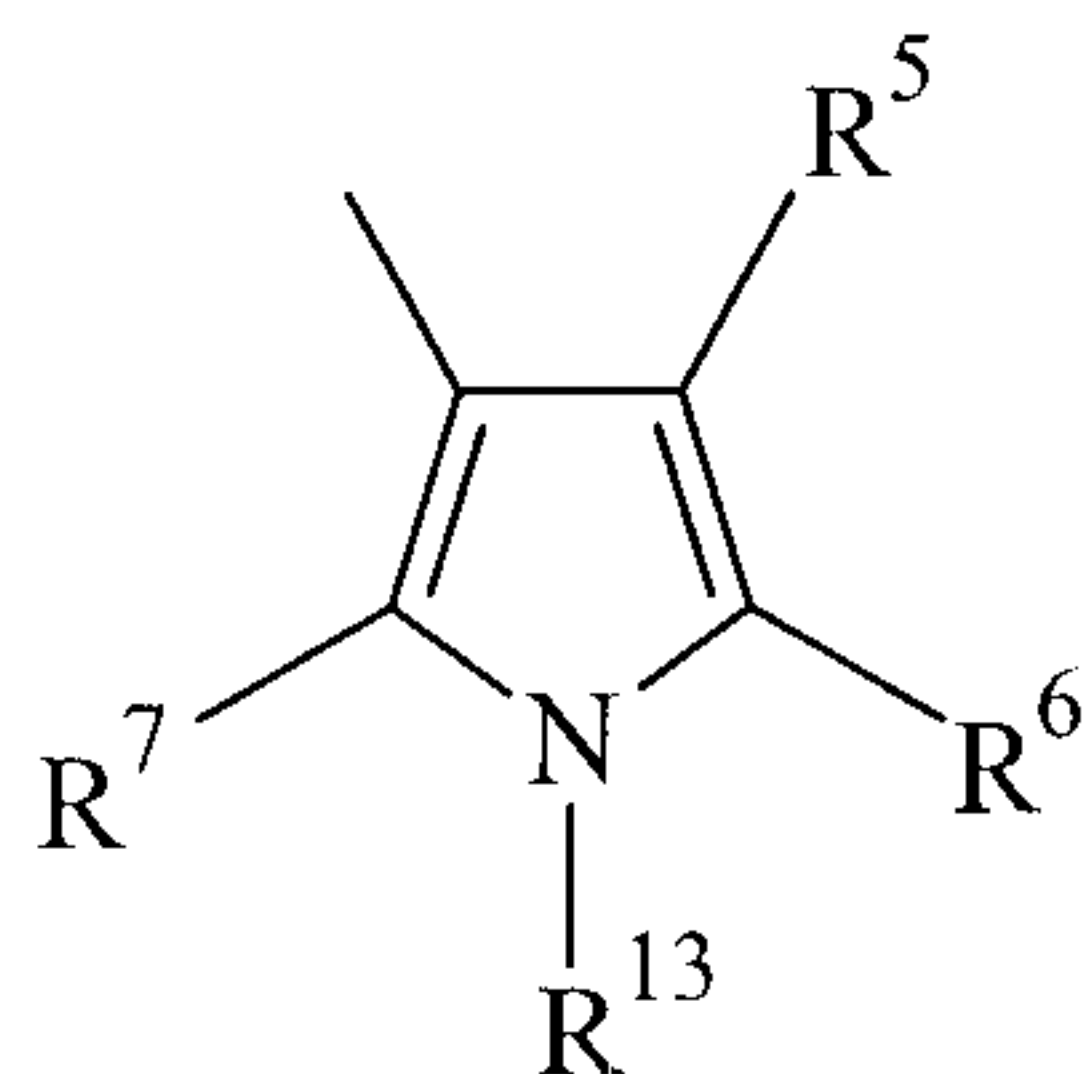
R^2 is H, a halogen, OH, an alkyl, an alkoxy, a
haloalkyl, a haloalkoxy or an (alkoxy)carbonyl,

R^3 is H, a halogen, OH, CN, NO₂, a haloalkyl, a
haloalkoxy or $R^4S(O)_m-$, where R^4 is an alkyl and m is zero,
10 one or two,

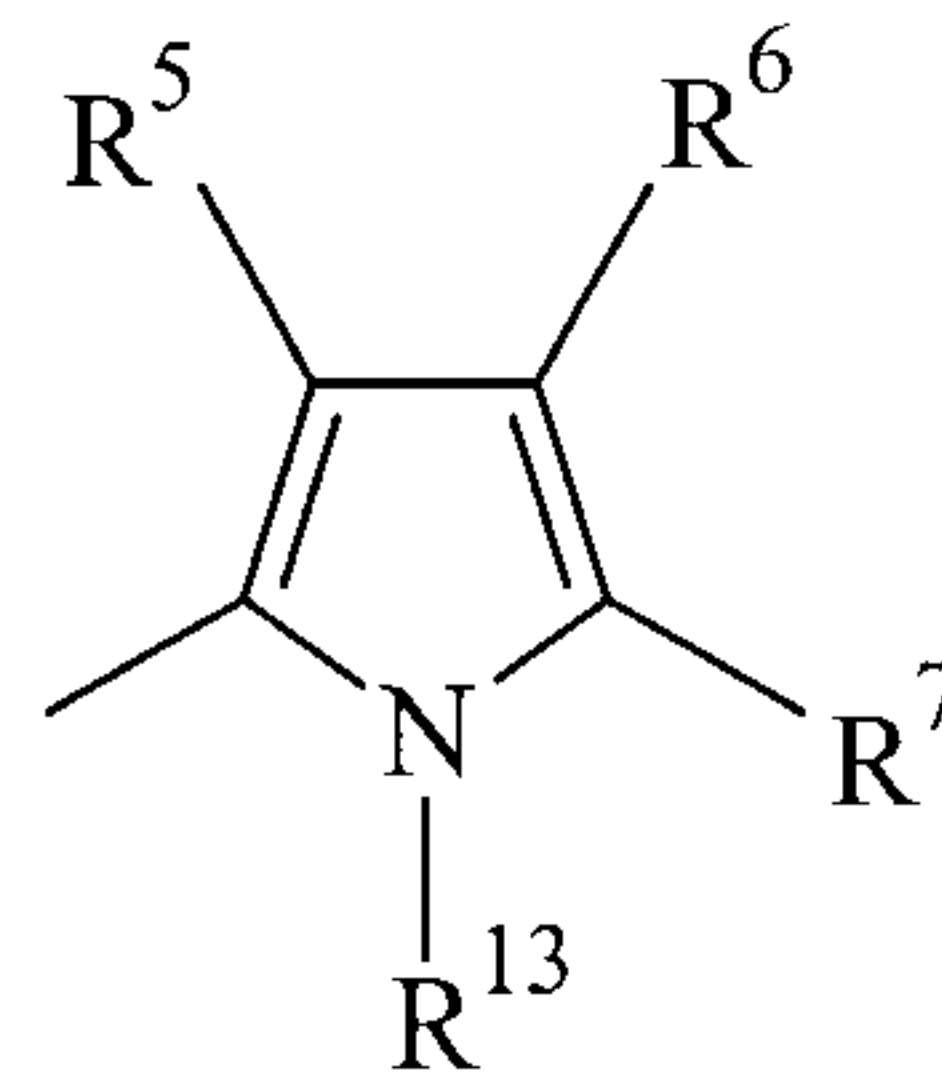
Q is a radical selected from the group of the
formulae



15



or



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in which R^5 , R^6 , R^7 , R^8 and R^9 independently of one another are H, a halogen, OH, CN, NO_2 , SO_3H , SO_3R^4 , $SO_2NR^{14}R^{15}$, $COOH$, $COOR^4$, $CONR^{14}R^{15}$, $O-COOR^4$, $O-COR^4$, an alkyl, an alkoxy, a haloalkyl or a haloalkoxy,

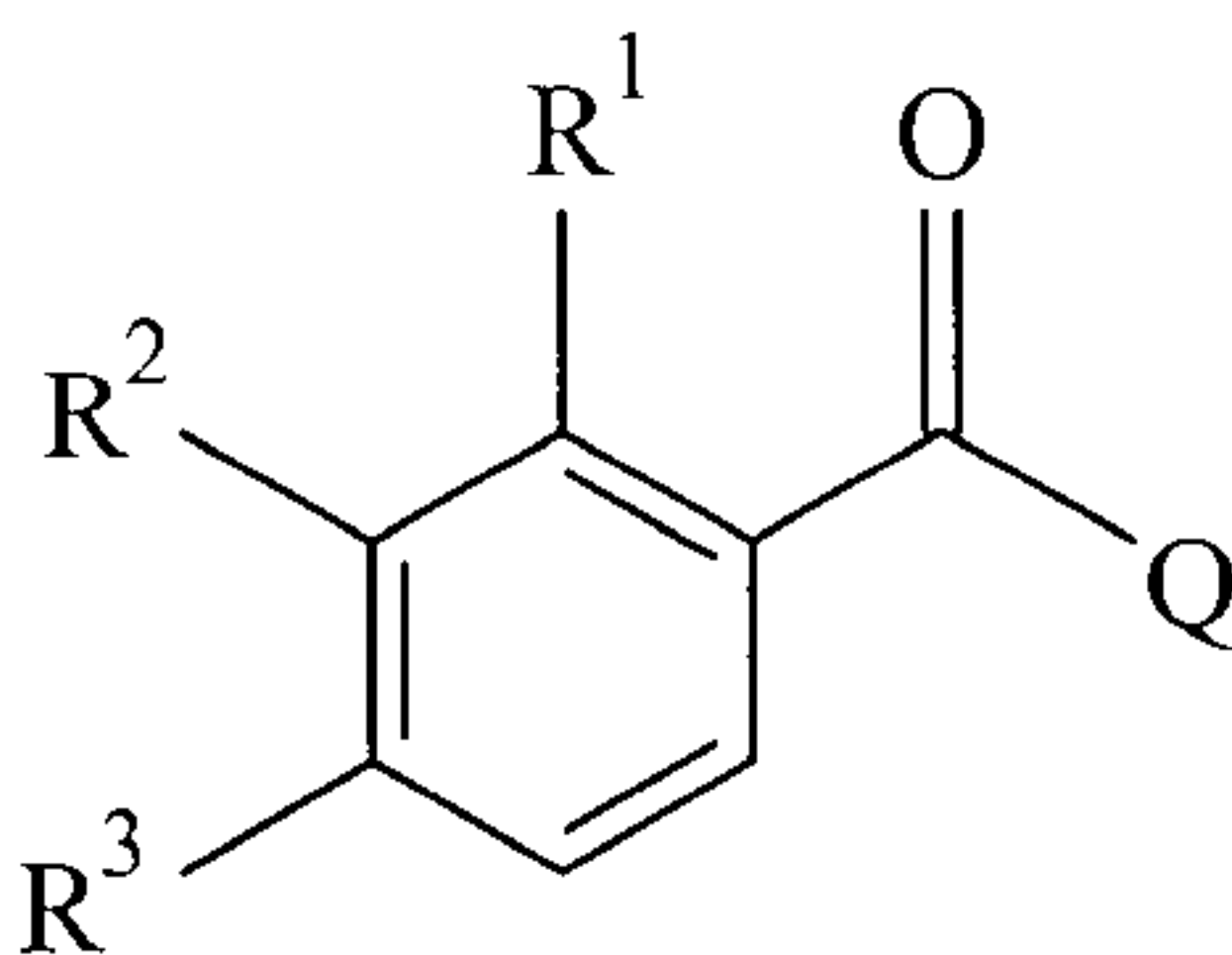
5 R^{10} , R^{11} and R^{12} independently of one another are H, a halogen, an alkyl, an alkoxy, a haloalkyl or a haloalkoxy,

R^{13} is H, phenylsulfonyl, an alkylsulfonyl or an alkylcarbonyl, and

R^{14} and R^{15} independently of one another are H, an alkyl, an aryl or benzyl.

In the formula (I), the radicals alkyl, alkoxy, haloalkyl and haloalkoxy can in each case be straight-chain or branched. Alkyl radicals are, for example, methyl, ethyl, n- or i-propyl or n-, i-, t- or 2-butyl. Aryl embraces aromatic and heteroaromatic radicals, such as, for example, phenyl, 2- or 3-naphthyl or 2-, 3- or 4-pyridyl. Halogen is fluorine, chlorine, bromine or iodine.

10 The invention further provides a compound of the formula (I),



(I)

in which

R^1 is H, a halogen, OH, C_1 - C_3 -alkoxy, CN, NO_2 or C_1 - C_3 -haloalkyl,

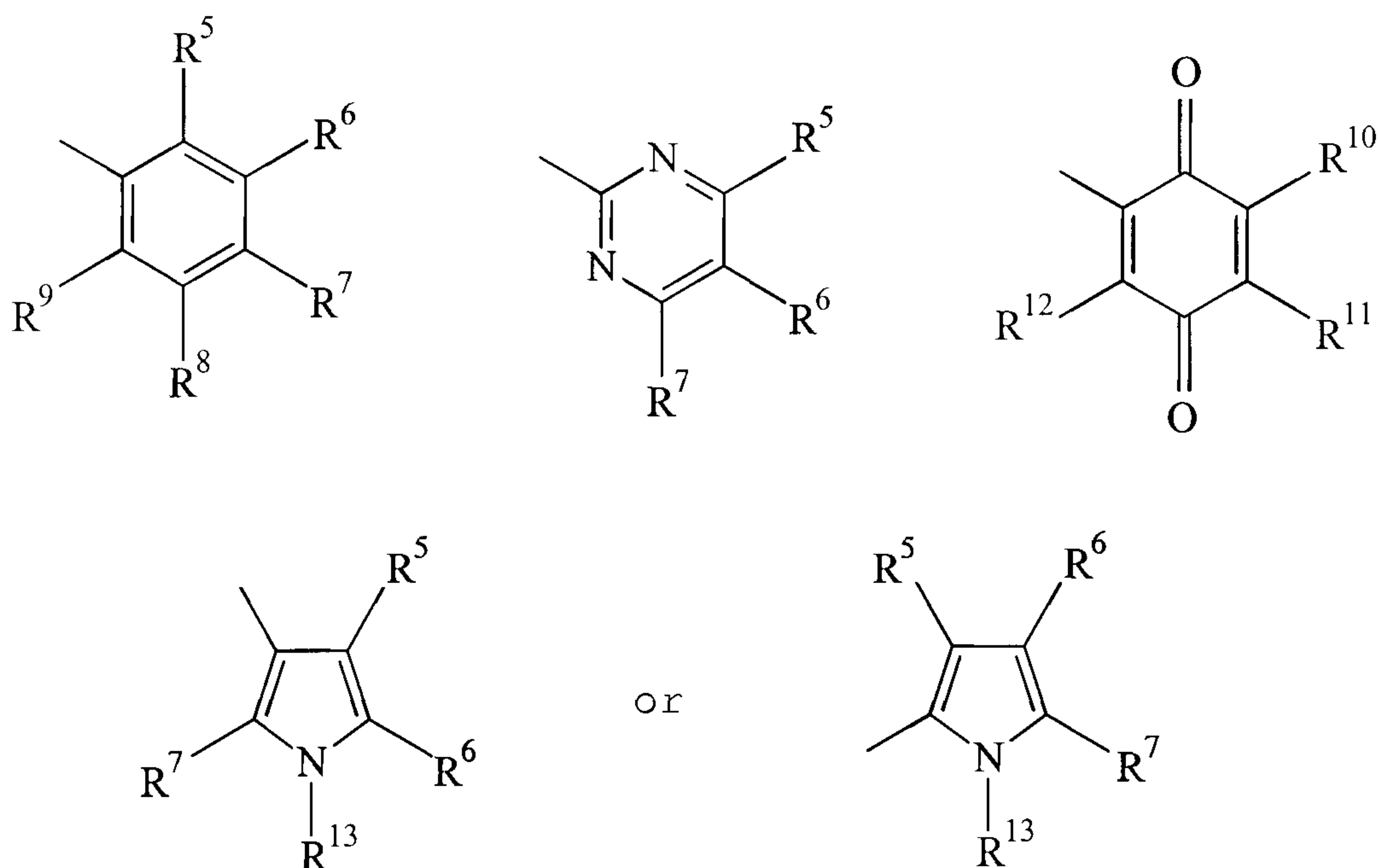
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R^2 is H, a halogen, OH, C_1 - C_3 -alkyl, C_1 - C_3 -alkoxy, C_1 - C_2 -haloalkyl, C_1 - C_2 -haloalkoxy or $(C_1$ - C_2 -alkoxy)carbonyl,

R^3 is H, a halogen, OH, CN, NO_2 , C_1 - C_3 -haloalkyl, C_1 - C_2 -haloalkoxy or $R^4S(O)_m-$, where R^4 is C_1 - C_2 -alkyl and m is
5 zero, one or two,

Q is a radical selected from the group of the formulae



R^5 , R^6 , R^7 , R^8 and R^9 independently of one another
10 are H, a halogen, OH, CN, NO_2 , SO_3H , SO_3R^4 , $SO_2NR^{14}R^{15}$, COOH, $COOR^4$, $CONR^{14}R^{15}$, O-COOR⁴, O-COR⁴, C_1 - C_4 -alkyl, C_1 - C_2 -alkoxy, C_1 - C_3 -haloalkyl or C_1 - C_2 -haloalkoxy,

R^{10} , R^{11} and R^{12} independently of one another are H,
a halogen, C_1 - C_3 -alkyl, C_1 - C_2 -alkoxy, C_1 - C_3 -haloalkyl or
15 C_1 - C_2 -haloalkoxy,

R^{13} is H, phenylsulfonyl, C_1 - C_2 -alkylsulfonyl or C_1 - C_2 -alkylcarbonyl,

R^{14} and R^{15} independently of one another are H, C_1 - C_4 -alkyl, phenyl or benzyl.

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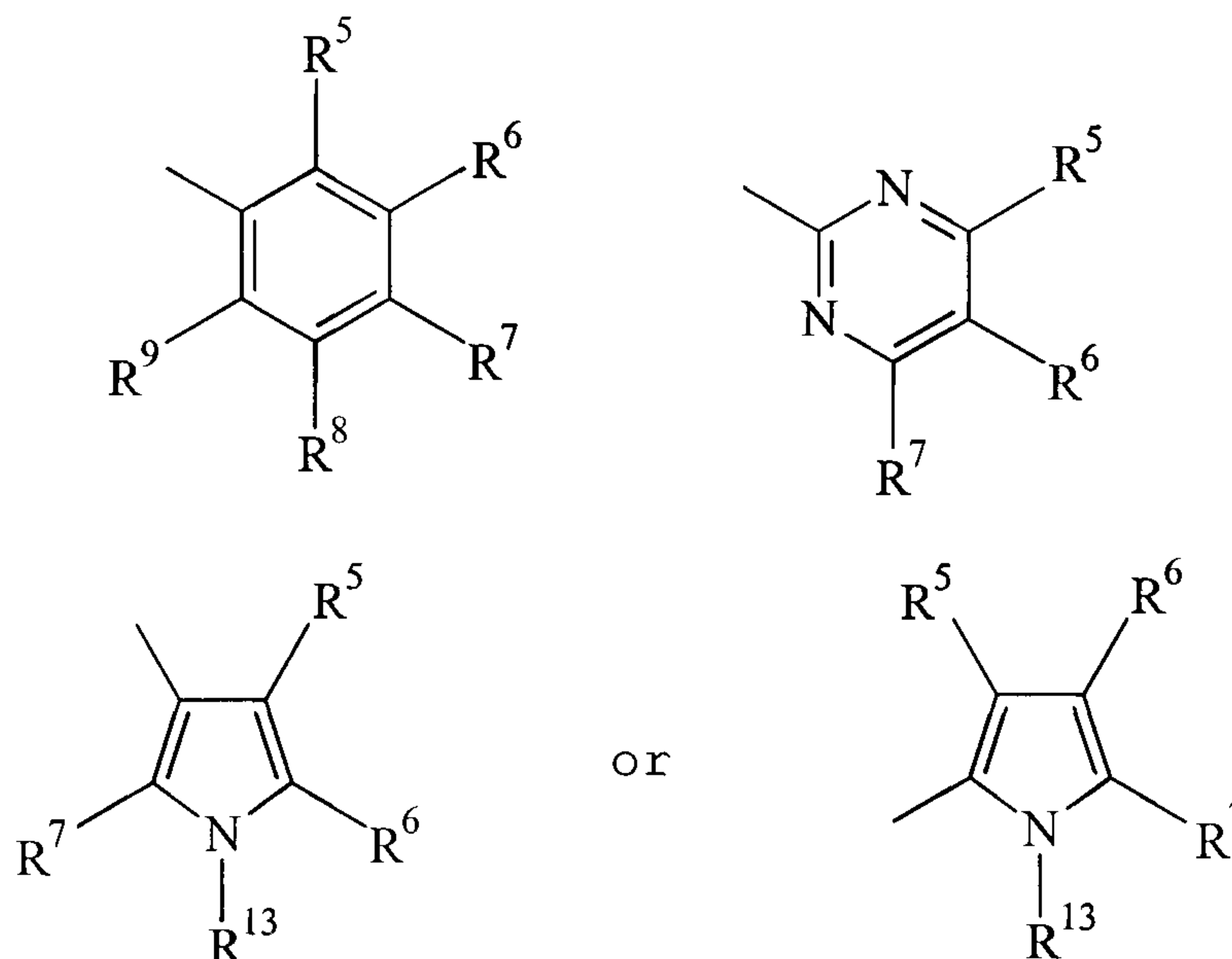
In yet another embodiment, the invention provides the compound of the formula (I) as described above, wherein

R^1 is hydrogen, hydroxyl, methoxy, fluorine, chlorine, bromine, cyano, nitro, difluoromethyl, trifluoromethyl, chloromethyl, trichloromethyl, 2,2,2-trifluoroethyl or pentafluoroethyl,

R^2 is hydrogen, fluorine, chlorine, hydroxyl, propyl, ethyl, methyl, methoxy, ethoxy, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, methoxycarbonyl or ethoxycarbonyl,

R^3 is hydrogen, hydroxyl, fluorine, chlorine, bromine, nitro, difluoromethyl, trifluoromethyl, chloromethyl, trichloromethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, difluoromethoxy, trifluoromethoxy, methylsulfonyl or ethylsulfonyl;

Q is a radical selected from the group of the formulae



20 where

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R^5 , R^6 , R^7 , R^8 and R^9 independently of one another are hydrogen, fluorine, chlorine, bromine, cyano, nitro, hydroxyl, hydroxysulfonyl, ethoxysulfonyl, ethylaminosulfonyl, methylaminosulfonyl, carboxyl, ethoxycarbonyl, methoxycarbonyl, ethylaminocarbonyl, methylaminocarbonyl, ethoxycarbonyloxy, methoxycarbonyloxy, methylcarbonyloxy, t-butyl, i-propyl, propyl, ethyl, methyl, difluoromethyl, trifluoromethyl, chloromethyl, trichloromethyl, methoxy, ethoxy, difluoromethoxy or trifluoromethoxy,

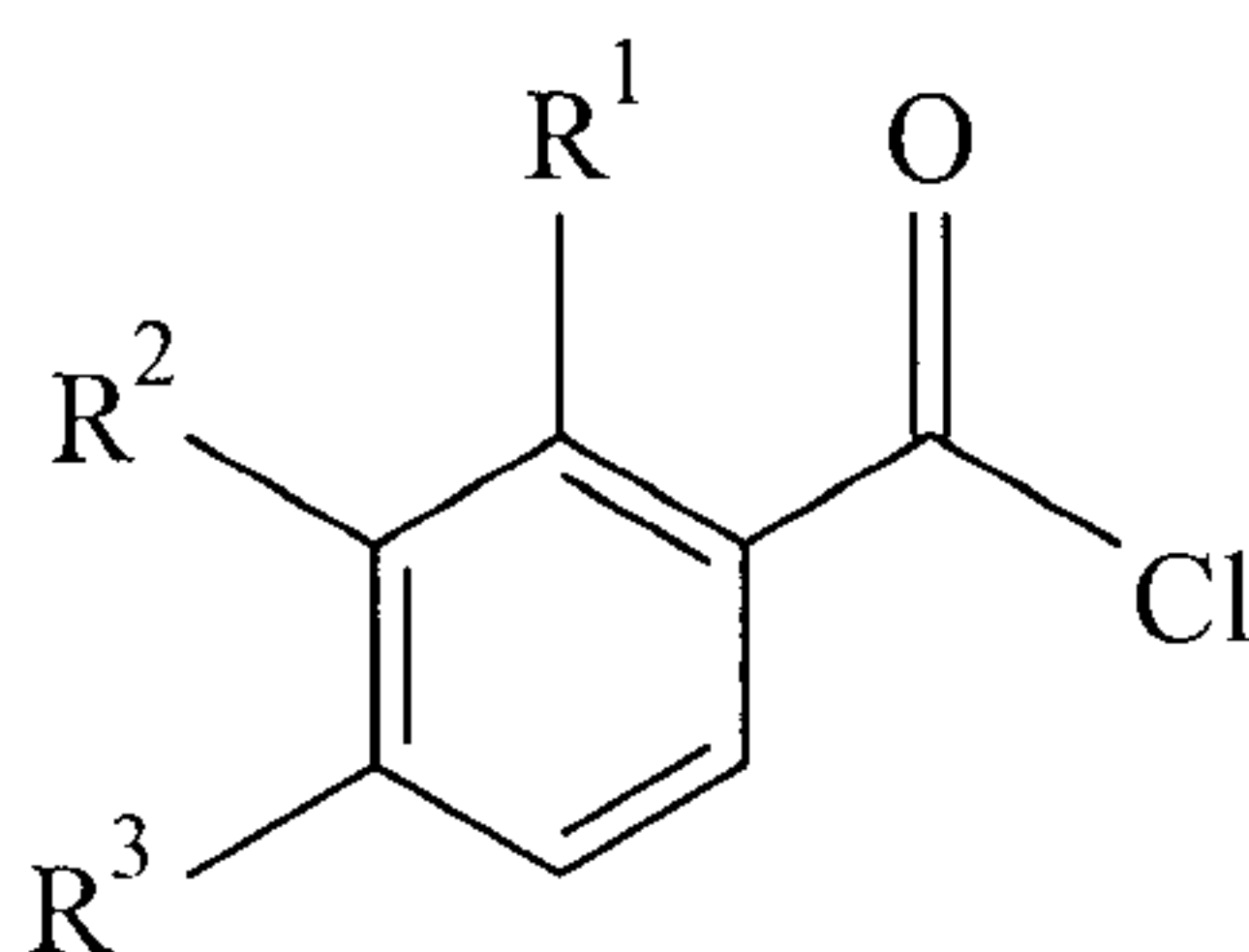
R^{10} , R^{11} and R^{12} independently of one another are hydrogen, fluorine, chlorine, bromine, ethyl, methyl, difluoromethyl, trifluoromethyl, chloromethyl, trichloromethyl, methoxy, ethoxy, difluoromethoxy or trifluoromethoxy,

R^{13} is hydrogen, phenylsulfonyl, methylsulfonyl, ethylsulfonyl, methylcarbonyl or ethylcarbonyl,

R^{14} and R^{15} independently of one another are hydrogen, butyl, propyl, ethyl, methyl or benzyl.

The invention further provides a herbicidal composition which comprises the compound of the formula (I) as described above and conventional formulations auxiliaries.

The invention further provides a process for the preparation of the compound of the formula (I) as described above, which comprises reacting acid chlorides of the formula (II)



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in which R^1 , R^2 and R^3 are as defined in formula (I), with aromatic and heteroaromatic compounds of the formula (III)

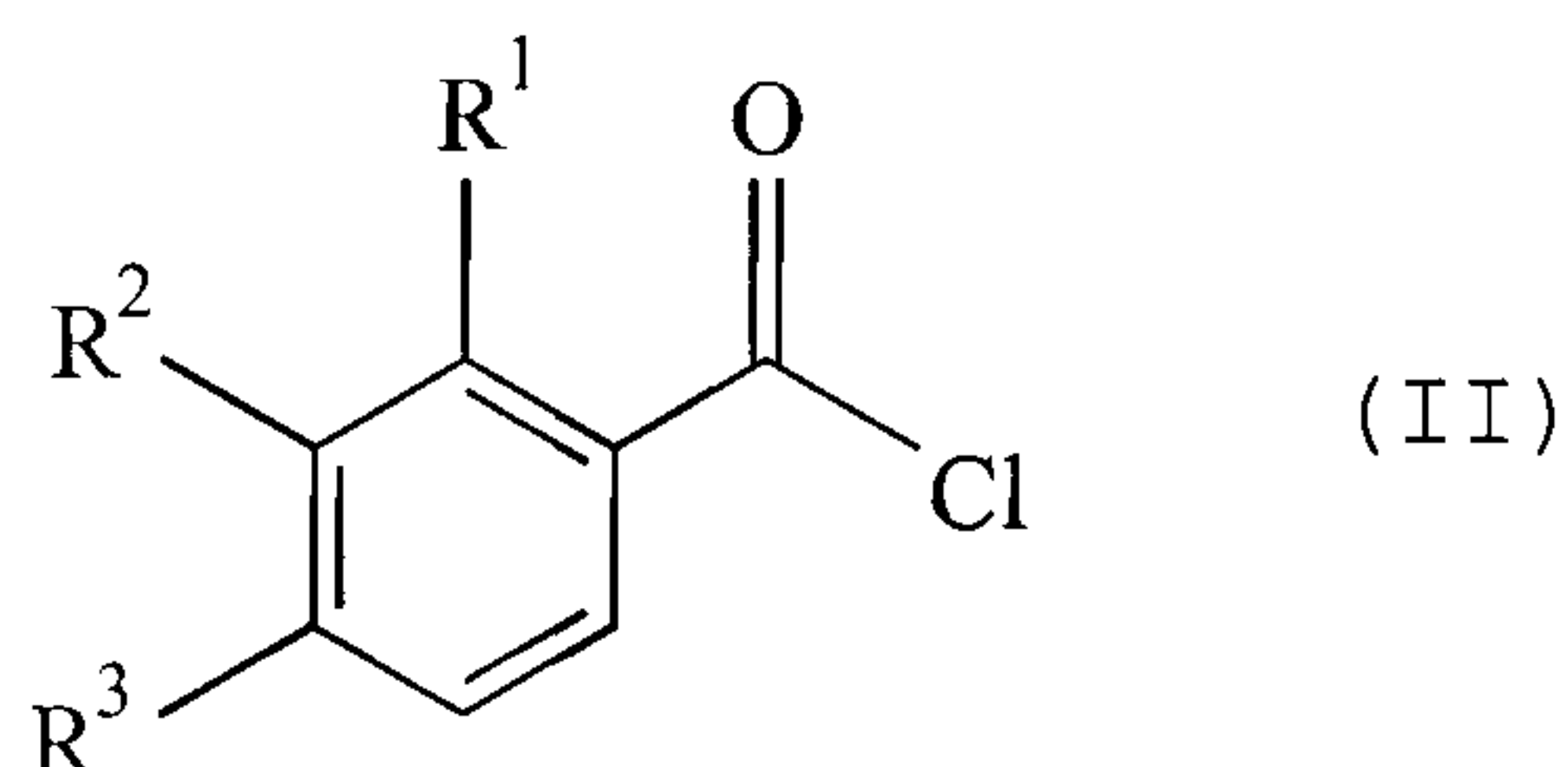


in which Q is as defined in formula (I), in the presence of
5 a Lewis acid, in a chlorinated hydrocarbon.

The invention further provides a method of controlling undesired plants, which comprises applying a herbicidally effective amount of the compound of the formula (I) as described above to the undesired plants or to the
10 areas on which the undesired plants grow.

The uses according to the invention of compounds of the formula (I) with a combination of the abovementioned preferred characteristics are also preferred.

The compounds of the abovementioned formula (I) can be prepared, for example, by reacting aromatic
15 carboxylic acid chlorides of the formula (II)



20 in which the substituents R^1 , R^2 and R^3 are as defined under formula (I), with aromatic or heteroaromatic compounds of the type H-Q, in which Q is as defined under formula (I), in an inert solvent in the presence of a Lewis acid.

The compounds (I) are preferably prepared in
25 aprotic solvents, in particular in halogenated hydrocarbons, such as, for example, dichloromethane, trichloromethane, 1,2-dichloromethane or 1,1,2,2-tetrachloroethane, at from -20°C up to the boiling point of the reaction mixture, in

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particular at from room temperature to 50°C, the reaction being carried out in the presence of a catalytically to stoichiometrically employed amount of Lewis acid, such as, for example, aluminum chloride, titanium tetra-chloride or
5 boron trifluoride.

A. Preparation Examples

- a) 3-(2,4-Dichlorobenzoyl)-1-phenylsulfonylpyrrole
(Table 1, Example No. 150)

5 4.0 ml of 2,4-dichlorobenzoyl chloride and 4.00 g of
aluminum chloride are stirred for 10 minutes at room
temperature in 50 ml of 1,2-dichloroethane. A solu-
tion of 5.10 g of phenylsulfonylpyrrole in 20 ml of
1,2-dichloroethane is added dropwise to the mixture,
and this is stirred for 2 hours at room temperature.
10 The mixture is poured into ice-water and extracted
using dichloromethane. The organic phase is dried
and evaporated. Recrystallization of the residue
from a mixture of ethyl acetate and petroleum ether
gives 8.3 g (89% of theory) of 3-(2,4-dichloro-
15 benzoyl)-1-phenylsulfonylpyrrole in the form of
white crystals with a melting point of 122°C.

- b) 2,5'-Dichloro-2'-hydroxy-3'-methyl-4-methylsulfonyl-
benzophenone (Table 1, Example No. 100)

20 5.06 g of 2-chloro-4-methylsulfonylbenzoyl chloride
are added in portions at room temperature to a mix-
ture of 2.85 g of 4-chloro-2-methylphenol and 5.40 g
of aluminum chloride in 100 ml of 1,1,2,2-tetra-
chloroethane, and the mixture is subsequently
25 refluxed for 7 hours. When cold, the reaction mix-
ture is poured onto 200 g of ice and 500 ml of
concentrated hydrochloric acid. The organic phase is
separated off, and the aqueous phase is extracted
twice using 50 ml of dichloromethane. The combined
organic phases are washed until neutral, dried over
30 magnesium sulfate and evaporated. Recrystallization
from a mixture of ethyl acetate and diisopropyl
ether gives 4.2 g (60% of theory) of 2,5'-dichloro-
2'-hydroxy-3'-methyl-4-methylsulfonylbenzophenone in
the form of colorless crystals with a melting point
35 of 175-180°C.

- c) 2-(2,4-Dichlorobenzoyl)-1,4-quinone (Table 1, Example No. 91)

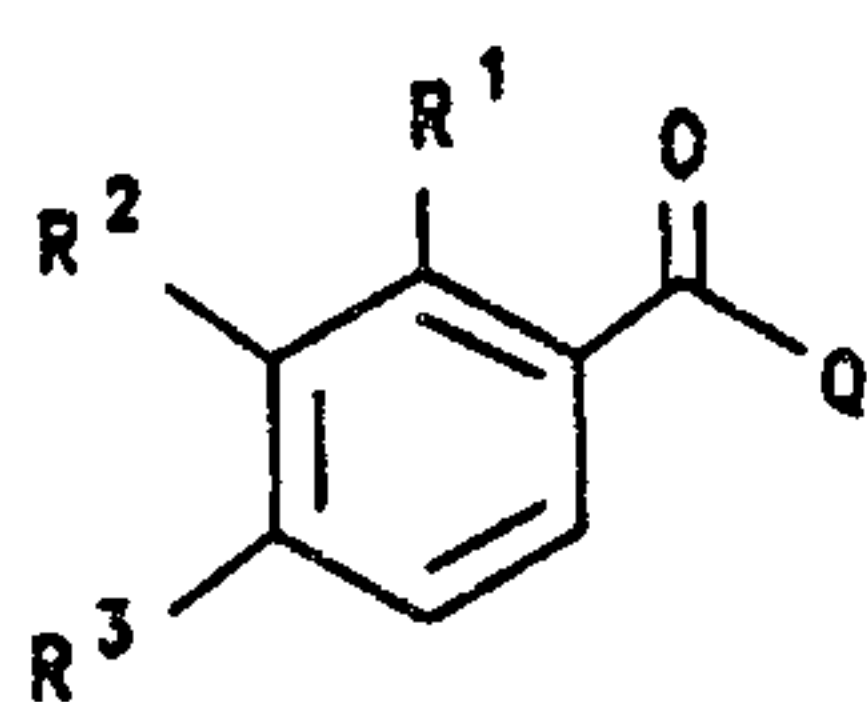
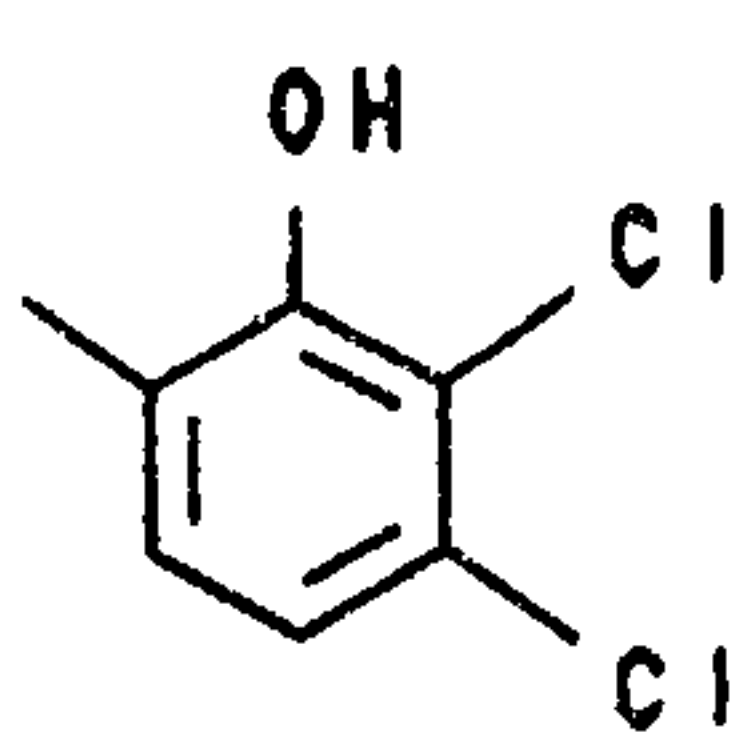
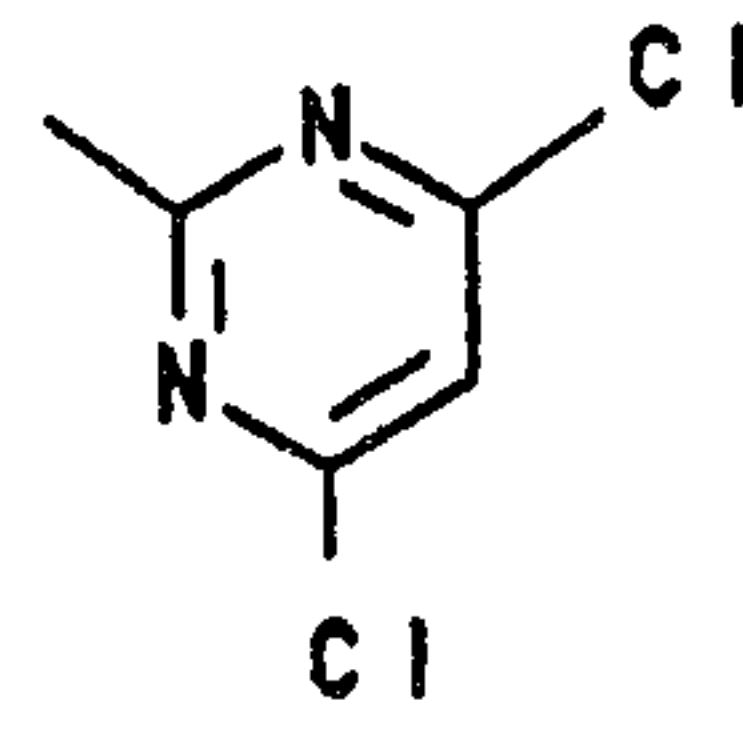
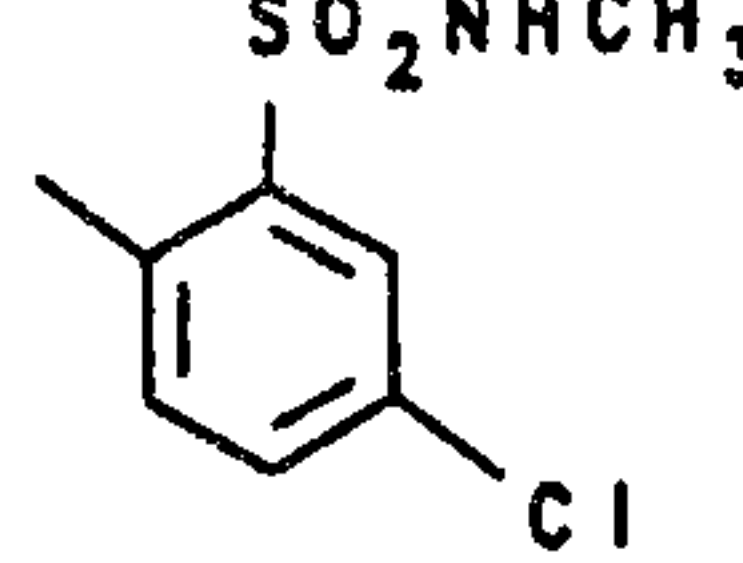
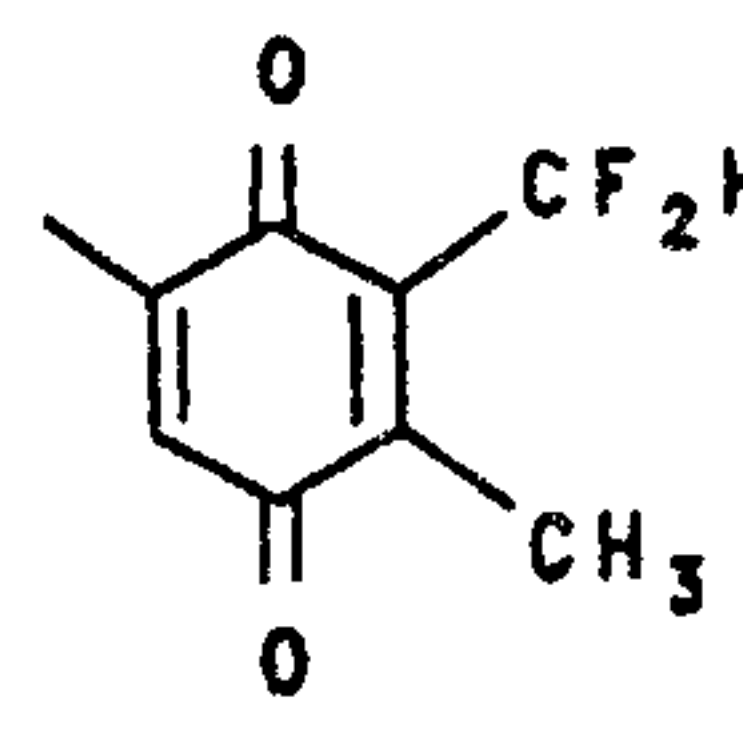
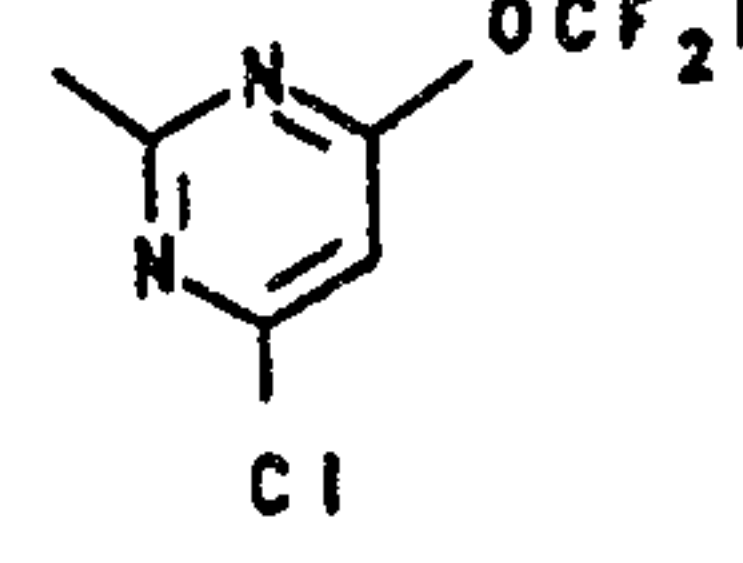
5 A solution of 2.49 g of 2-(2,4-dichlorobenzoyl)-1,4-dihydroxybenzene in 20 ml of glacial acetic acid is added dropwise at 10°C in the course of 3 minutes to a solution of 1.60 g of sodium dichromate in 2 g of concentrated sulfuric acid and 60 ml of water. The reaction mixture is stirred vigorously for a further 30 minutes at 10-15°C and then filtered. The
10 residue is washed with water until free from acid and recrystallized from diisopropyl ether. 1.74 g (70% of theory) of 2-(2,4-dichlorobenzoyl)-1,4-quinone are obtained in the form of yellowish-orange crystals with a melting point of 100°C.

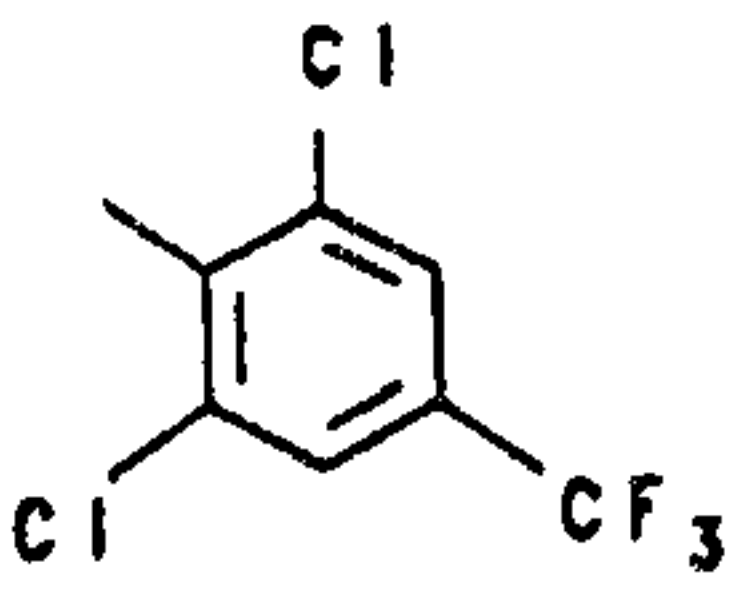
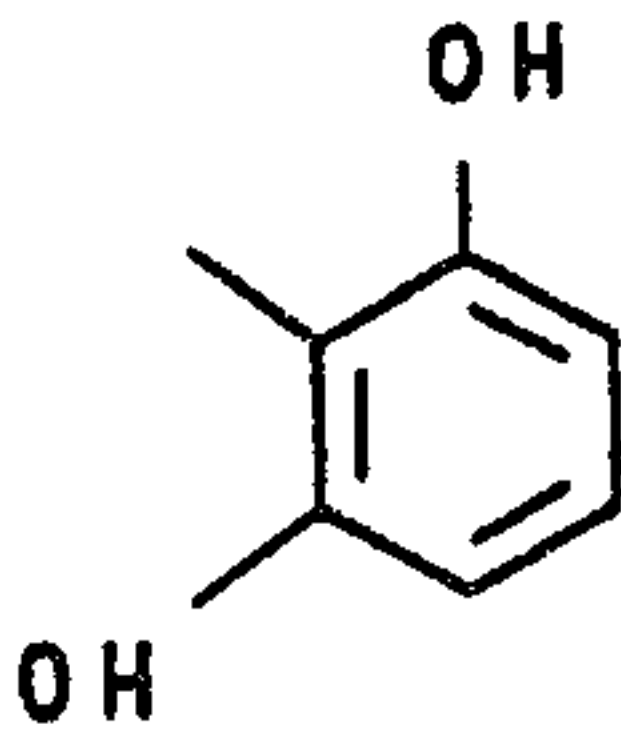
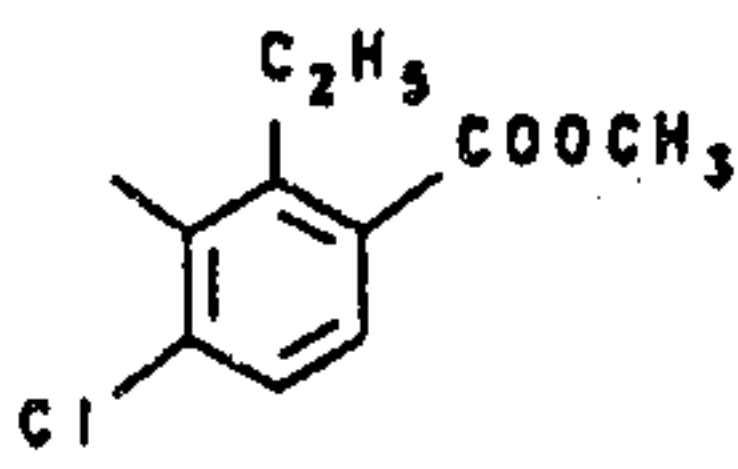
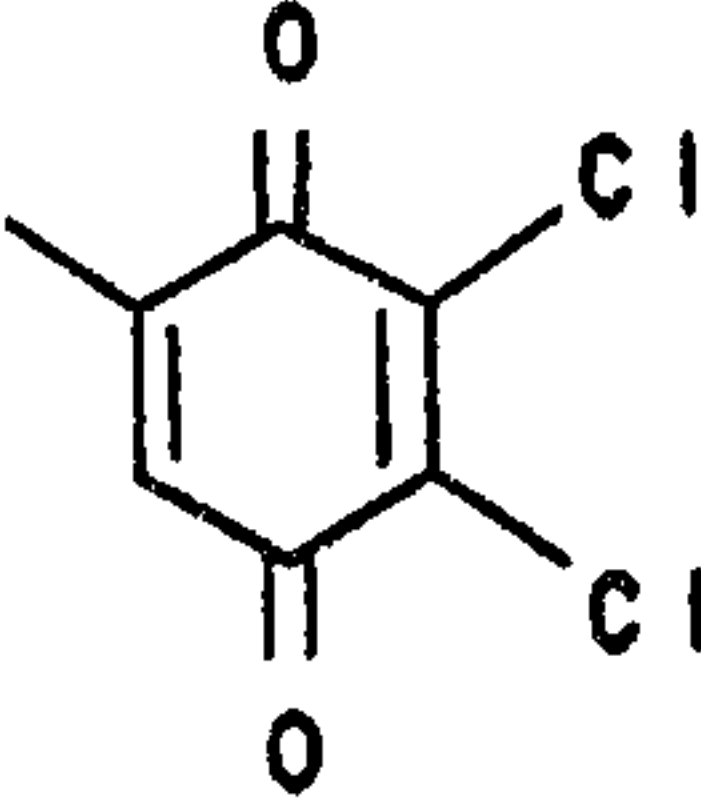
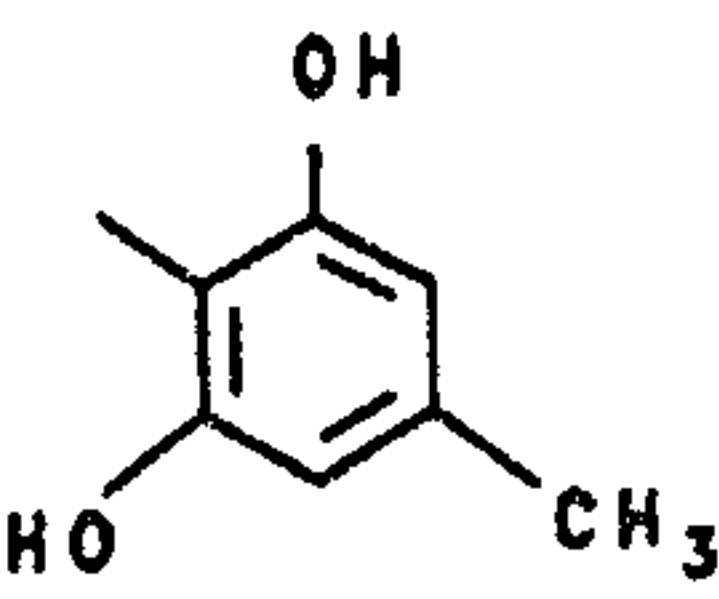
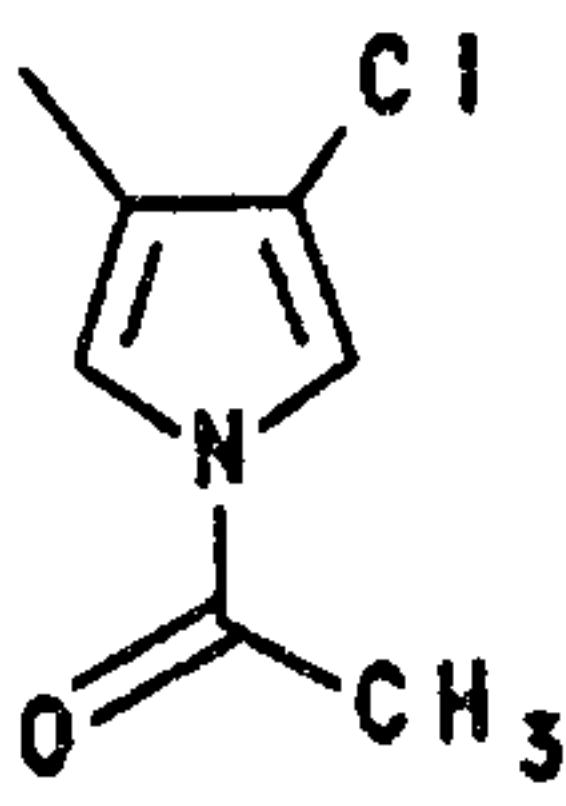
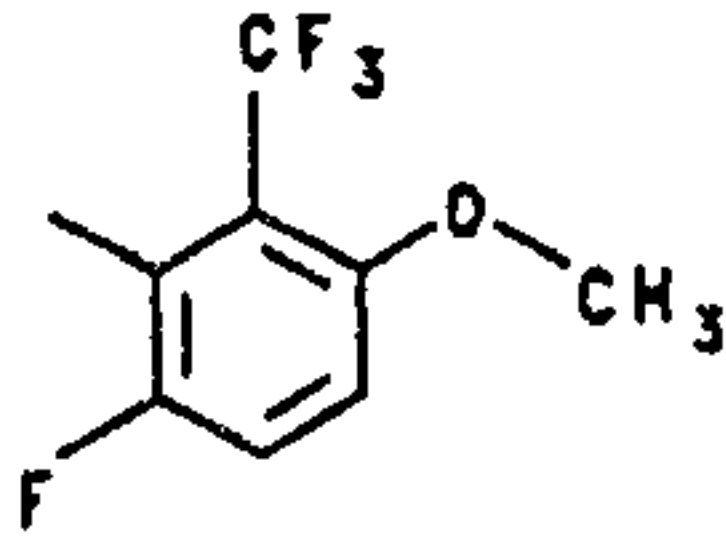
- 15 d) 2,2',4'-Trichloro-6'-hydroxy-4-methylsulfonylbenzophenone (Table 1, Example No. 183)

3.00 g of 2-chloro-4-methylsulfonylbenzoyl chloride are added in portions at room temperature to a mixture of 1.97 g of 3,5-dichlorophenone and 3.23 g
20 of aluminum chloride in 50 ml of 1,1,2,2-tetrachloroethane, and the mixture is subsequently refluxed for 7 hours. When cold, the reaction mixture is poured onto 100 g of ice and 20 ml of concentrated hydrochloric acid. The organic phase is removed, and the aqueous phase is extracted twice
25 using 50 ml of dichloromethane. The combined organic phases are washed until neutral and subsequently extracted three times using in each case 25 ml of 2 N sodium hydroxide solution. The combined alkaline extracts are brought to a pH of 2 using concentrated
30 hydrochloric acid. The precipitate is filtered off, washed with water until neutral and dried. This gives 3.194 g (70% of theory) of 2,2',4'-trichloro-6'-hydroxy-4-methylsulfonylbenzophenone in the form of colorless crystals with a melting point of
35 123-126°C.

The compounds listed in Table 1 are obtained analogously to the preparation examples described above.

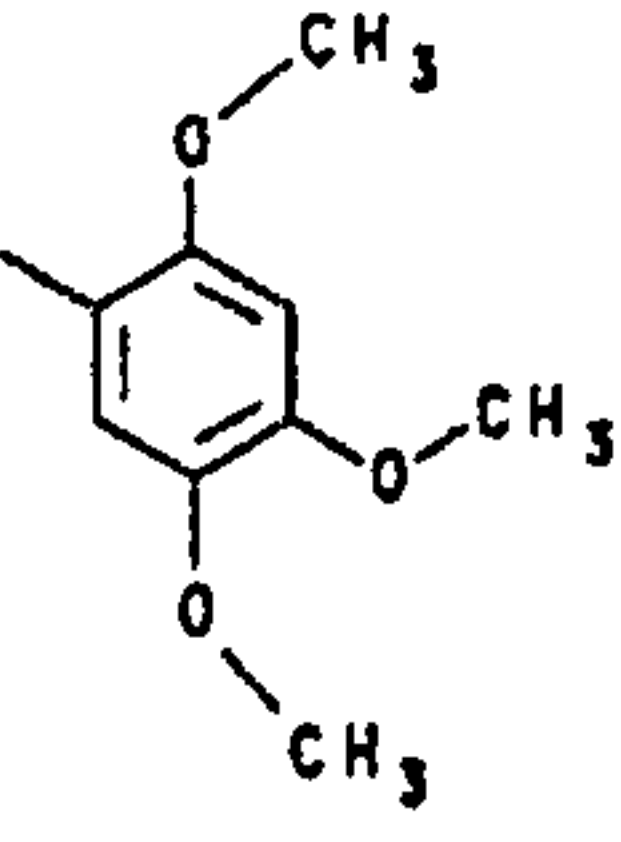
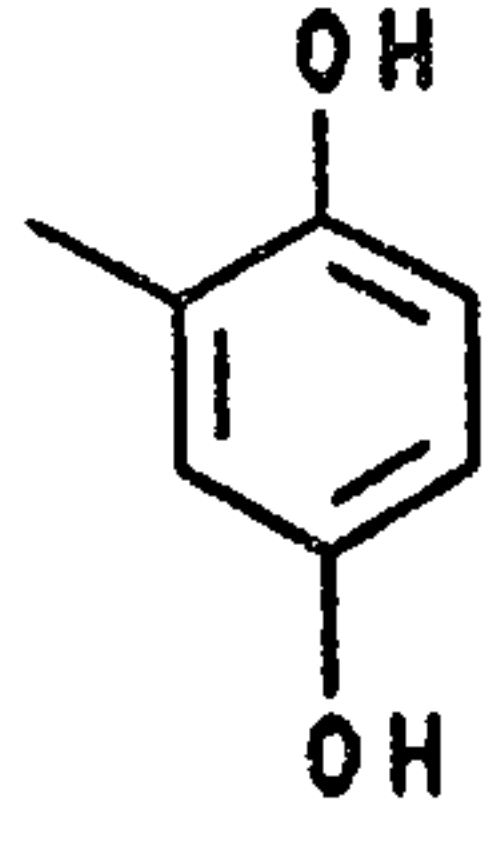
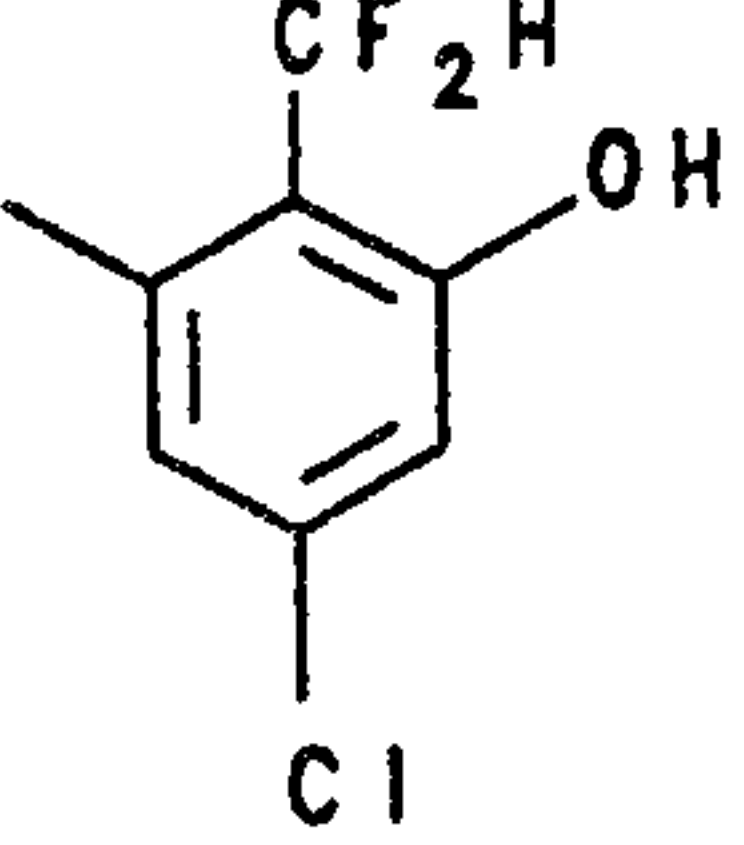
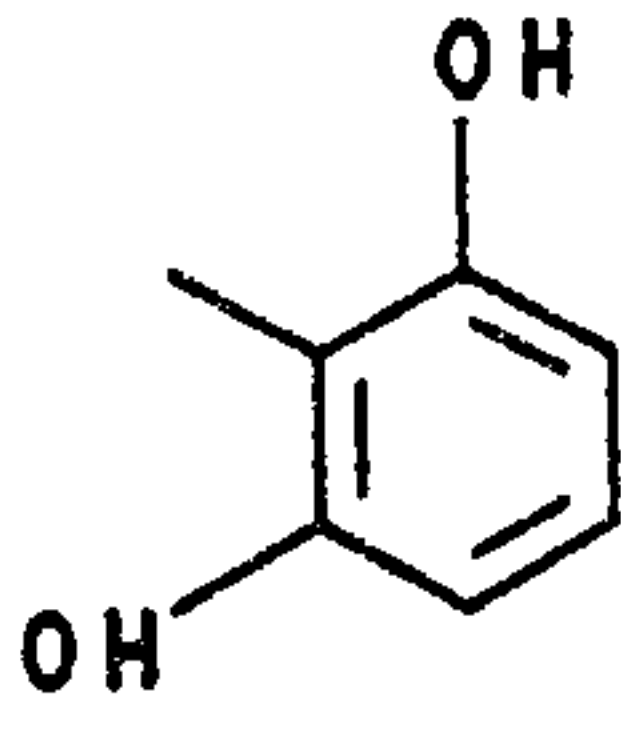
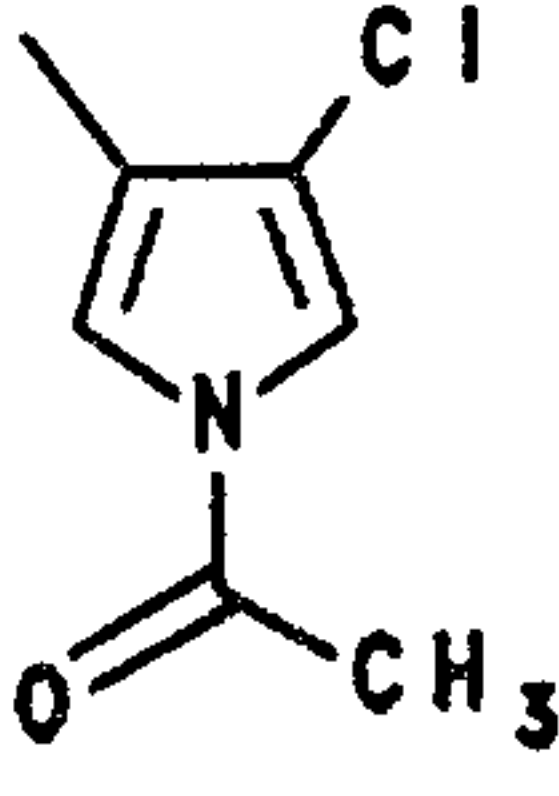
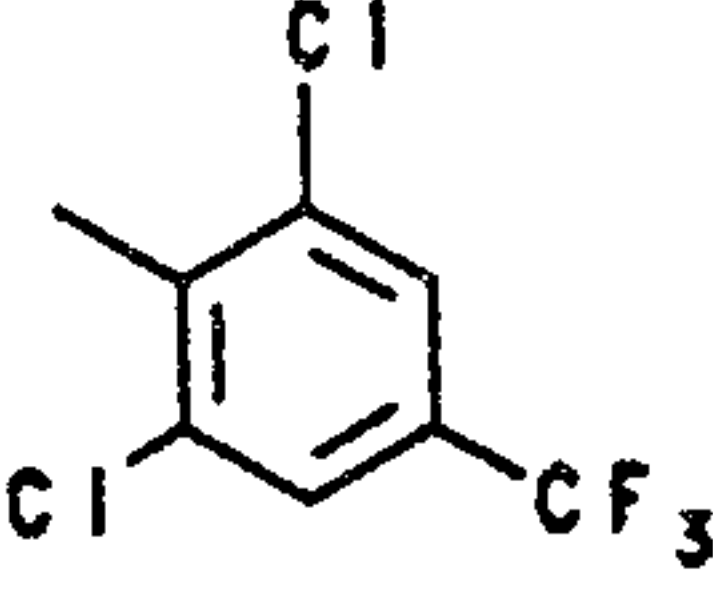
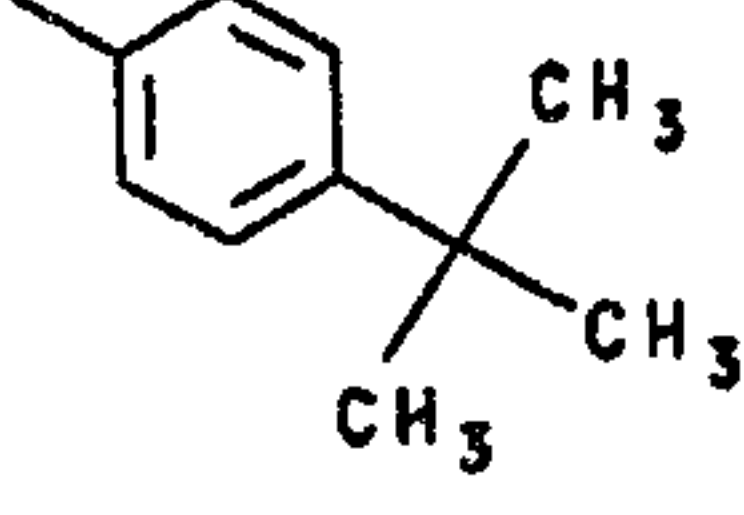
Table 1

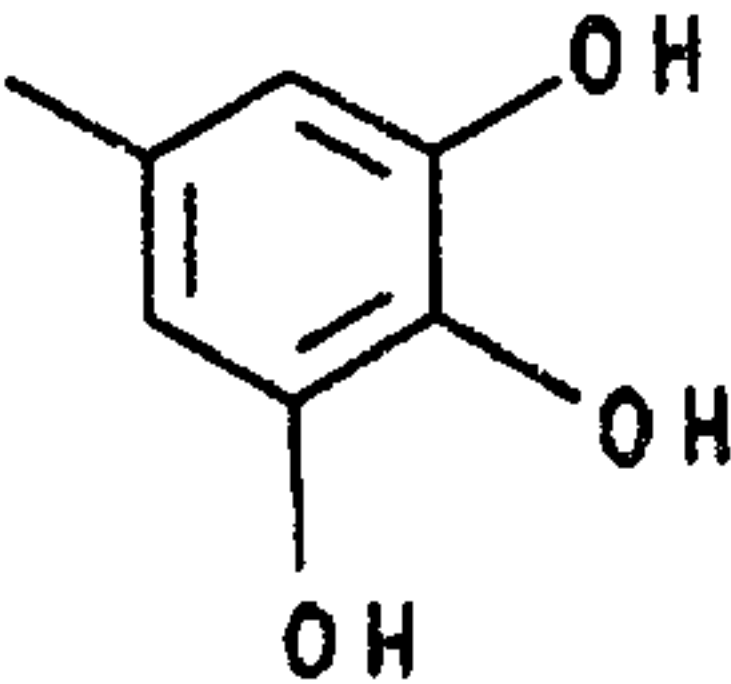
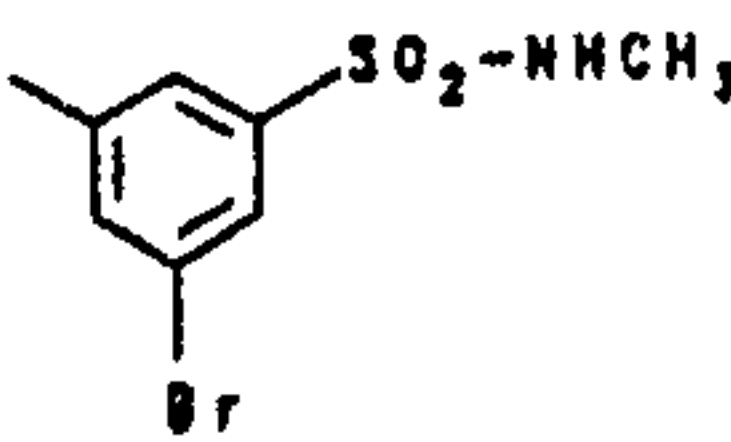
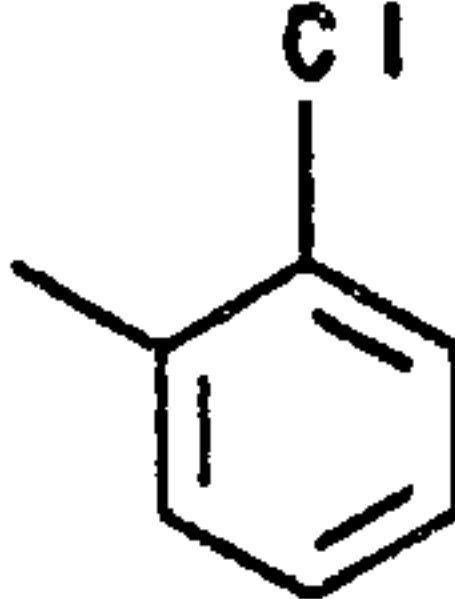
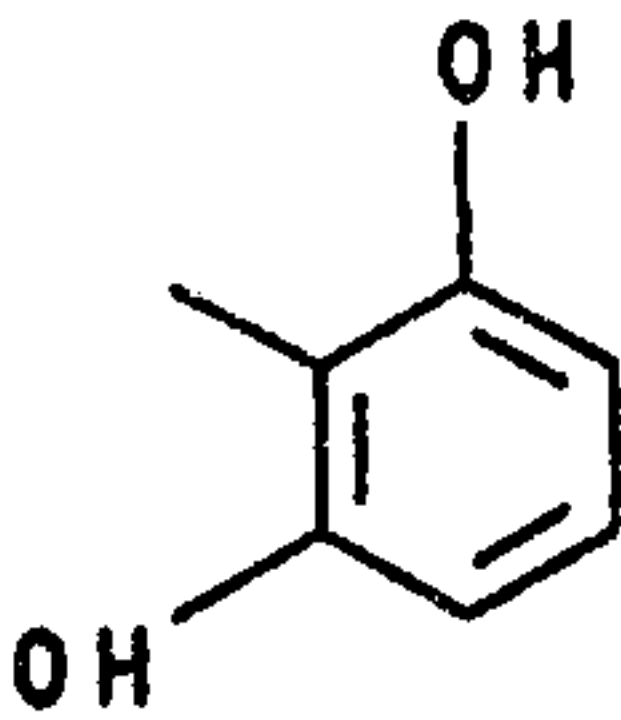
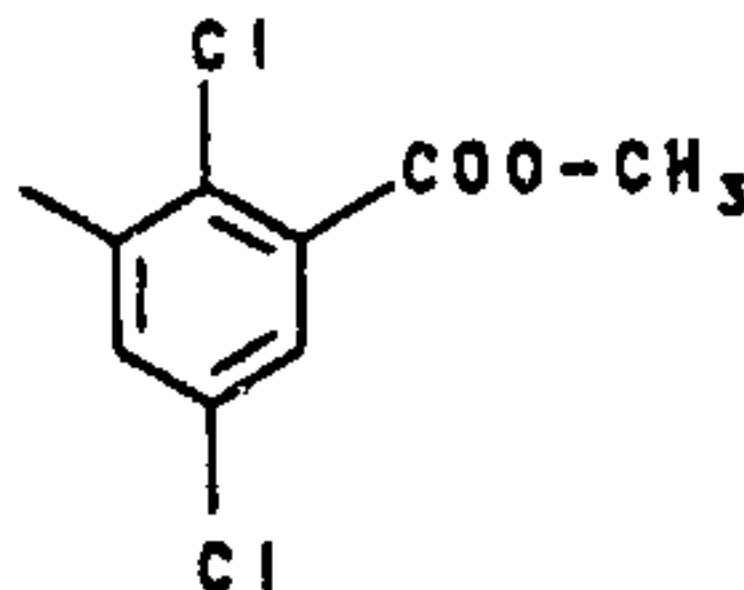
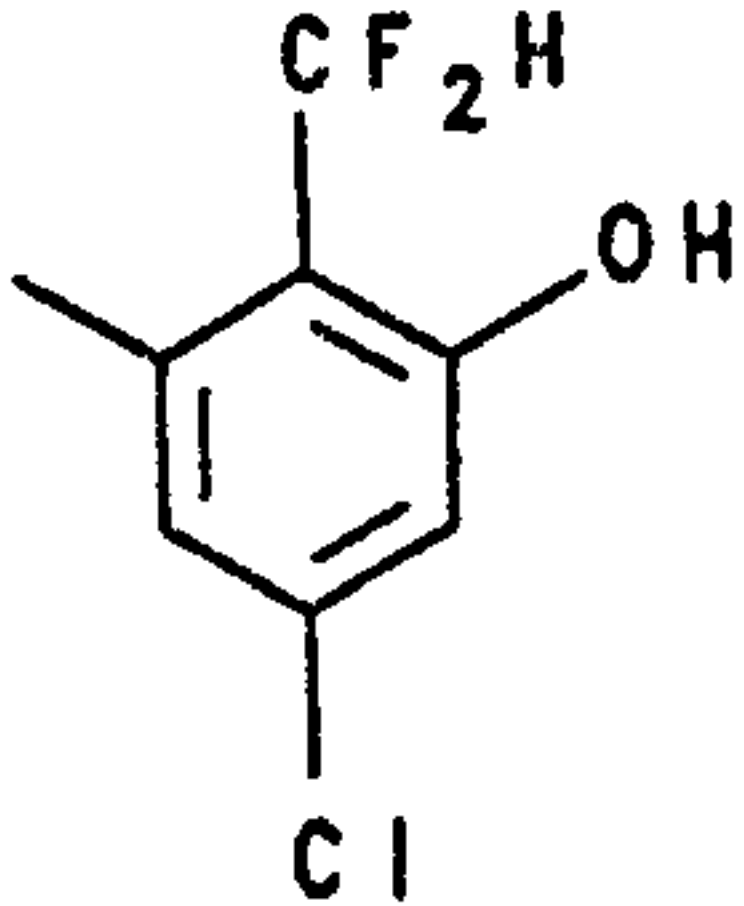
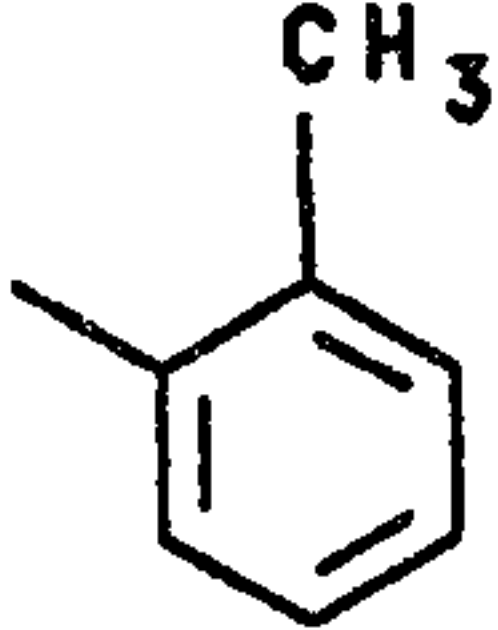
Compounds of the formula (I) according to the invention						
 (I)						
No.	R ¹	R ²	R ³	Q	M.p. [°C]	IC ₅₀
1	Cl	H	NO ₂		135-139	< 10 ⁻⁹
2	Cl	CH ₃	SO ₂ CH ₃			
3	Cl	H	OCF ₂ H			
4	Br	H	CN			
5	Br	H	NO ₂			

6	Cl	OC ₂ H ₅	SO ₂ CH ₃			
7	Cl	H	SO ₂ CH ₃		228	5.7×10 ⁻⁷
8	F	OH	CH ₂ CF ₃			
9	NO ₂	F	CH ₂ Cl			
10	Cl	H	SO ₂ CH ₃		225 (decomp.)	1.8×10 ⁻⁷
11	OC ₂ H ₅	CF ₂ H	SO ₂ CH ₃			
12	OCH ₃	H	Br			

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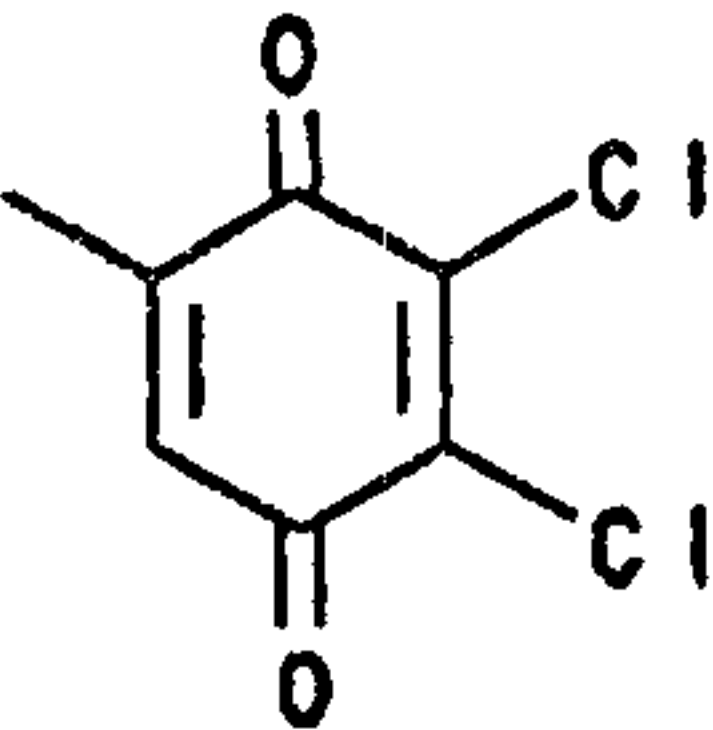
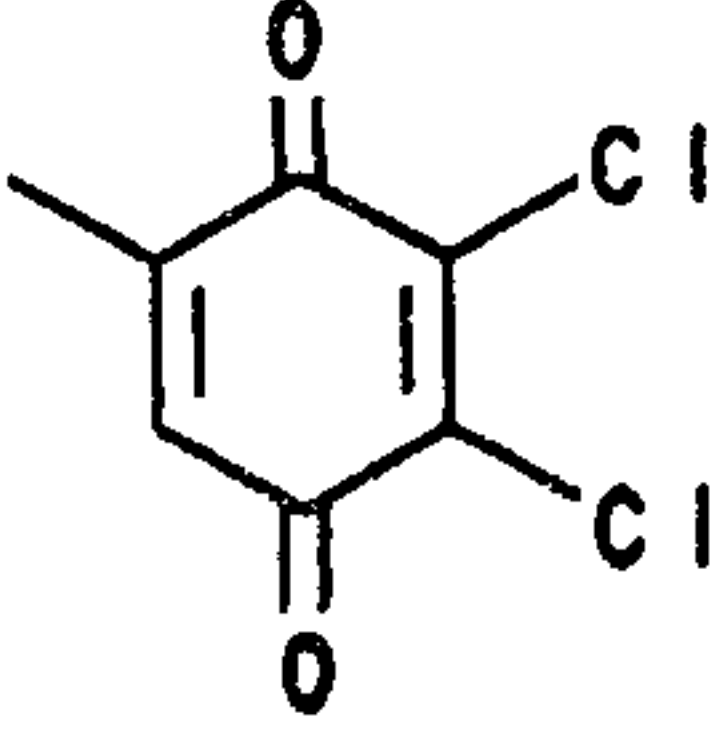
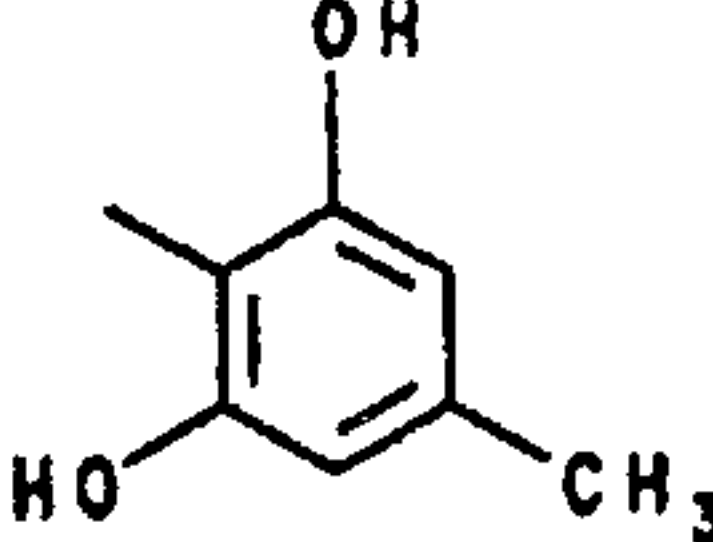
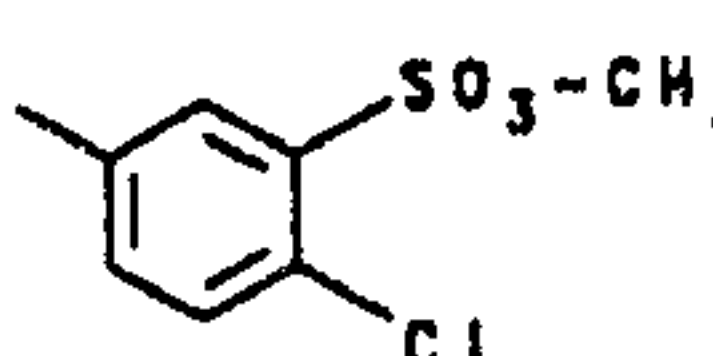
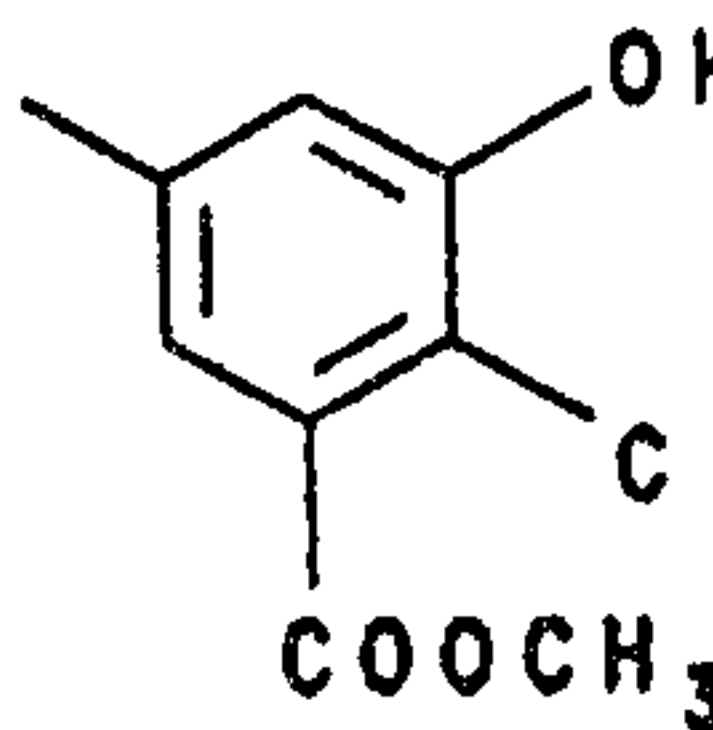
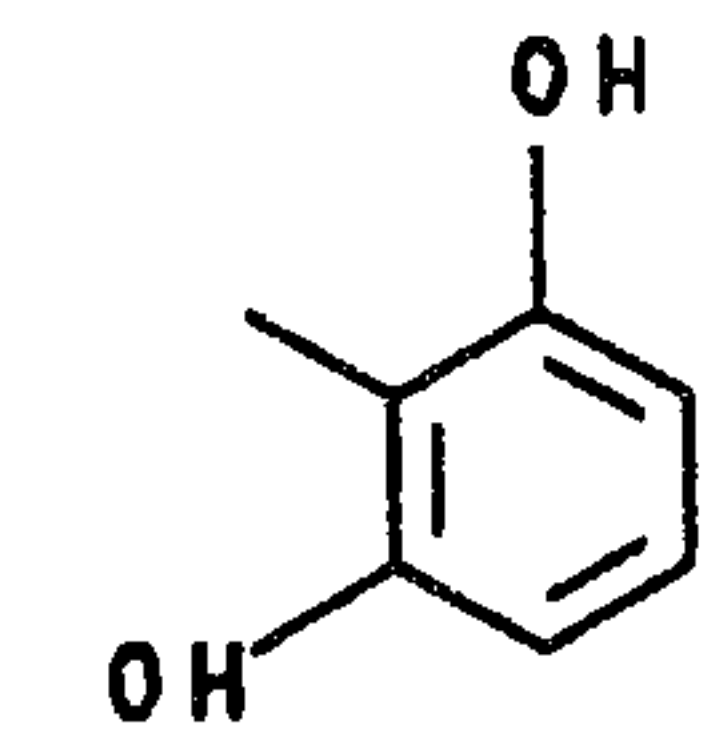
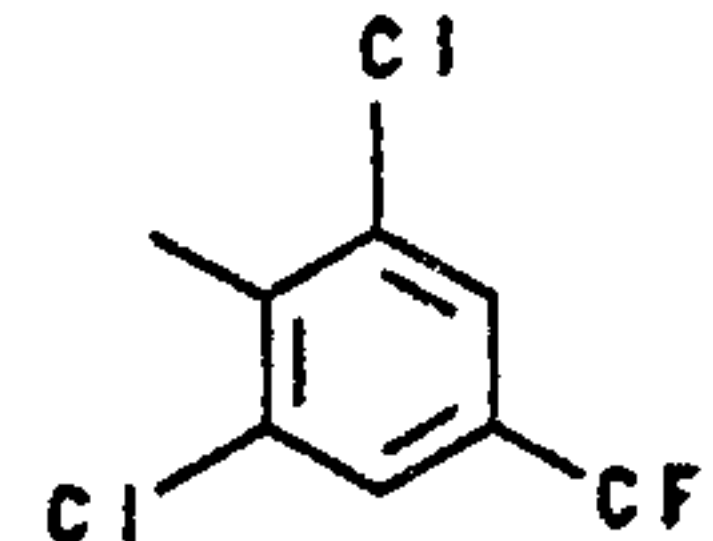
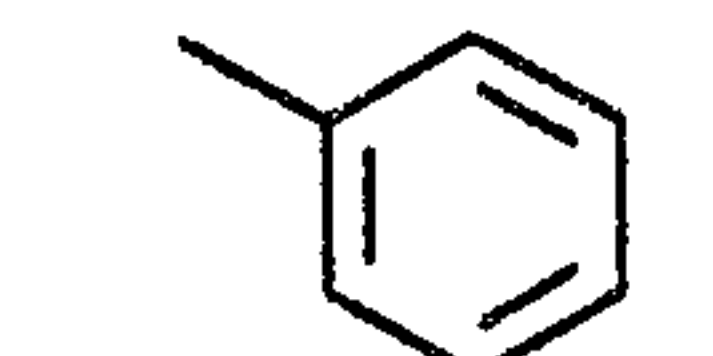
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14	Cl	H	SO ₂ CH ₃		267 (decomp.)	
15	F	COOCH ₃	CH ₂ CF ₃			
16	Cl	H	Cl		147	
17	Cl	Cl	Br			
18	CN	F	CH ₂ Cl			
19	OH	Cl	Cl		95-101	

20	<chem>CH2Cl</chem>	<chem>OCH3</chem>	<chem>NO2</chem>			
21	<chem>Br</chem>	<chem>Cl</chem>	<chem>Cl</chem>			
22	<chem>OH</chem>	<chem>Cl</chem>	<chem>Cl</chem>		126-128	
23	<chem>H</chem>	<chem>H</chem>	<chem>SO2CH3</chem>		224	
24	<chem>CH2CF3</chem>	<chem>COOCH3</chem>	<chem>Cl</chem>			
25	<chem>F</chem>	<chem>Cl</chem>	<chem>SO2CH3</chem>			
26	<chem>OH</chem>	<chem>Cl</chem>	<chem>Cl</chem>		97-100	

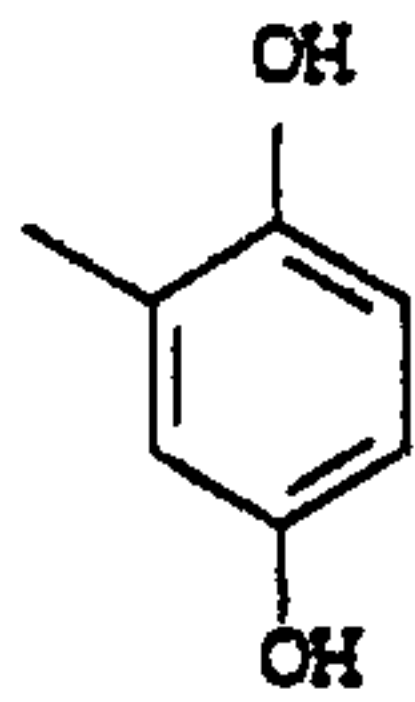
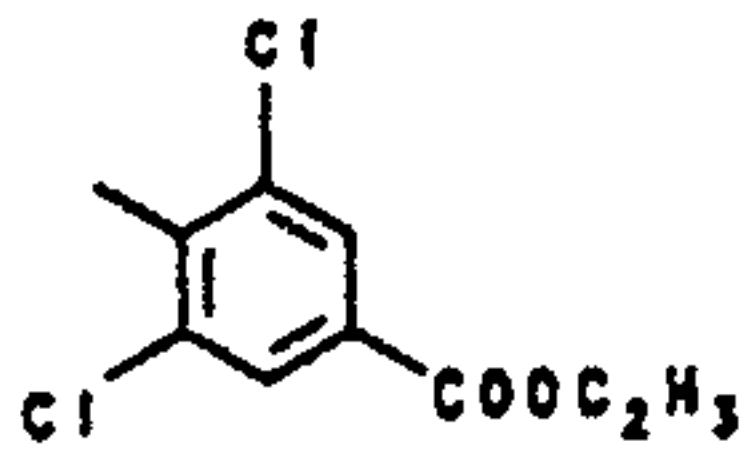
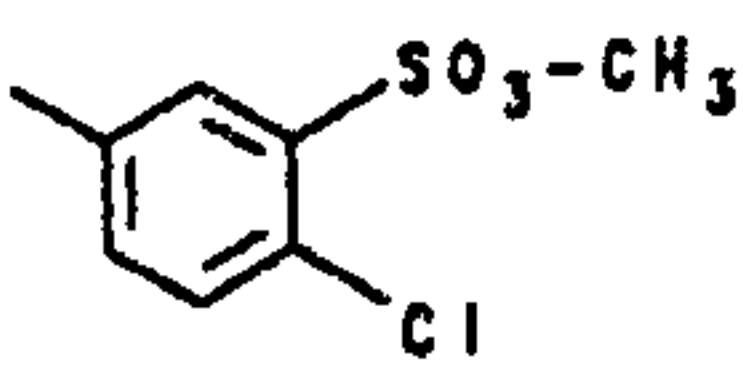
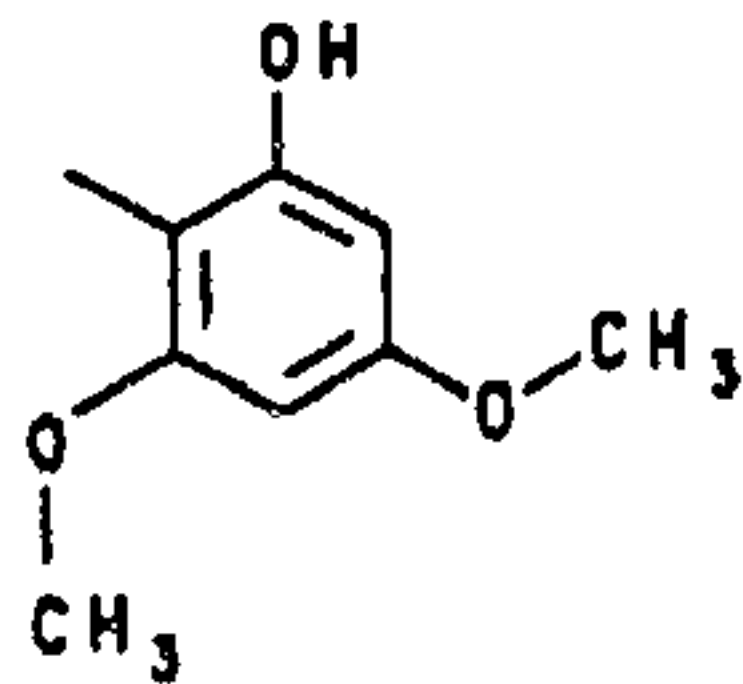
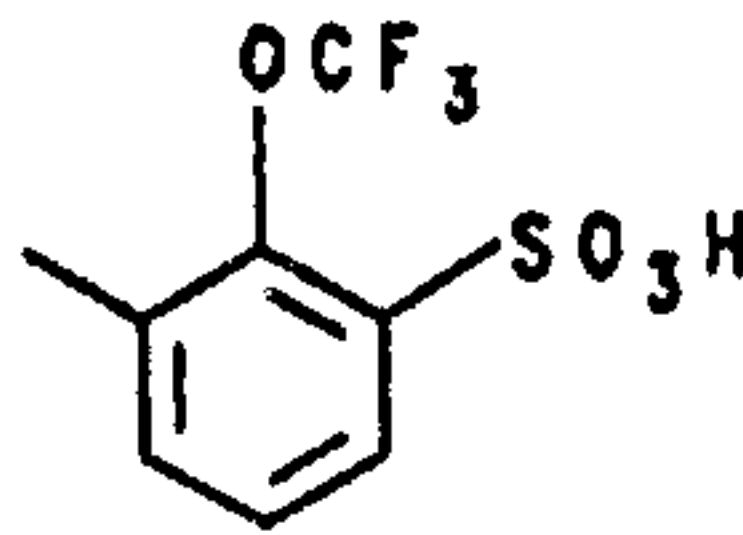
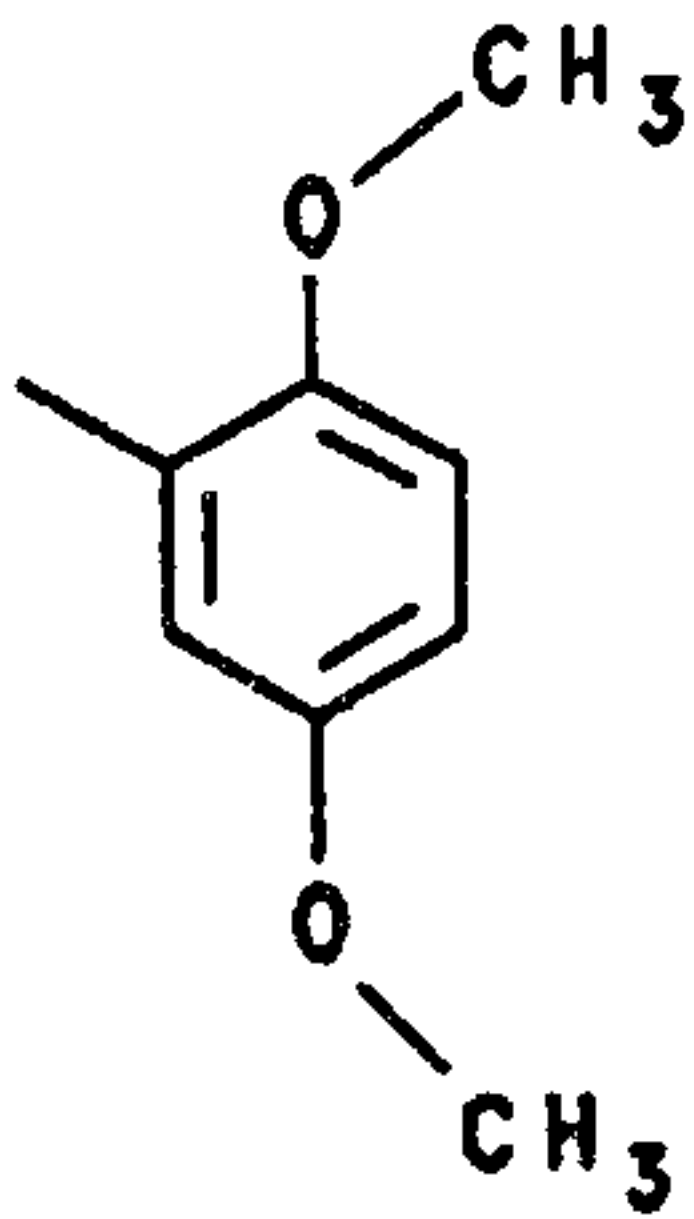
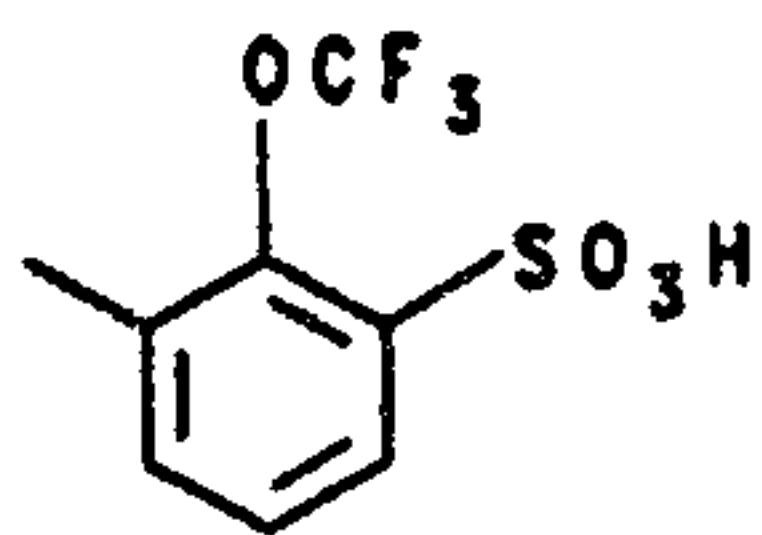
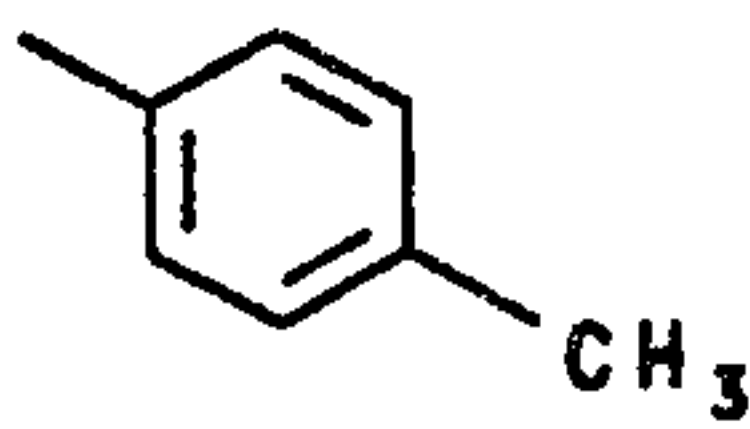
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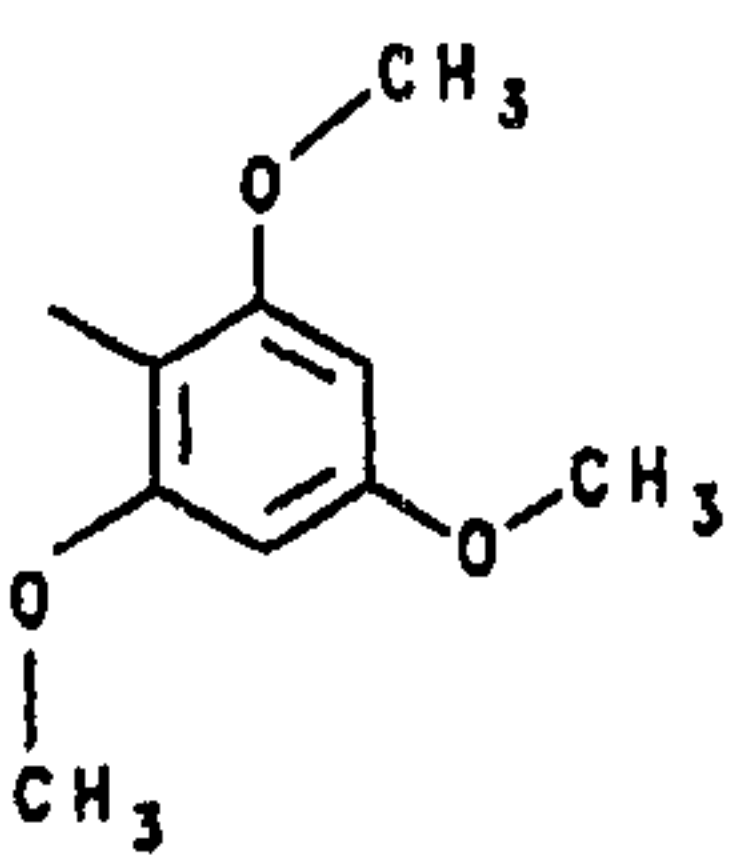
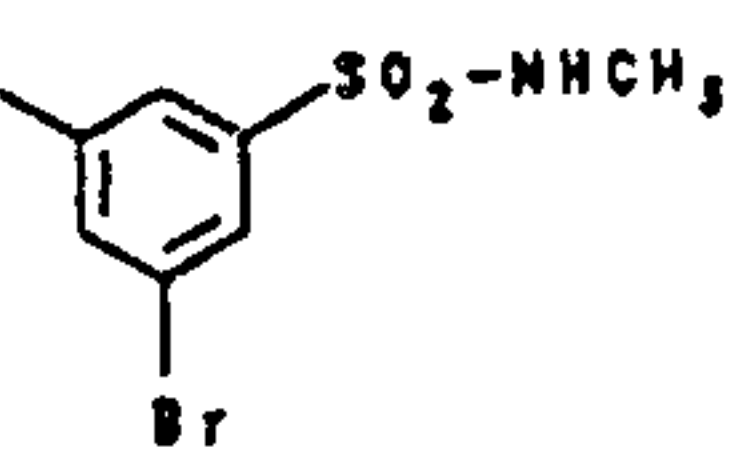
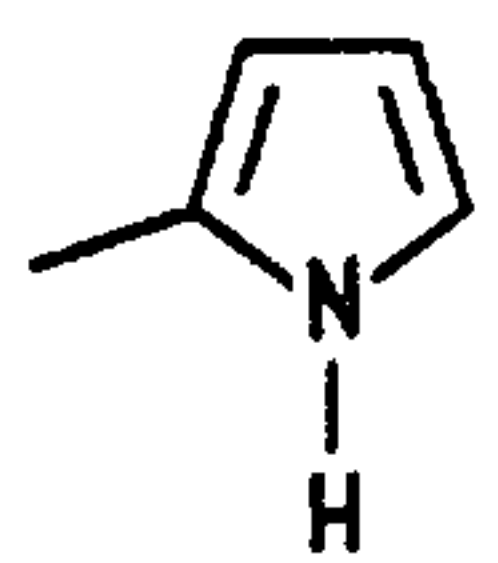
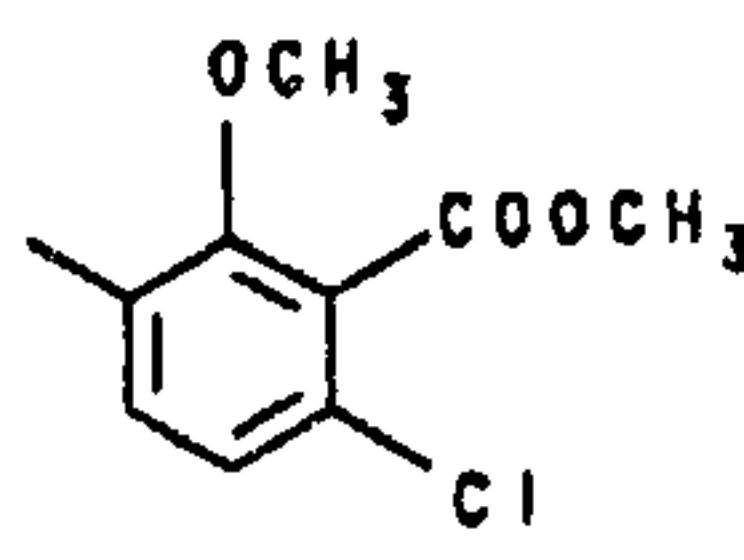
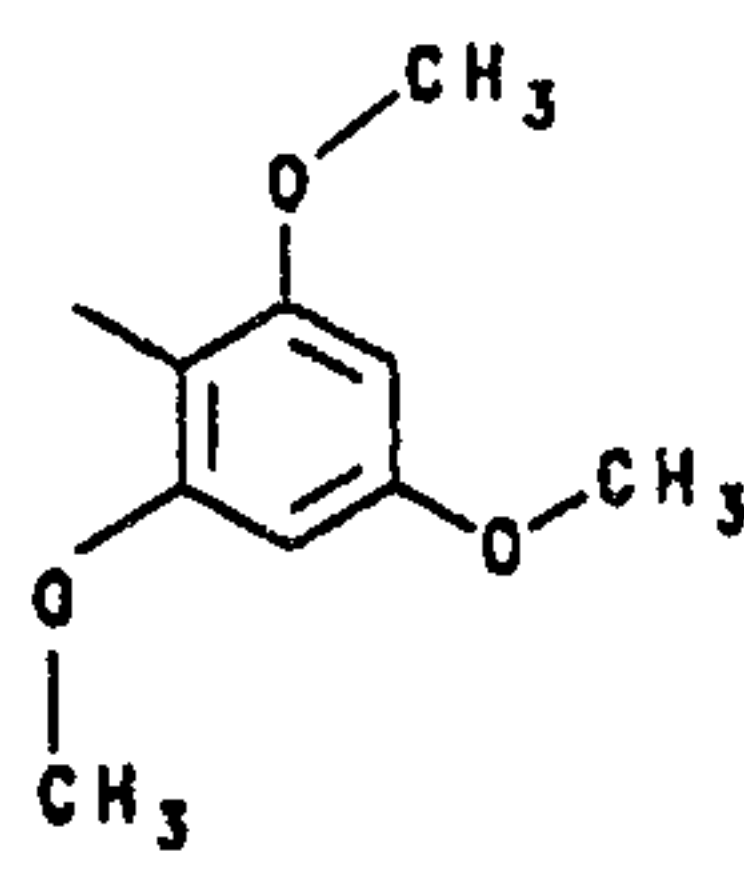
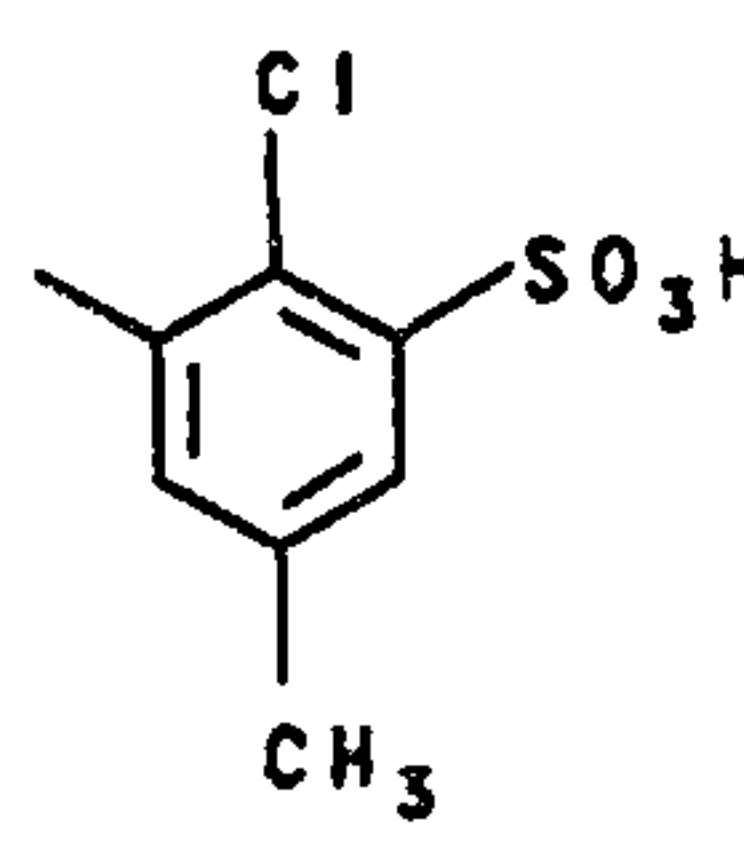
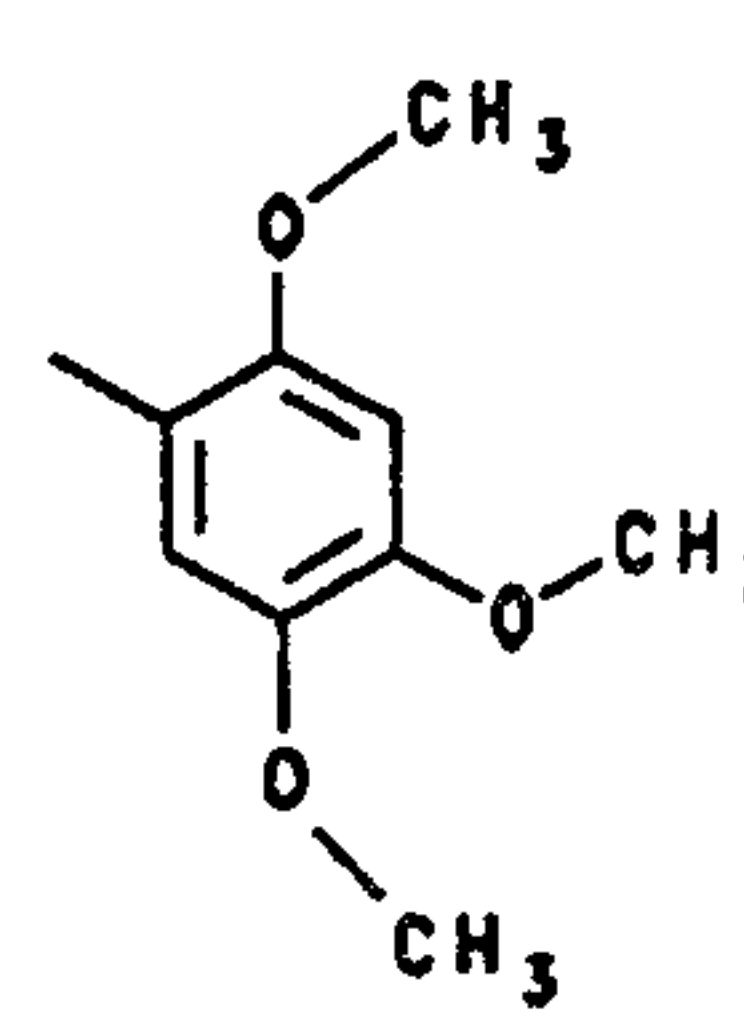
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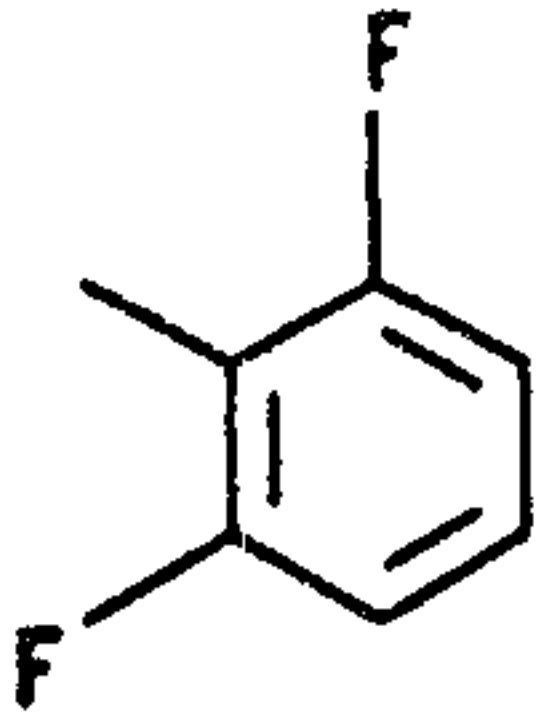
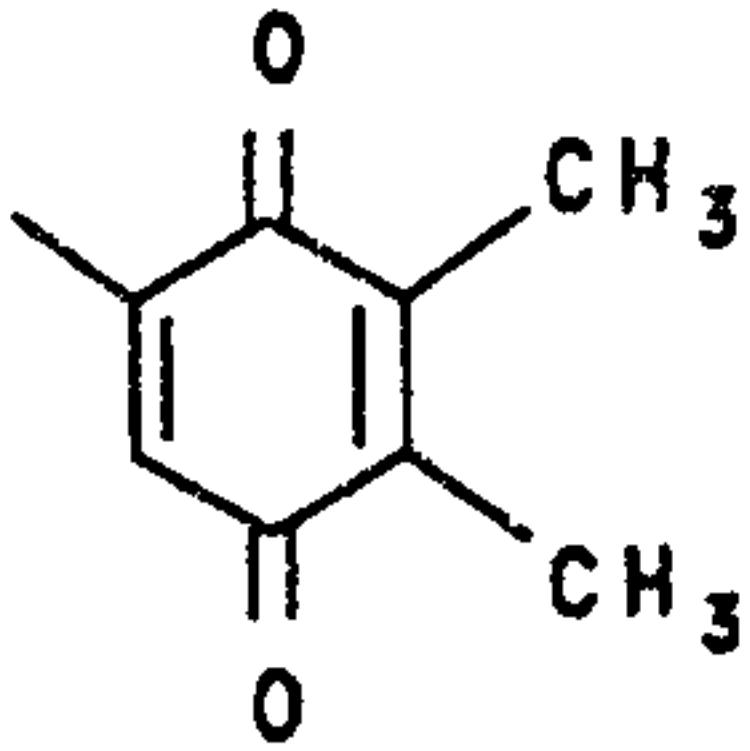
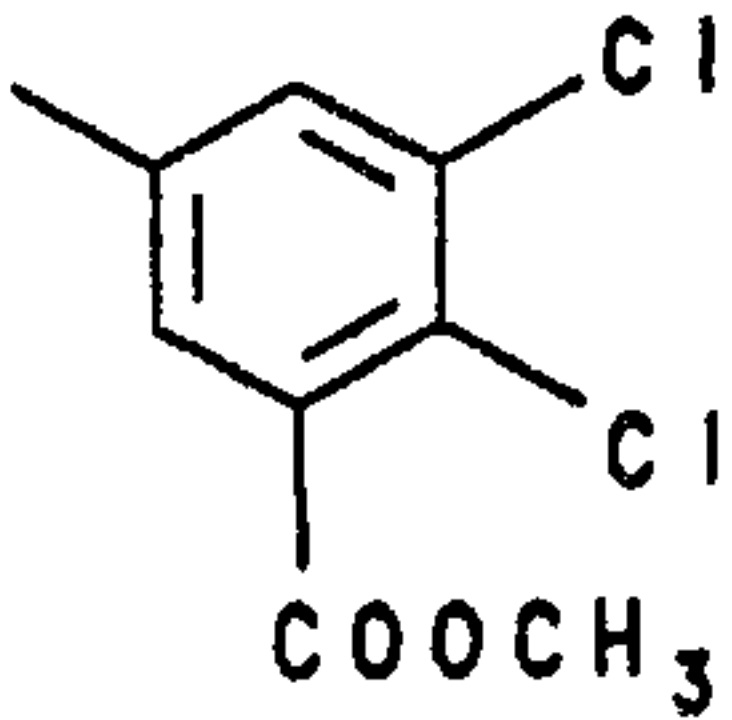
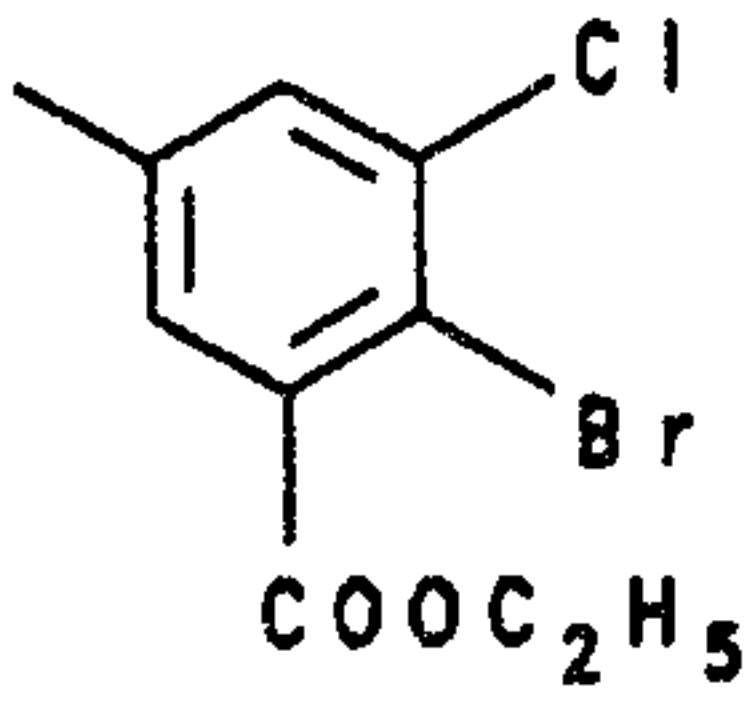
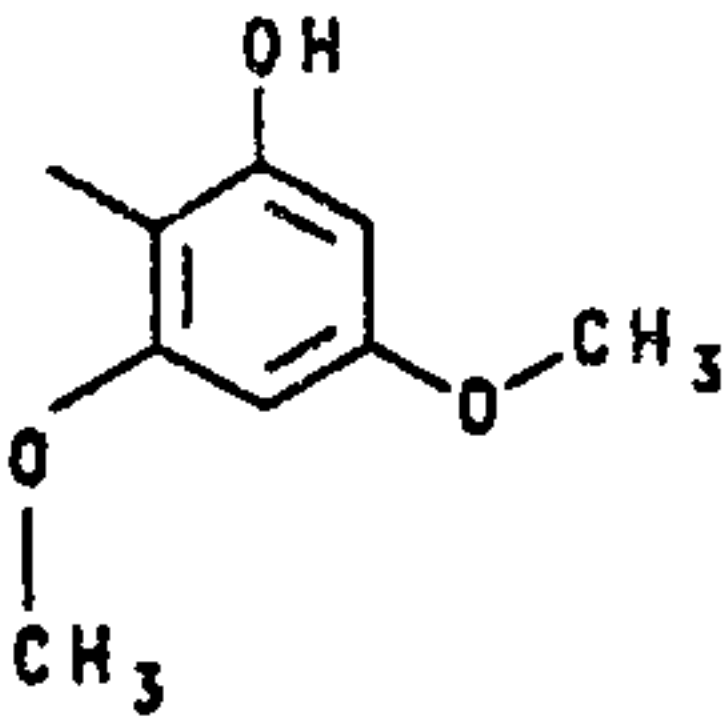
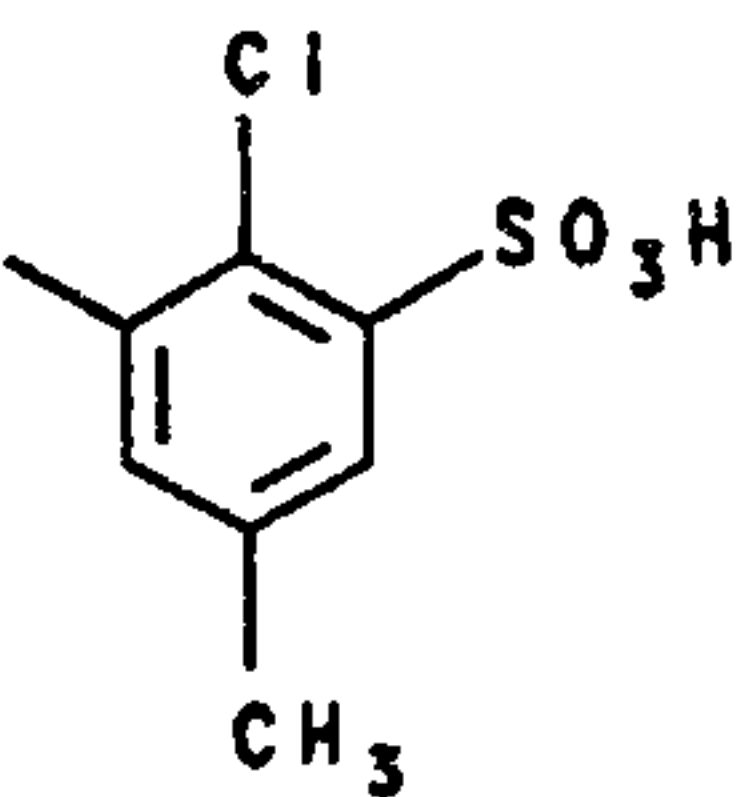
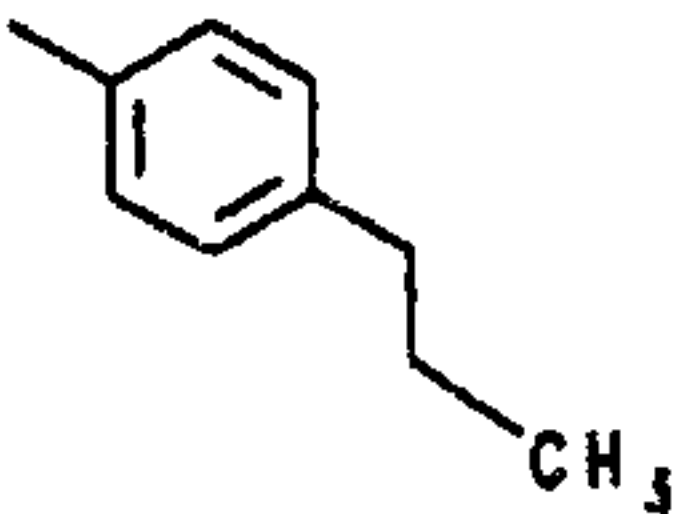
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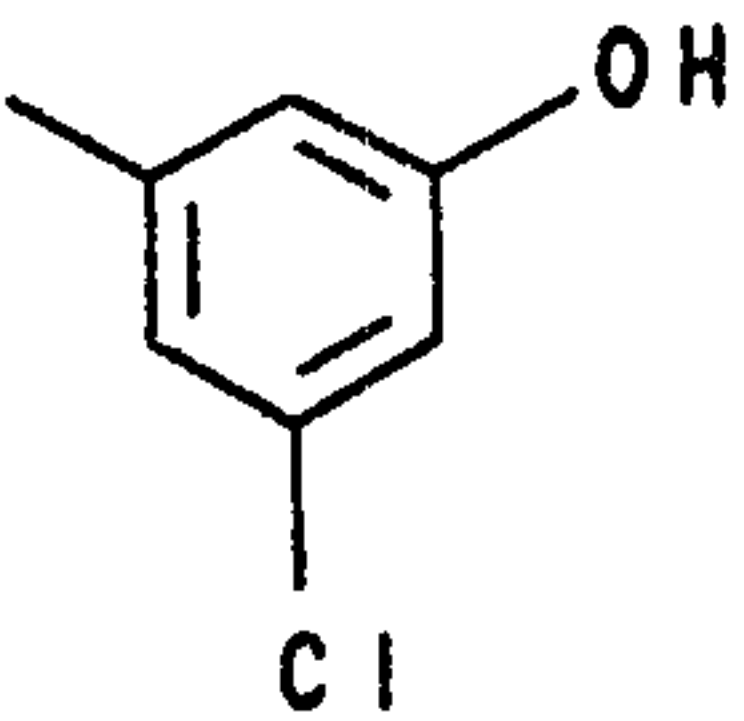
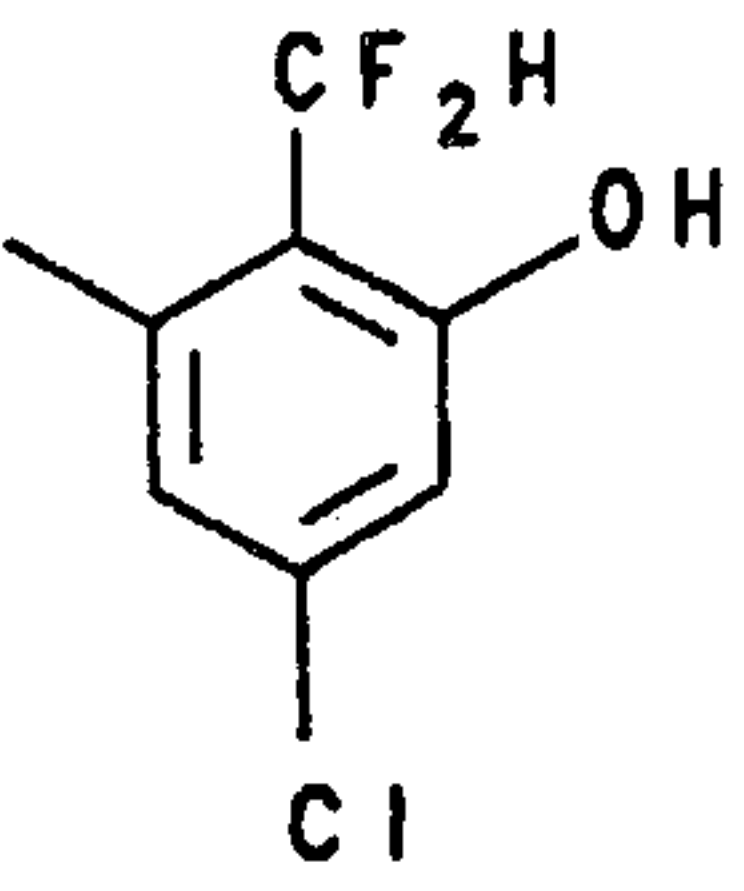
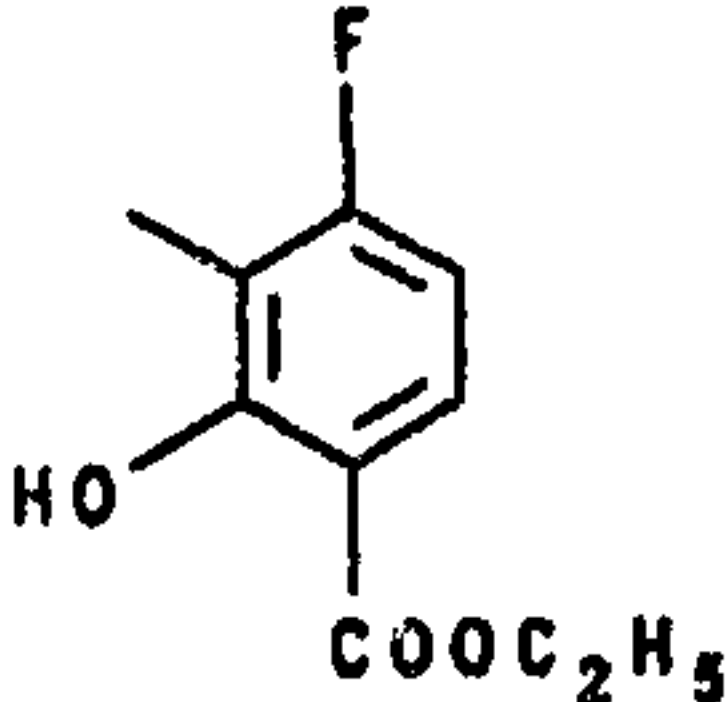
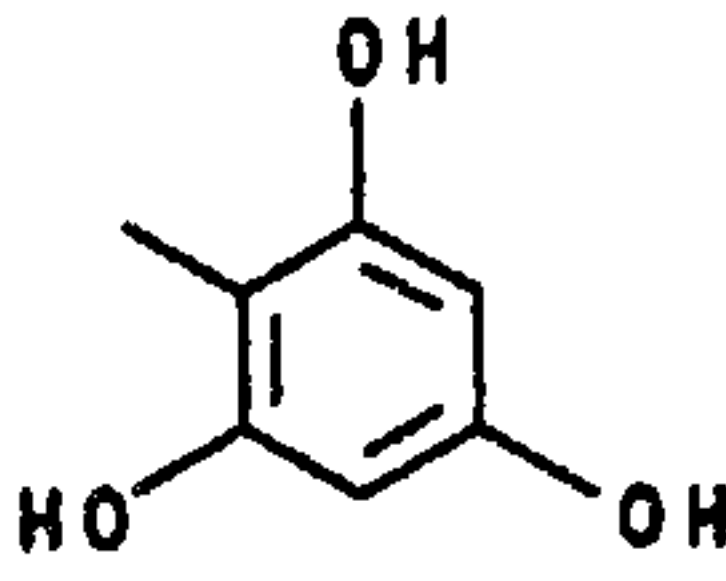
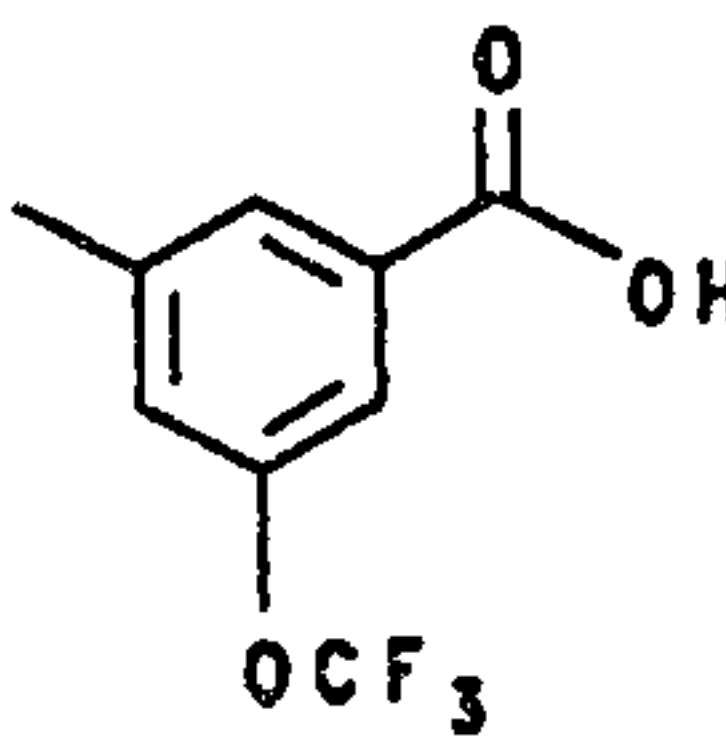
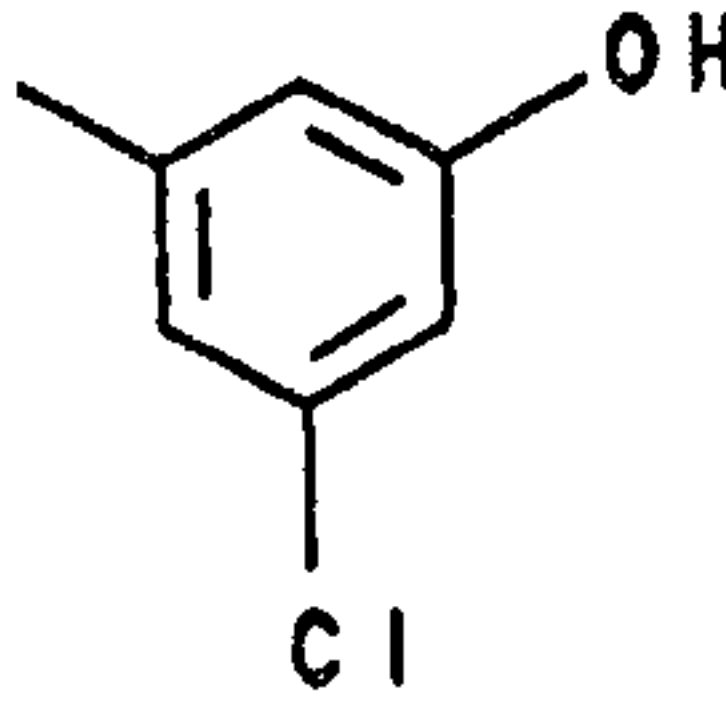
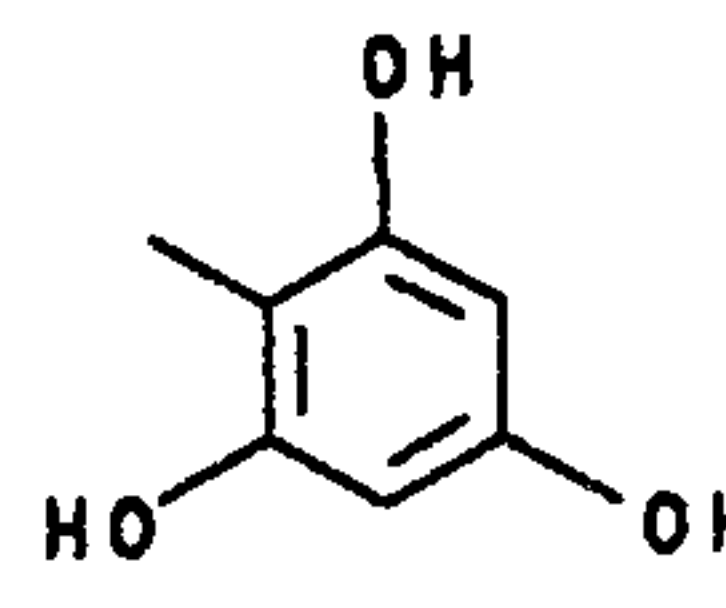
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28	Br	Cl	OCF ₂			
29	Cl	H	NO ₂		192	
30	NO ₂	H	Cl			
31	CCl ₃	F	SO ₂ CH ₃			
32	Cl	H	NO ₂		178	
33	NO ₂	Cl	Cl			
34	OH	Cl	Cl		124-128	

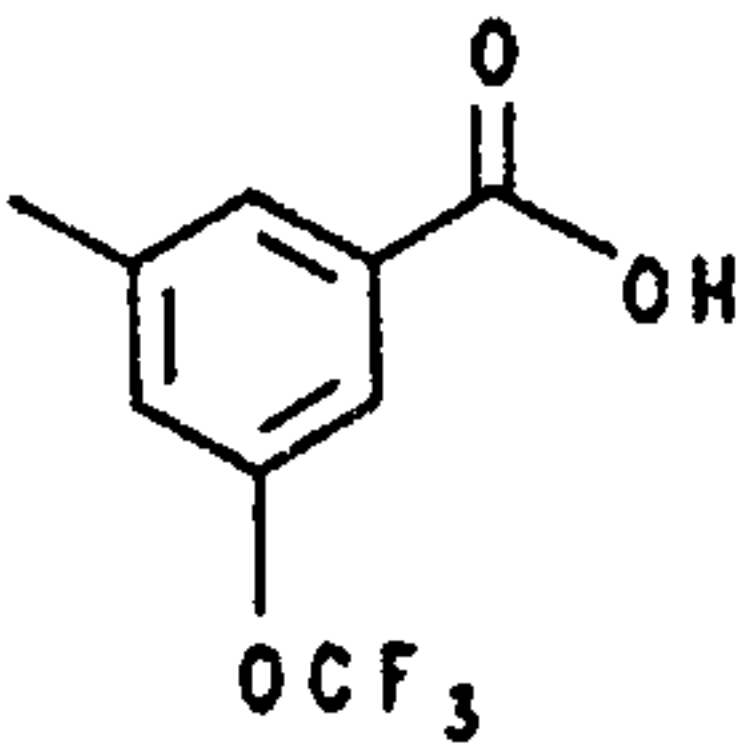
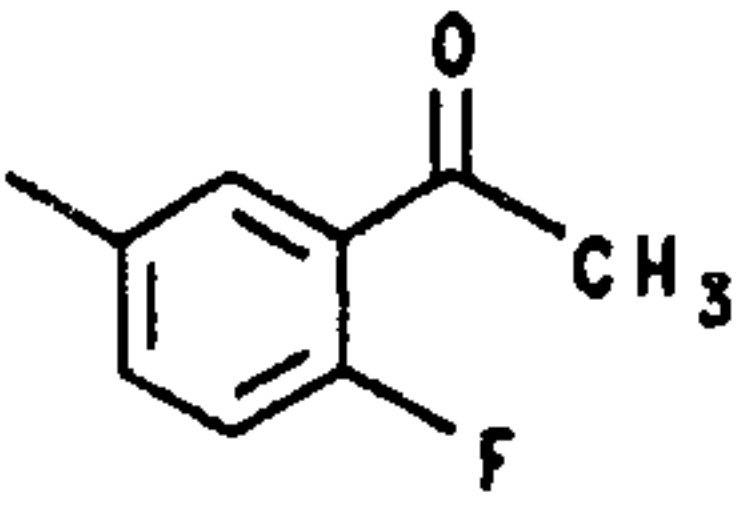
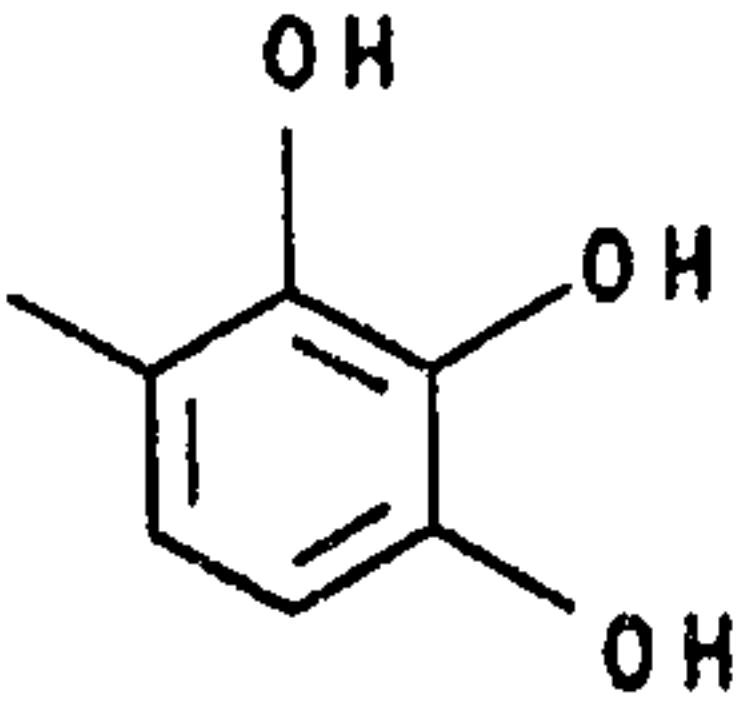
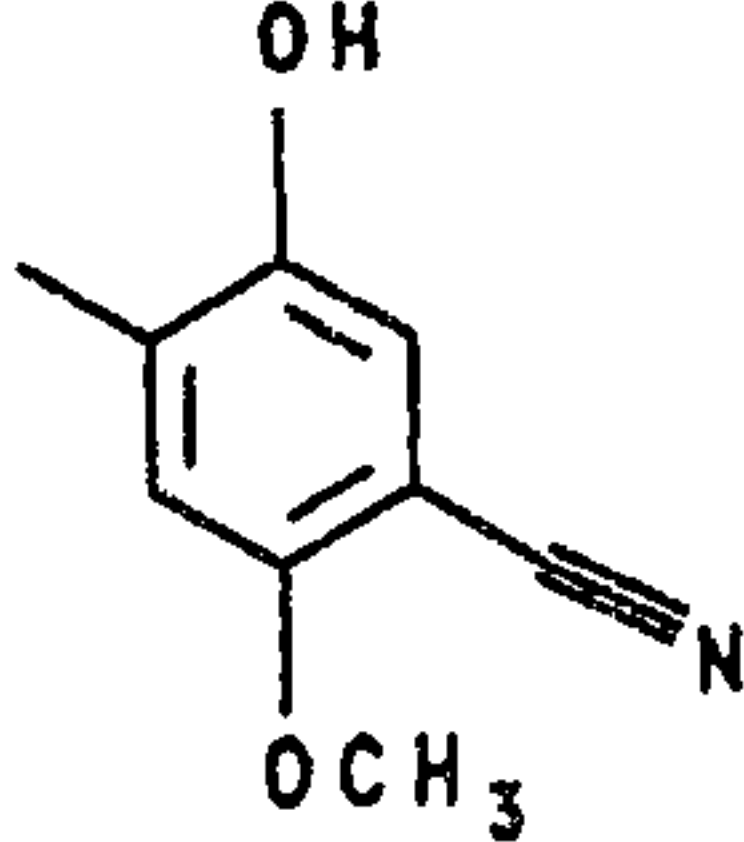
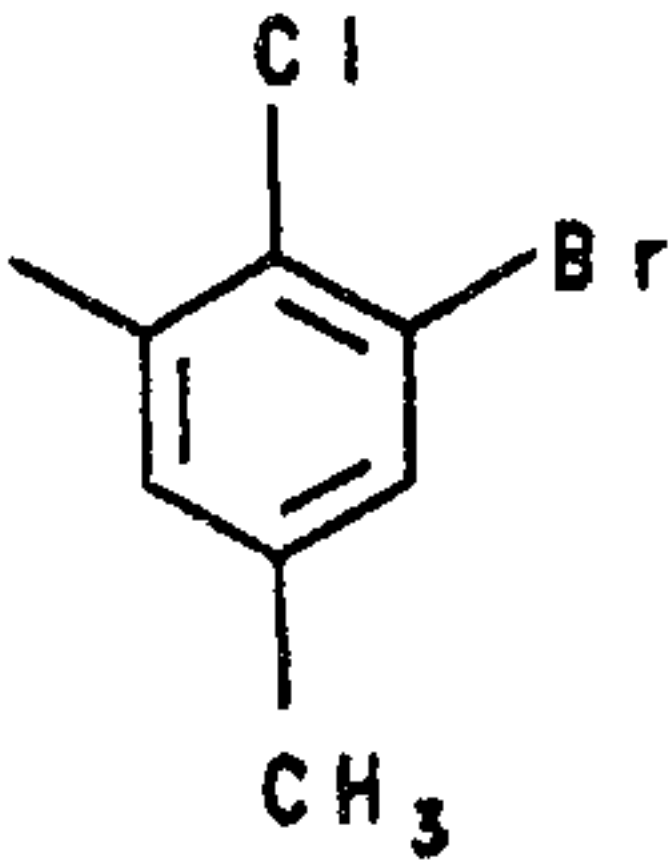
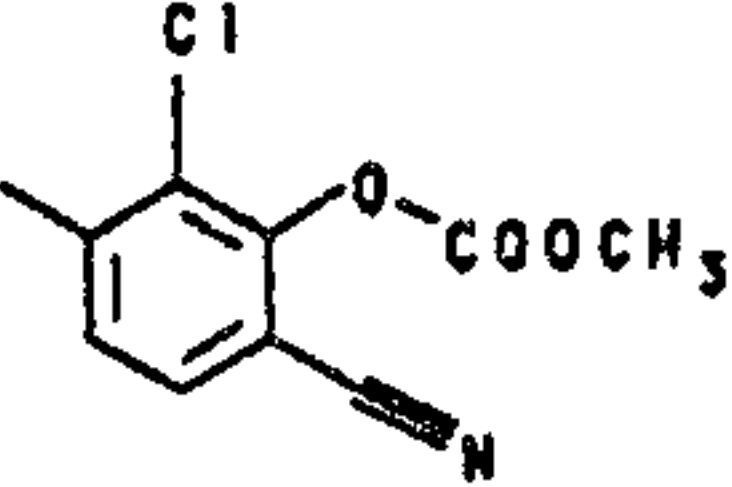
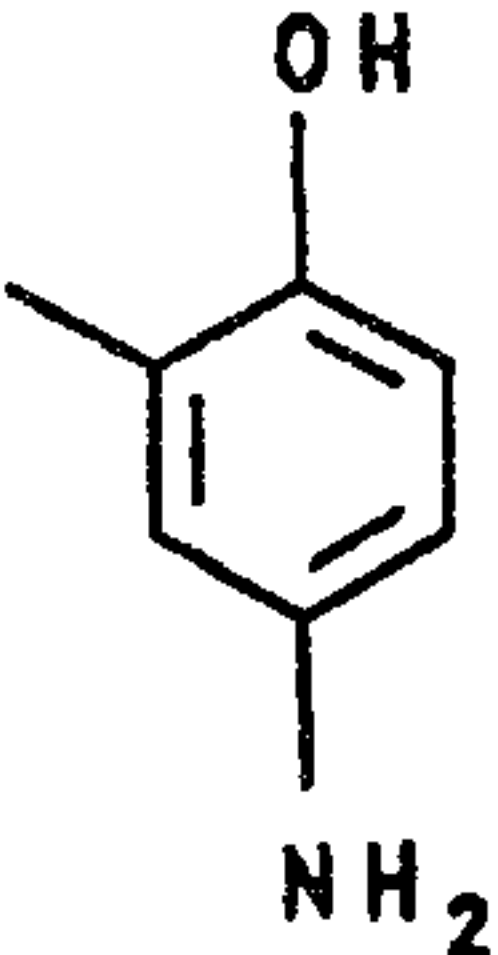
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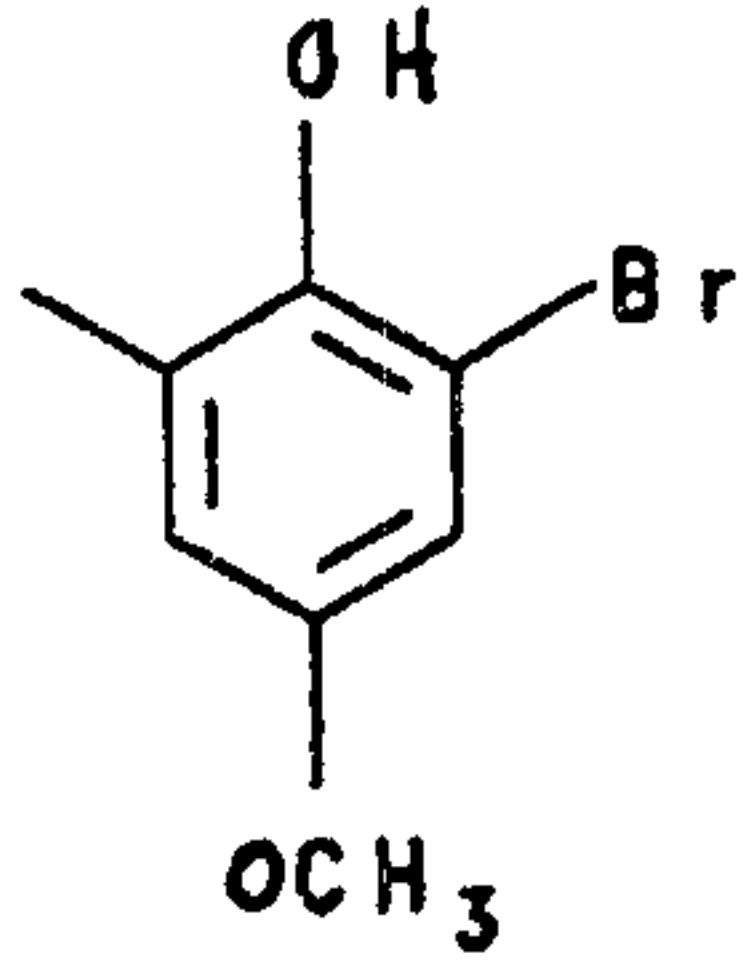
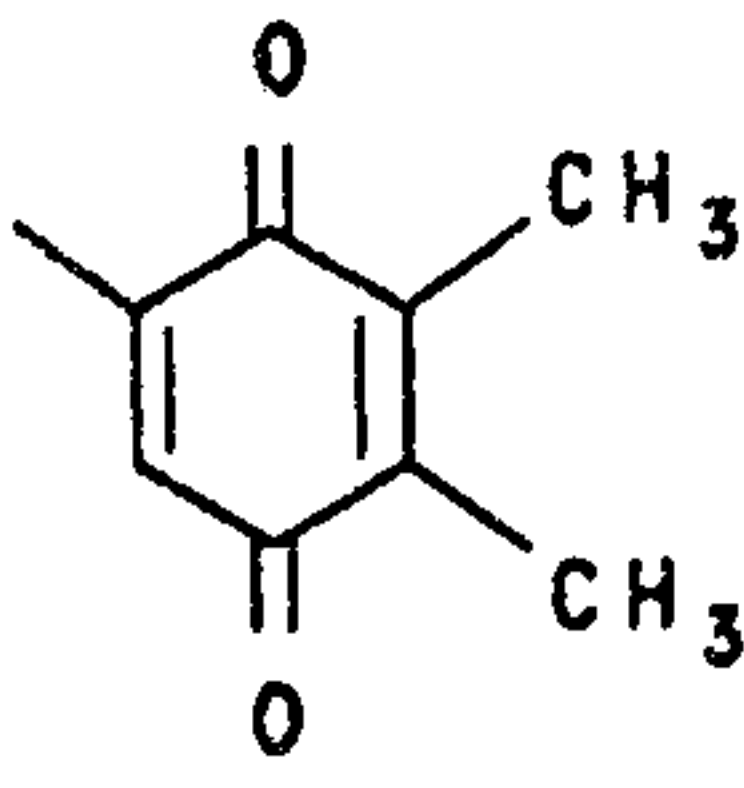
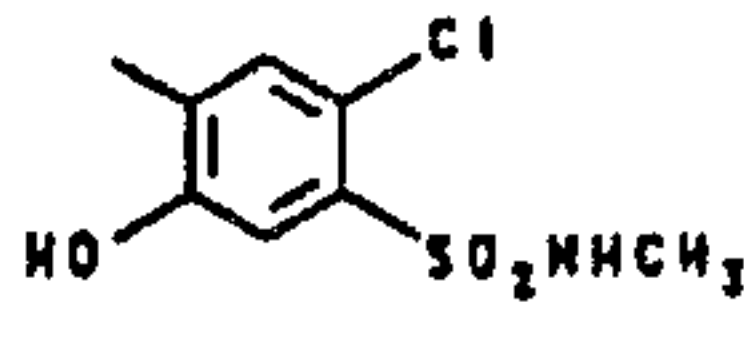
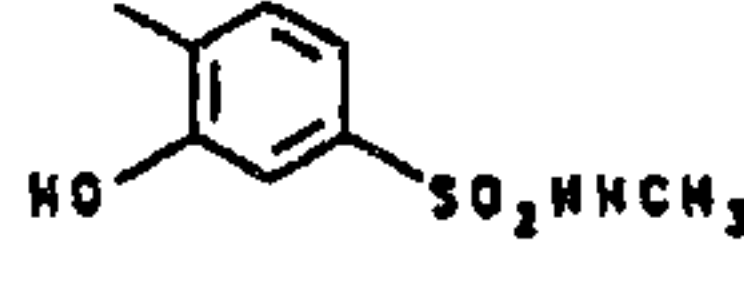
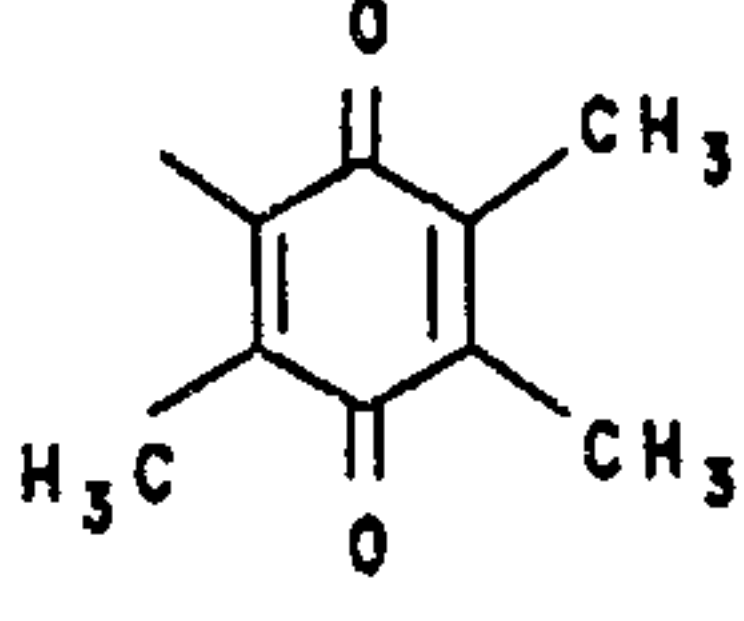
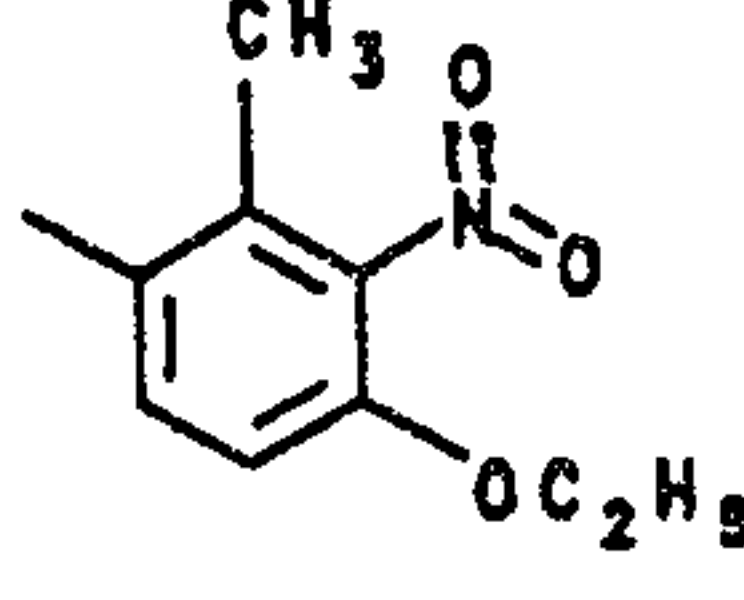
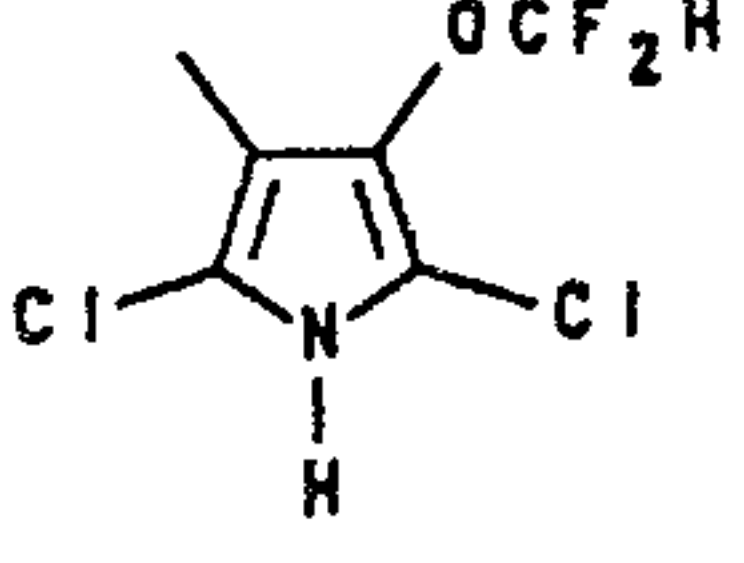
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36	Cl	Cl	CN			
37	Cl	H	SO ₂ CH ₃			
38	Cl	H	SO ₂ CH ₃		147	
39	Cl	COOCH ₃	SO ₂ CH ₃			
40	Cl	H	Cl		86	9.7×10^{-7}
41	Cl	C ₃ H ₇	SO ₂ CH ₃			
42	OH	Cl	Cl		134-136	3.5×10^{-6}

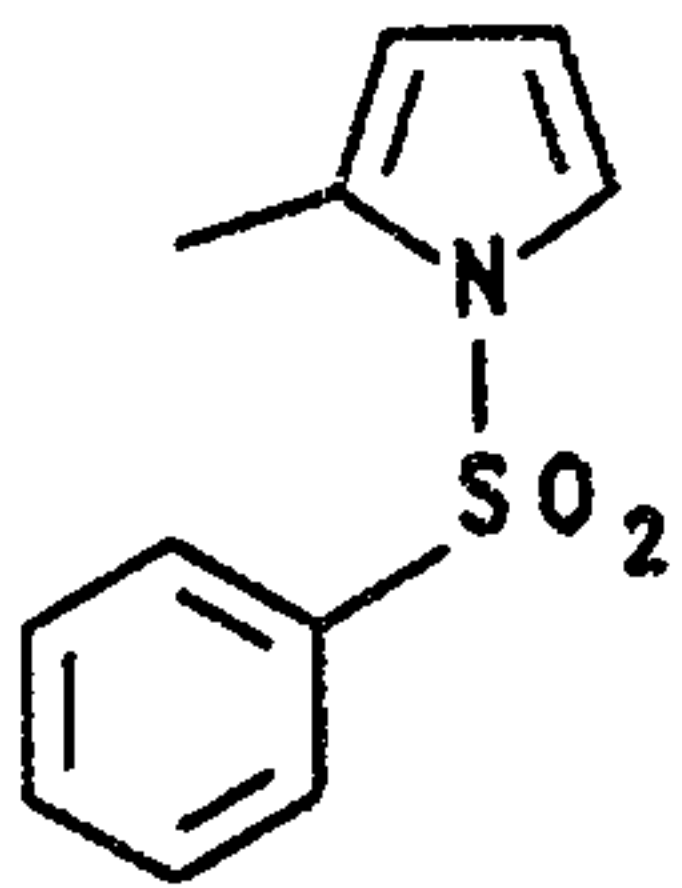
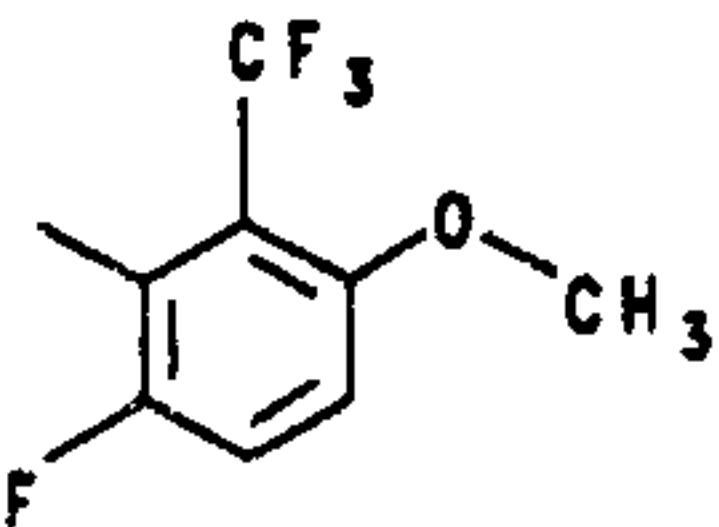
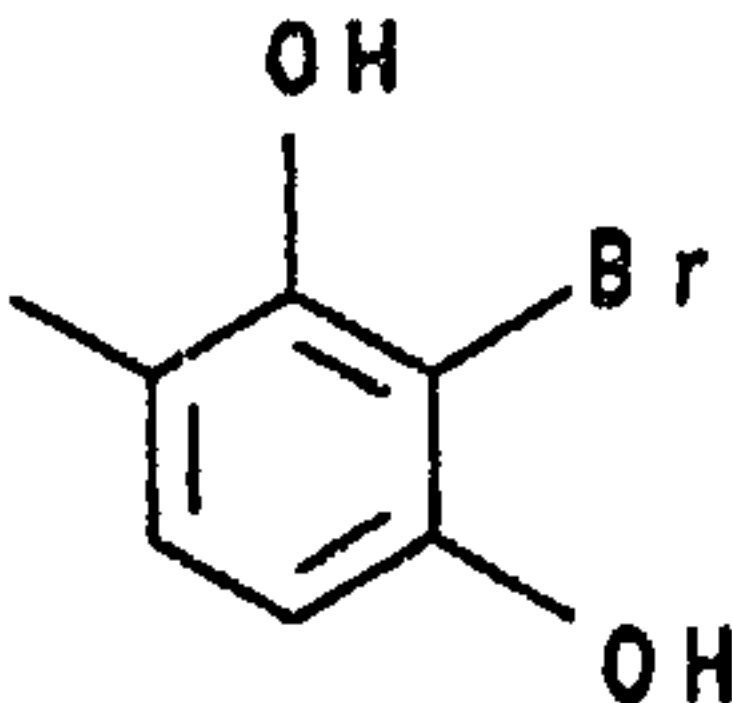
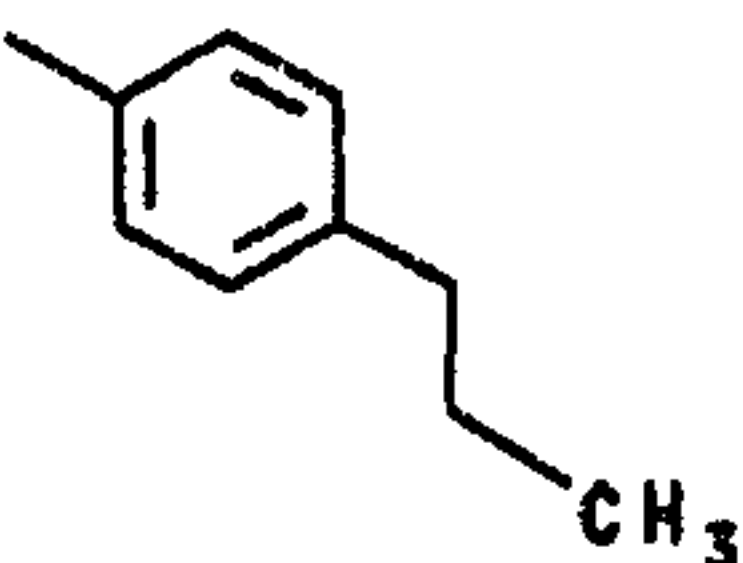
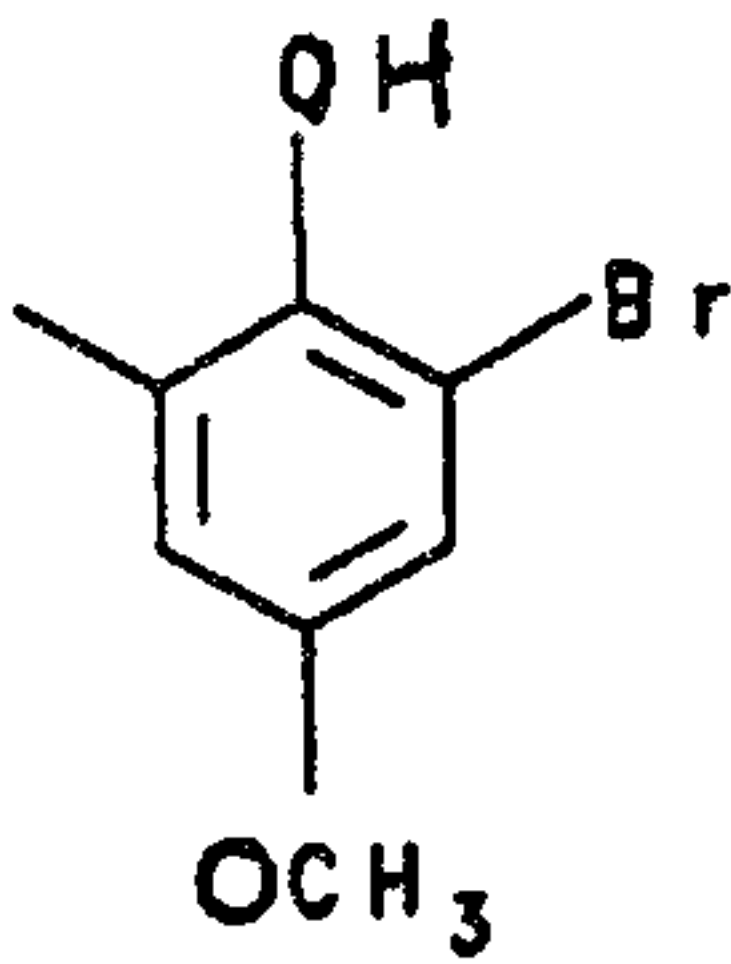
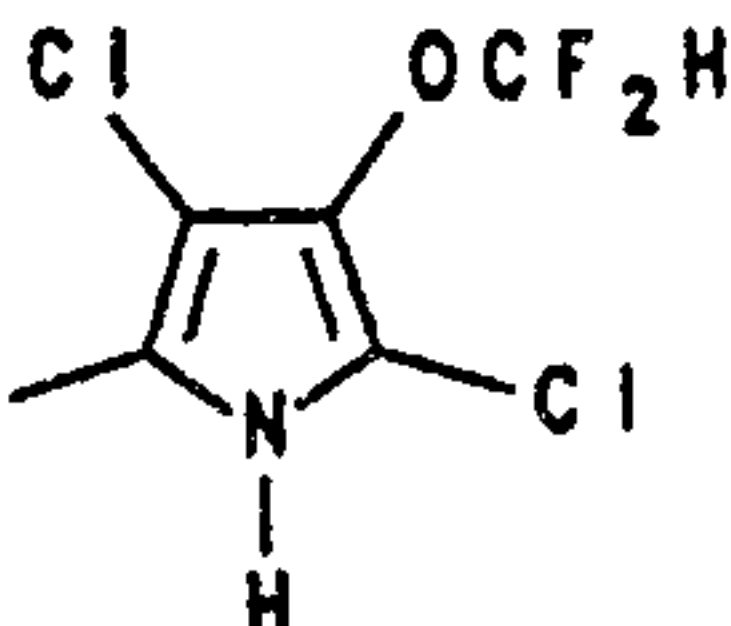
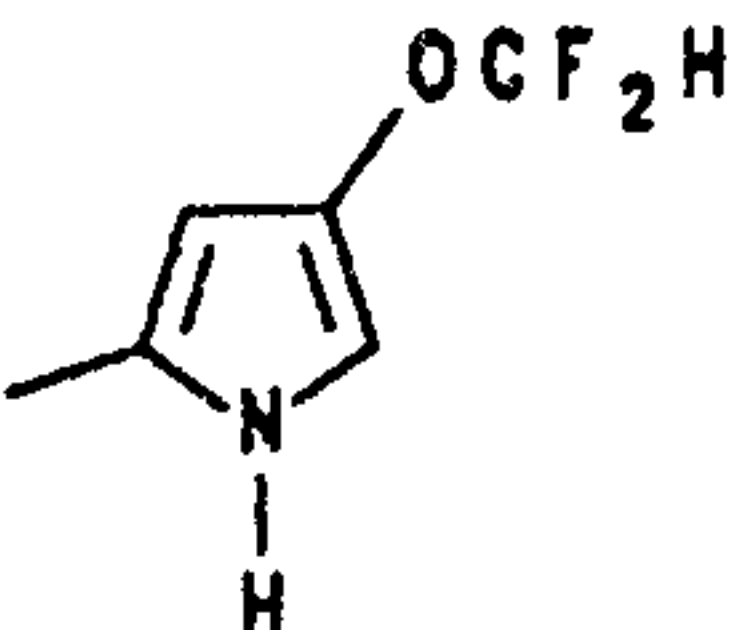
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44	H	OCF ₃	F			
45	NO ₂	H	Cl		125	
46	Cl	CH ₃	CF ₂ H			
47	Cl	H	SO ₂ CH ₃		163-166	5.7×10^{-6}
48	F	COOCH ₃	OCF ₂ H			
49	Cl	H	Cl		99	

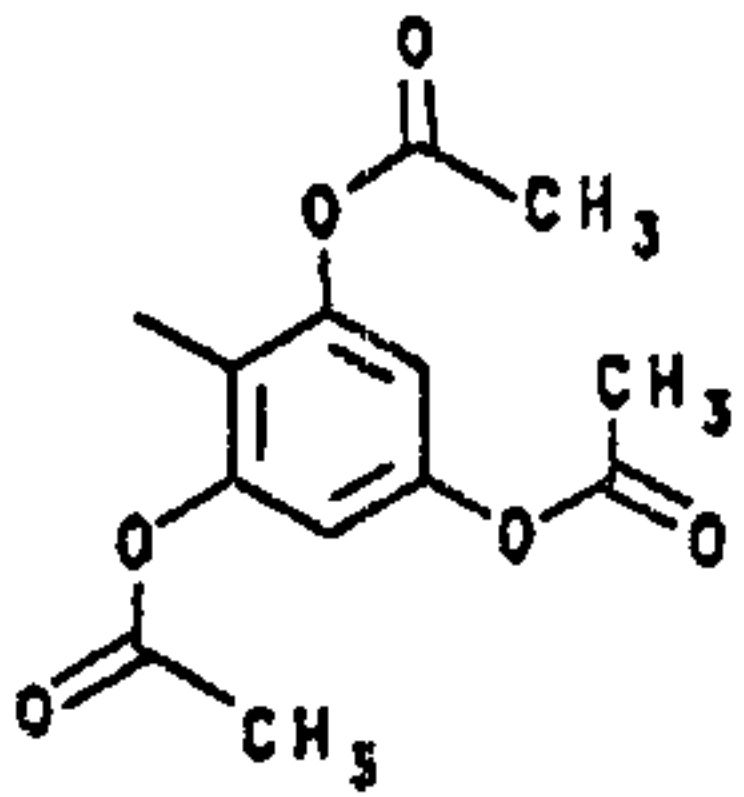
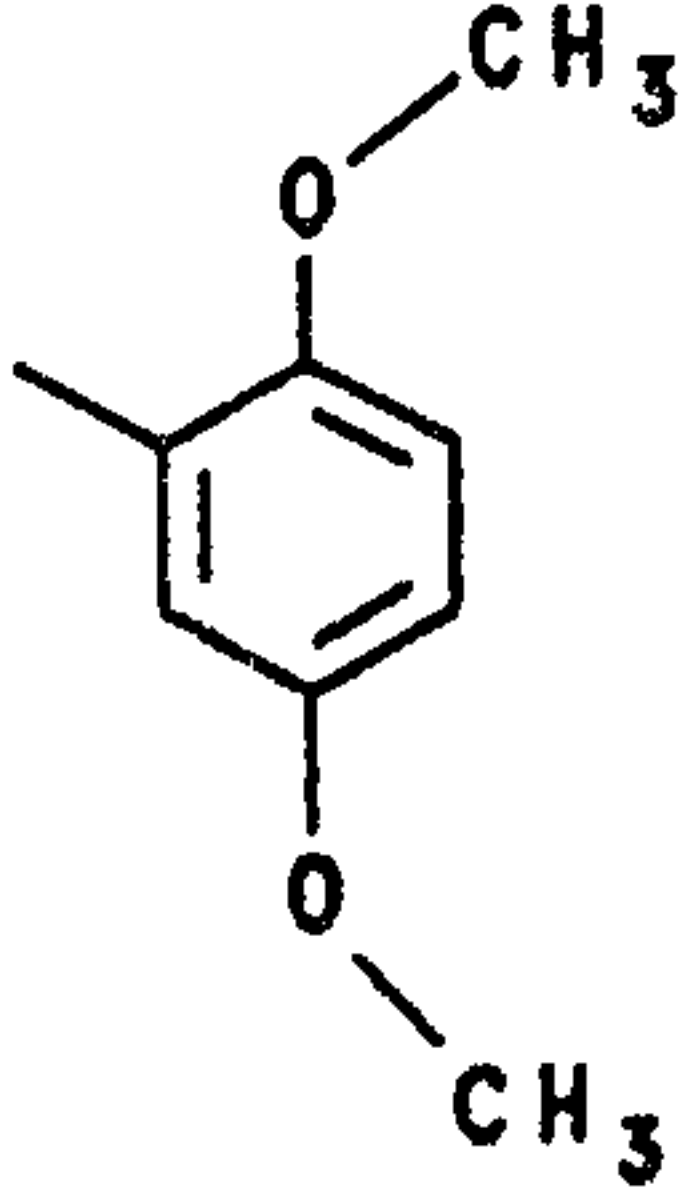
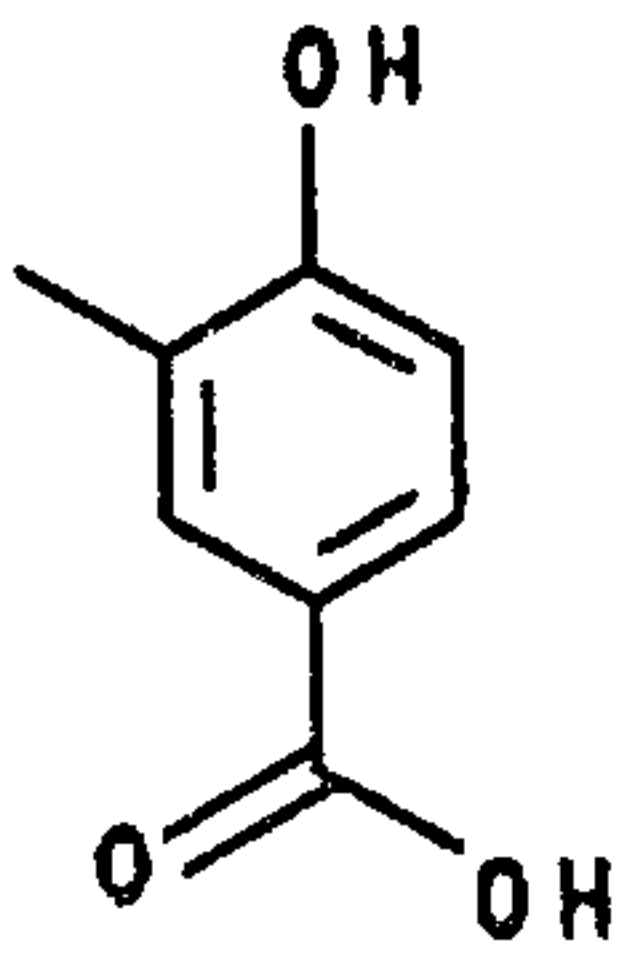
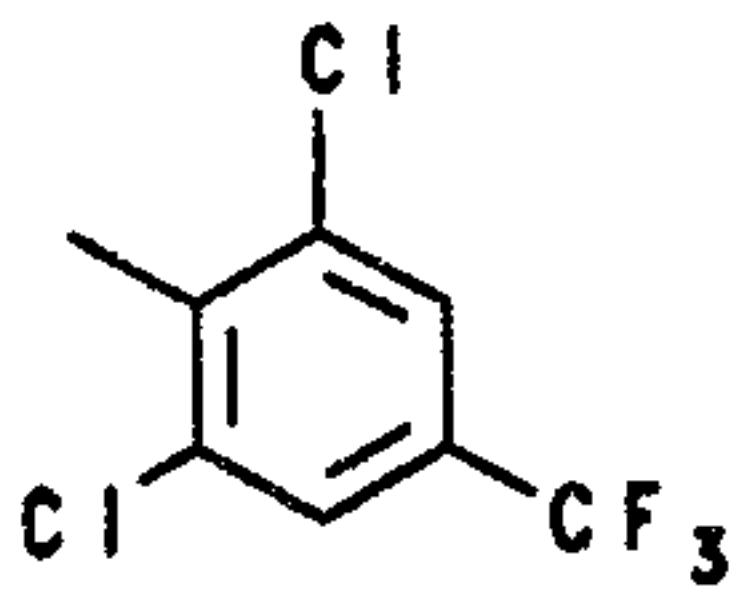
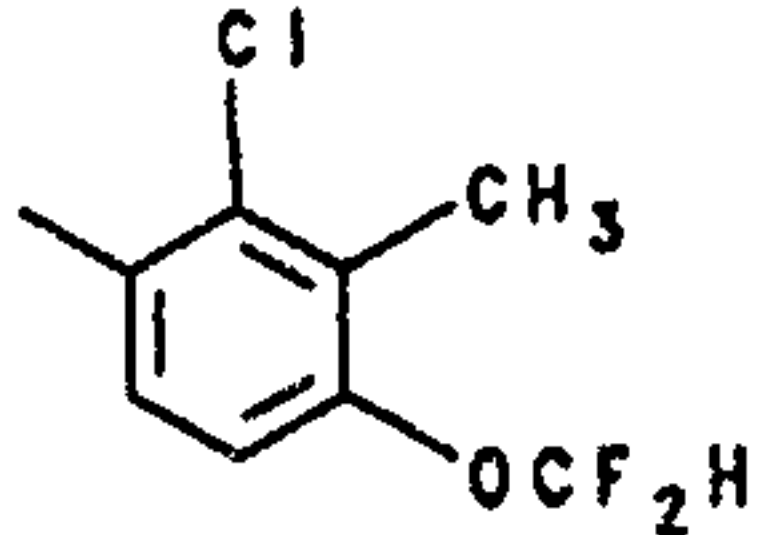
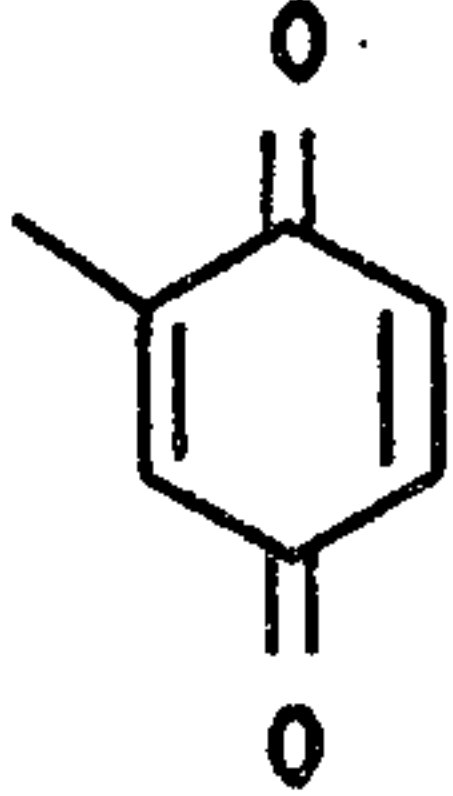
50	OH	Cl	Cl		98-103	
51	CH ₂ Cl	C ₃ H ₇	SO ₂ CH ₃			
52	NO ₂	OH	Br			
53	CF ₃	H	Cl			
54	Cl	H	Cl			
55	Cl	Cl	Cl			
56	OH	Cl	Cl		64-65	5.0x10 ⁻⁸

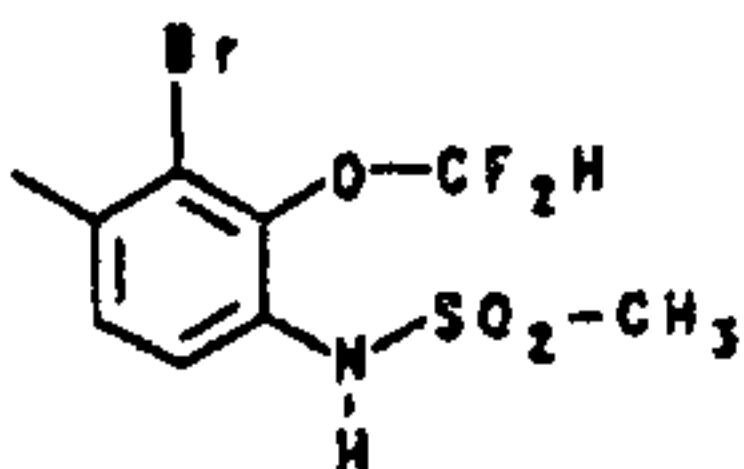
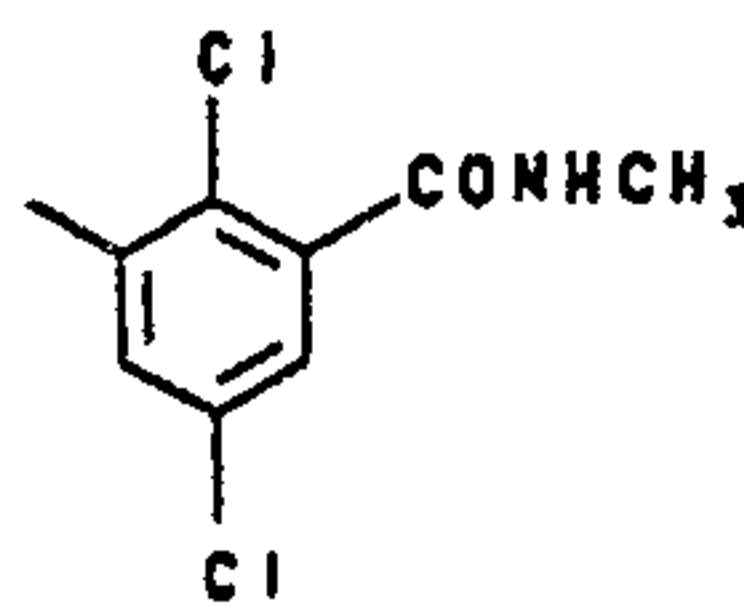
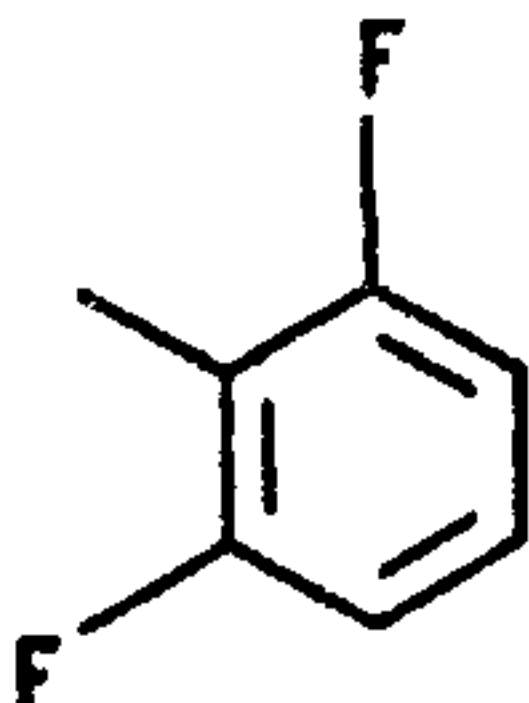
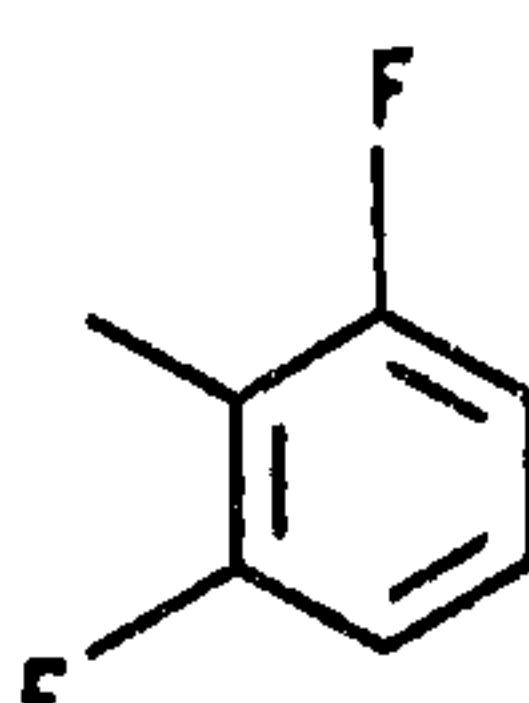
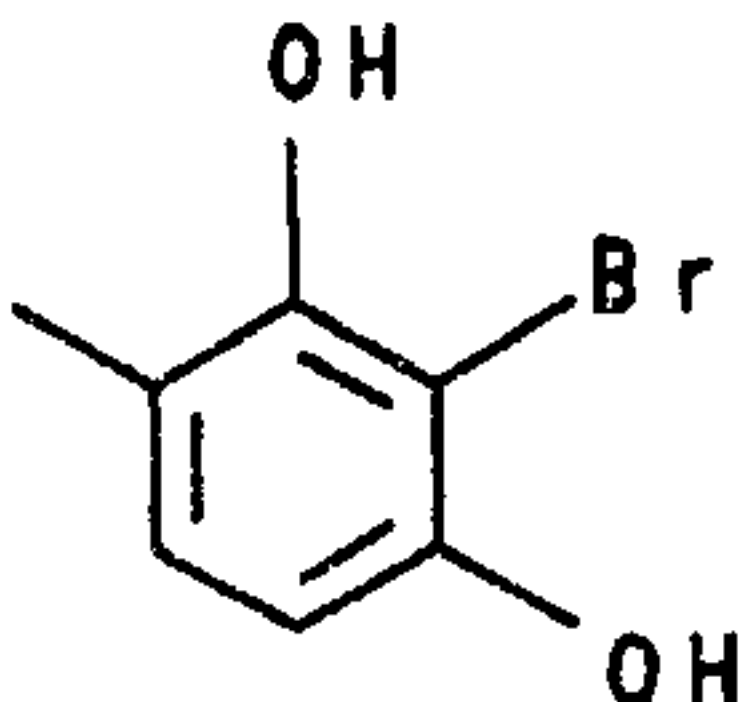
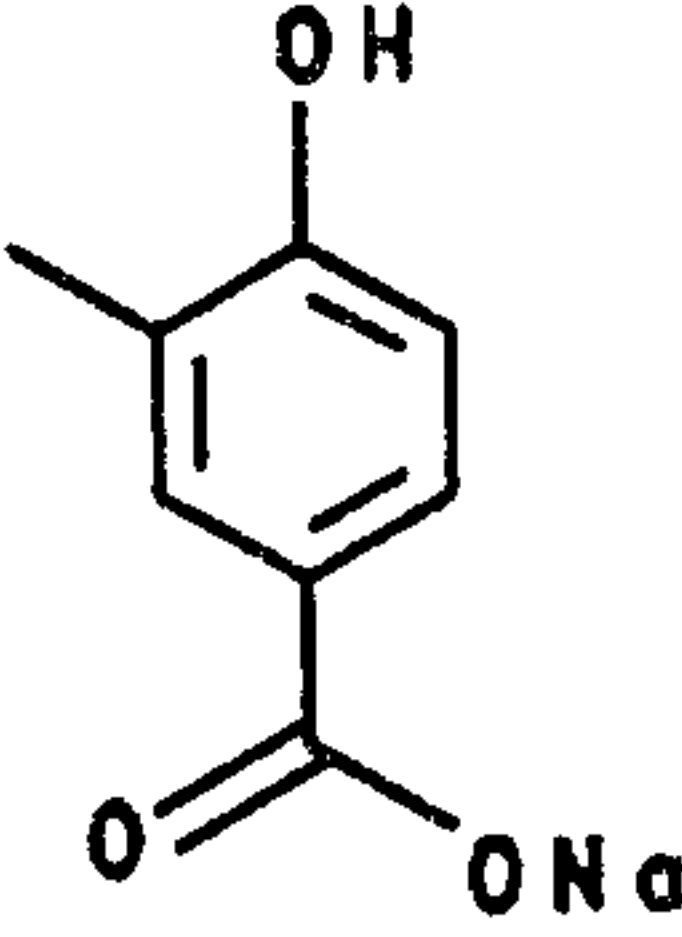
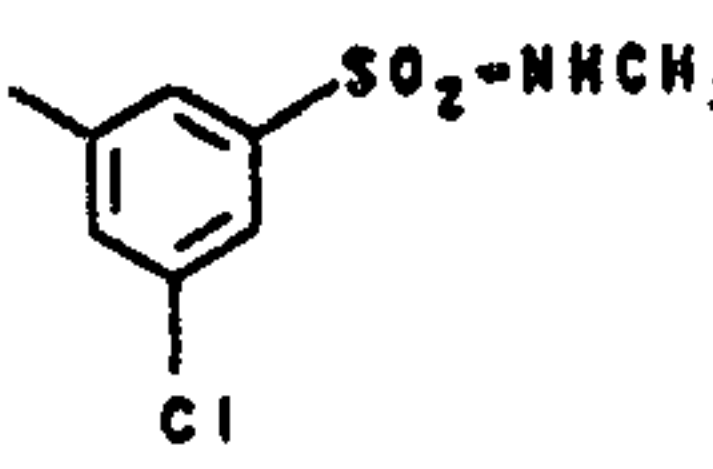
57	Br	H	OCF ₃			
58	F	CH ₃	F			
59	Br	Cl	Cl			
60	Cl	H	SO ₂ CH ₃		165	
61	NO ₂	H	OCF ₂ H			
62	CF ₃	Cl	Cl			
63	Cl	H	SO ₂ CH ₃		227	

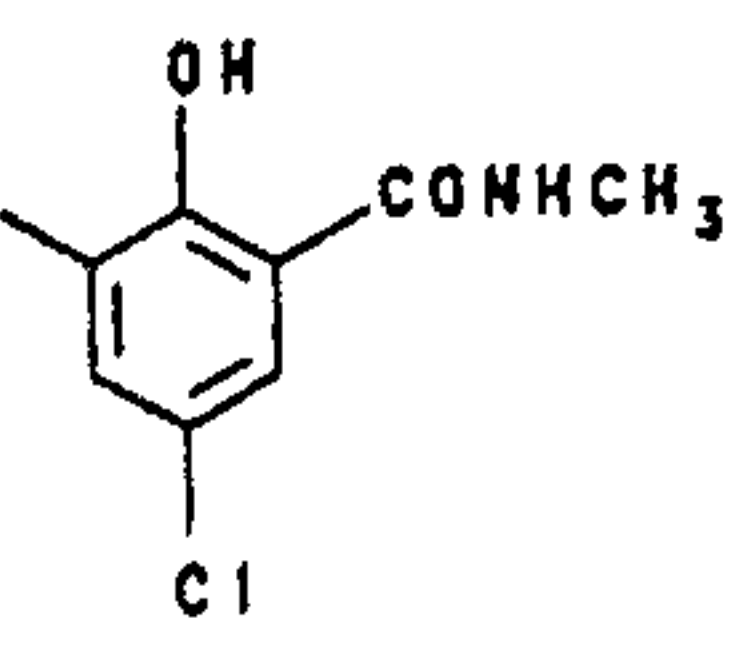
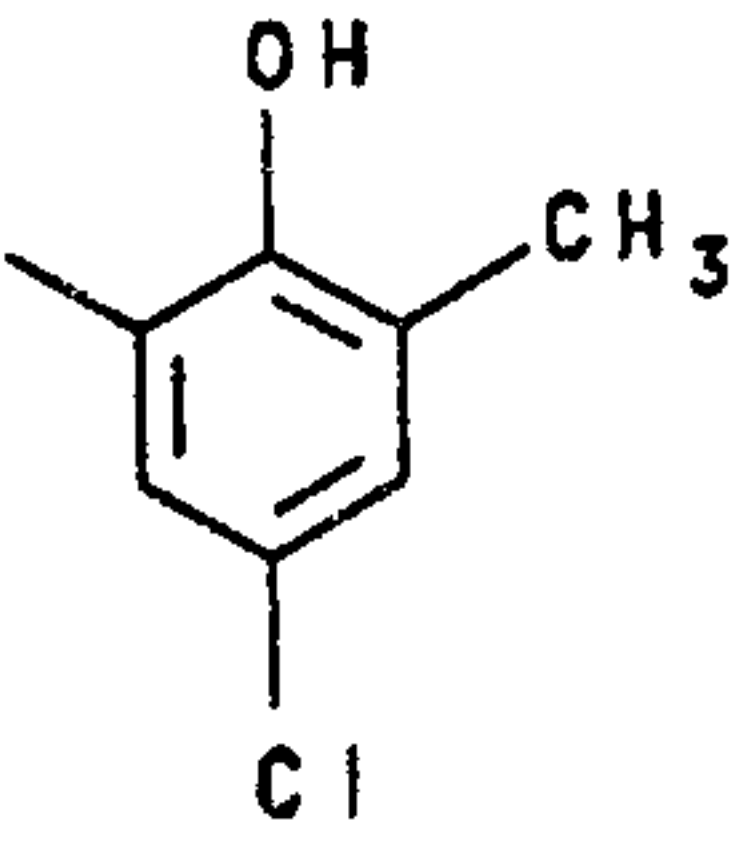
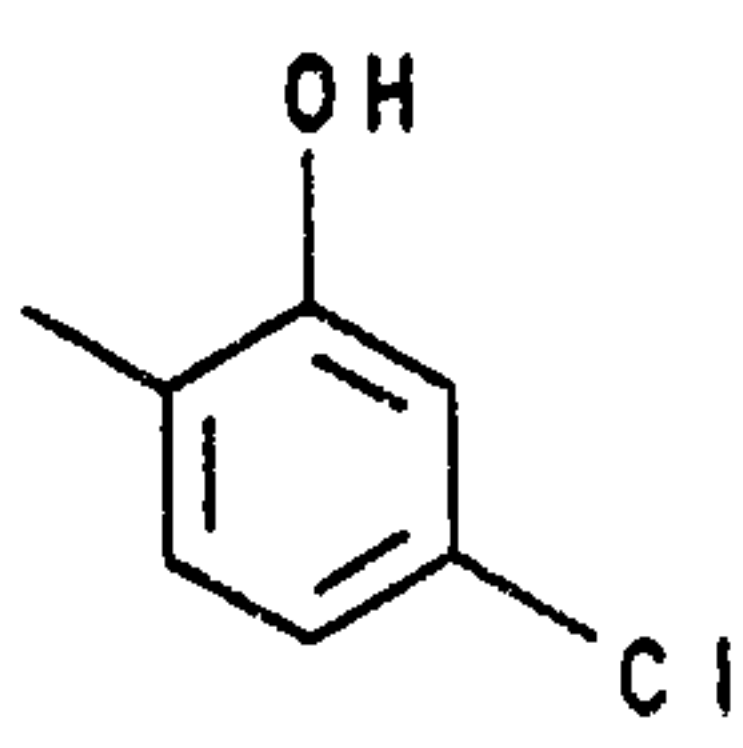
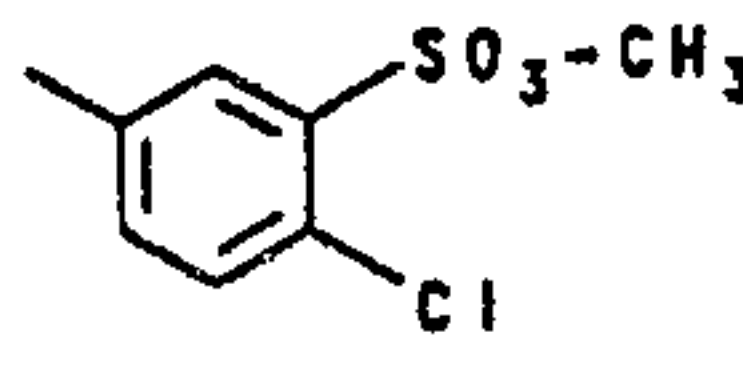
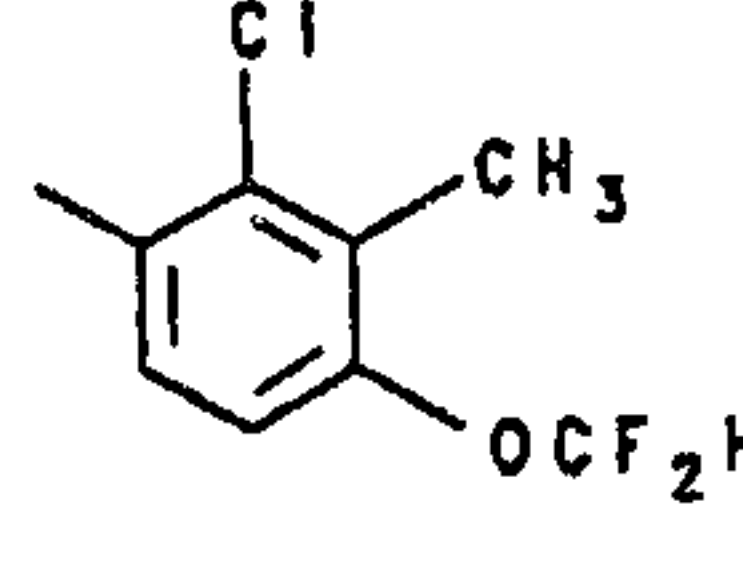
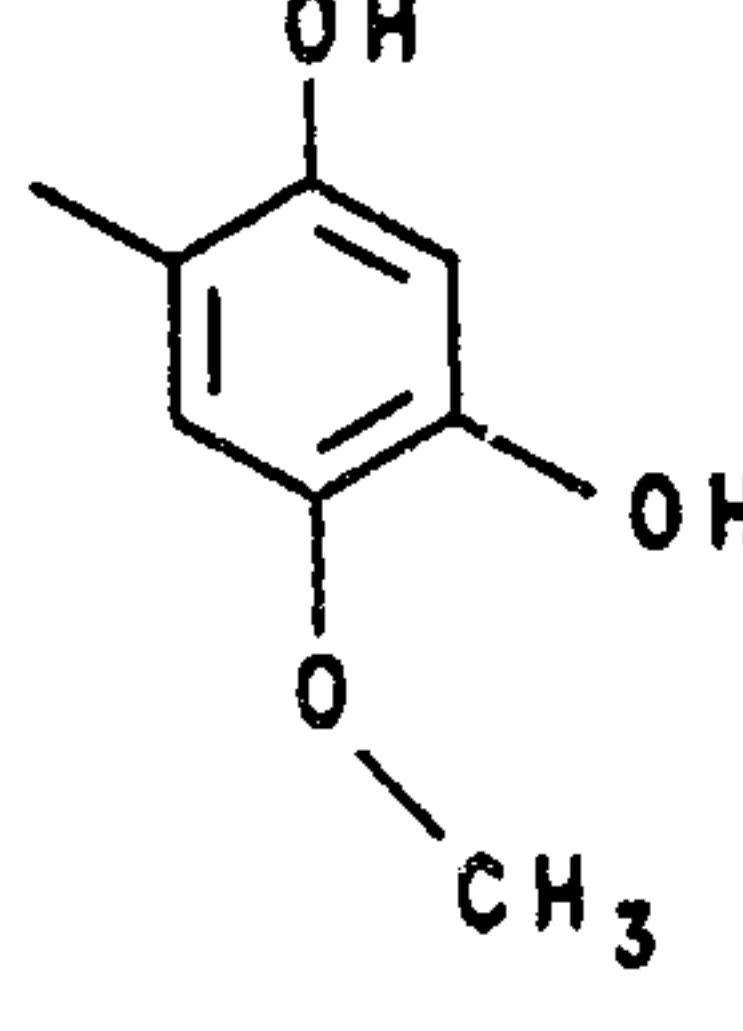
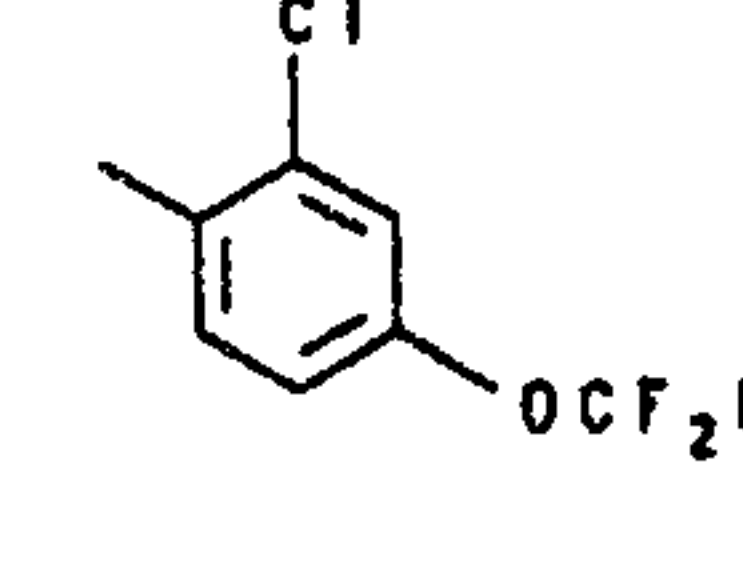
64	CCl ₃	H	Cl			
65	Cl	H	CF ₃			
66	Cl	H	SO ₂ CH ₃		228	
67	Cl	CH ₃	OCF ₂ H			
68	Cl	CF ₃	OCF ₂ H			
69	Cl	H	SO ₂ CH ₃			
70	Cl	H	SO ₂ CH ₃		240 (decomp.)	4.0×10 ⁻⁸

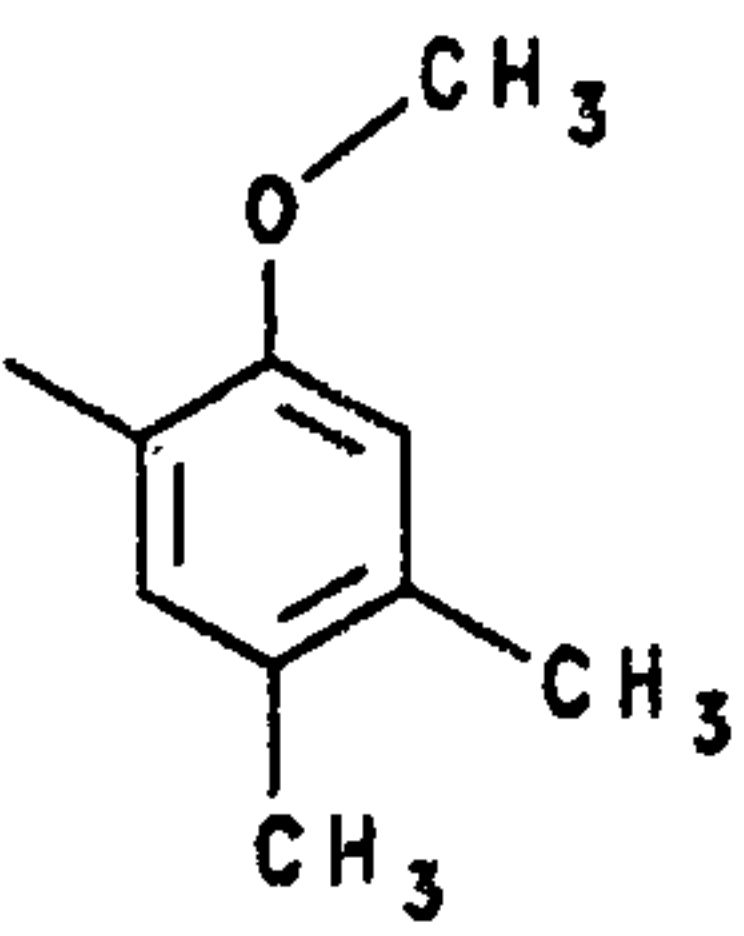
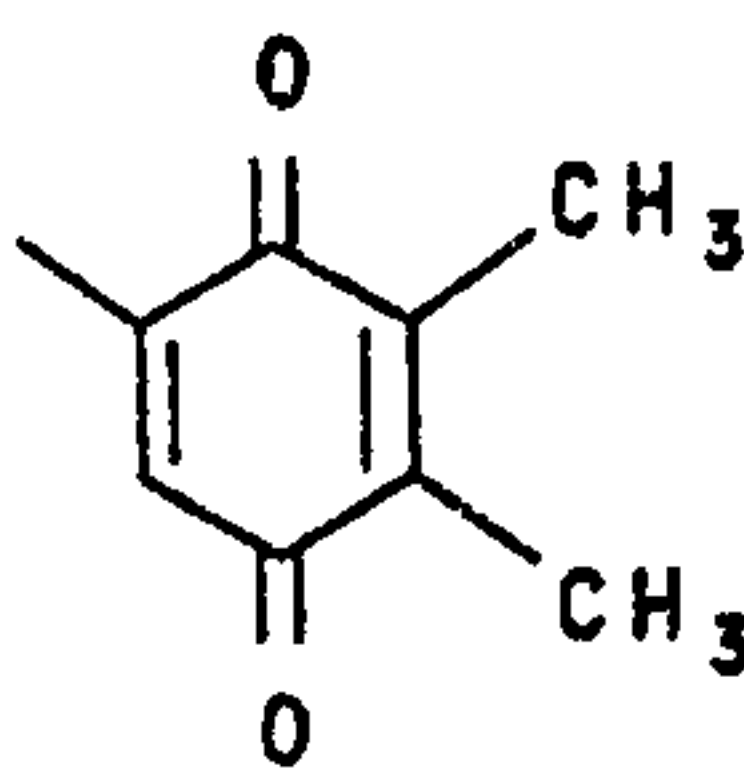
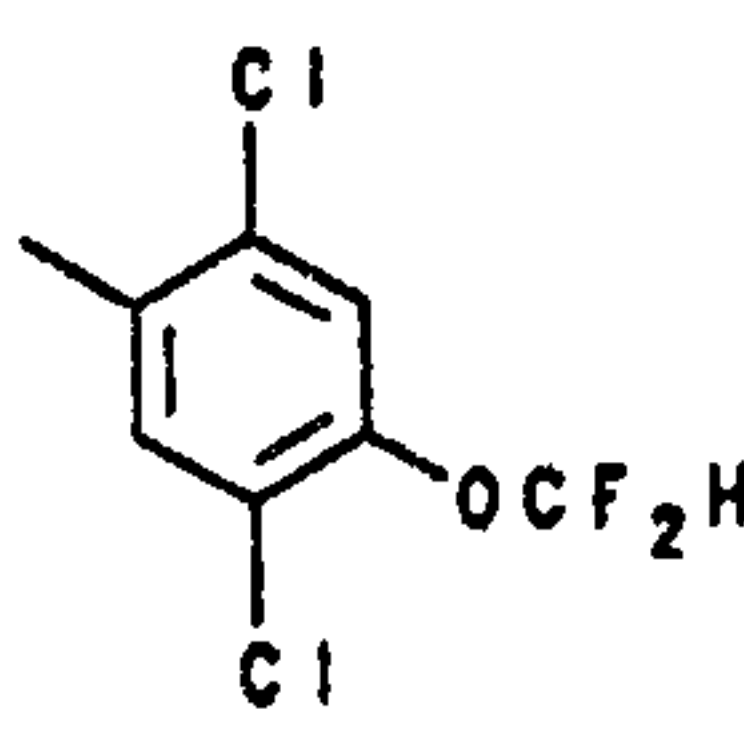
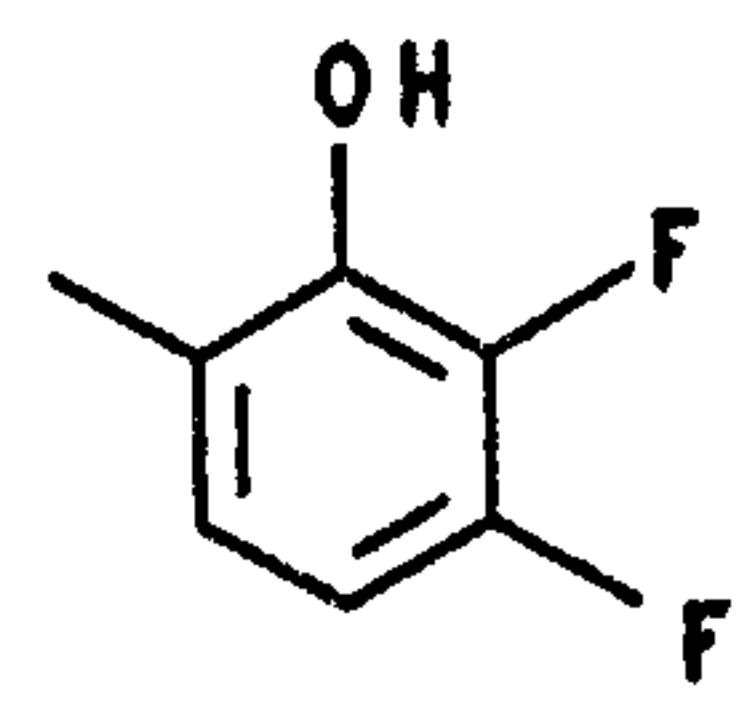
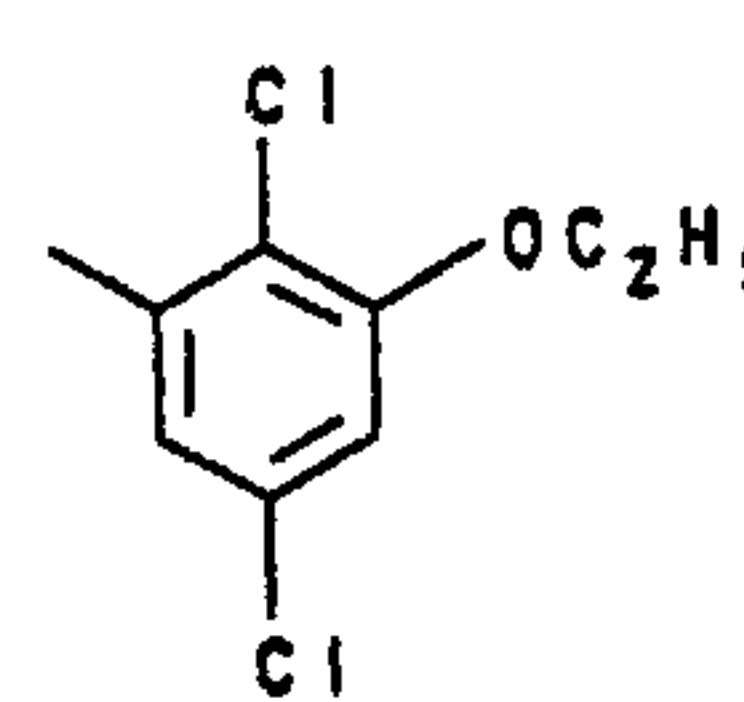
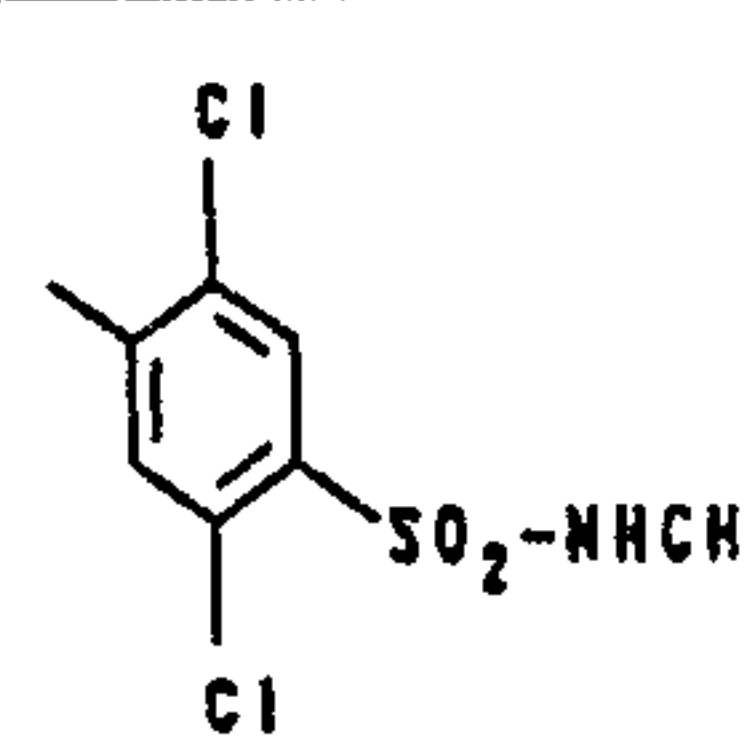
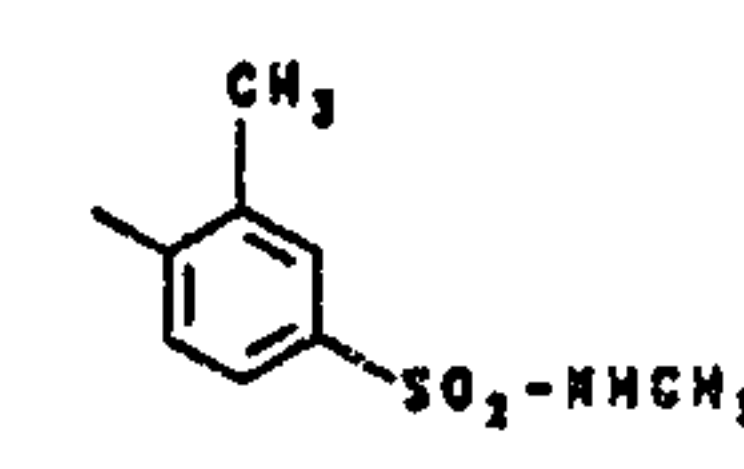
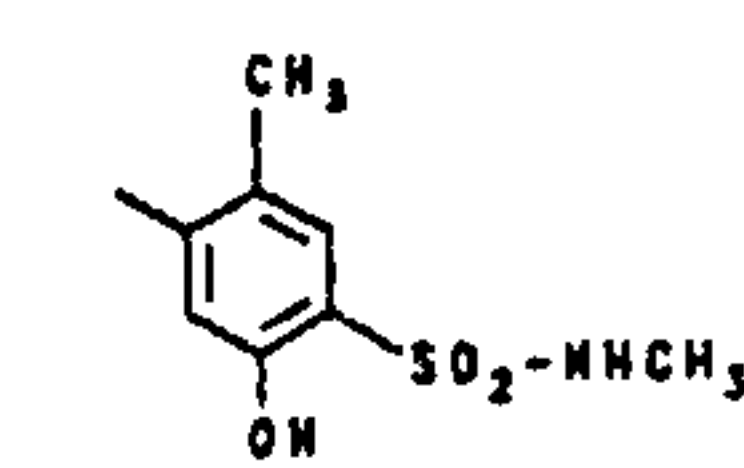
71	OCH_3	COOCH_3	SO_2CH_3			
72	Cl	H	$\text{SO}_2\text{C}_2\text{H}_5$			
73	CF_3	CH_3	Cl			
74	Cl	H	SO_2CH_3		151-153	
75	F	OCF_3	Cl			
76	Cl	CF_3	Cl			
77	H	COOC_2H_5	SO_2CH_3			
78	Cl	H	SO_2CH_3			

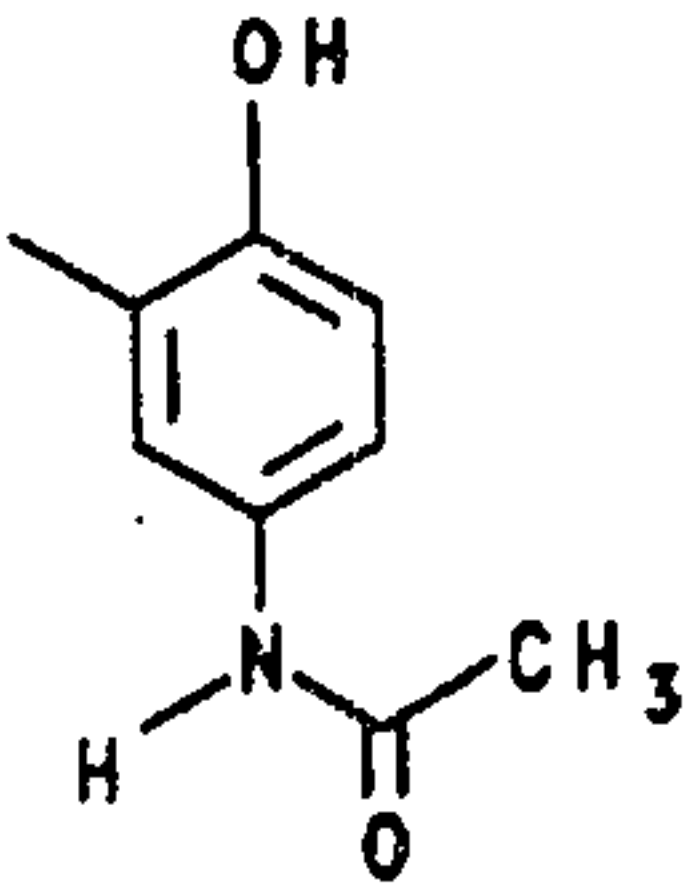
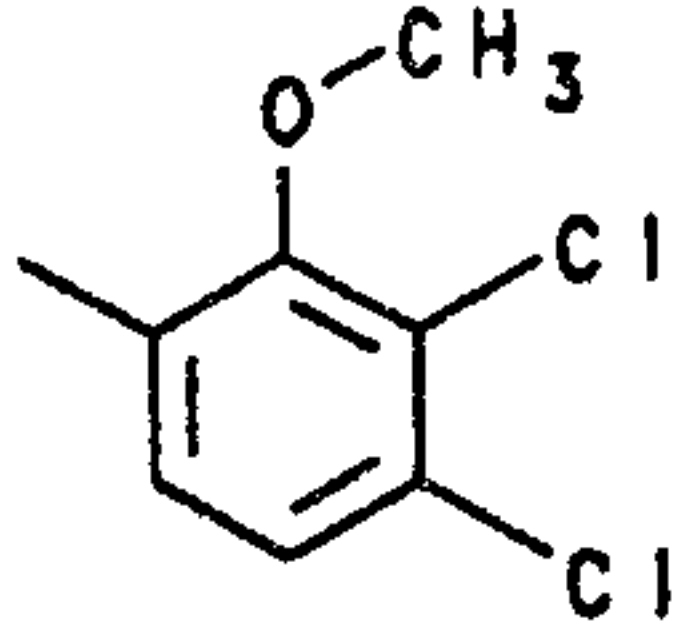
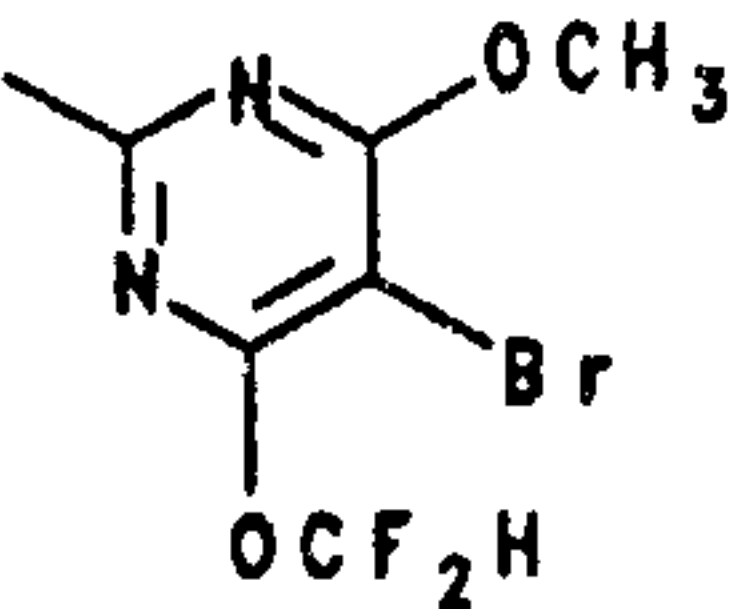
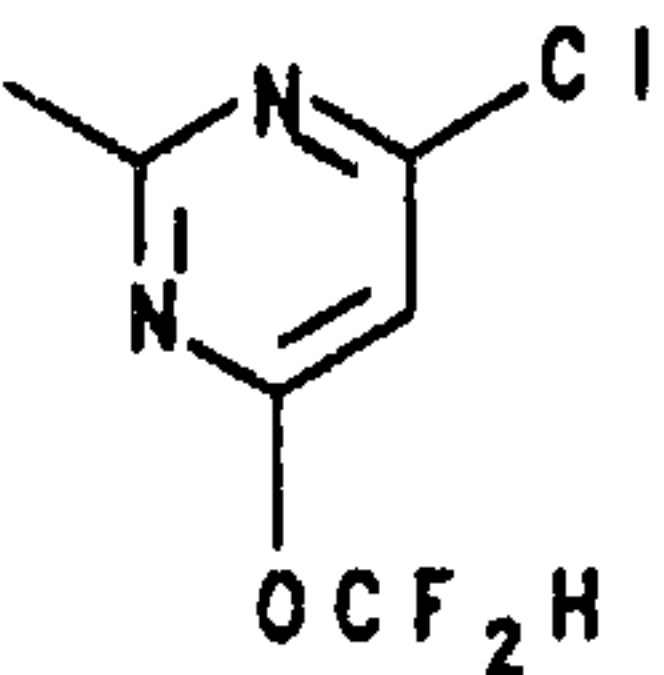
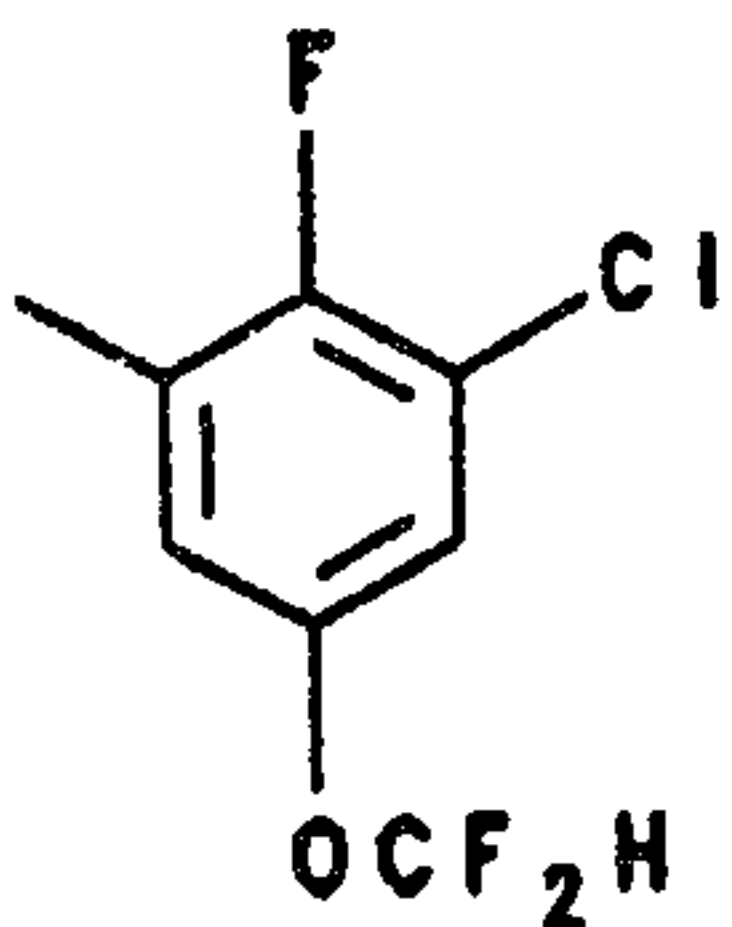
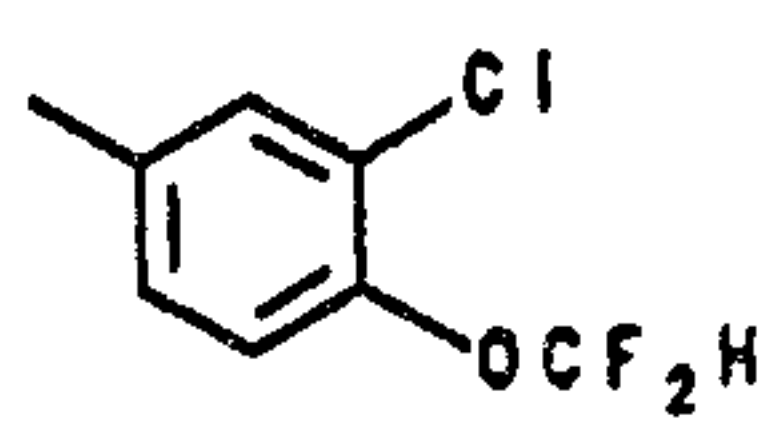
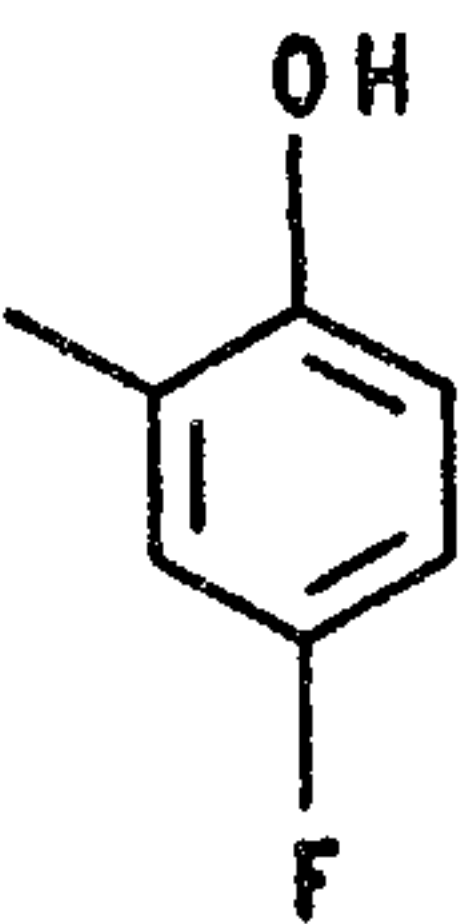
79	NO ₂	H	Cl		160-162	
80	F	Cl	Cl			
81	OCH ₃	COOCH ₃	SO ₂ CH ₃			
82	Cl	Cl	OH		137-139	
83	Cl	Cl	CF ₃			
84	F	C ₂ H ₅	Cl			
85	OCF ₂ H	Cl	Cl			

86	Cl	H	SO ₂ CH ₃		157	
87	Cl	H	SO ₂ CH ₃		108	2.4x10 ⁻⁷
88	Cl	H	SO ₂ CH ₃		254-256	7.0x10 ⁻⁸
89	CF ₂ H	Cl	Cl			
90	Br	H	SO ₂			
91	Cl	H	Cl		100	1.8x10 ⁻⁸

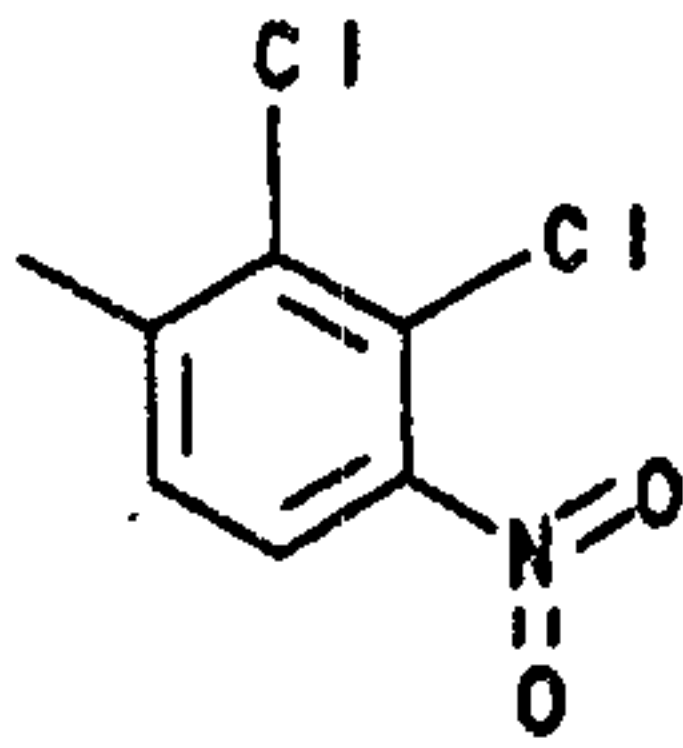
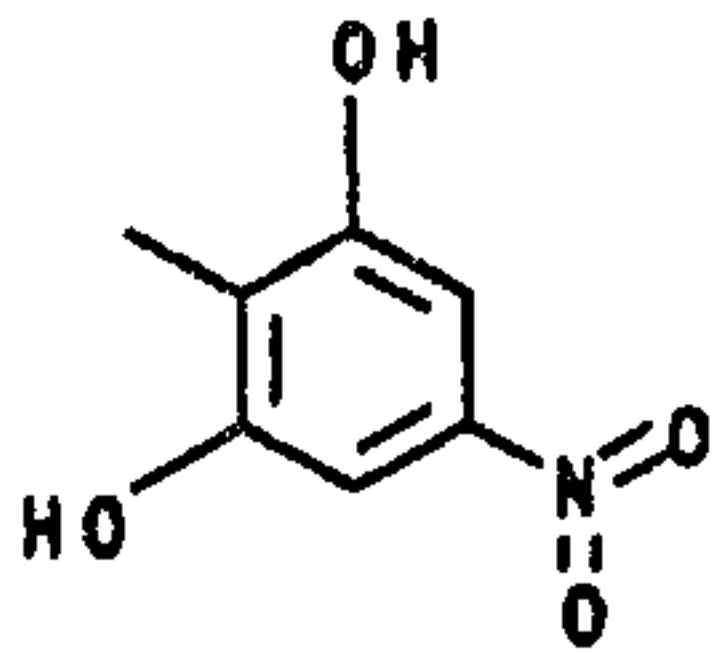
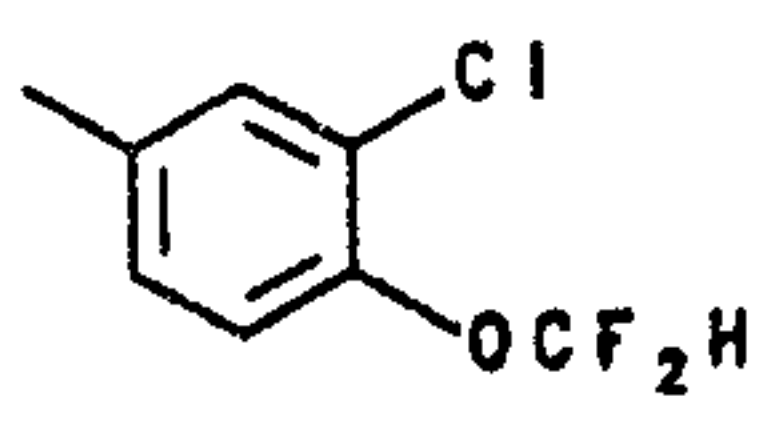
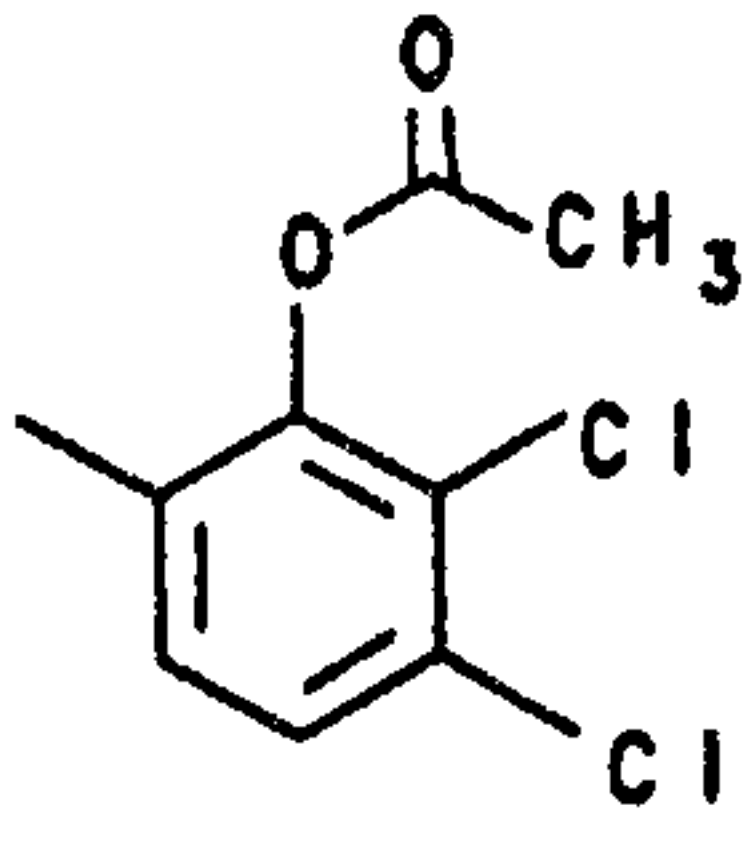
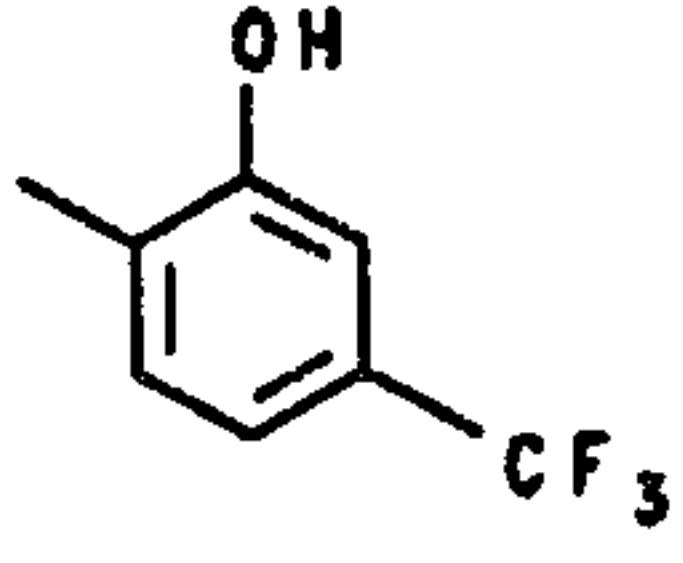
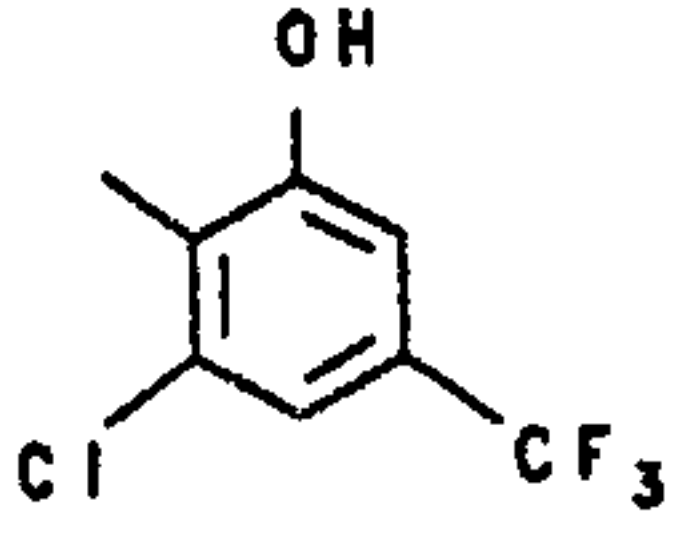
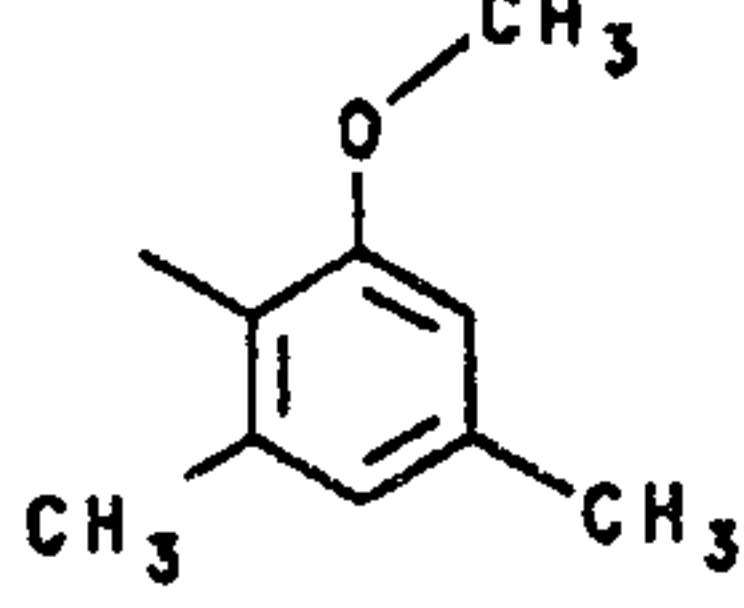
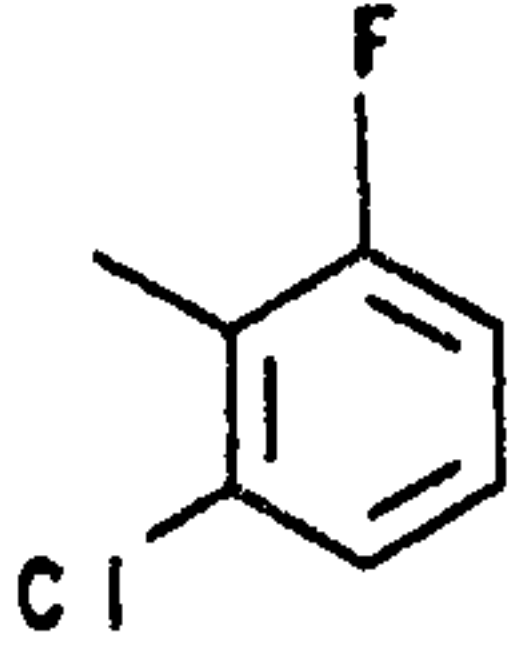
92	Cl	C ₂ H ₅	CF ₃			
93	F	F	F			
94	Cl	Cl	OH		149-152	
95	OH	Cl	Cl		118-121	
96	OC ₂ H ₅	Cl	CF ₃			
97	Cl	H	SO ₂ CH ₃		180 (decomp.)	6.0×10 ⁻⁸
98	CN	F	F			

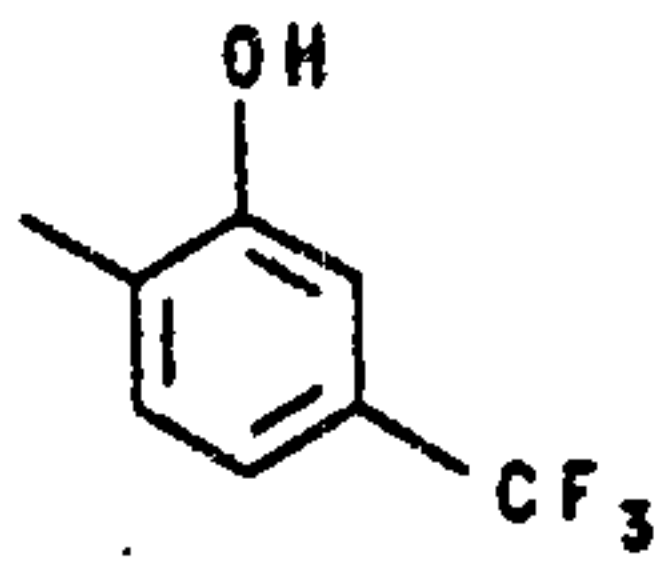
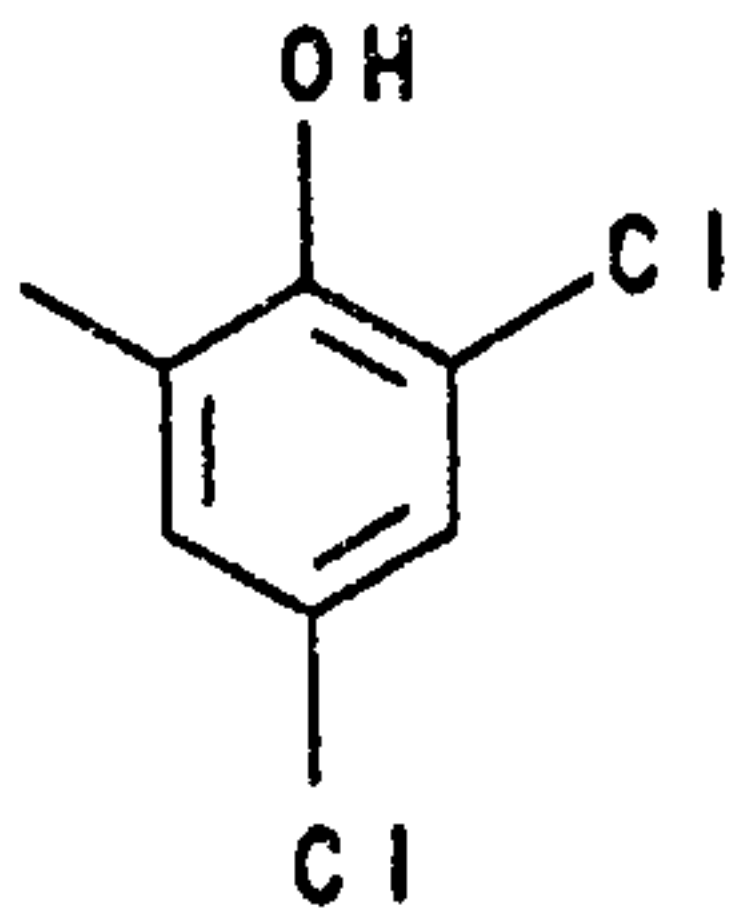
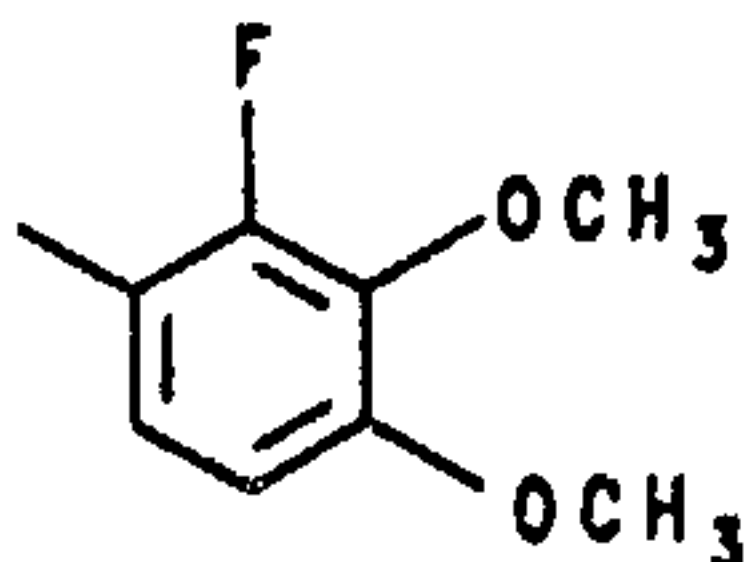
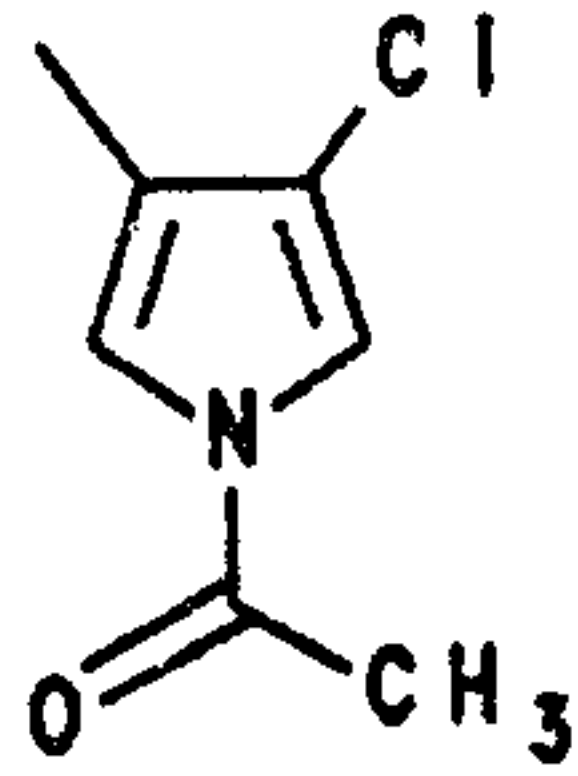
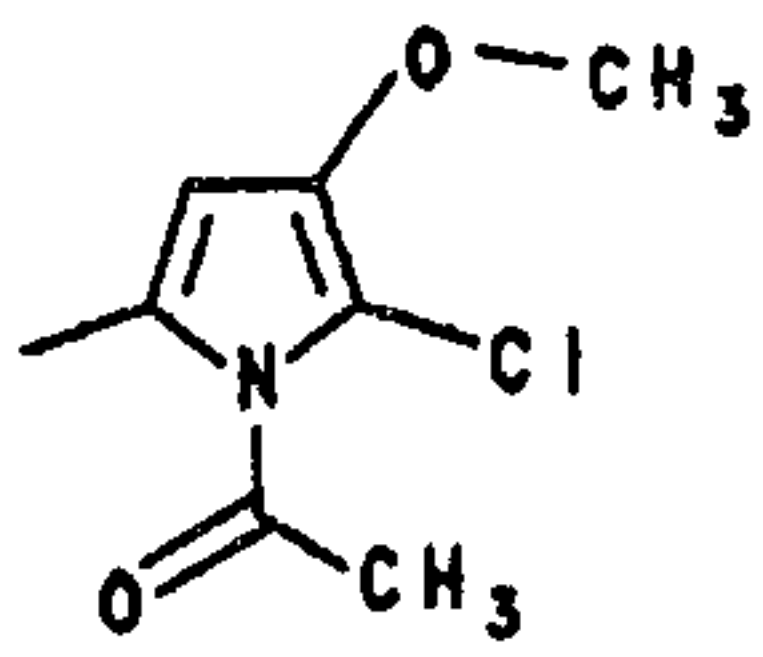
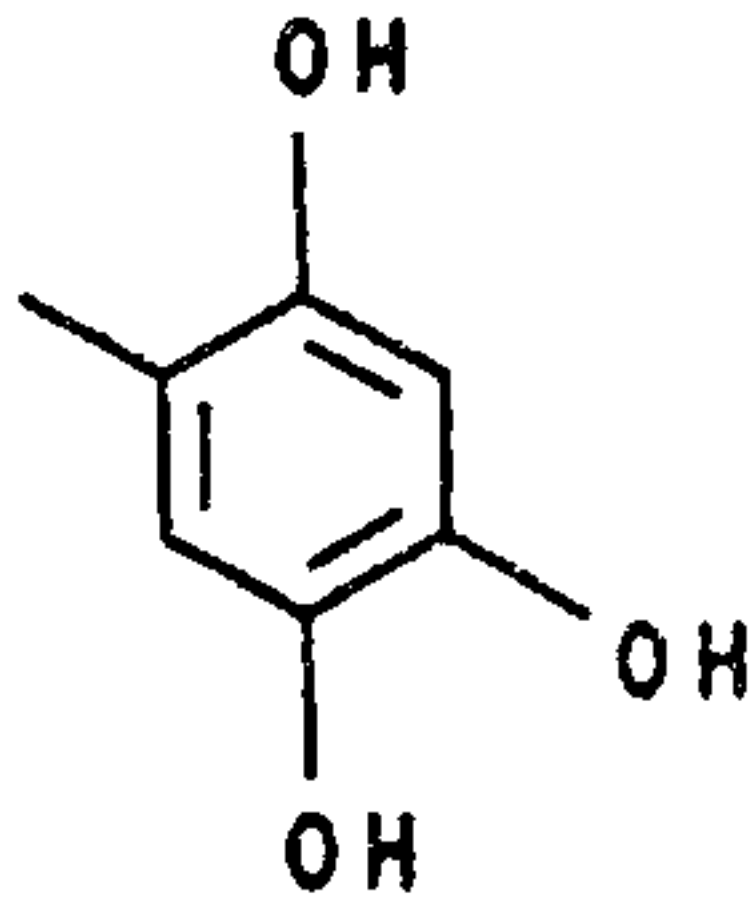
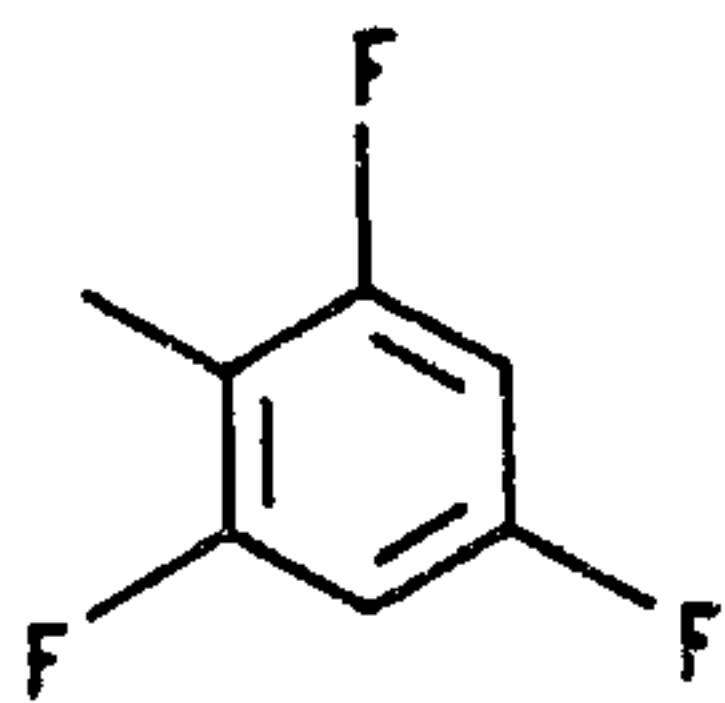
99	Cl	H	SO ₂ CH ₃			
100	Cl	H	SO ₂ CH ₃		175-180	6.2×10 ⁻⁹
101	Cl	H	SO ₂ CH ₃		183	< 10 ⁻⁹
102	Cl	OCH ₃	NO ₂			
103	F	Cl	Cl			
104	Cl	H	Cl		90	
105	Cl	H	SO ₂ C ₂ H ₅			

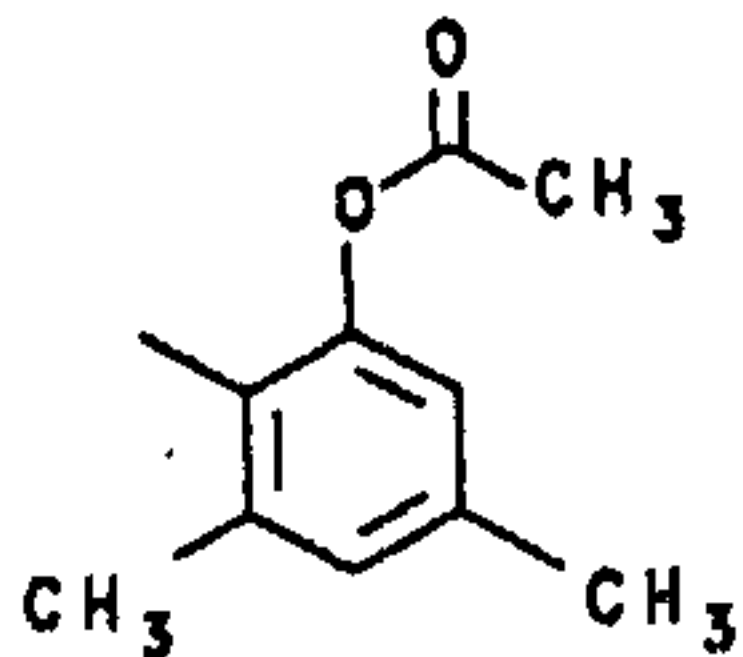
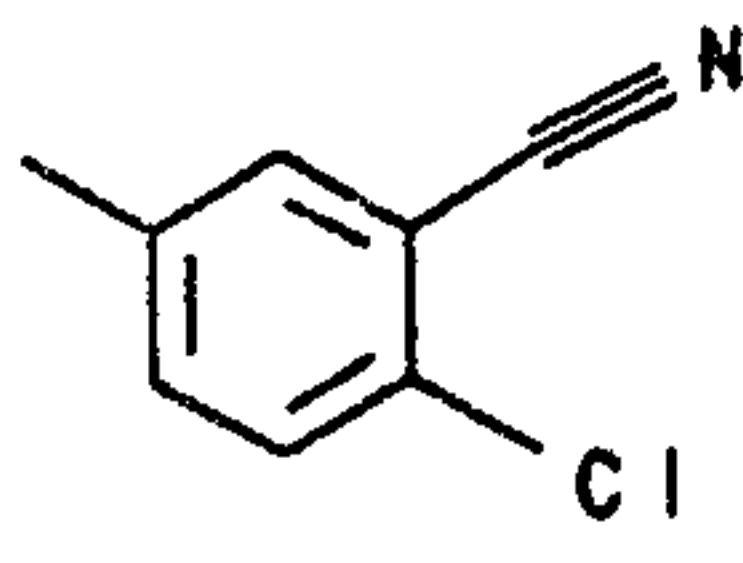
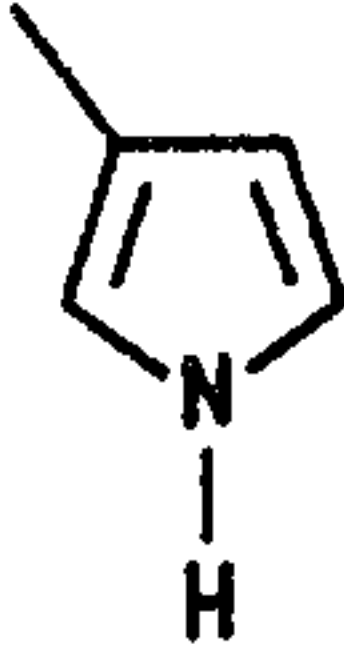
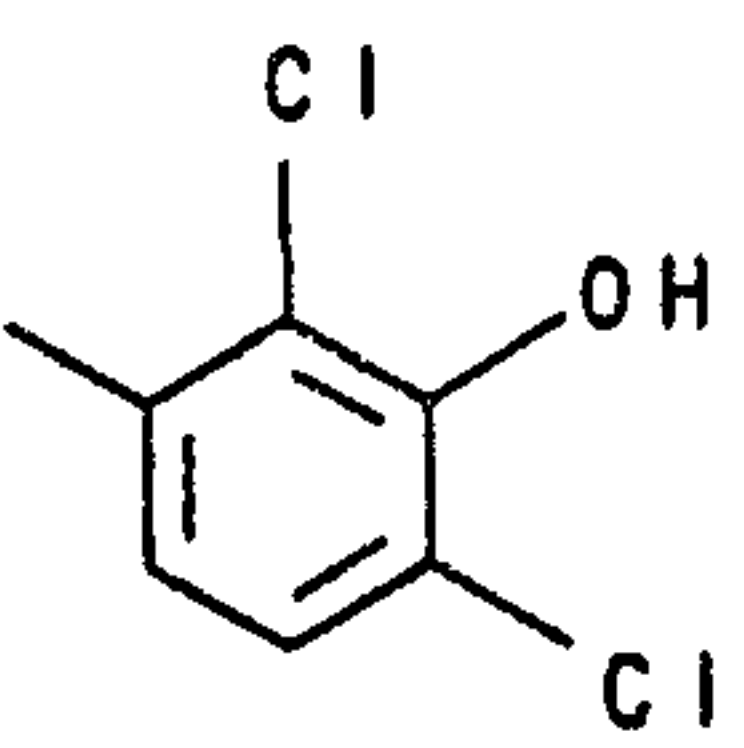
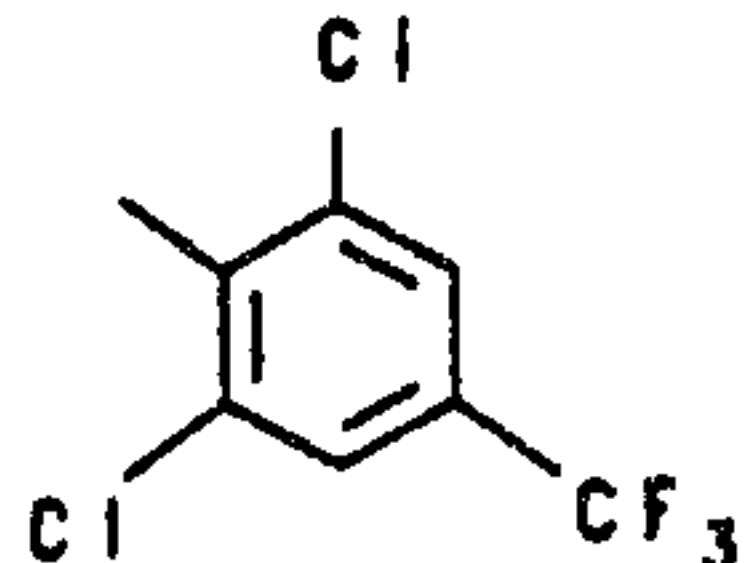
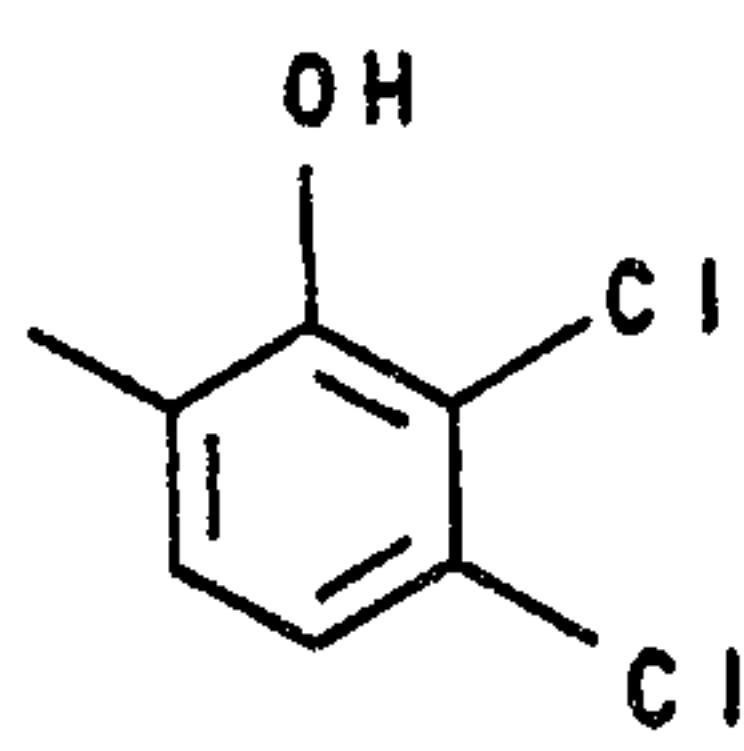
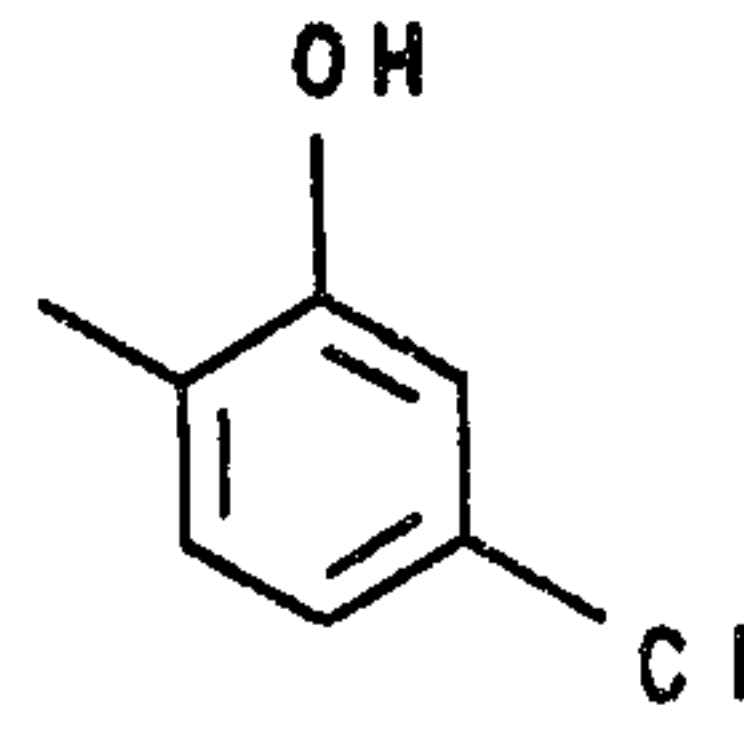
106	Cl	H	SO ₂ CH ₃		141-143	
107	H	COOC ₂ H ₅	CN			
108	OCH ₃	H	CF ₃			
109	Cl	H	SO ₂ CH ₃		171-175	< 10 ⁻⁸
110	H	COOC ₂ H ₅	CF ₃			
111	CCl ₃	Cl	Cl			
112	CCl ₃	Cl	Cl			
113	CF ₃	OCH ₃	Cl			

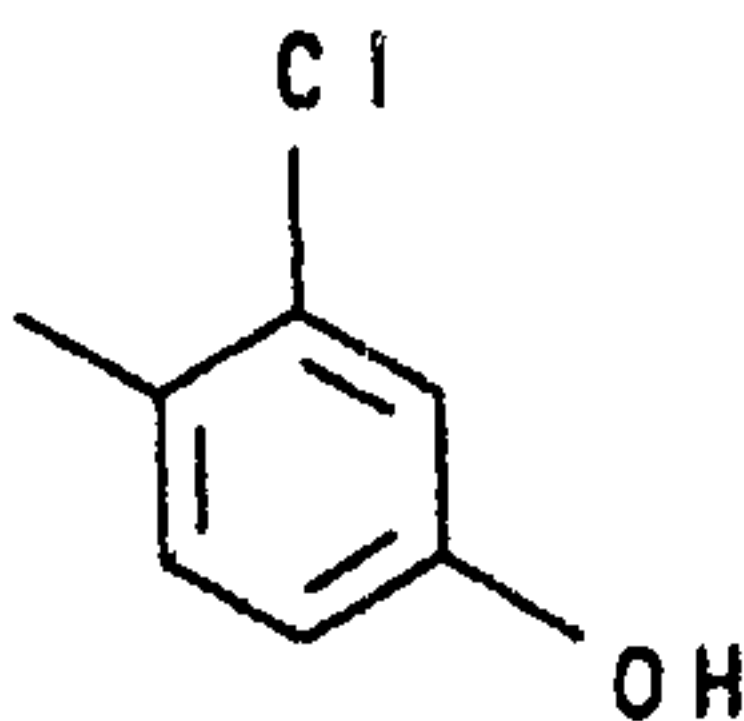
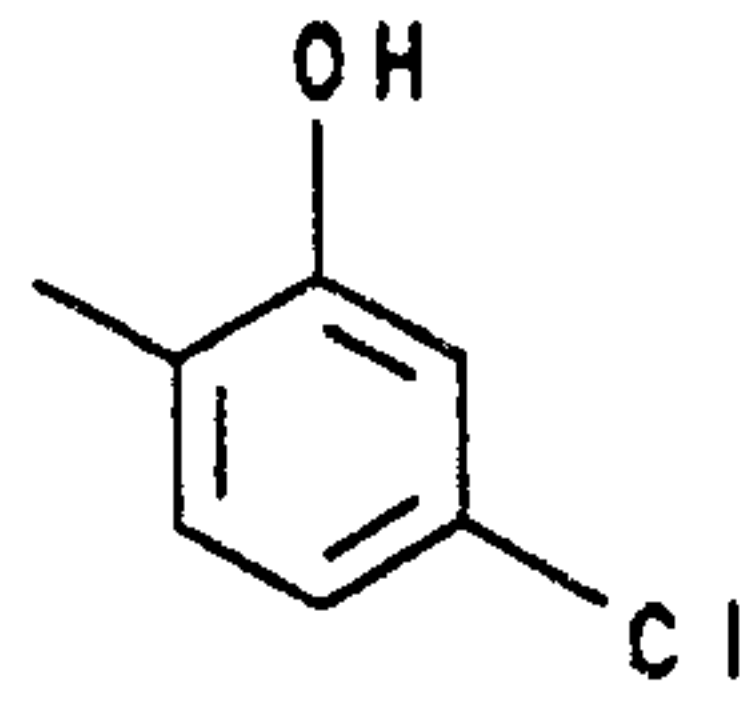
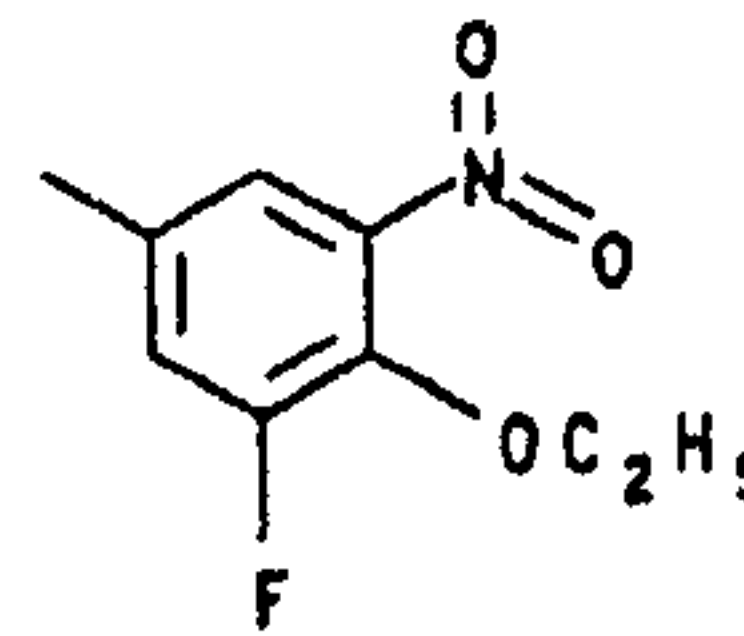
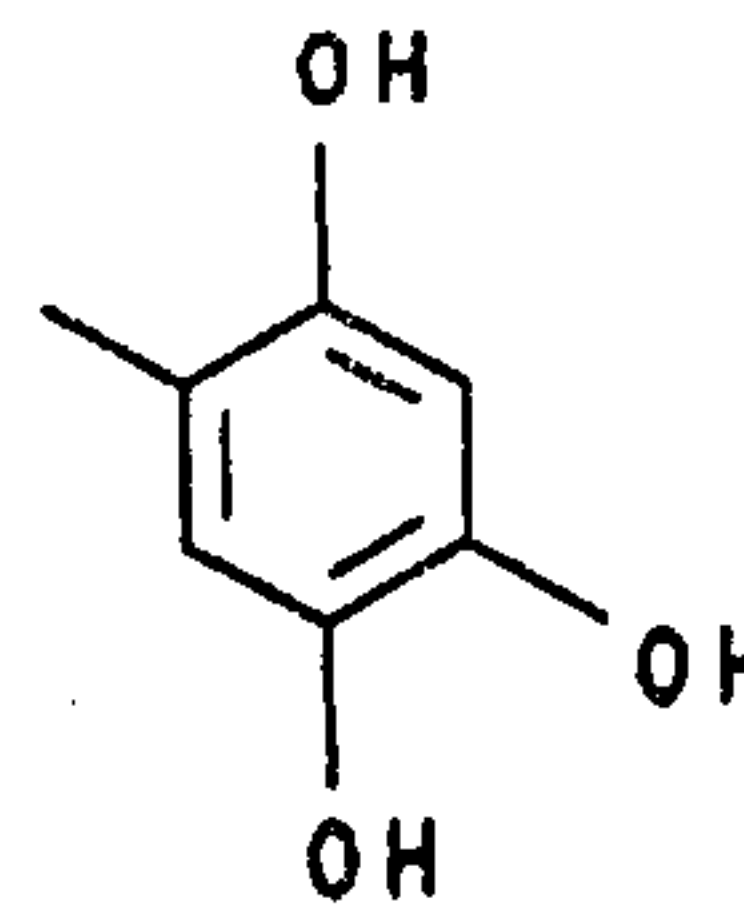
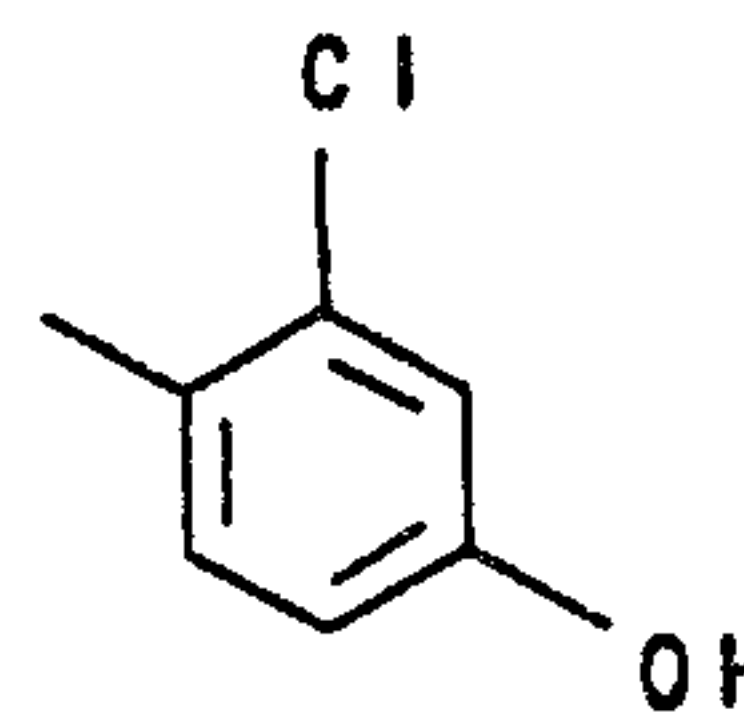
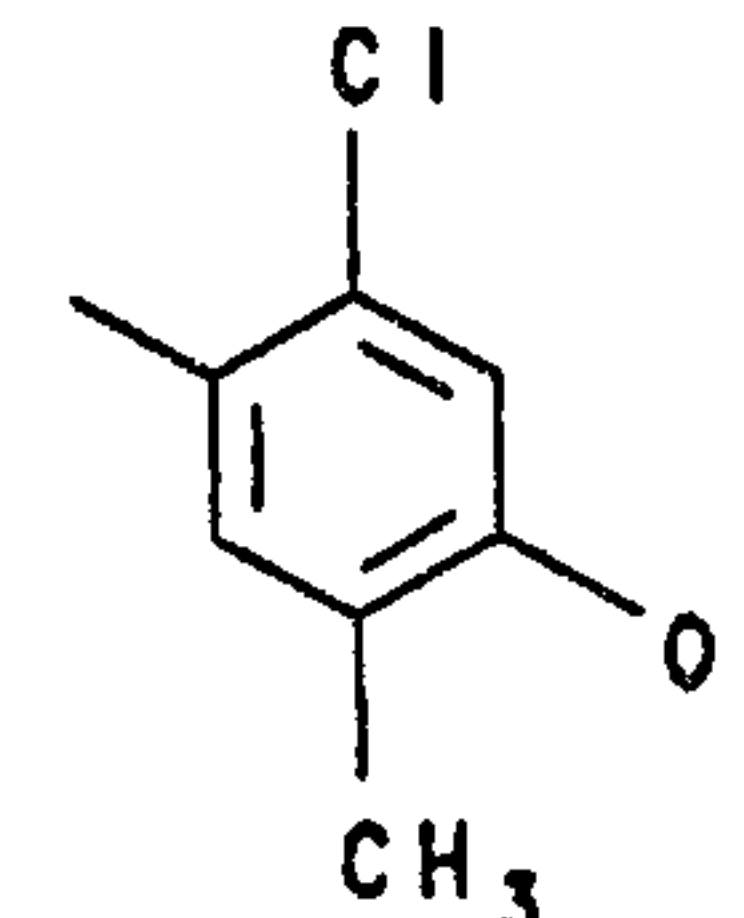
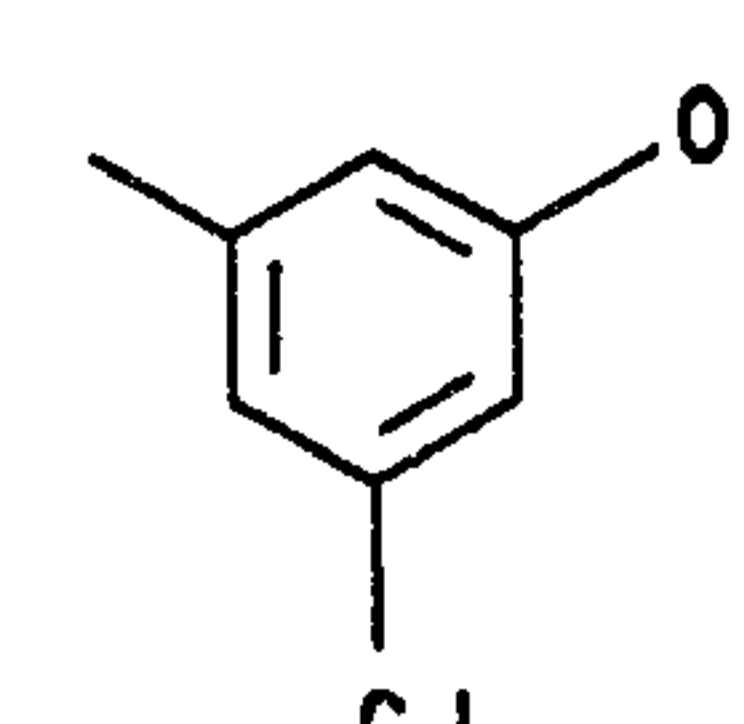
114	Cl	H	SO ₂ CH ₃		234-235	9.0×10 ⁻⁹
115	Cl	H	SO ₂ CH ₃		98-100	
116	Cl	Cl	Br			
117	CN	H	Cl			
118	Cl	CF ₃	Cl			
119	NO ₂	OC ₂ H ₅	Cl			
120	Cl	H	SO ₂ CH ₃		182-187	< 10 ⁻⁹

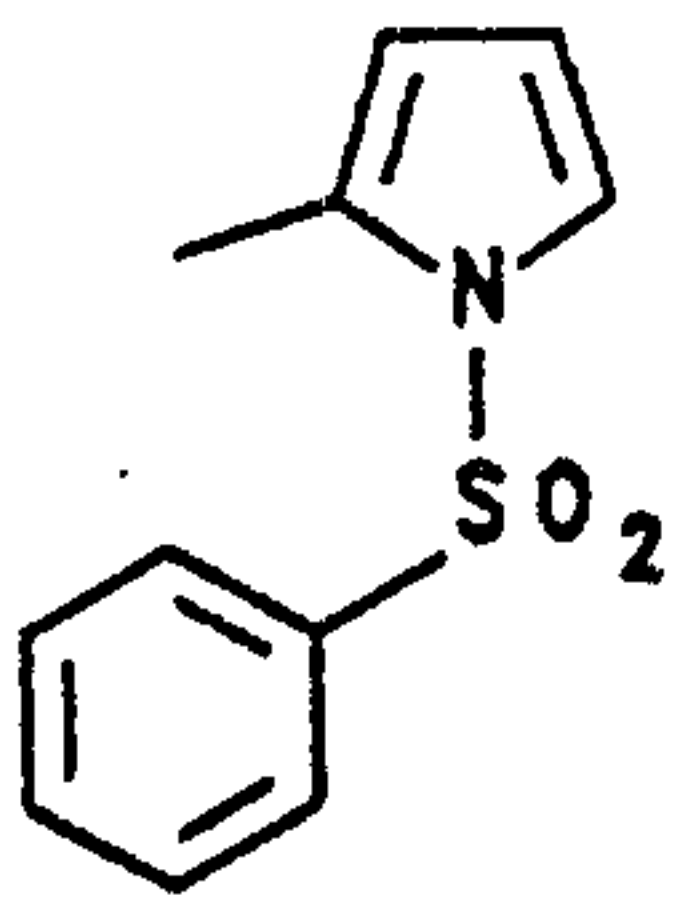
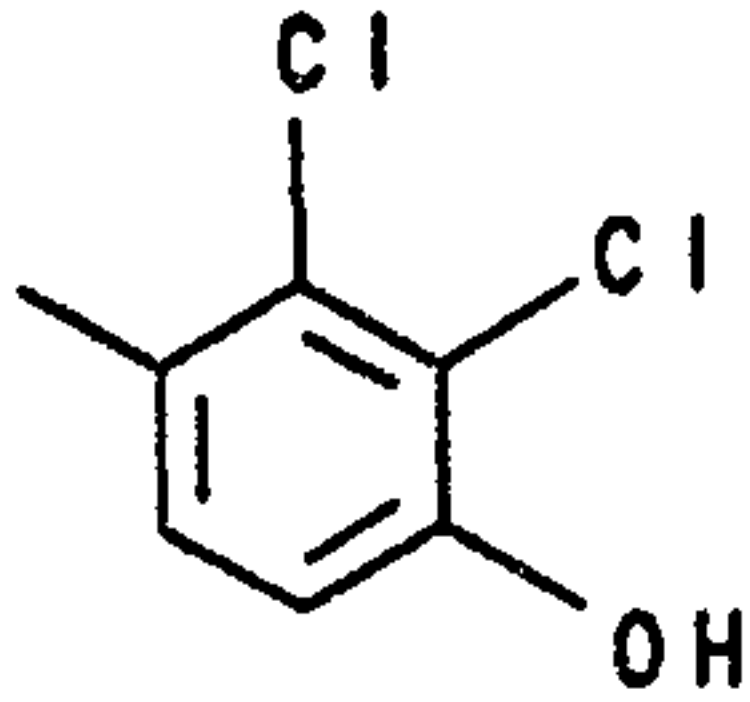
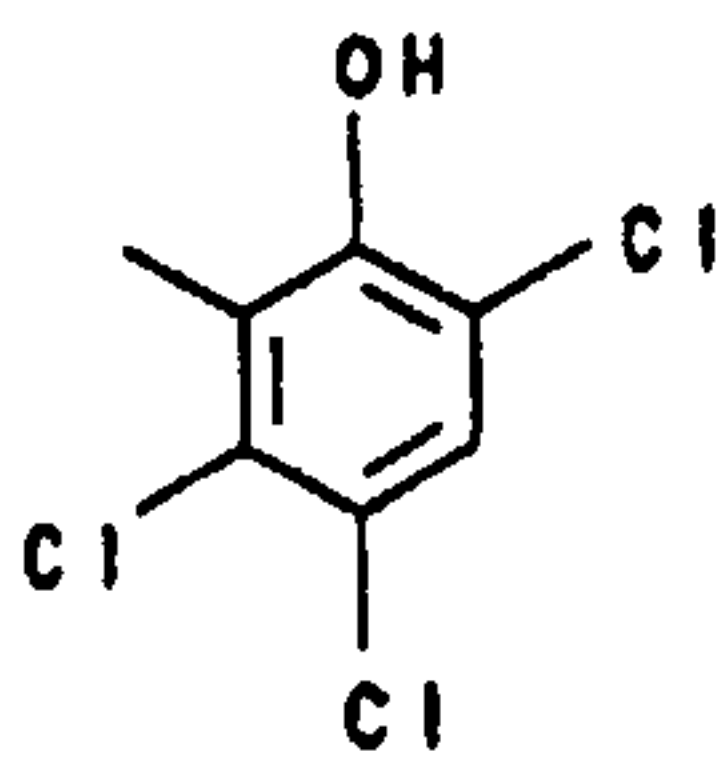
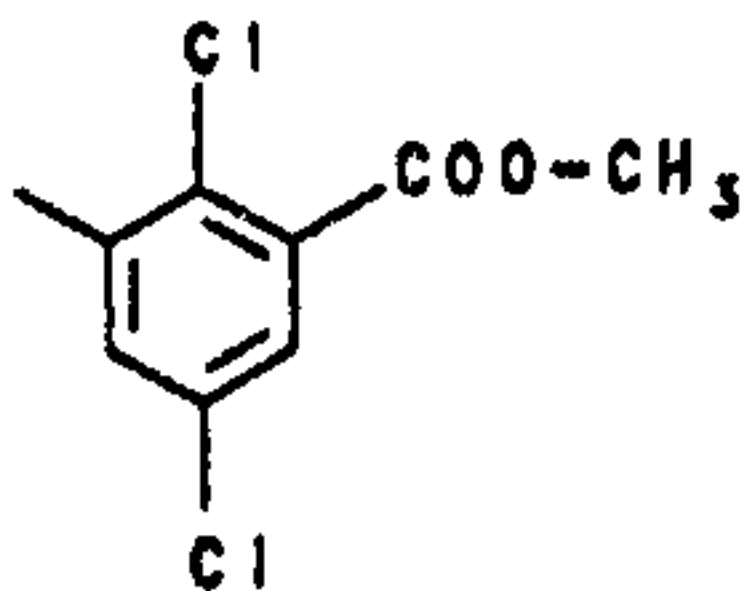
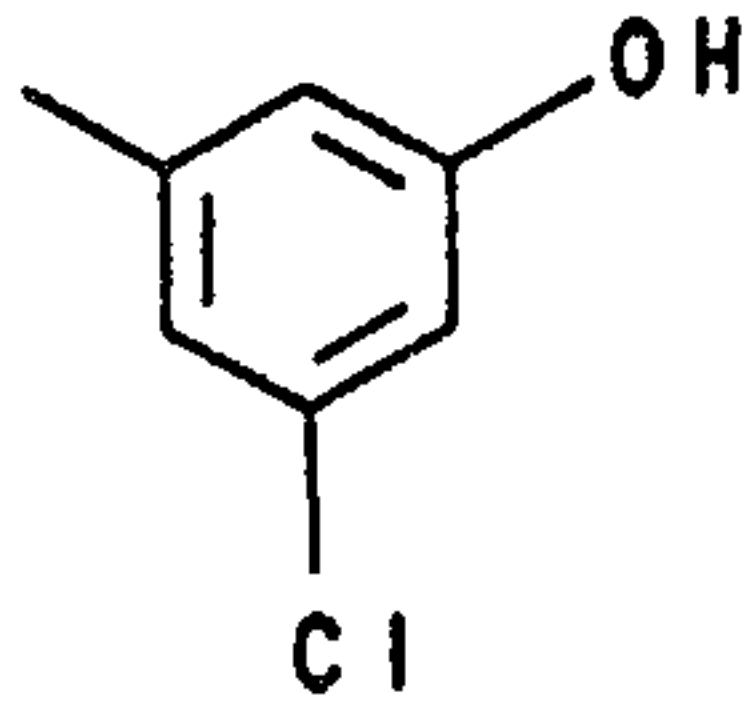
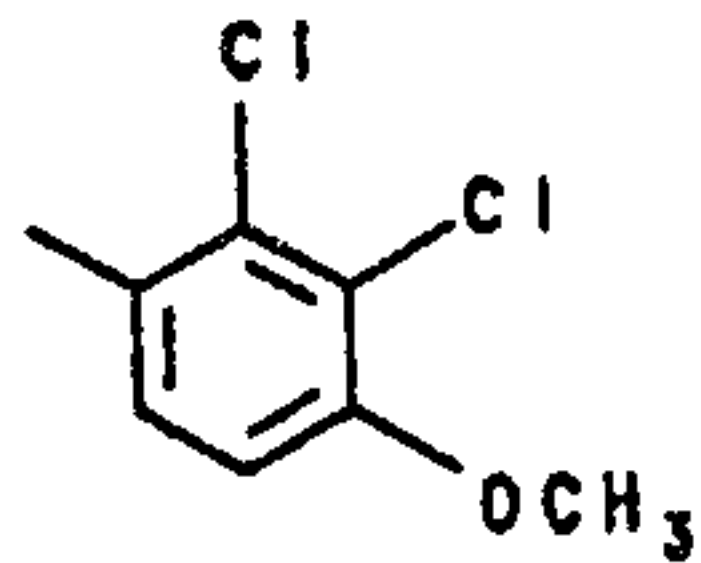
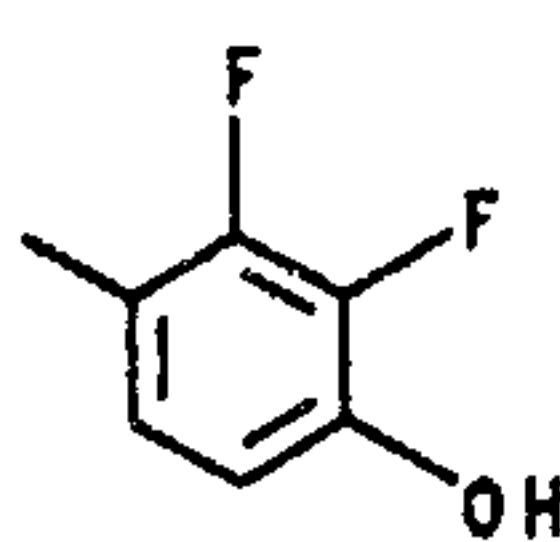
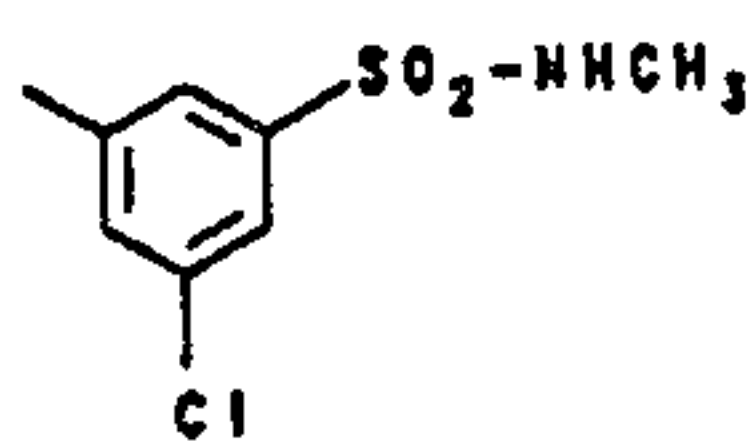
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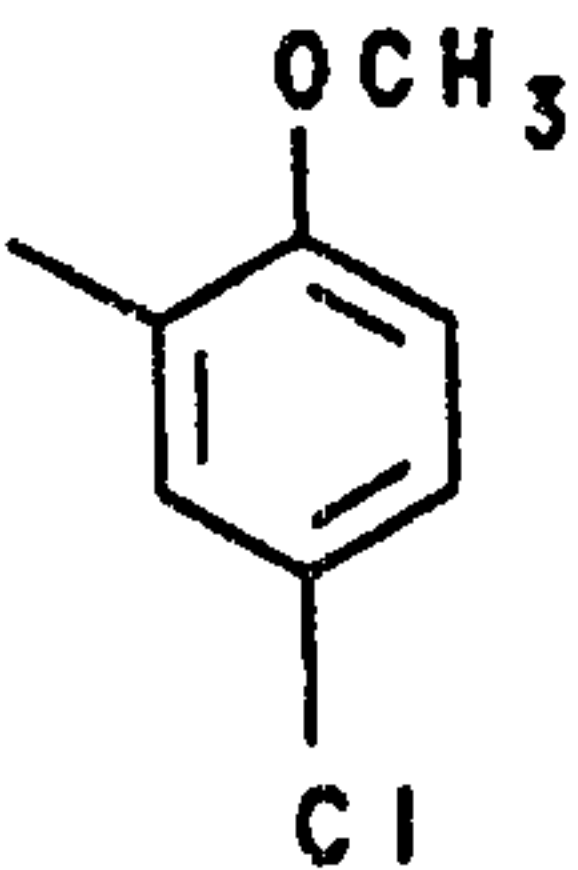
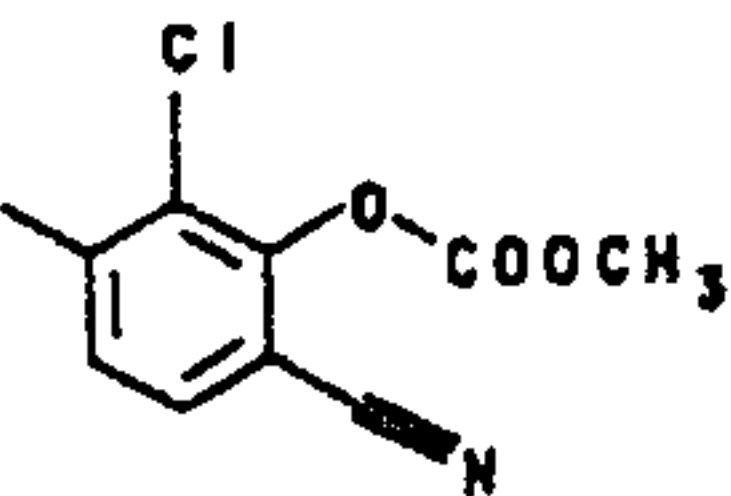
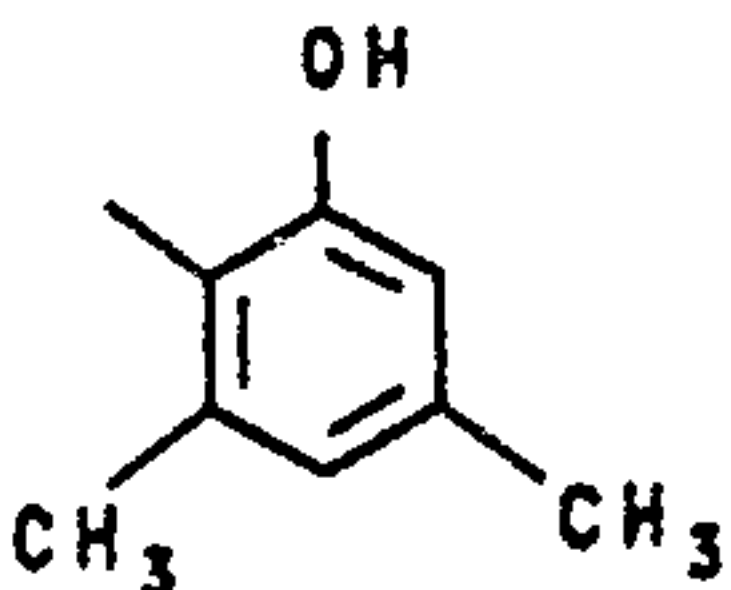
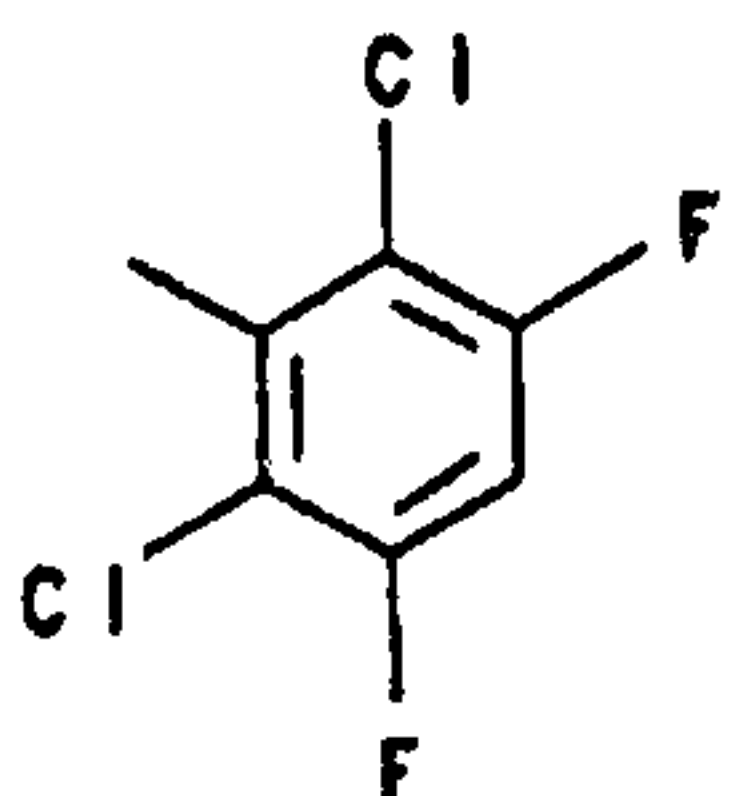
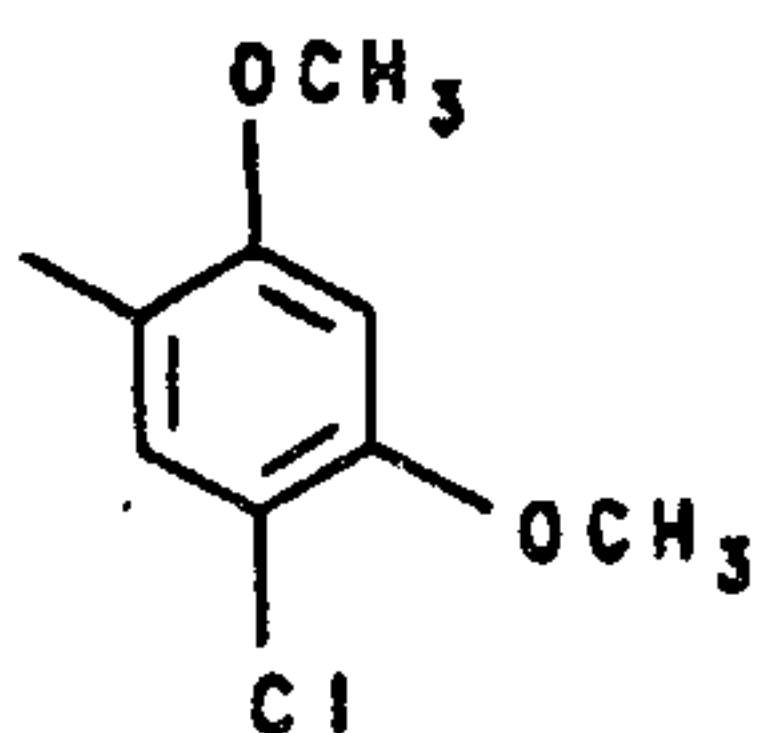
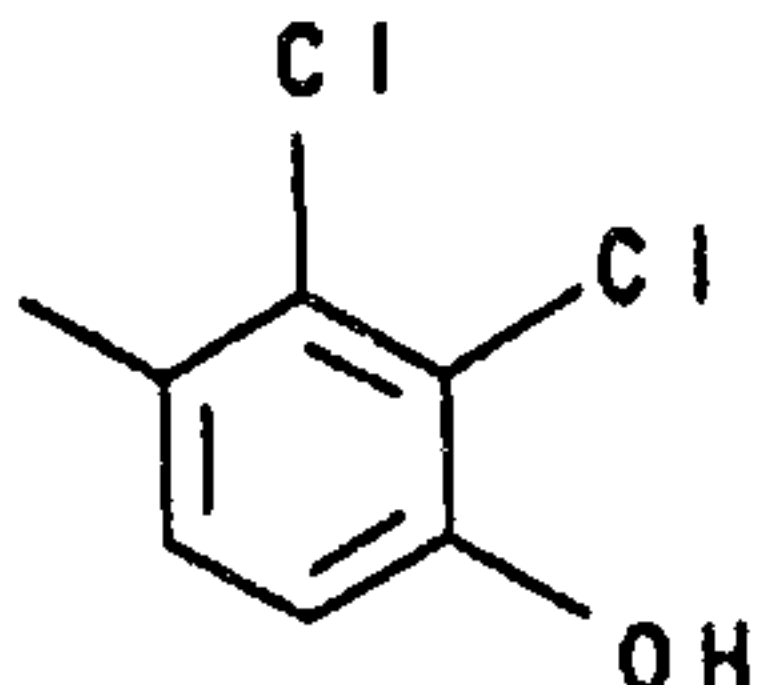
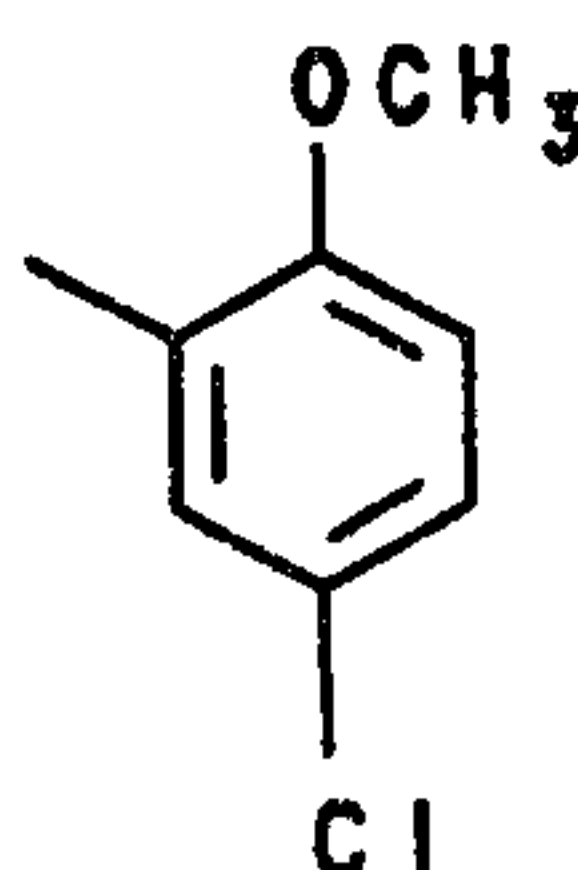
121	F	OCH ₃	F			
122	Cl	Cl	Cl			
123	CF ₃	COOCH ₃	Cl			
124	Cl	H	SO ₂ CH ₃		188-192	
125	Cl	COOC ₂ H ₅	Cl			
126	NO ₂	H	Cl			
127	Cl	H	SO ₂ CH ₃		136-140	
128	OH	CF ₂ H	Br			

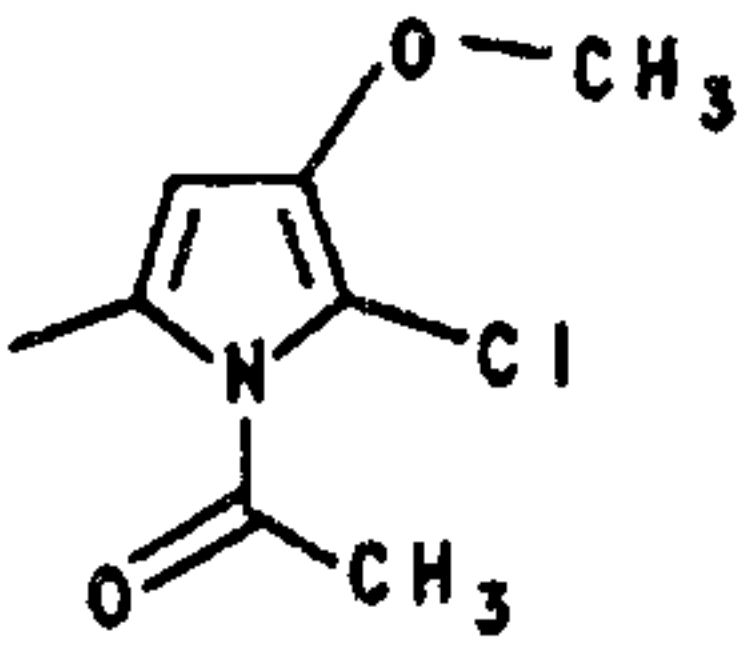
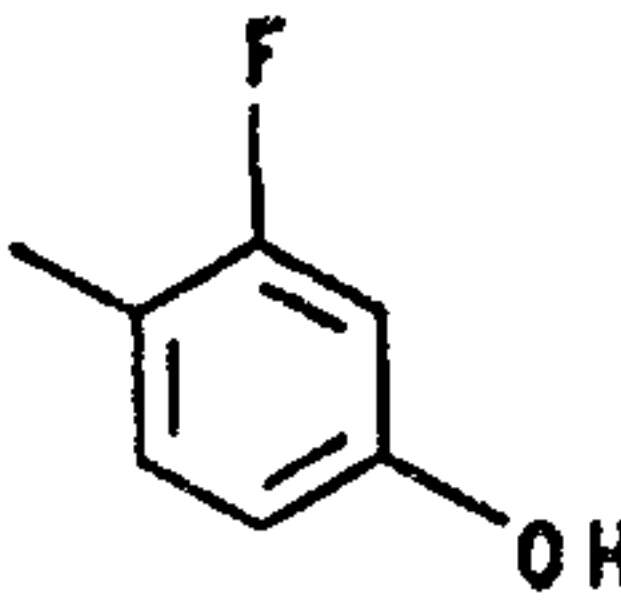
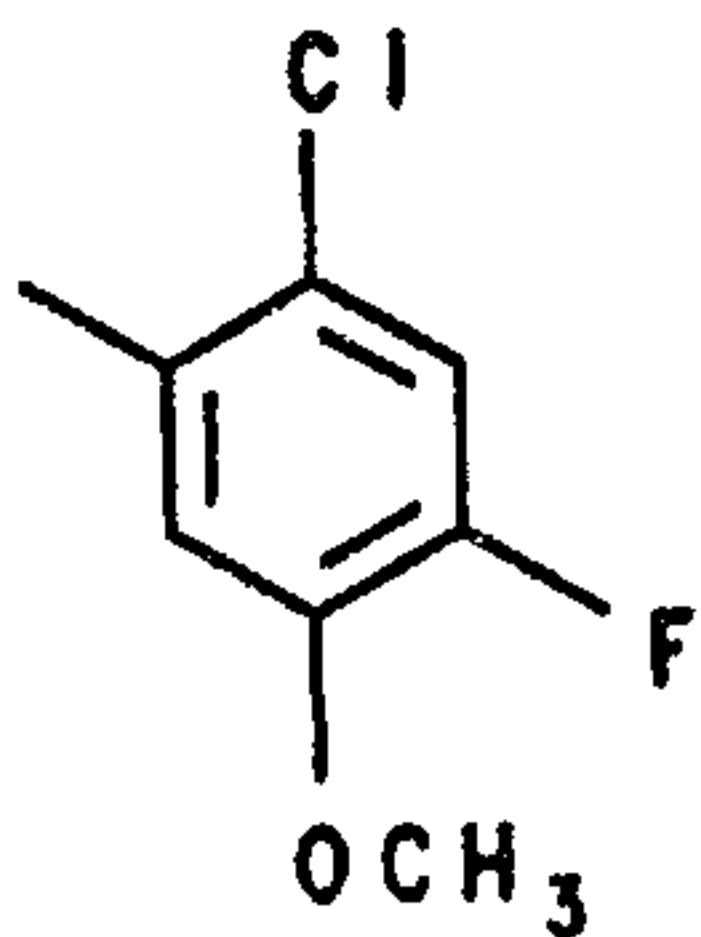
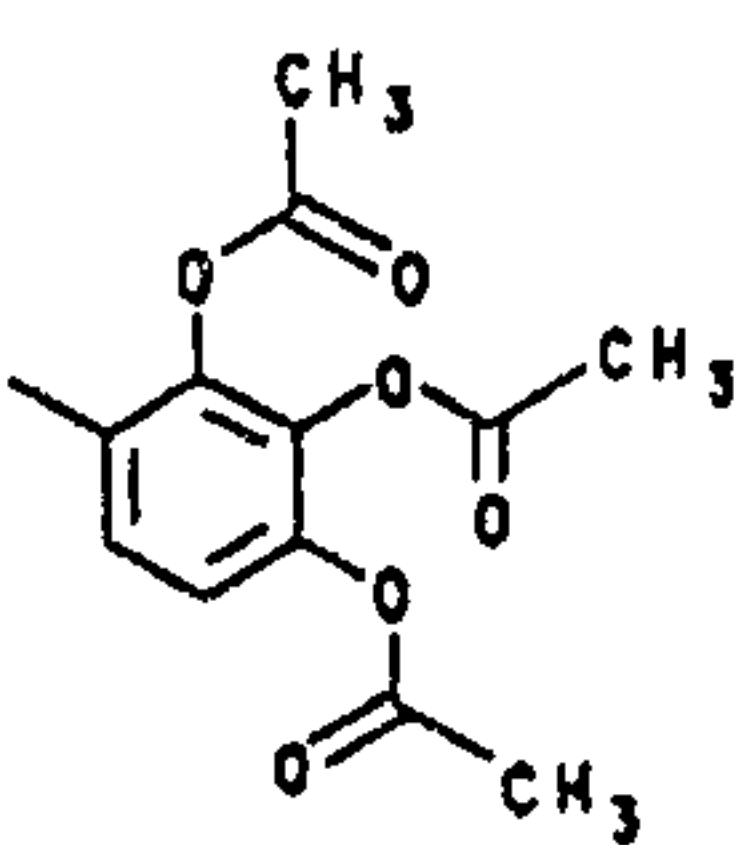
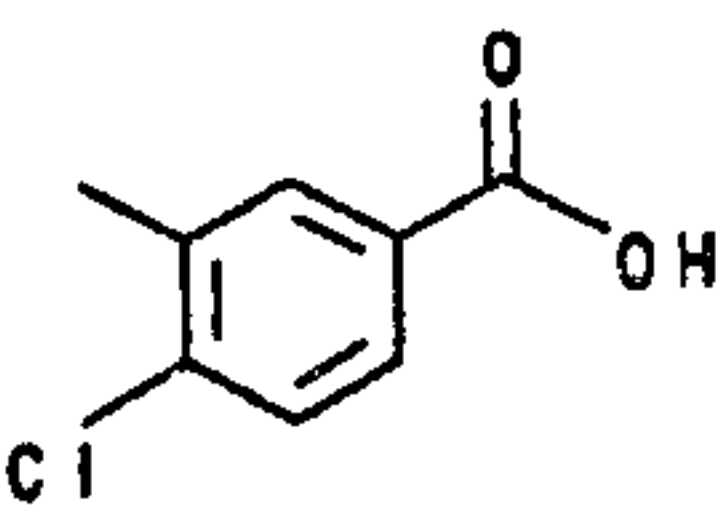
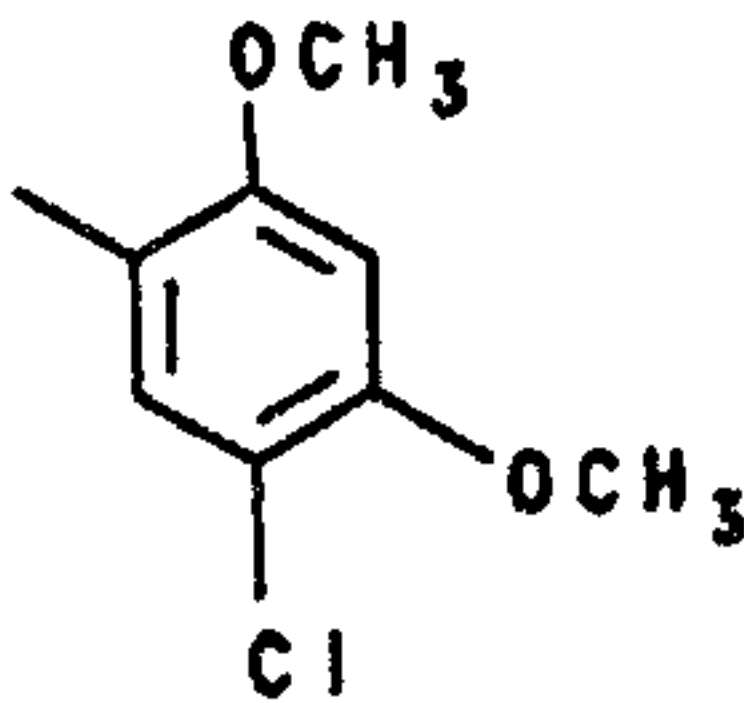
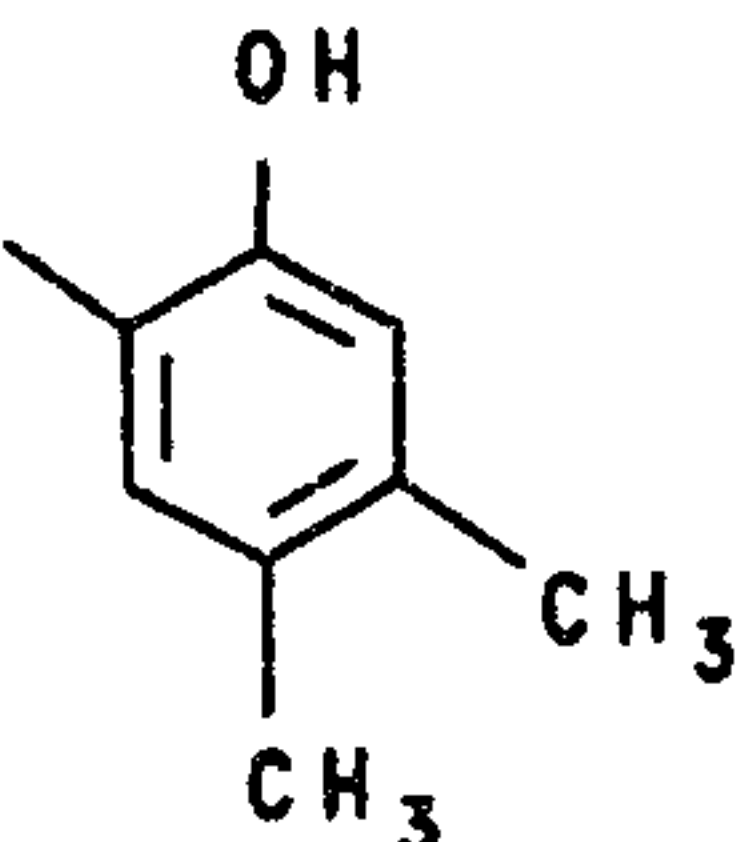
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130	Cl	H	SO ₂ CH ₃		198-202	1.0x10 ⁻⁹
131	Cl	H	CF ₃			
132	Cl	H	Cl			
133	H	Cl	Cl			
134	Cl	H	SO ₂ CH ₃		278	
135	Cl	OC ₂ H ₅	C ₂ F ₅			

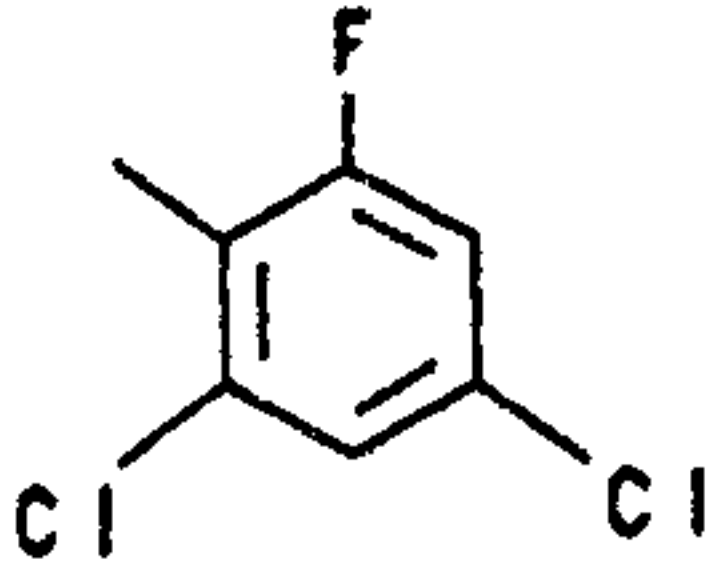
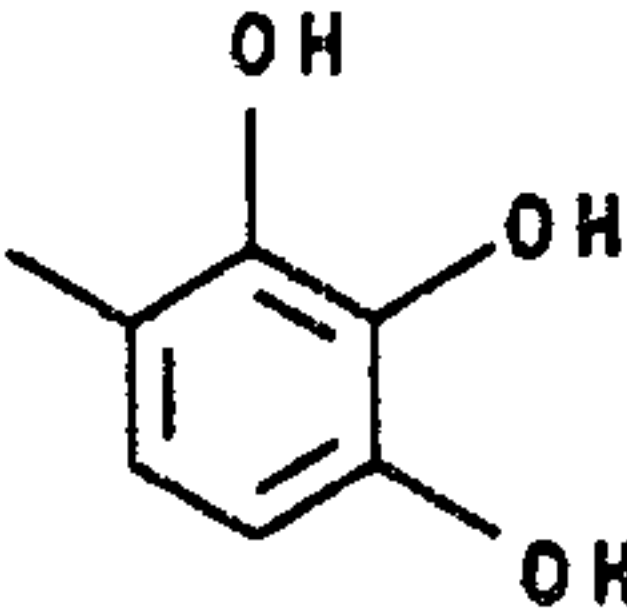
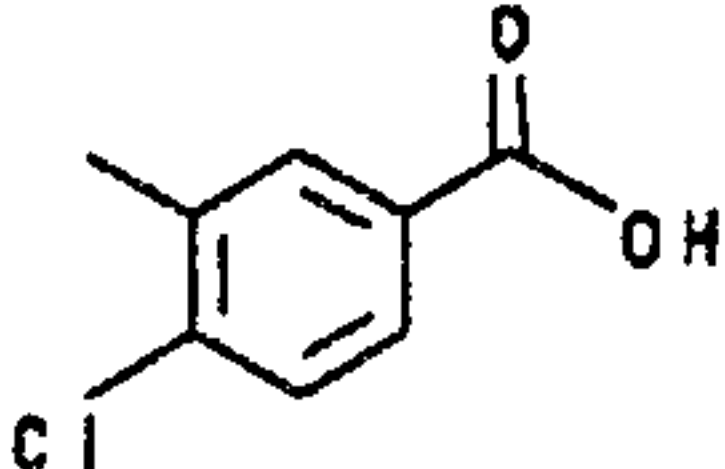
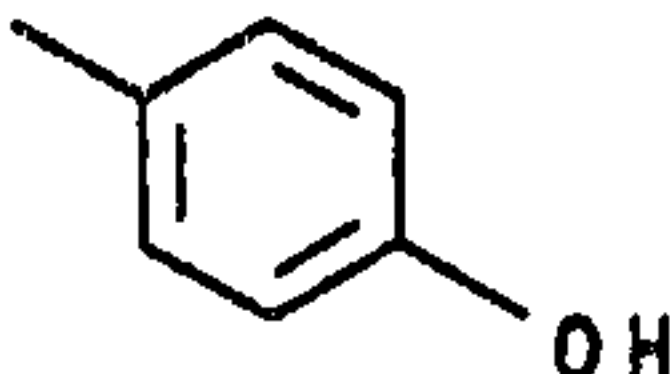
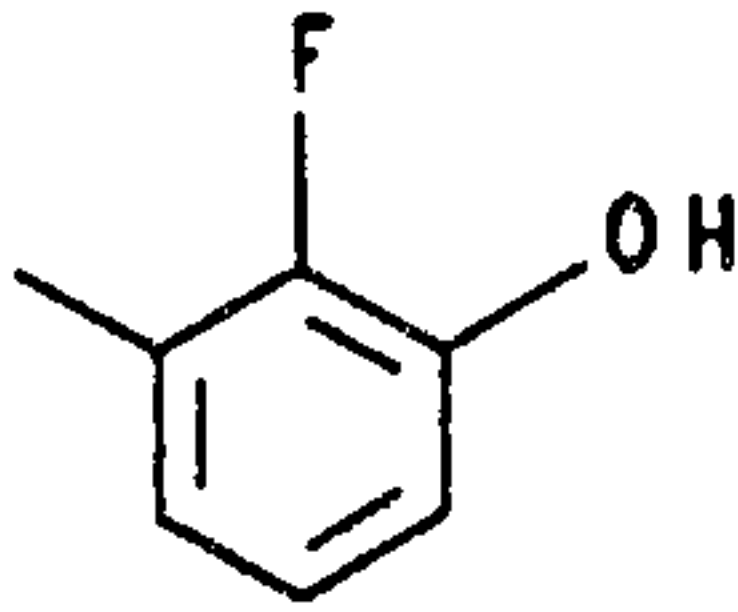
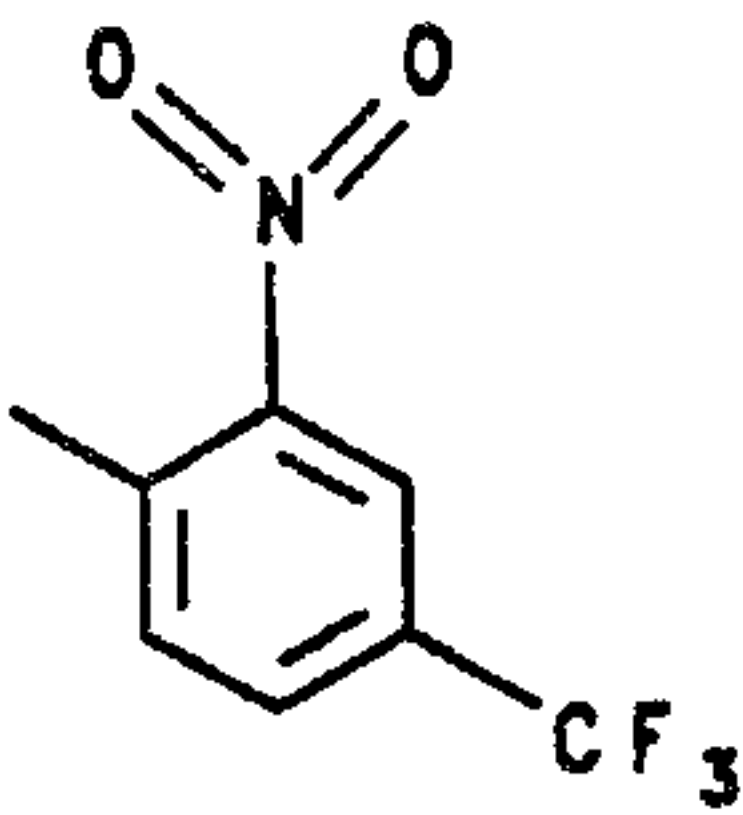
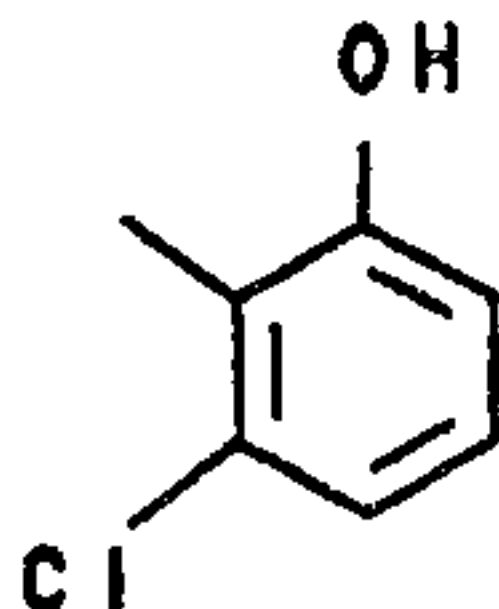
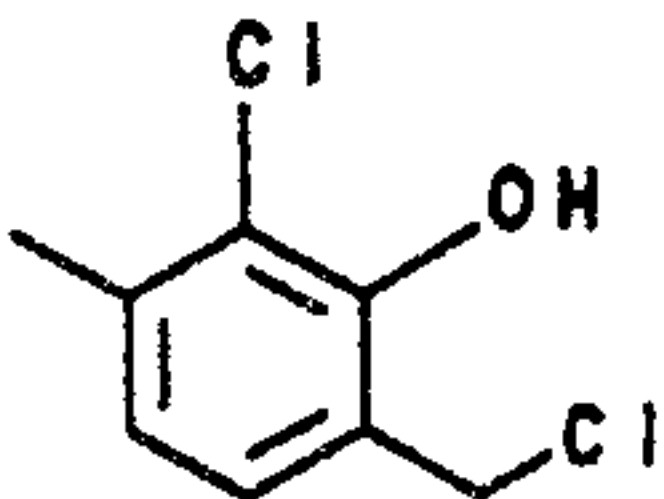
136	Cl	H	SO ₂ CH ₃		105-108	3.0×10 ⁻⁷
137	C ₂ F ₅	COOCH ₃	Cl			
138	Cl	H	Cl		173	
139	CN	F	Cl			
140	H	Cl	SO ₂ CH ₃			
141	Cl	H	SO ₂ CH ₃		182-185	1.1×10 ⁻⁹
142	Cl	CF ₂ H	SO ₂ C ₂ H ₅			

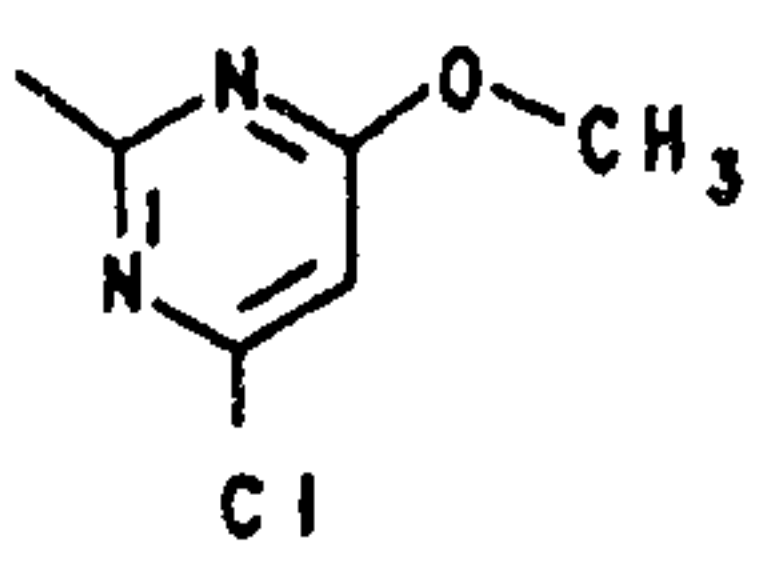
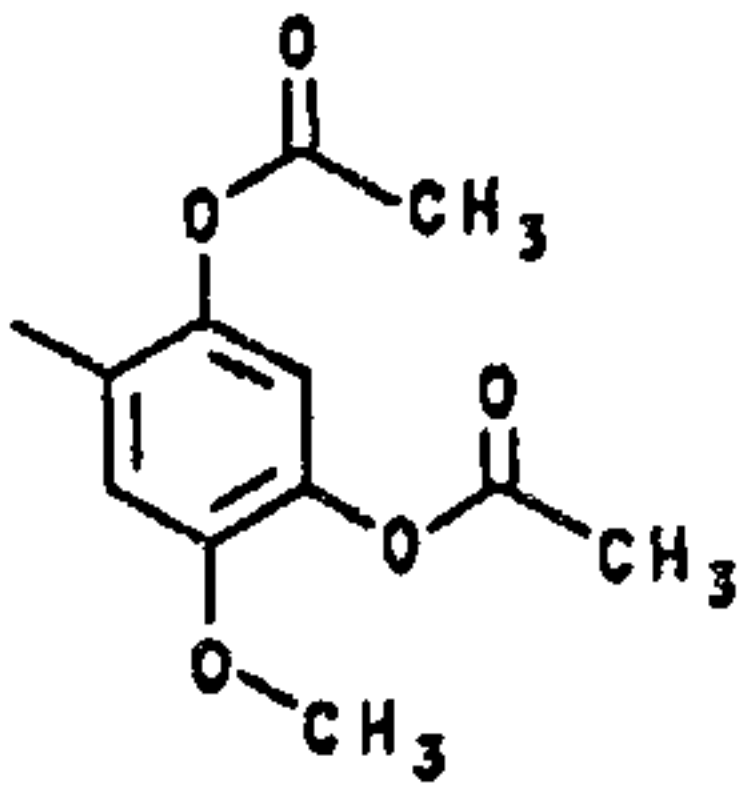
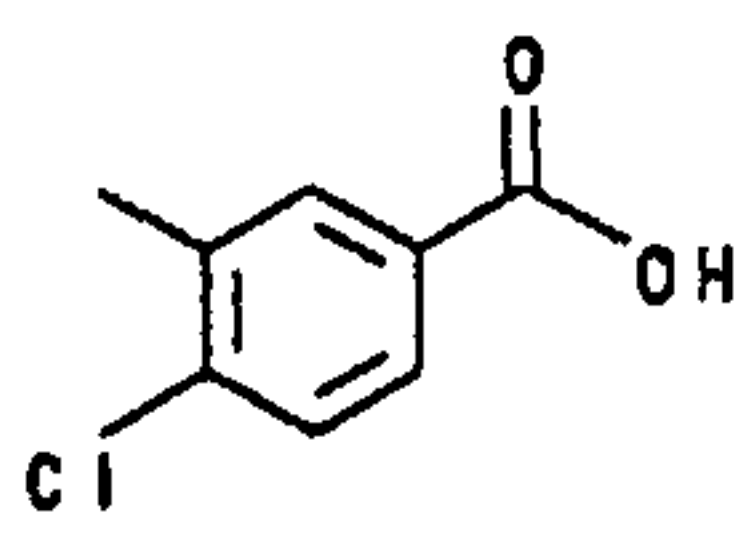
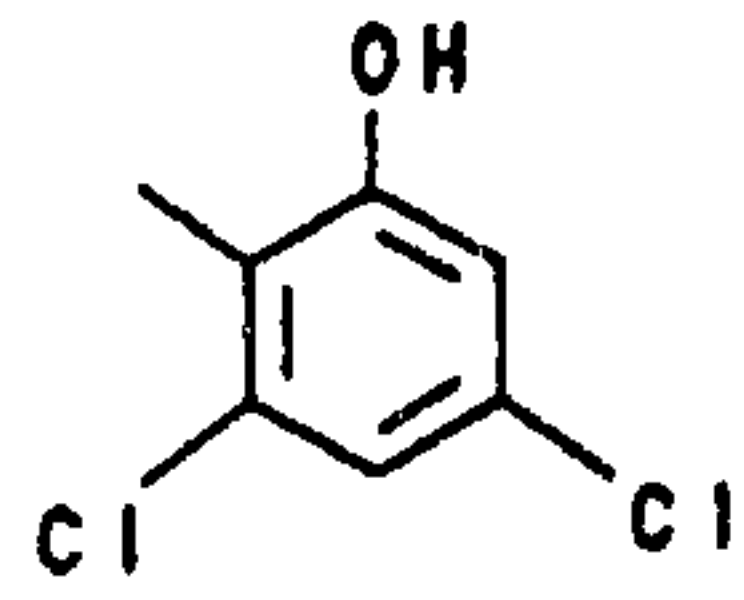
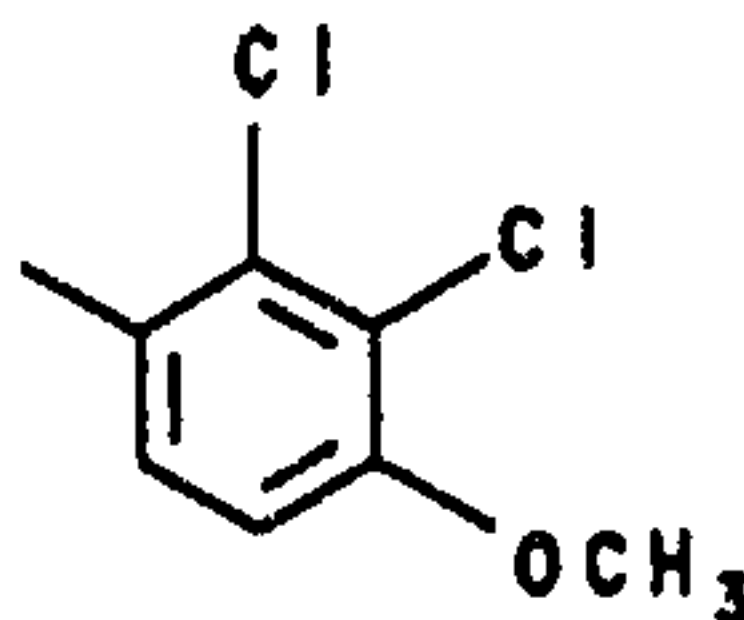
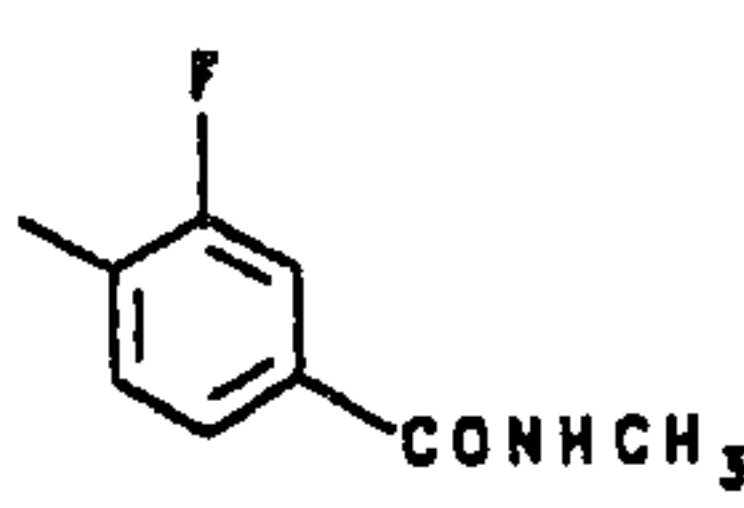
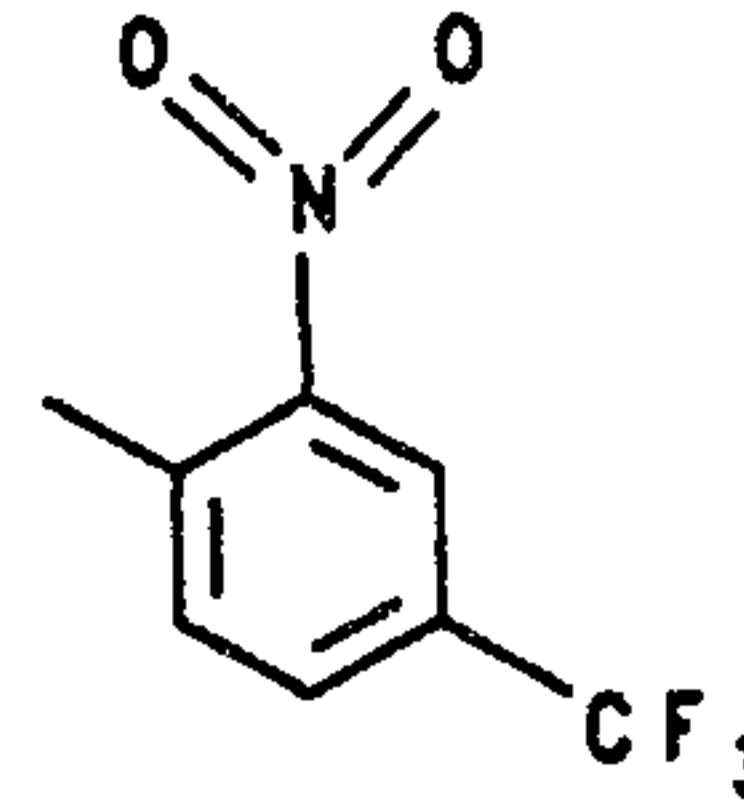
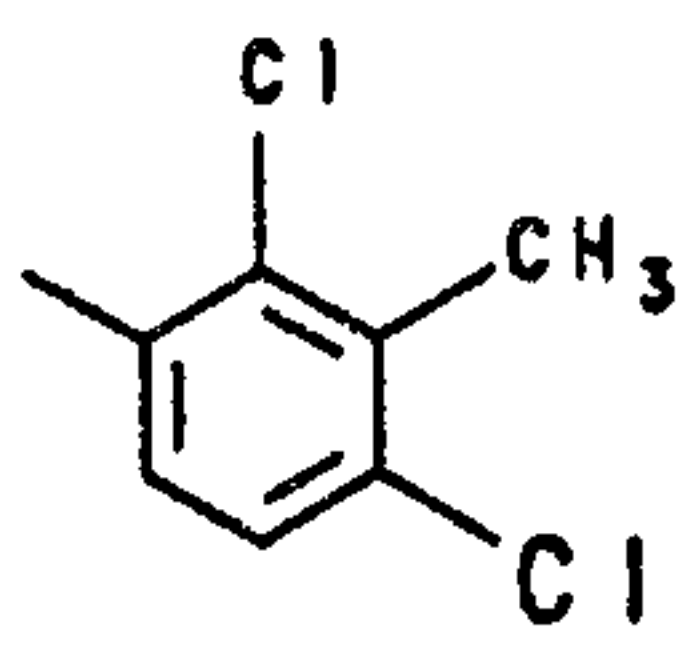
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144	CF_3	Cl	SO_2CH_3			
145	NO_2	Cl	OCF_2H			
146	Cl	H	Cl		178	
147	CH_2Cl	Cl	SO_2CH_3			
148	Cl	H	SO_2CH_3		193-195	9.2×10^{-7}
149	CF_2H	H	OCF_3			

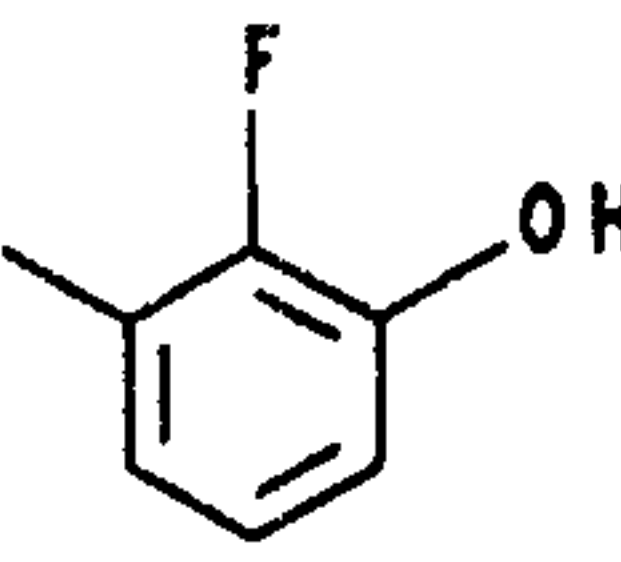
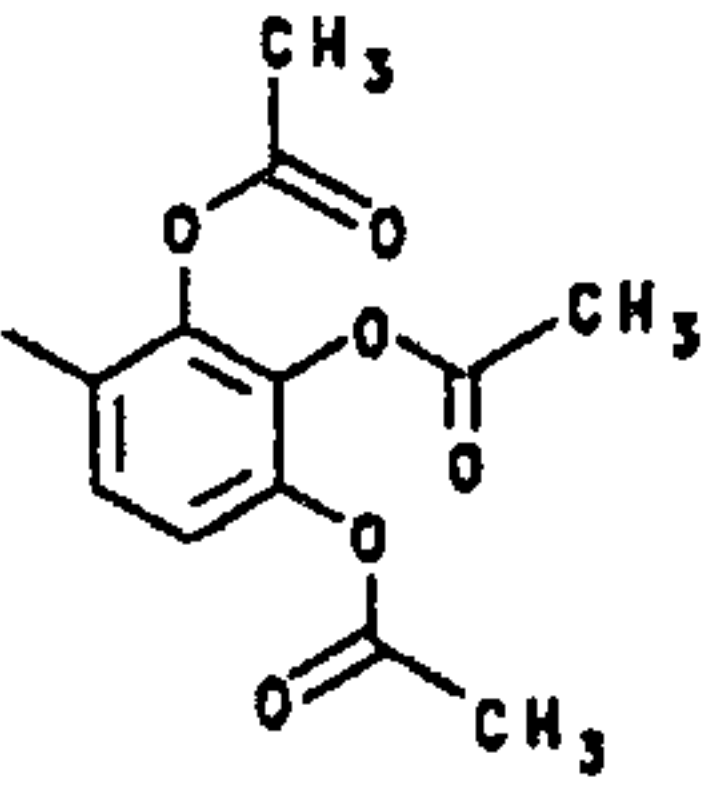
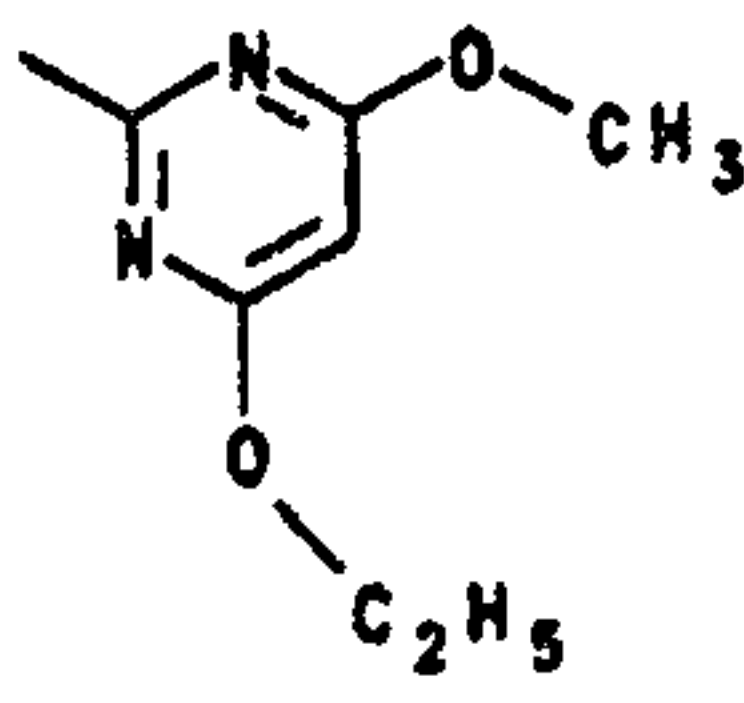
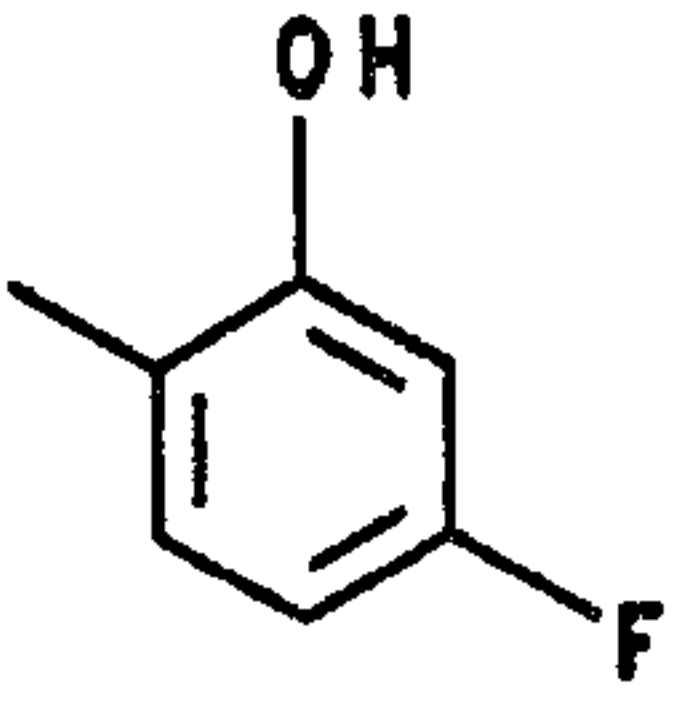
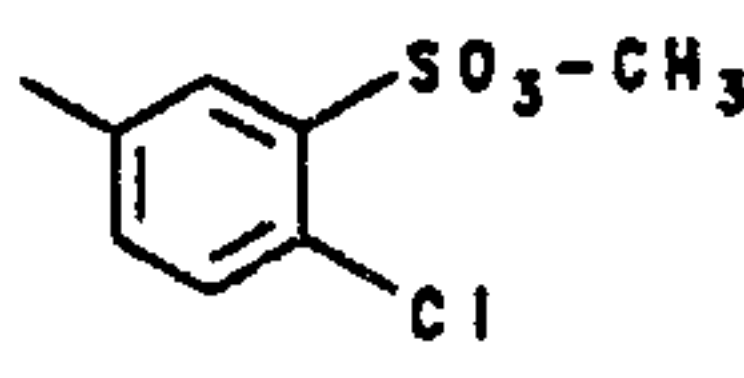
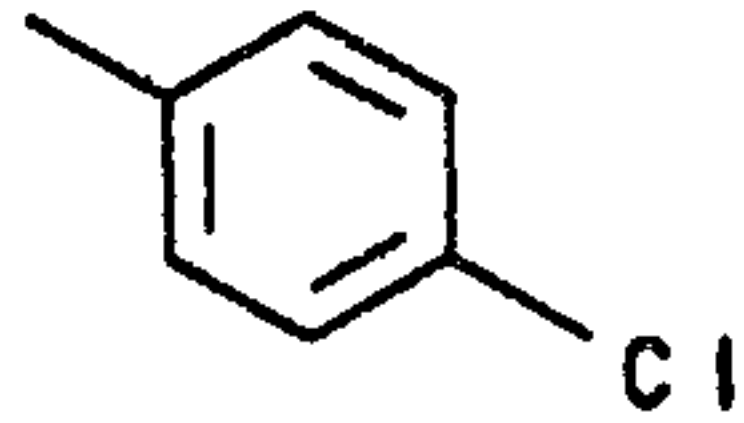
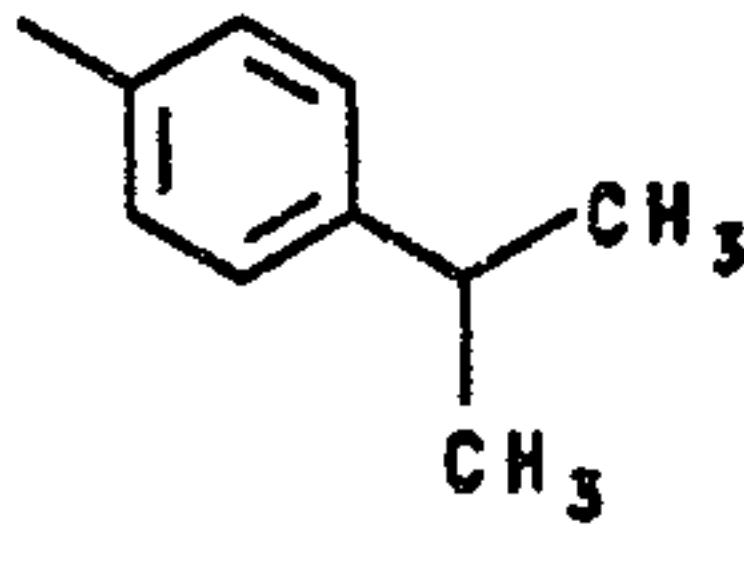
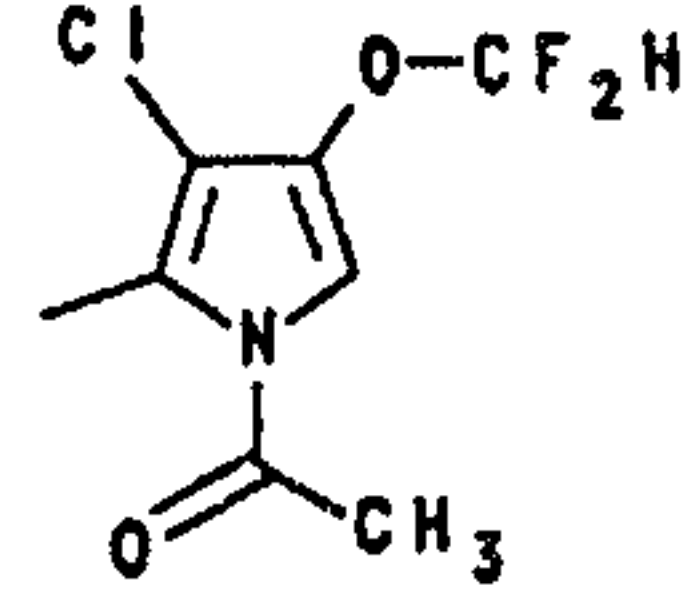
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151	F	CF ₃	F			
152	Cl	H	SO ₂ CH ₃		143-144	1.2×10 ⁻⁷
153	Cl	Cl	Cl			
154	Cl	COOCH ₃	CF ₃			
155	C ₂ F ₅	H	NO ₂			
156	Cl	H	SO ₂ CH ₃		160-165	< 10 ⁻⁹
157	CF ₃	H	F			

158	Cl	CF ₂ H	SO ₂ C ₂ H ₅			
159	C ₂ F ₅	H	Cl			
160	Cl	H	SO ₂ CH ₃		142-145	2.3×10 ⁻⁷
161	CCl ₃	H	SO ₂ CH ₃			
162	Cl	CF ₃	Cl			
163	Cl	H	SO ₂ CH ₃		167-170	1.2×10 ⁻⁸
164	Br	OCF ₂ H	CF ₃			

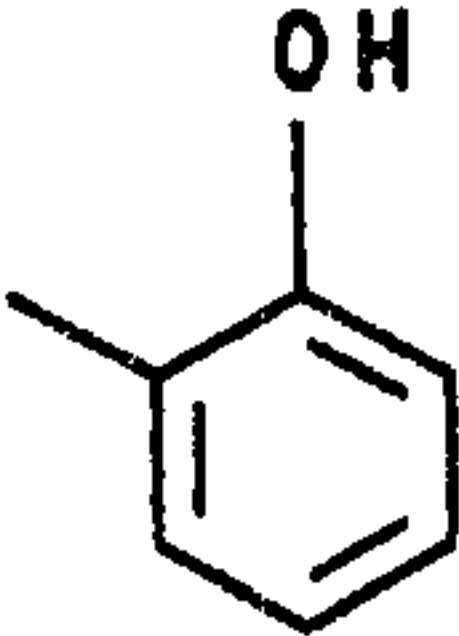
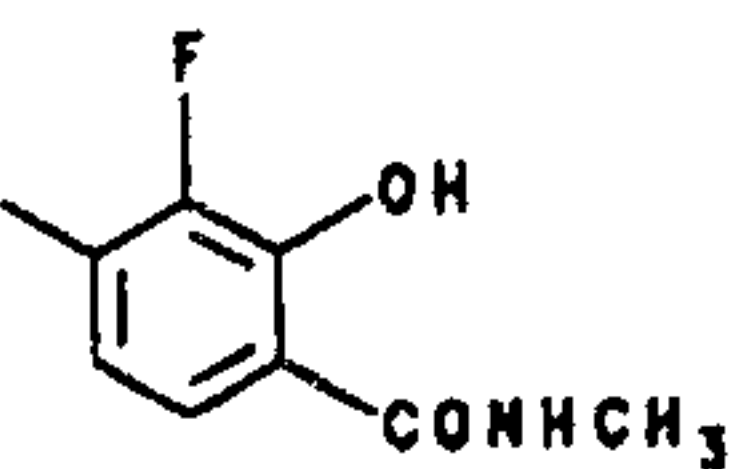
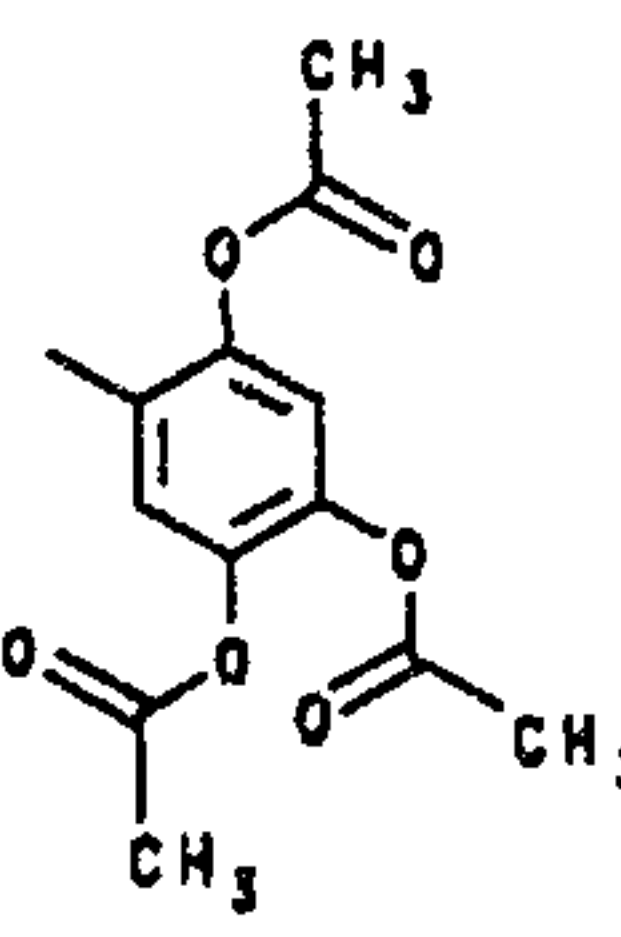
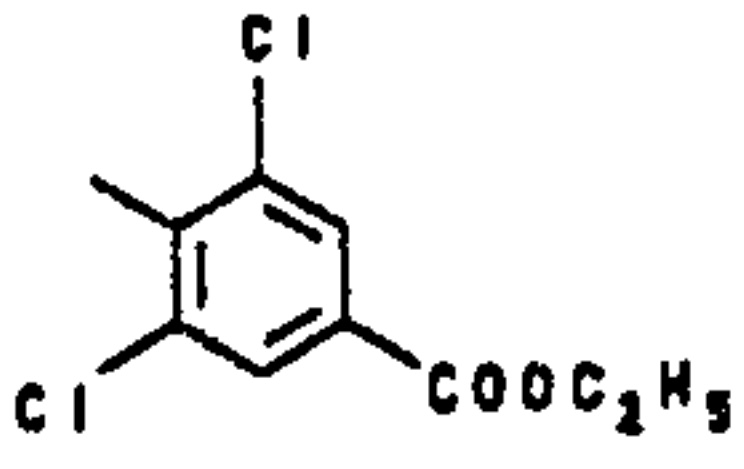
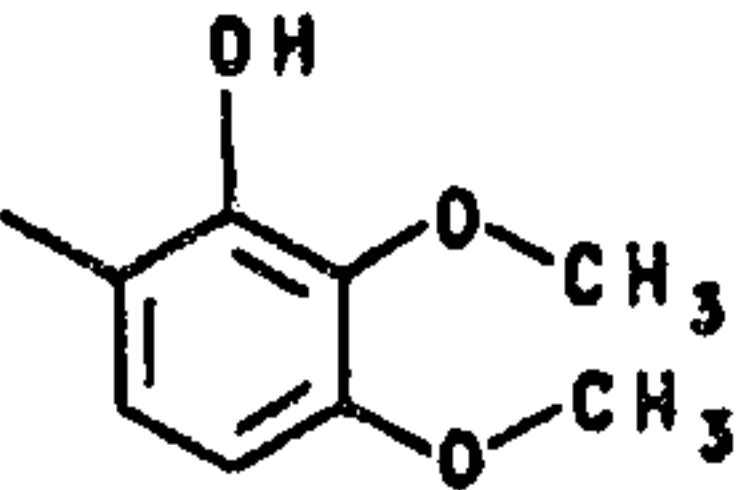
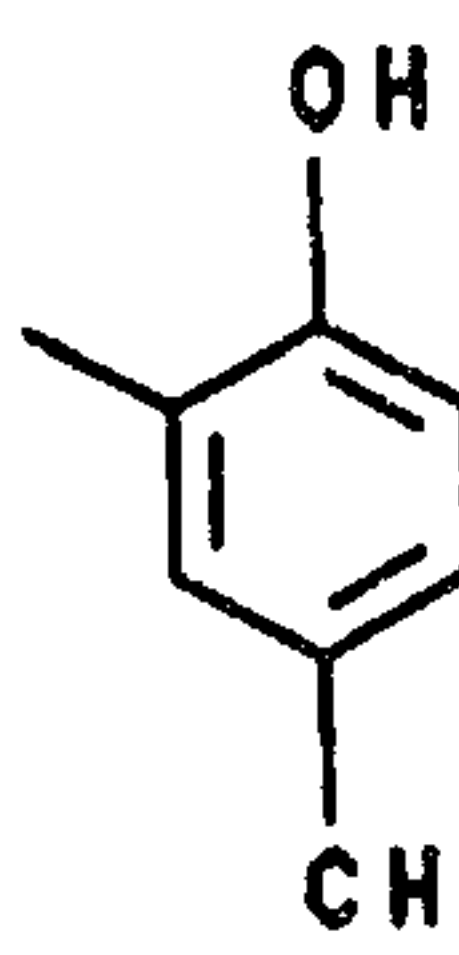
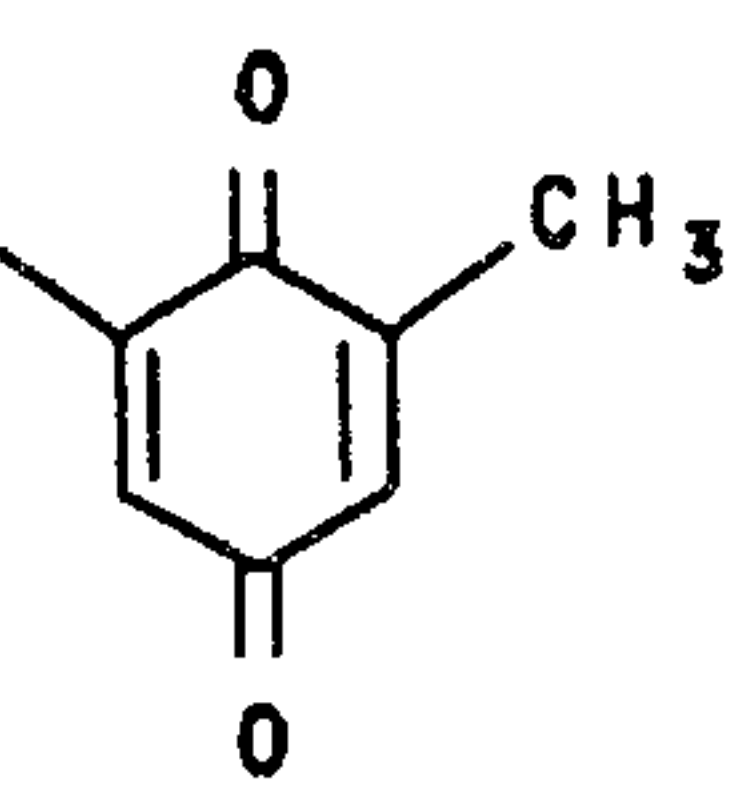
165	Cl	OCH ₃	SO ₂ CH ₃			
166	Cl	H	SO ₂ CH ₃		154-155	2.0×10 ⁻⁸
167	H	F	CCl ₃			
168	Cl	H	SO ₂ CH ₃		161	
169	CH ₂ CF ₃	Cl	Cl			
170	CF ₂ H	OCH ₃	CN			
171	Cl	H	SO ₂ CH ₃		228-230	2.2×10 ⁻⁸

172	CF ₃	H	Cl			
173	Cl	H	Cl		92	
174	Br	OCF ₃	CH ₂ Cl			
175	Cl	H	SO ₂ CH ₃		195-196	1.2×10 ⁻⁸
176	OH	COOC ₂ H ₅	CF ₂ H			
177	H	OCH ₃	F			
178	Cl	H	SO ₂ CH ₃		118-120	4.0×10 ⁻⁹
179	Br	OCH ₃	CF ₃			

180	NO ₂	COOCH ₃	OCF ₂ H			
181	Cl	H	Cl		134	
182	CN	F	CH ₂ CF ₃			
183	Cl	H	SO ₂ CH ₃		123-125	4.8×10 ⁻⁹
184	Br	OCH ₃	CF ₂ H			
185	Cl	OCF ₂ H	NO ₂			
186	OC ₂ H ₅	COOC ₂ H ₅	Cl			
187	Cl	H	SO ₂ CH ₃		117-121	4.0×10 ⁻⁷

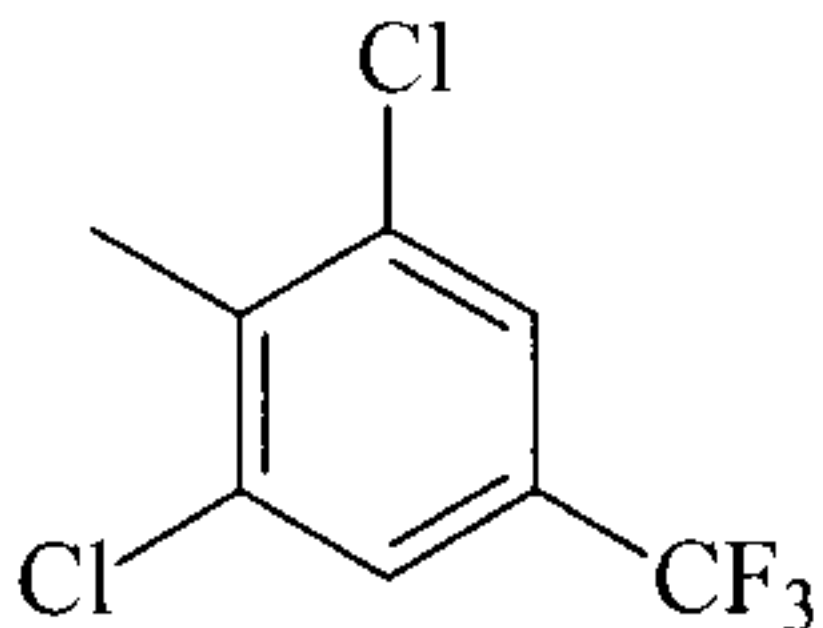
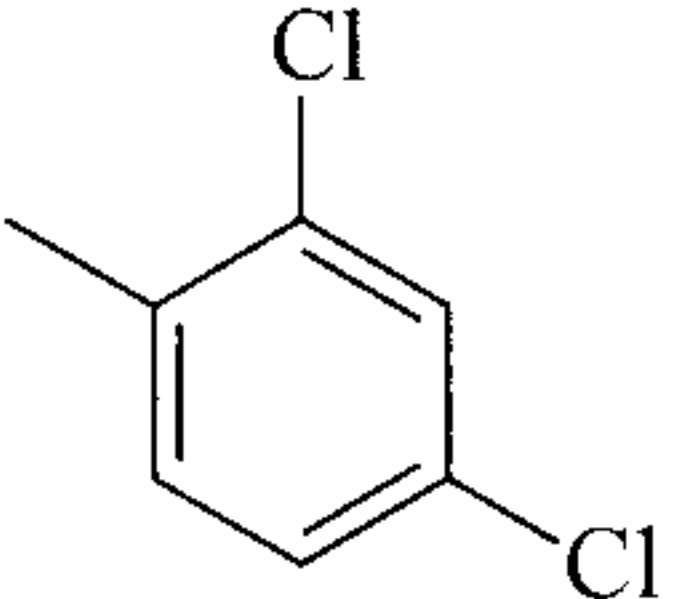
188	F	Cl	CCl ₃			
189	Cl	H	Cl		101	
190	Cl	OCF ₃	SO ₂ CH ₃			
191	Cl	H	SO ₂ CH ₃		164-166	< 10 ⁻⁸
192	Br	OH	CF ₃			
193	OH	Cl	Cl		116-118	
194	Cl	Cl	OH		69-71	
195	Br	H	CCl ₃			

5

196	Cl	H	SO ₂ CH ₃		162-168	< 10 ⁻⁹
197	F	H	Br			
198	Cl	H	Cl		132	
199	Cl	Br	CF ₃			
200	Cl	H	Cl		135	
201	Cl	H	SO ₂ CH ₃		115-118	< 10 ⁻⁹
202	F	COOCH ₃	SO ₂ CH ₃			

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203	CH ₂ CF ₃	H	Br			
204	Cl	H	SO ₂ CH ₃		118-121	<10 ⁻⁵

The invention furthermore relates to the use of the herbicidal active substances identified by means of the assay method according to the invention in plant
5 populations.

Suitable plant populations are, in particular, crop plants.

The invention further relates to a method of controlling undesired plants which comprises applying a
10 herbicidally effective amount of a compound of formula (I) as previously defined to the plants or to the areas where the plants grow.

In a preferred embodiment, the methods described herein are used in crops of useful plants selected from the
15 group consisting of wheat, barley, rye, rice and maize.

In the examples which follow, the invention is described further and illustrated in greater detail with the aid of examples. Percentages are by weight unless otherwise specified.

20 Example 1: Enriching HPPD from maize plants

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To enrich the anabolic HPPD from plant tissues, young etiolated maize plants were homogenized in extraction buffer (20 mM phosphate buffer pH 7.0; 0.14 M KCl; 0.1 mg/ml glutathione and 1% insoluble polyvinyl-pyrrolidone) for 5 3 x 10 seconds, for example in a Waring* blender. The extract was filtered (all other isolation steps were carried out at 4°C) and centrifuged (20 minutes; 10,000 g). The supernatant was subjected to fractional ammonium sulfate precipitation. At from 20 to 40% saturation of the solution 10 with ammonium sulfate, HPPD precipitated. At this stage, it was possible to store the enzyme at -80°C following dialysis in a

*Trade-mark

suitable buffer, such as, for example, 20 mM phosphate buffer pH 7.0; 0.14 M KCl; 0.1 mg/ml glutathione. This degree of purity of the enzyme is sufficient for identifying inhibitors.

5 Example 2: Method for the identification of potential HPPD inhibitors

10 The enzyme assays were performed in 20 ml polyethylene screw-top containers. Two hypodermic needles (0.9 x 40 mm) were pushed through the screw-top cap. One of the hypodermic needles was bent to form a hook onto which a small filter paper disk of diameter 10 mm was placed. The filter paper was moistened with 25 μ l of methylbenzethonium hydroxide (Sigma). The second hypodermic needle was used for injecting start and stop
15 solution into the screw-top container.

The enzyme reaction mix contained:

20 1 ml of 0.1 M phosphate buffer, pH 7.3;
 2 g/l of bovine liver catalase;
 100 μ l of a mixture of 3 mM dichlorophenol-indophenol and
 150 mM glutathione (reduced);
 25 μ l of acetone (or potential inhibitors dissolved in acetone) and
 enzyme in a total volume of 1,635 μ l.

25 After preincubation for 5 minutes at 30°C, the reaction was started by injecting 800 μ l of ^{14} C-p-hydroxyphenylpyruvate. The reaction was stopped by injecting 600 μ l of 1 N H₂SO₄, incubation was continued for 15 minutes, and the radioactivity which was liberated was determined on
30 the small filter paper disks in a liquid scintillation counter.

Example 3: Demonstration of the inhibition of plastoquinone biosynthesis in wheat by SC-0051

Thin-layer chromatography analysis of the incorporation of radioactivity from ^{14}C -tyrosine into plastoquinone.

5 Wheat plants were either not treated (A), or sprayed with a standard screening formulation (B) or with 100 g/ha of SC-0051 in this screening formulation (C), and then incubated with ^{14}C -tyrosine. The lipophilic metabolites of the wheat were extracted using chloroform, separated on

10 silica gel 60 HPTLC plates using chloroform: diethyl ether (99:1), and the radioactivity was analyzed by thin-layer scanner. The incorporation of radioactivity from tyrosine into plastoquinone (see Fig. 1, band 2) can be seen clearly in the control batches (A) and (B), while

15 plastoquinone biosynthesis is inhibited by the use of SC-0051 (C).

Example 4: Inhibition of partially purified maize HPPD by the herbicide SC-0051

The test was carried out analogously to Example 3, but a

20 different inhibitor which also results in bleaching symptoms was used (clomazone). While SC-5001 shows a marked inhibition of HPPD (°), the other bleaching herbicide has no inhibitory action on HPPD (•) (see Fig. 2).

25 Example 5: Demonstration of the correlation between HPPD inhibition and herbicidal activity

HPPD catalyzes the transformation of p-hydroxyphenylpyruvate to homogentisic acid. If HPPD inhibition is responsible for the herbicidal activity of an inhibitor,

30 then it should be possible to neutralize the herbicidal effect by supplementation with homogentisic acid. This was demonstrated by an experiment with the dockweed *Lemna gibba*. The plant was grown in a sterile aqueous medium supplemented as described in Table 1.

Table 1: Neutralization of the effect of SC-0051 by homogentisic acid

Supplementation of the medium	Number of L. gibba plants	
	Control	10^{-7} M SC-0051
-	25	3
1 mM HPPD	22	2
1 mM HGA	29	32

Batches of three Lemna plants in 100 ml of sterile medium were incubated for six days with sterile-filtered supplements. SC-0051 was added in the form of a 10^{-3} M stock solution (active substance in acetone). The number of newly formed plants was determined on day six.

Example 6: Effect of benzophenones

Example No. from Table I	IC ₅₀ value (M)	Growth inhibition of Lemna (%)		
		10^{-4} M	10^{-5} M	10^{-6} M
183	4.8×10^{-9}	98	82	81
160	2.3×10^{-7}	80	72	12
204	$> 10^{-5}$	28	12	-
171	2.2×10^{-8}	98	93	93
100	6.2×10^{-9}	98	96	92

Table 2 shows IC₅₀ values of p-hydroxyphenylpyruvate dioxygenase inhibition by a range of benzophenone derivatives in comparison with growth inhibition of Lemna gibba.

The IC₅₀ value is the molar concentration of the inhibitor at which 50% of the enzyme activity are inhibited. The growth of Lemna was measured as described in: Schulz, A., Ort, O., Beyer, P. and Kleinig, H.; SC-0051, a 2-benzoyl-

cyclohexane-1,3-dione bleaching herbicide, is a potent inhibitor of the enzyme p-hydroxyphenylpyruvate dioxygenase. FEBS-Letters, 1993, 318 (2), 162-166.

5 It can be seen from this table that the herbicidal activity of the benzophenone derivatives is correlated with the in vitro activity.

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CLAIMS:

1. A method for inhibiting plant growth by inhibiting p-hydroxyphenylpyruvate dioxygenase of a plant which comprises:

5 i) identifying an inhibitor of p-hydroxyphenylpyruvate dioxygenase of the plant by an assay for identifying inhibitors of anabolic p-hydroxyphenylpyruvate dioxygenase from plants, said assay comprising the steps of:

10 a) incubating an isolated p-hydroxyphenylpyruvate dioxygenase from the plant with a potential inhibitor and,

b) after a suitable substrate reaction time, determining the enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant with the
15 potential inhibitor in comparison with the enzymatic activity of p-hydroxyphenylpyruvate dioxygenase from the plant which has not been so incubated with the potential inhibitor, whereby a decrease in enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant incubated
20 with the potential inhibitor identifies that the potential inhibitor is an inhibitor of the plant p-hydroxyphenylpyruvate dioxygenase; and

ii) applying to the plant the identified inhibitor of the p-hydroxyphenylpyruvate dioxygenase of the
25 plant.

2. A method for inhibiting plant growth by inhibiting p-hydroxyphenylpyruvate dioxygenase of a plant which comprises:

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applying an inhibitor of p-hydroxyphenylpyruvate dioxygenase to the plant, wherein the inhibitor is identified by an assay for identifying inhibitors of anabolic p-hydroxyphenylpyruvate dioxygenase from plants,
5 which assay comprises:

a) incubating an isolated p-hydroxyphenylpyruvate dioxygenase from a plant with a potential inhibitor and,

b) after a suitable substrate reaction time, determining the enzymatic activity of the
10 p-hydroxyphenylpyruvate dioxygenase from a plant incubated with the potential inhibitor in comparison with the enzymatic activity of p-hydroxyphenylpyruvate dioxygenase from a plant which has not been so incubated with the potential inhibitor, whereby a decrease in enzymatic
15 activity of the p-hydroxyphenylpyruvate dioxygenase from a plant incubated with the potential inhibitor indicates that the potential inhibitor is an inhibitor of a plant p-hydroxyphenylpyruvate dioxygenase.

3. A method for inhibiting growth of undesired plants
20 by inhibiting p-hydroxyphenylpyruvate dioxygenase of undesired plants and thereby having a herbicidal effect on the undesired plants which comprises:

i) identifying an inhibitor of p-hydroxyphenylpyruvate dioxygenase of the plants by an
25 assay for identifying inhibitors of anabolic p-hydroxyphenylpyruvate dioxygenase from plants, said assay comprising the steps of:

a) incubating an isolated p-hydroxyphenylpyruvate dioxygenase from a plant with a potential inhibitor and,

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b) after a suitable substrate reaction time, determining the enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant incubated with the potential inhibitor in comparison with the enzymatic activity of p-hydroxyphenylpyruvate dioxygenase from a plant which has not been so incubated with the potential inhibitor, whereby a decrease in enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant incubated with the potential inhibitor identifies that the potential inhibitor is an inhibitor of the plant p-hydroxyphenylpyruvate dioxygenase; and

ii) applying to the plants or areas in which they grow a herbicidally effective amount of the identified inhibitor of the p-hydroxyphenylpyruvate dioxygenase of the plant.

4. A method for inhibiting the growth of undesired plants by inhibiting p-hydroxyphenylpyruvate dioxygenase of undesired plants and thereby having a herbicidal effect on the undesired plants which comprises:

applying a herbicidally effective amount of inhibitor of p-hydroxyphenylpyruvate dioxygenase to the plants or areas in which they grow, wherein the inhibitor is identified by an assay for identifying inhibitors of anabolic p-hydroxyphenylpyruvate dioxygenase from plants, which assay comprises:

a) incubating an isolated p-hydroxyphenylpyruvate dioxygenase from a plant with a potential inhibitor and

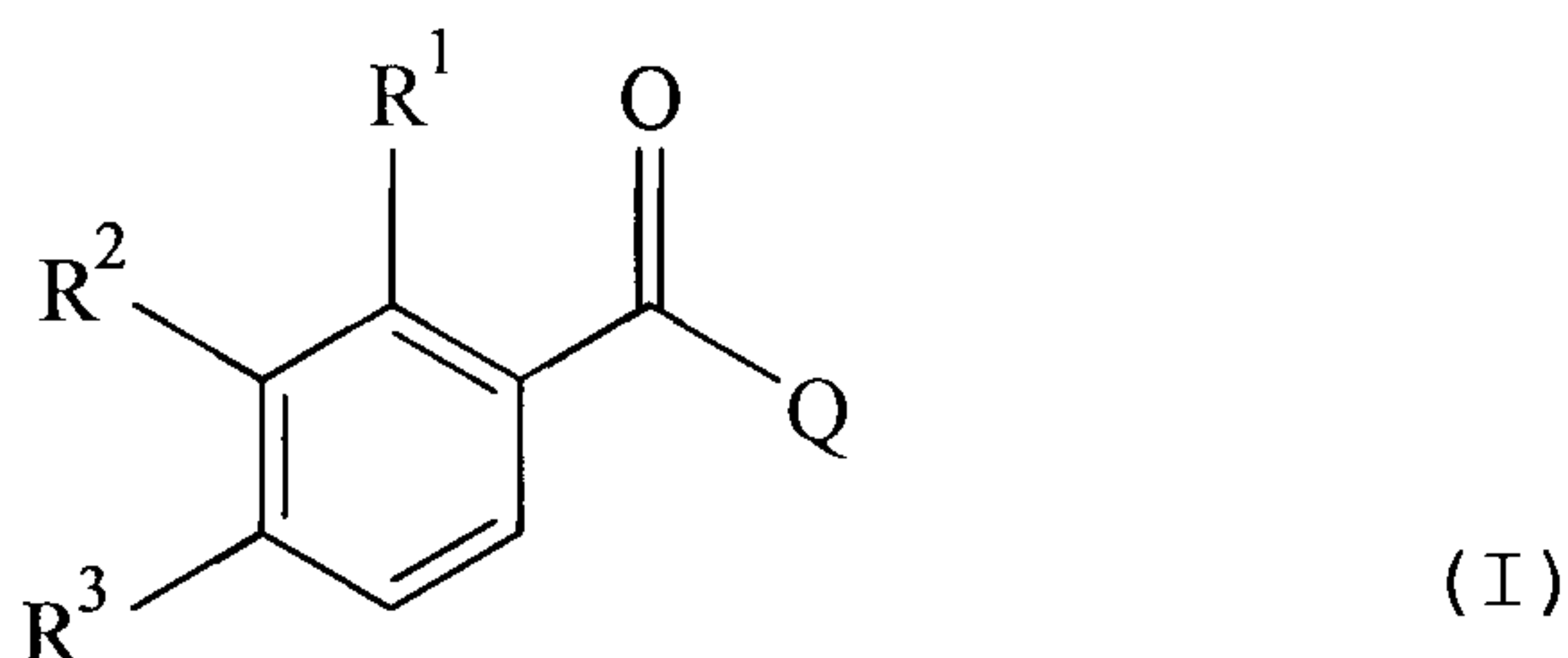
b) after a suitable substrate reaction time, determining the enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant incubated

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with the potential inhibitor in comparison with the enzymatic activity of p-hydroxyphenylpyruvate dioxygenase from a plant which has not been so incubated with the potential inhibitor, whereby a decrease in enzymatic activity of the p-hydroxyphenylpyruvate dioxygenase from the plant incubated with the potential inhibitor indicates that the potential inhibitor is an inhibitor of plant p-hydroxyphenylpyruvate dioxygenase.

5. A compound of the formula (I)



10 in which

R^1 is H, a halogen, OH, an alkoxy, CN, NO₂ or a haloalkyl,

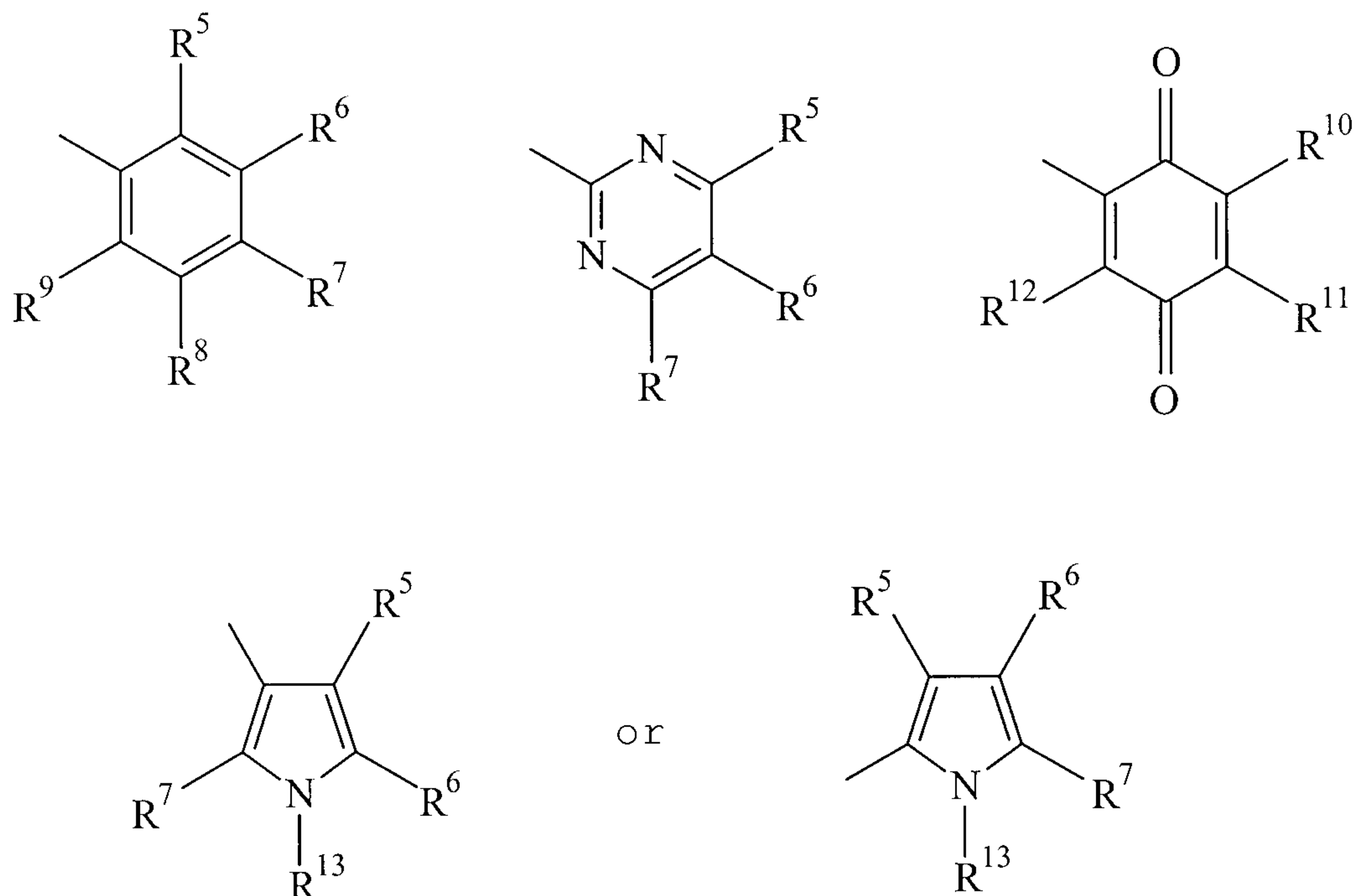
R^2 is H, a halogen, OH, an alkyl, an alkoxy, a haloalkyl, a haloalkoxy or an (alkoxy)carbonyl,

15 R^3 is H, a halogen, OH, CN, NO₂, a haloalkyl, a haloalkoxy or $R^4S(O)_m-$, where R^4 is an alkyl and m is zero, one or two,

Q is a radical selected from the group of the formulae

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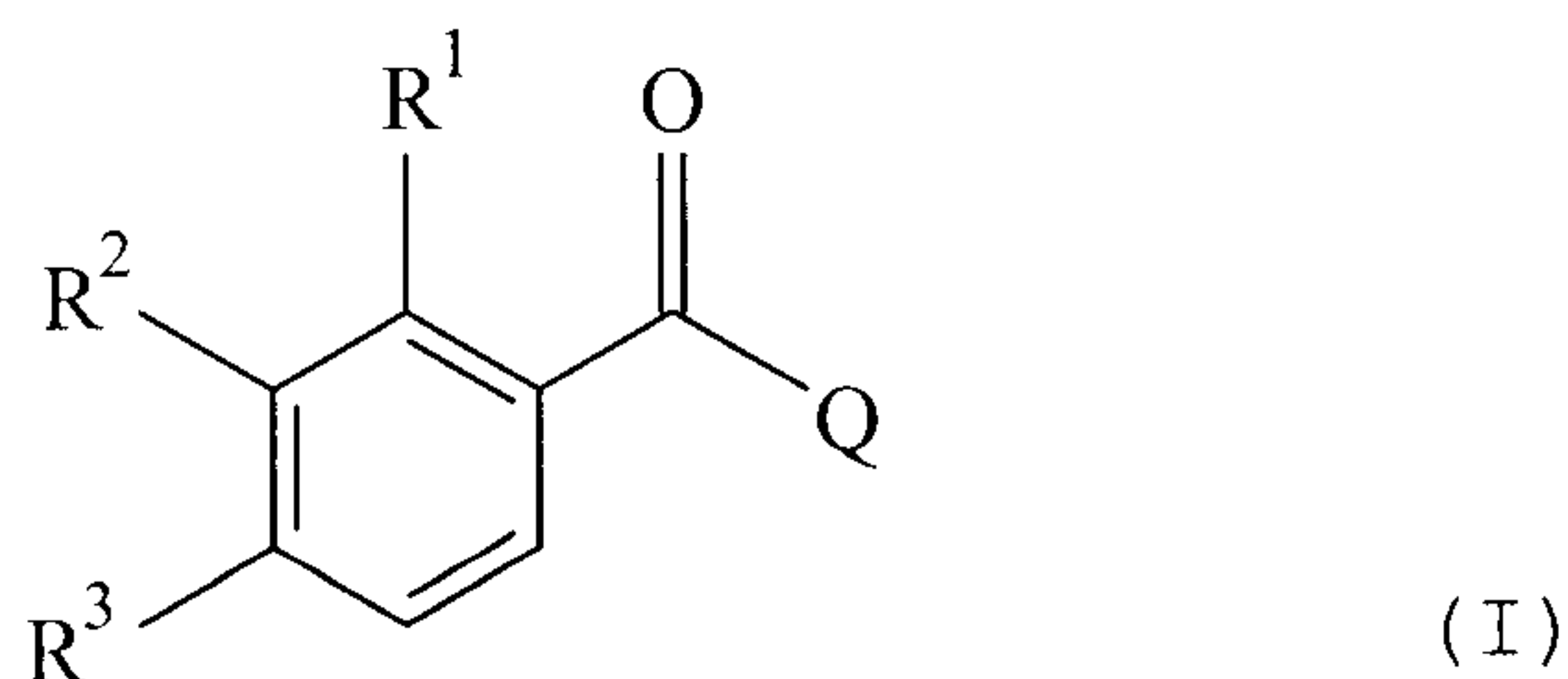
in which R^5 , R^6 , R^7 , R^8 and R^9 independently of one another are H, a halogen, OH, CN, NO_2 , SO_3H , SO_3R^4 , $\text{SO}_2\text{NR}^{14}\text{R}^{15}$, COOH , COOR^4 , $\text{CONR}^{14}\text{R}^{15}$, O-COOR^4 , O-COR^4 , an alkyl, an alkoxy, a
5 haloalkyl or a haloalkoxy,

R^{10} , R^{11} and R^{12} independently of one another are H, a halogen, an alkyl, an alkoxy, a haloalkyl or a haloalkoxy,

R^{13} is H, phenylsulfonyl, an alkylsulfonyl or an alkylcarbonyl, and

10 R^{14} and R^{15} independently of one another are H, an alkyl, an aryl or benzyl.

6. A compound of the formula (I),



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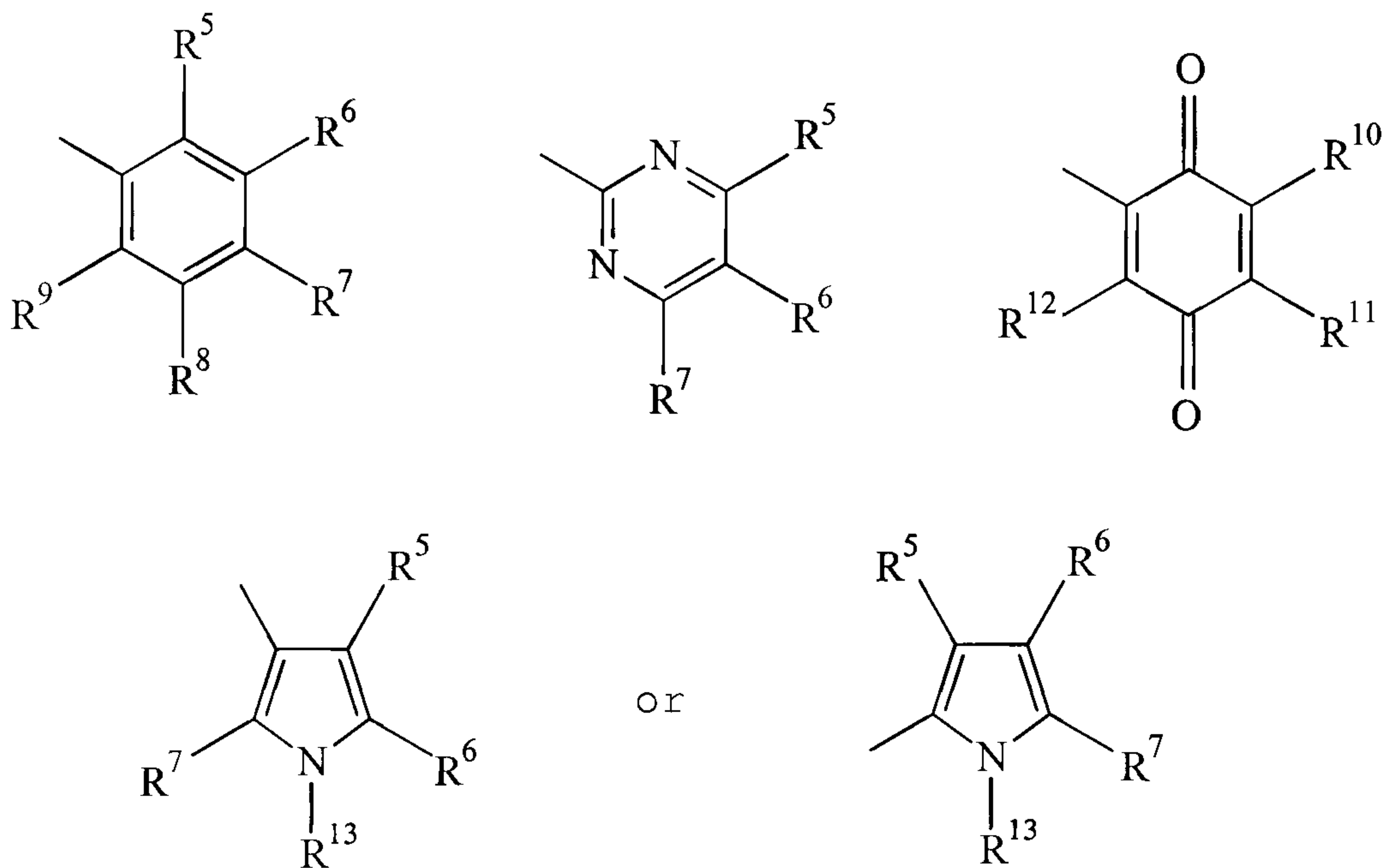
in which

R^1 is H, a halogen, OH, C₁-C₃-alkoxy, CN, NO₂ or C₁-C₃-haloalkyl,

R^2 is H, a halogen, OH, C₁-C₃-alkyl, C₁-C₃-alkoxy,
5 C₁-C₂-haloalkyl, C₁-C₂-haloalkoxy or (C₁-C₂-alkoxy)carbonyl,

R^3 is H, a halogen, OH, CN, NO₂, C₁-C₃-haloalkyl, C₁-C₂-haloalkoxy or $R^4S(O)_m-$, where R^4 is C₁-C₂-alkyl and m is zero, one or two,

Q is a radical selected from the group of the
10 formulae



R^5 , R^6 , R^7 , R^8 and R^9 independently of one another are H, a halogen, OH, CN, NO₂, SO₃H, SO₃R⁴, SO₂NR¹⁴R¹⁵, COOH, COOR⁴, CONR¹⁴R¹⁵, O-COOR⁴, O-COR⁴, C₁-C₄-alkyl, C₁-C₂-alkoxy,
15 C₁-C₃-haloalkyl or C₁-C₂-haloalkoxy,

R^{10} , R^{11} and R^{12} independently of one another are H, a halogen, C₁-C₃-alkyl, C₁-C₂-alkoxy, C₁-C₃-haloalkyl or C₁-C₂-haloalkoxy,

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R^{13} is H, phenylsulfonyl, C_1 - C_2 -alkylsulfonyl or C_1 - C_2 -alkylcarbonyl,

R^{14} and R^{15} independently of one another are H, C_1 - C_4 -alkyl, phenyl or benzyl.

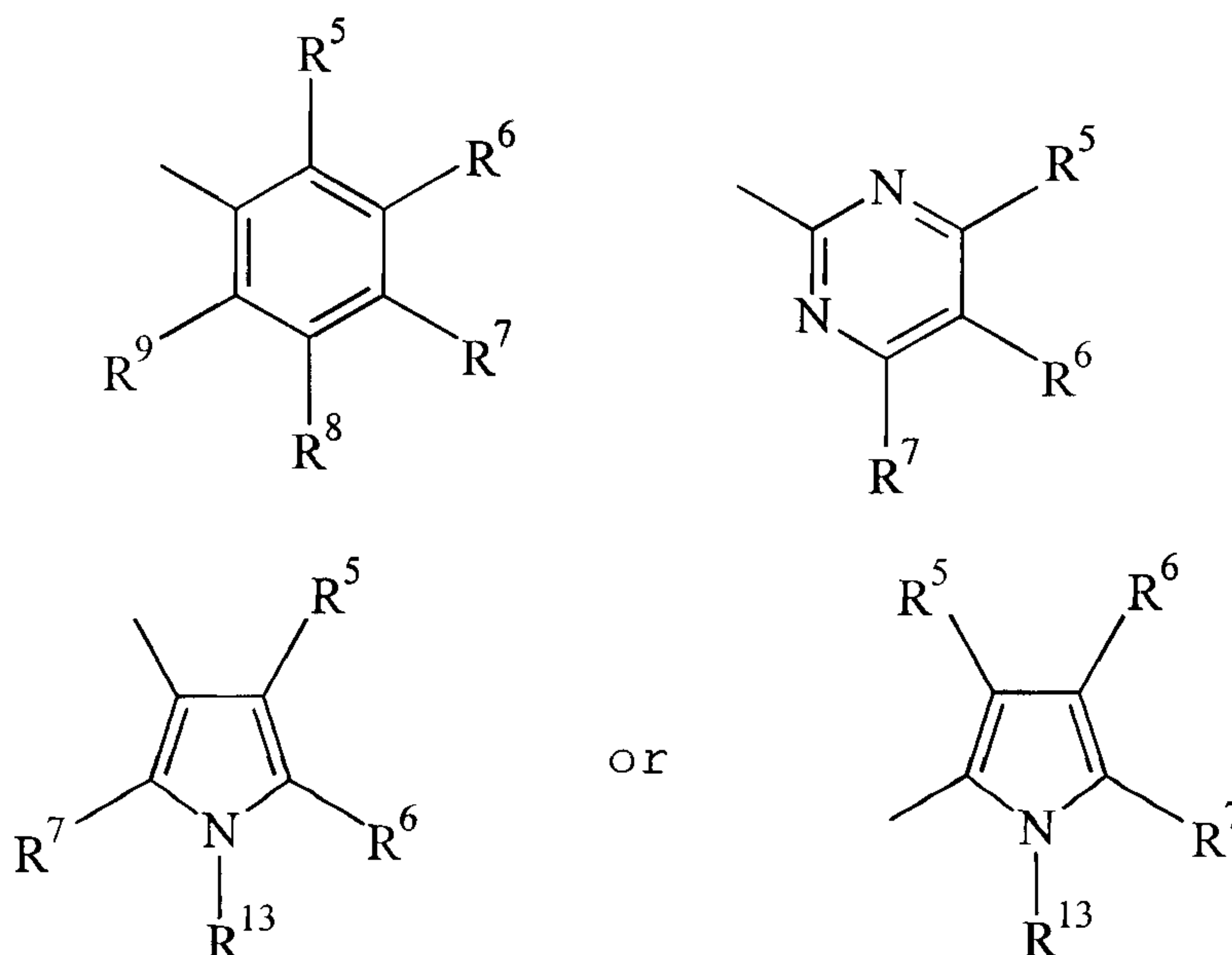
5 7. The compound of the formula (I) of claim 5, wherein

R^1 is hydrogen, hydroxyl, methoxy, fluorine, chlorine, bromine, cyano, nitro, difluoromethyl, trifluoromethyl, chloromethyl, trichloromethyl,
10 2,2,2-trifluoroethyl or pentafluoroethyl,

R^2 is hydrogen, fluorine, chlorine, hydroxyl, propyl, ethyl, methyl, methoxy, ethoxy, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, methoxycarbonyl or ethoxycarbonyl,

15 R^3 is hydrogen, hydroxyl, fluorine, chlorine, bromine, nitro, difluoromethyl, trifluoromethyl, chloromethyl, trichloromethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, difluoromethoxy, trifluoromethoxy, methylsulfonyl or ethylsulfonyl;

20 Q is a radical selected from the group of the formulae



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where

R⁵, R⁶, R⁷, R⁸ and R⁹ independently of one another are hydrogen, fluorine, chlorine, bromine, cyano, nitro, hydroxyl, hydroxysulfonyl, ethoxysulfonyl, ethylaminosulfonyl, methylaminosulfonyl, carboxyl, ethoxycarbonyl, methoxycarbonyl, ethylaminocarbonyl, methylaminocarbonyl, ethoxycarbonyloxy, methoxycarbonyloxy, methylcarbonyloxy, t-butyl, i-propyl, propyl, ethyl, methyl, difluoromethyl, trifluoromethyl, chloromethyl, trichloromethyl, methoxy, ethoxy, difluoromethoxy or trifluoromethoxy,

R¹⁰, R¹¹ and R¹² independently of one another are hydrogen, fluorine, chlorine, bromine, ethyl, methyl, difluoromethyl, trifluoromethyl, chloromethyl, trichloromethyl, methoxy, ethoxy, difluoromethoxy or trifluoromethoxy,

R¹³ is hydrogen, phenylsulfonyl, methylsulfonyl, ethylsulfonyl, methylcarbonyl or ethylcarbonyl,

R¹⁴ and R¹⁵ independently of one another are hydrogen, butyl, propyl, ethyl, methyl or benzyl.

8. A herbicidal composition which comprises the compound of the formula (I) of any one of claims 5 to 7 and conventional formulations auxiliaries.

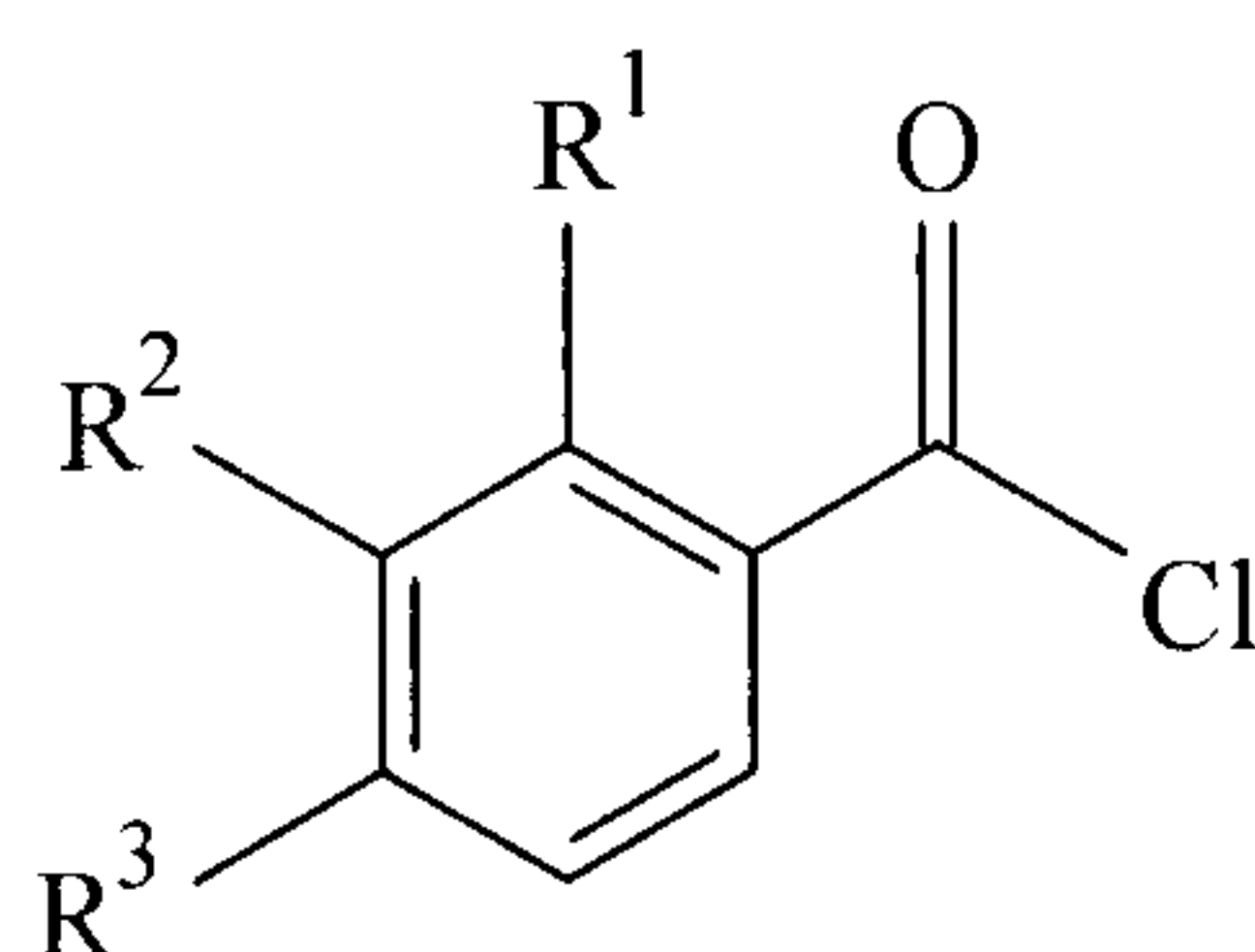
9. The composition of claim 8, in a formulation selected from the group consisting of a wettable powder, a water-soluble powder, an emulsifiable concentrate, an aqueous solution or concentrate, an emulsion, a sprayable solution, a capsule suspension, a dispersion on an oil or water basis, a suspoemulsion, a suspension concentrate, a dust, an oil-miscible solution, a seed-dressing agent, a

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microgranule, a spray granule, a coated granule, an adsorption granule, a granule for soil application and broadcasting, a water-dispersible granule, an ultra low volume formulation, a micro-capsule and a wax.

- 5 10. A process for the preparation of the compound of the formula (I) of any one of claims 5 to 7, which comprises reacting acid chlorides of the formula (II)



- 10 in which R^1 , R^2 and R^3 are as defined in formula (I), with aromatic and heteroaromatic compounds of the formula (III)



in which Q is as defined in formula (I), in the presence of a Lewis acid, in a chlorinated hydrocarbon.

- 15 11. The process according to claim 10, wherein the Lewis acid is aluminum chloride, titanium tetrachloride or boron trifluoride.
12. The process of claim 10 or 11, wherein the chlorinated hydrocarbon is dichloromethane.
- 20 13. A method of controlling undesired plants, which comprises applying a herbicidally effective amount of the compound of the formula (I) of any one of claims 5 to 7 to the undesired plants or to the areas on which the undesired plants grow.

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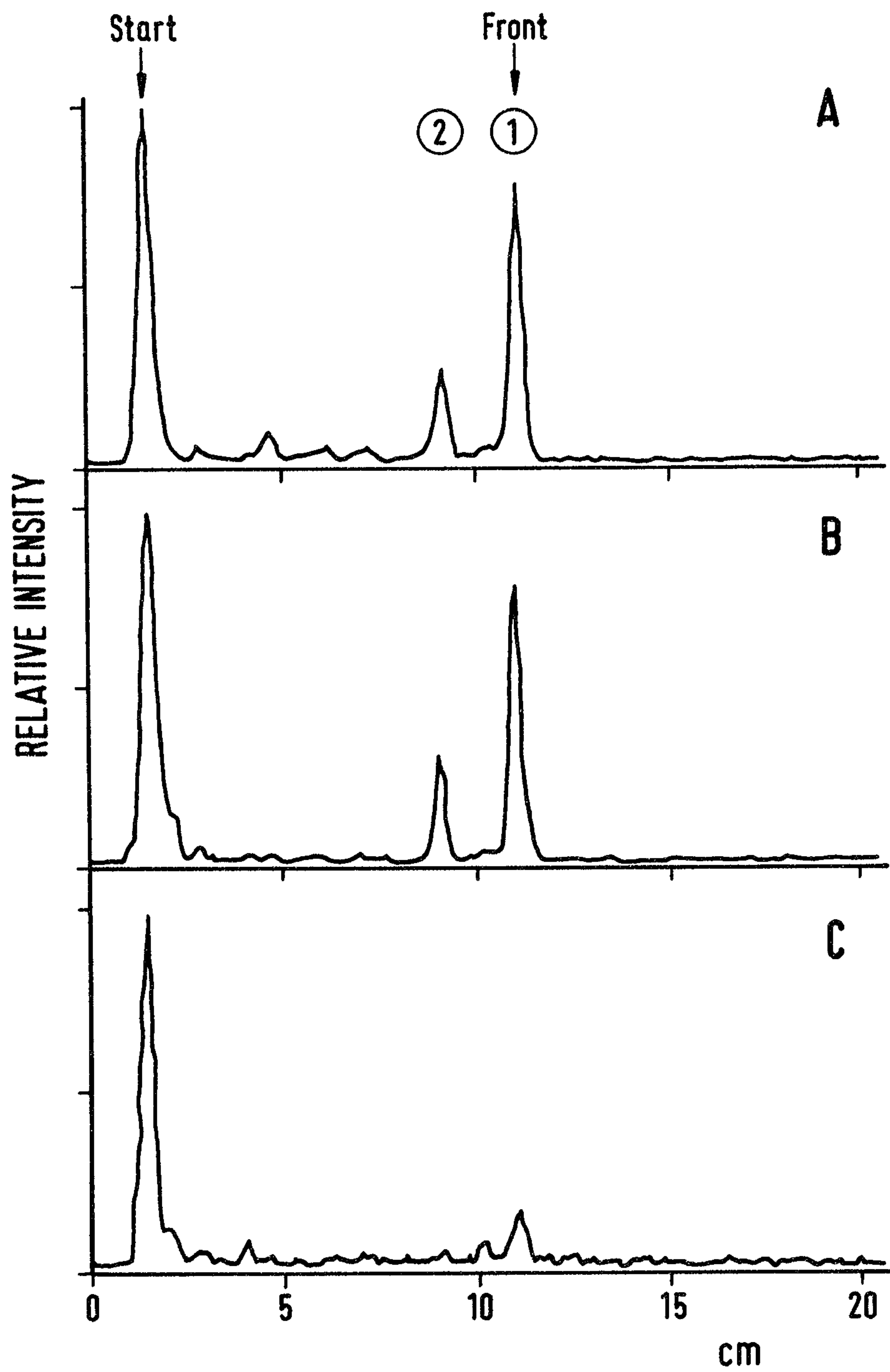
14. The method of claim 13, wherein the undesired plants are located in crops of useful plants.

15. The method of claim 14, wherein the crop of useful plants is selected from the group consisting of wheat,
5 barley, rye, rice and maize.

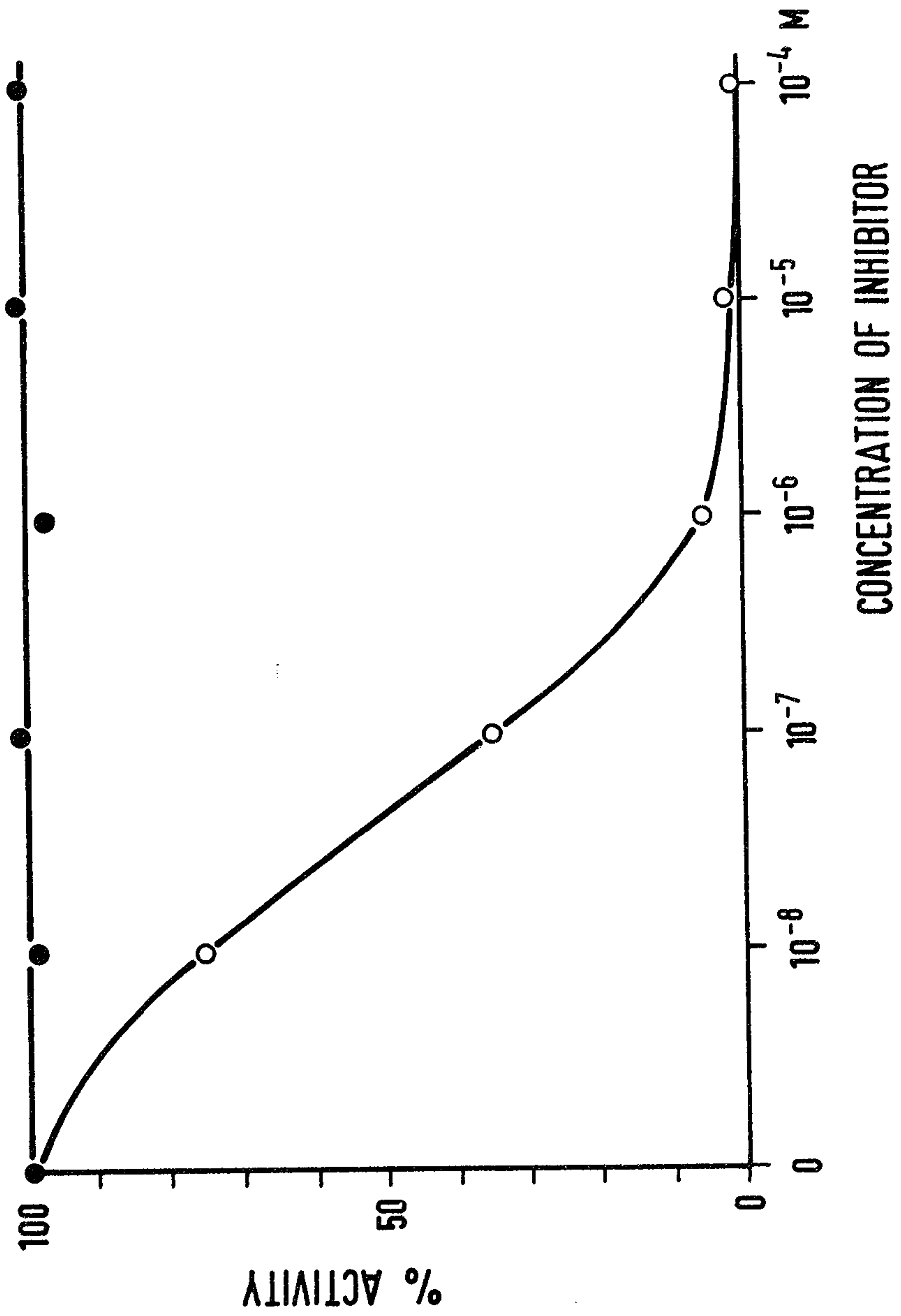
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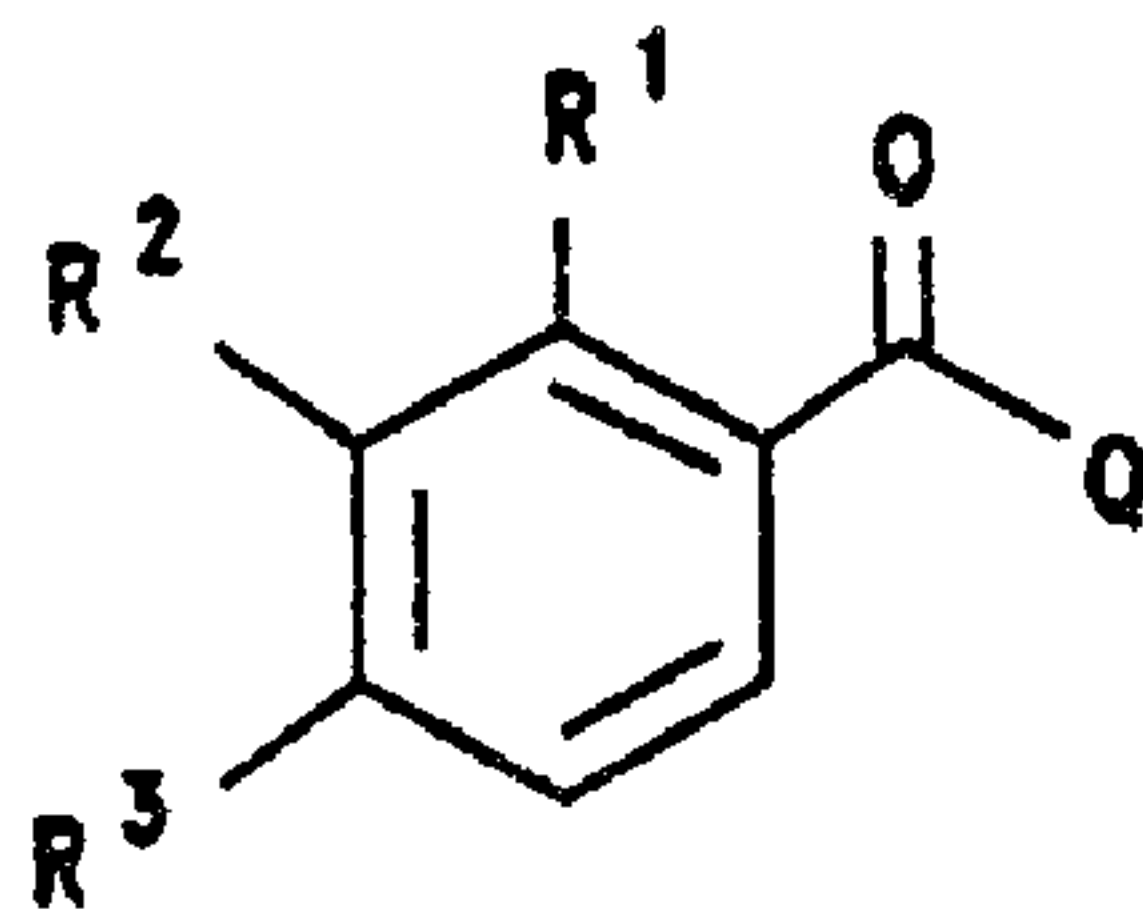
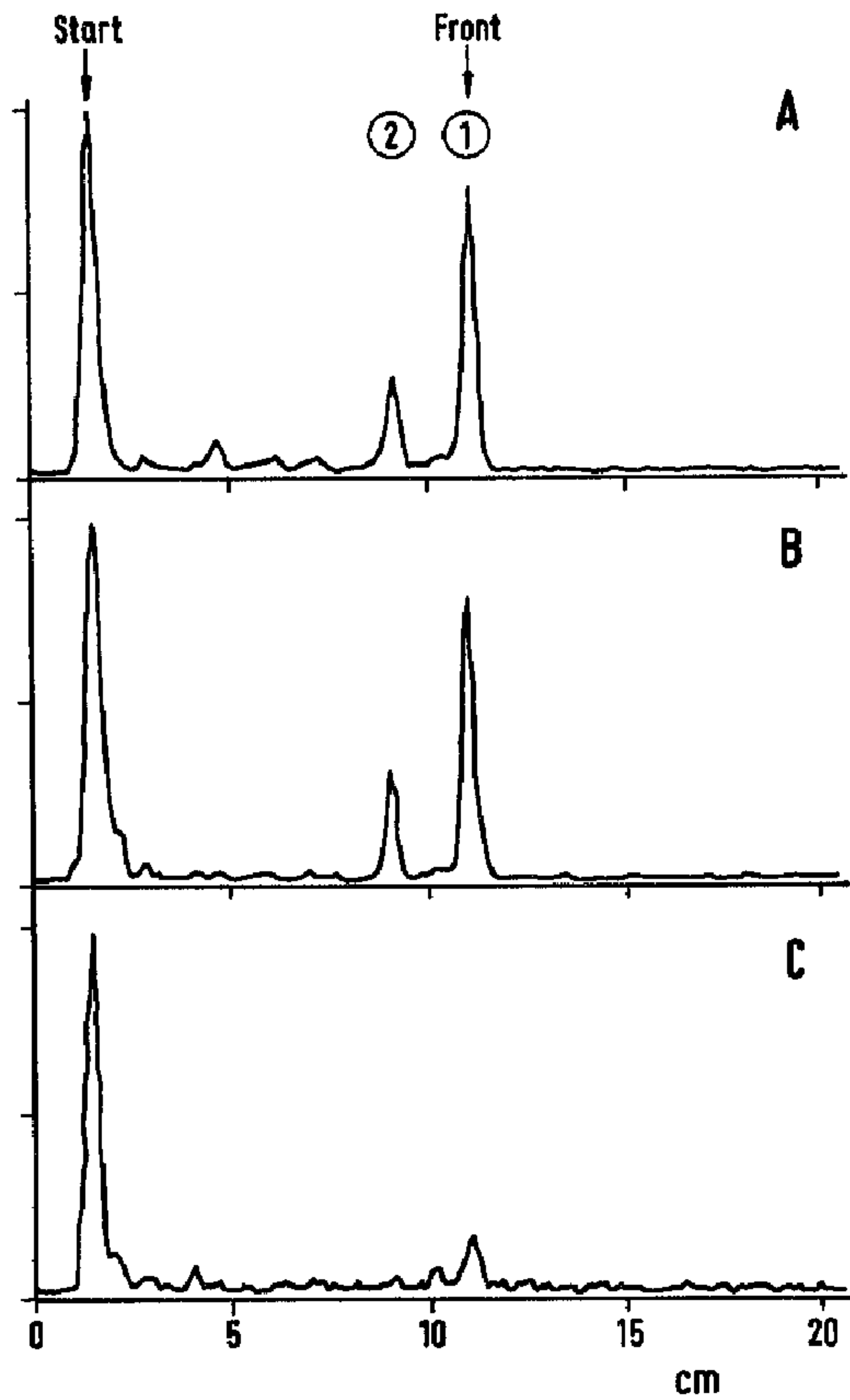
PATENT AGENTS

**Fig. 1**

Patent Agents
Guthrie & Co.

Fig. 2

Patent Agents
Fetherstonhaugh & Co.



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