N-Arylmethyl Derivatives of Isoproturon as Models for Potential Photoactivatable Herbicides

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We have synthesized a series of 17 N-arylmethyl derivatives of isoproturon, and we have studied their photochemical properties. Some arylmethyl groups (naphthylmethyl, aminobenzyl) allow the corresponding N-(arylmethyl)isoproturons to absorb solar light and to be photolyzed with production of isoproturon in natural conditions. N-(Arylmethyl)isoproturons are representative of a new concept of potential photoactivatable herbicides, which can also apply to many other classes of pesticides.

INTRODUCTION

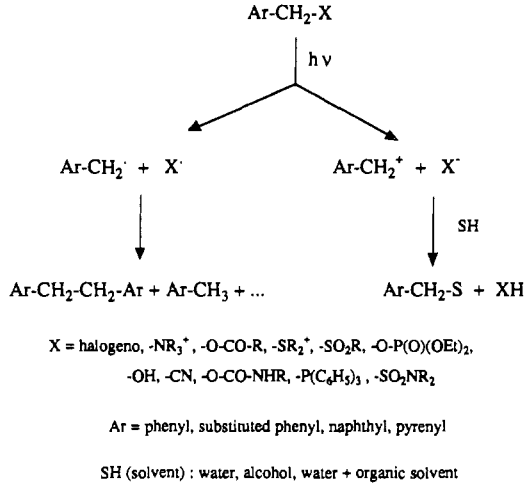
The photocleavage of the C–X bond in arylmethyl derivatives Ar–CH_2–X has been extensively studied, in various situations (Cristol and Bindel, 1983). The model compounds used in these studies were often arylmethyl halides (X = halogeno) (Ivanov et al., 1973; Appleton et al., 1980; Cristol and Greenwald, 1976; Hyomaki and Koskikallio, 1977; Larson et al., 1980; Cristol et al., 1978; Cristol and Bindel, 1980; Slocum and Schuster, 1984; Arnold et al., 1985; Choudhry et al., 1982), but data were also obtained from other arylmethyl derivatives [X = NR_3^+, OC(=O)R, SR_2^+, SO_2R, OP(=O)$(OEt)_2$ (Arnold et al., 1985); OH (Wan and Chak, 1986); CN (Zimmerman and Sandel, 1963; Choudhry et al., 1982); OC(=O)NHR (Chamberlin, 1966); $(C_6H_5)_3P^+$ (Griffin and Kaufman, 1965); SO_2NR_2 (Pincock and Jurgens, 1979; Epling and Walker, 1982); Ar = phenyl, substituted phenyl, naphthyl, and pyrenyl (Iwamura et al., 1987)].

Two concurrent mechanisms have been generally proposed, resulting from homolysis or heterolysis of the C–X bond (Scheme I), although flash laser photolysis studies of benzyl chloride in water revealed additional more complex mechanisms (Lillie and Koskikallio, 1984). Photosolvolysis which results from the ionic cleavage of the C–X bond predominates in polar solvents, and in the specific case of substituted benzylic derivatives (Ar = substituted phenyl), its rate depends upon the nature and the position of the substituents (Cristol and Bindel, 1983).

The photolysis of N-arylmethyl derivatives of N-containing compounds has been described for only two kinds of compounds: arylmethylammoniums (Arnold et al., 1985) and N-(arylmethyl)adenines (Er-Rhaimini et al., 1990). N–H-containing functional groups are very frequently found in pesticide compounds. We wanted to investigate the possibility of obtaining photoactivatable pesticides by changing known pesticides into their N-arylmethyl derivatives. As a model pesticide, we chose isoproturon [1,1-dimethyl-3-(4-isopropyl)phenylurea (1)] a commercial herbicide, which was expected to be stable under natural light, as a consequence of its low quantum yield of photolysis (Kulsrestha and Mukerjee, 1986) and of its UV absorption spectrum (upper limit at 290 nm).

We have prepared a series of N-arylmethyl derivatives 2–18 of this compound, and we have studied their photochemical behavior. The aryl groups studied were 1- and 2-naphthyl or benzyl bearing various substituents: o- and m-methoxy, -chloro, -amino or -(dimethylamino), which generally favor photosolvolysis in benzyl derivatives by acting as electrodonors at the excited-state level of the molecule (Zimmerman and Sandel, 1963; Wan, 1985; Wan and Chak, 1986); p-chloro, which also allowed photosolvolysis products to be observed in p-chlorobenzyl chloride (Choudhry et al., 1982), together with some unusual secondary products; m-nitro, which has its own photochemistry (Chow, 1982) and whose corresponding benzyl alcohols were found to be prone to photoredox reactions, with no photosolvolysis products observed (Wan and Yates, 1986; Wan et al., 1987).

Scheme I



Some of the N-(arylmethyl)isoproturons 2–18, when exposed to solar light, released isoproturon (1) by losing their arylmethyl substituent. Therefore, the derivatives that exhibit this property might act as photoactivatable herbicides whose activity should be attributed to isoproturon. On the other hand, the N-(arylmethyl)isoproturons 2–18 were additional models for the study of the photolysis of arylmethyl derivatives. In particular, in substituted benzylisoproturons, it was important to learn about the influence of the substituents, expected initially to behave as in simple benzyl derivatives, on the course of the photolysis, to design further potential photoactivatable isoproturons or other classes of photoactivatable pesticides.

MATERIALS AND METHODS

General Procedures. IR spectra were recorded on Perkin-Elmer 117 or Beckman Acculab II spectrometers, from samples suspended in paraffin oil. ^1H NMR spectra were determined on a Varian EM 360 spectrometer with TMS as internal standard and are expressed in δ. UV spectra were recorded on a Kontron Uvikon 860 spectrometer by using cells of 1 cm path length.

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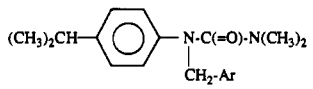
Table I. UV Spectra of *N*-(Arylmethyl)isoproturons 2–18 (in Ethanol)



no.	Ar	λ_{max}, nm	ϵ, cm mol L^{-1}	upper λ of absorption[a]
2	phenyl	251	10300	300
3	4-chlorophenyl	250	8500	290
4	3,5-dimethoxyphenyl	250	10600	300
5	3,4-dichlorophenyl	249	11200	300
6	1-naphthyl	250	8300	305
		271	6100	
		281	7000	
		292	4600	
7	2-naphthyl	250	13700	320
		274 (sh)	7300	
		286 (sh)	4500	
8	3-(dimethylamino)phenyl	250	17300	345
		305 (sh)	1200	
9	3-nitrophenyl	251	16200	370
10	3,5-dinitrophenyl	242	26000	380
11	2-chloro-5-nitrophenyl	245	16000	370
		270 (sh)	7900	
12	2-methoxy-5-nitrophenyl	241	14900	390
		310	9900	
13	4-chloro-3-nitrophenyl	244	14100	390
14	3-aminophenyl	245	16200	320
15	3,5-diaminophenyl	245	16500	320
		285 (sh)	2500	
16	3-amino-4-chlorophenyl	246	15400	320
		293	3400	
17	5-amino-2-chlorophenyl	247	19500	340
		289 (sh)	2200	
18	5-amino-2-methoxyphenyl	243	14900	340
		301	3200	

[a] $A < 0.01$ for a 10^{-4} M solution.

Melting points were determined on a Tottoli melting point apparatus and are uncorrected. Microanalyses were performed by the Service d'Analyses du CNRS at Vernaison, France.

High-performance liquid chromatography (HPLC) experiments were performed with a Waters apparatus (M6000A pump, U6K injector, and M440 UV spectrophotometric detector set at 254 nm), on Lichrosorb RP 8 or RP 18 columns [4 mm (i.d.) × 25 cm] of 10-μm particle size, eluted with water–methanol mixtures of variable composition. Ion-pairing chromatography was used with compounds containing amino groups, by adding sodium heptanesulfonate (0.005 M) and 1% acetic acid to the eluent. Gas chromatography (GC) analyses were performed on a Carlo Erba 6100 Vega chromatograph equipped with a flame ionization detector (FID) and a split–splitless injector, on a capillary OV1 column [0.22 mm (i.d.) × 25 m], with nitrogen as carrier gas.

General Method of Synthesis of 1-(Arylmethyl)-1-(4-isopropylphenyl)-3,3-dimethylureas [*N*-(Arylmethyl)isoproturons] 2–13. To isoproturon 1 (6.18 g, 30 mmol) dissolved in 50 mL of tetrahydrofuran (THF) was added a 50% suspension of sodium hydride in Vaseline oil (2.6 g, 54 mmol). The mixture was stirred until gas evolution ceased. The appropriate arylmethyl bromide or chloride (33 mmol) in 20 mL of THF was then added, and the mixture was stirred at room temperature for 24 h–5 days, the reaction being monitored by HPLC. After dilution with diethyl ether (20 mL), the reaction mixture was poured into a separatory funnel. Water (50 mL) was then added, and the organic layer was washed with 50 mL of water and dried over sodium sulfate. After concentration under reduced pressure, the residue was recrystallized from hexane or hexane–benzene (H–B). For some products, analytic samples devoid of residual trace of isoproturon (1) were obtained only by silica gel column chromatography, with the eluent indicated. The UV spectra of compounds 2–13 are described in Table I. In NMR spectra (described below), δ of the isopropyl C*H* was given only for compound 4, the low intensity of the heptuplet signal not allowing its determination in the other compounds.

1-Benzyl-3,3-dimethyl-1-(4-isopropylphenyl)urea (2): (from benzyl bromide); reaction time 3 days; 57% yield; chromatography eluent dichloromethane; mp 83 °C (hexane); NMR ($CDCl_3$) 1.29 [6 H, d, CH_3)$_2$CH], 2.71 [6 H, s, $(CH_3)_2$N], 4.85 (2 H, s, CH_2), 7.08 (4 H, m, phenyl Hs), 7.35 (5 H, s, Ar benzyl Hs). Anal. Calcd for $C_{19}H_{24}N_2O$: C, 76.69; H, 8.16; N, 9.45. Found: C, 76.81; H, 8.26; N, 9.42.

1-(4-Chlorobenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)urea (3): (from 4-chlorobenzyl chloride); reaction time 5 days; 47% yield; mp 79 °C (hexane); NMR ($CDCl_3$) 1.21 [6 H, d, $(CH_3)_2$CH], 2.76 [6 H, s, $(CH_3)_2$N], 4.78 (2 H, s, CH_2), 7.06 (4 H, m, phenyl Hs), 7.31 (4 H, s, Ar benzyl Hs). Anal. Calcd for $C_{19}H_{23}ClN_2O$: C, 68.97; H, 7.00; Cl, 10.71; N, 8.46. Found: C, 69.24; H, 7.03; Cl, 10.66; N, 8.41.

1-(3,5-Dimethoxybenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)-urea (4): (from 3,5-dimethoxybenzyl bromide); reaction time 24 h; chromatography eluent dichloromethane; 65% yield; oil; NMR ($CDCl_3$) 1.21 [6 H, d, $(CH_3)_2$CH], 2.73 [6 H, s, $(CH_3)_2$N], 2.75 [1 H, m, C*H*$(CH_3)_2$], 3.75 (6 H, s, 2 CH_3O), 4.86 (2 H, s, CH_2), 6.35 (1 H, t, benzyl 4-H), 6.52 (2 H, d, benzyl 2 and 6 H), 7.08 (4 H, m, phenyl Hs). Anal. Calcd for $C_{21}H_{28}N_2O_3$: C, 70.75; H, 7.91; N, 7.85. Found: C, 70.63; H, 8.01; N, 7.39.

1-(3,4-Dichlorobenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)-urea (5): (from 3,4-dichlorobenzyl bromide); reaction time 4 days; 40% yield; mp 45 °C (hexane); NMR ($CDCl_3$) 1.21 [6 H, d, $(CH_3)_2$CH], 2.68 [6 H, s, $(CH_3)_2$N], 4.73 (2 H, s, CH_2), 7.06 (4 H, m, phenyl Hs), 7.16–7.5 (3 H, m, Ar benzyl Hs). Anal. Calcd for $C_{19}H_{22}Cl_2N_2O$: C, 62.47; H, 6.07; Cl, 19.41; N, 7.67. Found: C, 62.66; H, 5.96; Cl, 19.59; N, 7.51.

3,3-Dimethyl-1-(4-isopropylphenyl)-1-(1-naphthylmethyl)-urea (6): [from 1-(bromomethyl)naphthyl bromide]; reaction time 4 days; 54% yield; mp 70 °C (hexane); NMR ($CDCl_3$) 1.20 [6 H, d, $CH_3)_2$CH], 2.76 [6 H, s, $(CH_3)_2$N], 5.33 (2 H, s, CH_2), 7.06 (4 H, m, phenyl Hs), 7.1–7.96 (7 H, m, naphthyl Hs). Anal. Calcd for $C_{23}H_{26}N_2O$: C, 79.73; H, 7.56; N, 8.08. Found: C, 79.43; H, 7.53; N, 8.15.

3,3-Dimethyl-1-(4-isopropylphenyl)-1-(2-naphthylmethyl)-urea (7): [from 2-(bromomethyl)naphthyl bromide]; reaction time 3 days; 74% yield; chromatography eluent dichloromethane; mp 75 °C (hexane); NMR ($CDCl_3$) 1.20 [6 H, d, $(CH_3)_2$CH], 2.73 [6 H, s, $(CH_3)_2$N], 5.00 (2 H, s, CH_2), 7.06 (4 H, m, phenyl Hs), 7.1–8.06 (7 H, m, naphthyl Hs). Anal. Calcd for $C_{23}H_{26}N_2O$: C, 79.73; H, 7.56; N, 8.08. Found: C, 79.48; H, 7.70; N, 8.19.

3,3-Dimethyl-1-[3-(dimethylamino)benzyl]-1-(4-isopropylphenyl)urea (8): [from 3-(dimethylamino)benzyl bromide hydrobromide and 84 mmol of sodium hydride]; reaction time 24 h; 53% yield; mp 98 °C (hexane); NMR ($CDCl_3$) 1.21 [6 H, d, $(CH_3)_2$CH], 2.75 [6 H, s, $(CH_3)_2$NC=O], 2.91 [6 H, s, benzyl $(CH_3)_2$N], 4.83 (2 H, s, CH_2), 6.5–7.4 (4 H, m, Ar benzyl Hs), 7.06 (4 H, m, phenyl Hs). Anal. Calcd for $C_{21}H_{29}N_3O$: C, 74.30; H, 8.60; N, 12.37. Found: C, 74.06; H, 8.76; N, 12.15.

3,3-Dimethyl-1-(4-isopropylphenyl)-1-(3-nitrobenzyl)urea (9): (from 3-nitrobenzyl bromide); reaction time 4 days; 71% yield; chromatography eluent dichloromethane–acetone (98:2); mp 78 °C (H–B 50:50); NMR ($CDCl_3$) 1.23 [6 H, d, $CH_3)_2$CH], 2.75 [6 H, s, $(CH_3)_2$N], 4.93 (2 H, s, CH_2), 7.15 (4 H, m, phenyl Hs), 6.9–8.3 (4 H, m, Ar benzyl Hs). Anal. Calcd for $C_{19}H_{23}N_3O_3$: C, 66.84; H, 6.79; N, 12.30. Found: C, 66.55; H, 6.75; N, 12.26.

3,3-Dimethyl-1-(4-isopropylphenyl)-1-(3,5-dinitrobenzyl)-urea (10): (from 3,5-dinitrobenzyl bromide); reaction time 24 h; 44% yield; chromatography eluent dichloromethane–acetone 98:2, mp 122 °C (H–B 50:50); NMR ($CDCl_3$) 1.23 [6 H, d, $CH_3)_2$CH], 2.73 [6 H, s, $(CH_3)_2$N], 4.93 (2 H, s, CH_2), 7.13 (4 H, m, phenyl Hs), 8.55 (2 H, d, benzyl 2- and 6-H), 8.95 (1 H, t, benzyl 4-H). Anal. Calcd for $C_{19}H_{22}N_4O_5$: C, 59.05; H, 5.74; N, 14.49. Found: C, 59.01; H, 5.74; N, 14.46.

1-(2-Chloro-5-nitrobenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)urea (11): (from 2-chloro-5-nitrobenzyl bromide); reaction time 2 days; 47% yield; mp 88 °C (H–B 80:20); NMR ($CDCl_3$) 1.21 [6 H, d, $CH_3)_2$CH], 2.78 [6 H, s, $(CH_3)_2$N], 4.98 (2 H, s, CH_2), 7.11 (4 H, m, phenyl Hs), 7.3–8.4 (3 H, m, Ar benzyl Hs). Anal. Calcd for $C_{19}H_{22}ClN_3O_3$: C, 60.71; H, 5.90; Cl, 9.43; N, 11.18. Found: C, 61.03; H, 6.02; Cl, 8.86; N, 11.13.

3,3-Dimethyl-1-(4-isopropylphenyl)-1-(2-methoxy-5-nitrobenzyl)urea (12): (from 2-methoxy-5-nitrobenzyl bromide); reaction time 24 h; 71% yield; mp 115 °C (H–B 80:20); NMR ($CDCl_3$) 1.21 [6 H, d, $CH_3)_2$CH], 2.76 [6 H, s, $(CH_3)_2$N], 3.90 (3 H, s, CH_3O),

4.90 (2 H, s, CH_2), 7.13 (4 H, m, phenyl Hs), 6.8–8.5 (3 H, m, Ar benzyl Hs). Anal. Calcd for $C_{20}H_{25}N_3O_4$: C, 64.47; H, 6.79; N, 11.31. Found: C, 64.30; H, 6.97; N, 11.19.

1-(4-Chloro-3-nitrobenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)urea (13): (from 4-chloro-3-nitrobenzyl bromide); reaction time 24 h; 70% yield; mp 79 °C (hexane); NMR ($CDCl_3$), 1.21 [6 H, d, $(CH_3)_2CH$], 2.71 [6 H, s, $(CH_3)_2N$], 4.81 (2 H, s, CH_2), 7.10 (4 H, m, phenyl Hs), 7.33–7.83 (3 H, m, Ar benzyl Hs). Anal. Calcd for $C_{19}H_{22}ClN_3O_3$: C, 60.71; H, 5.90; Cl, 9.43; N, 11.18. Found: C, 60.66; H, 5.77; Cl, 9.46; N, 11.12.

General Method of Synthesis of 1-(Aminobenzyl)-1-(4-isopropylphenyl)-3,3-dimethylureas 14–18. A commercial aqueous suspension of Raney nickel (1 mL) was washed five times with absolute ethanol and was added to a solution of a nitrobenzyl derivative of isoproturons **9–13** (10 mmol) in 100 mL of ethanol. The resulting suspension was shaken under hydrogen gas at atmospheric pressure for 6 h. The Raney nickel was filtered off, and the filtrate was concentrated under reduced pressure. The residue was recrystallized from hexane, ethanol–diethyl ether or hexane–benzene (H–B) as indicated. The UV spectra of compounds **14–18** are described in Table I.

1-(3-Aminobenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)urea (14): 88% yield; mp 69 °C (H–B 80:20); NMR ($CDCl_3$) 1.21 [6 H, d, $(CH_3)_2CH$], 2.75 [6 H, s, $(CH_3)_2N$], 4.76 (2 H, s, CH_2), 6.4–7.3 (4 H, m, Ar benzyl Hs), 7.06 (4 H, m, phenyl Hs). Anal. Calcd for $C_{19}H_{25}N_3O$: C, 73.28; H, 8.09; N, 13.50. Found: C, 73.33; H, 8.28; N, 13.70.

1-(3,5-Diaminobenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)urea (15): isolated as its dihydrochloride, after addition of hydrochloric acid (10 mL of concentrated aqueous solution) to the ethanolic filtrate; 88% yield; mp 214 °C (ethanol–diethyl ether); NMR ($CDCl_3$), 1.20 [6 H, d, $(CH_3)_2CH$], 2.72 [6 H, s, $(CH_3)_2N$], 4.68 (2 H, s, CH_2), 6.2–7.8 (3 H, m, Ar benzyl Hs); 7.07 (4 H, m, phenyl Hs). Anal. Calcd for $C_{19}H_{26}N_4O$, 2 HCl: C, 57.14; H, 7.06; Cl, 17.75; N, 14.02. Found: C, 57.02; H, 7.27; Cl, 17.67; N, 13.86.

1-(3-Amino-4-chlorobenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)urea (16): 70% yield; mp 115 °C (H–B 80:20); NMR ($CDCl_3$), 1.21 [6 H, d, $(CH_3)_2CH$], 2.71 [6 H, s, $(CH_3)_2N$], 4.88 (2 H, s, CH_2), 6.6–7.5 (3 H, m, Ar benzyl Hs), 7.11 (4 H, m, phenyl Hs). Anal. Calcd for $C_{19}H_{24}ClN_3O$: C, 65.98; H, 6.99; Cl, 10.25; N, 12.15. Found: C, 65.98; H, 7.09; Cl, 10.06; N, 11.98.

1-(5-Amino-2-chlorobenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)urea (17): 30% yield; mp 122 °C (hexane); NMR ($CDCl_3$) 1.21 [6 H, d, $(CH_3)_2CH$], 2.76 [6 H, s, $(CH_3)_2N$], 4.73 (2 H, s, CH_2), 6.5–7.6 (3 H, m, Ar benzyl Hs), 7.11 (4 H, m, phenyl Hs). Anal. Calcd for $C_{19}H_{24}ClN_3O$: C, 65.98; N, 6.99; Cl, 10.25; N, 12.15. Found: C, 66.38; H, 7.03; Cl, 9.81; N, 12.11.

1-(5-Amino-2-methoxybenzyl)-3,3-dimethyl-1-(4-isopropylphenyl)urea (18): 64% yield; mp 94 °C (H–B 50:50); NMR ($CDCl_3$) 1.21 [6 H, d, $(CH_3)_2CH$], 2.71 [6 H, s, $(CH_3)_2N$], 3.71 (3 H, s, CH_3O), 4.83 (2 H, s, CH_2), 6.6–7.6 (3 H, m, Ar benzyl Hs), 7.11 (4 H, m, phenyl Hs). Anal. Calcd for $C_{20}H_{27}N_3O_2$: C, 64.47; H, 6.79; N, 11.31. Found: C, 64.30; H, 6.97; N, 11.19.

Photolysis Experiments. *Qualitative Studies.* Irradiations were carried out with a medium-pressure mercury vapor lamp (450 W) in a quartz immersion apparatus cooled internally by running water. The main radiations which were efficient for the photolysis of the compounds studied were at 254, 265, 302.5, 313, and 366 nm. The *N*-(arylmethyl)isoproturons **2–18** to be photolyzed were dissolved in water–methanol (50:50) (10^{-4} M solutions). A Pyrex filter was used with the compounds whose upper limit of absorption was higher than 300 nm (all except **2–5**; Table I). The products were analyzed by HPLC, and generally we just attempted to characterize isoproturon (**1**) or in some experiments to quantify it. In most cases, **1** gave rise to the main peak in the chromatograms. We did not try to characterize the arylmethyl-containing products expected to occur in each photolysis, most of them being not commercially available. However, the photolysis products of *N*-benzylisoproturon (**2**) were more carefully studied by GC. In addition to the expected isoproturon (**1**), they were found to be benzyl alcohol and benzyl methyl ether, which were the main products, and bibenzyl.

All *N*-(nitrobenzyl)isoproturons **9–12** were photolyzed very slowly. Numerous peaks appeared in the chromatograms of their reaction mixtures, besides a small peak of isoproturon (**1**) (Figure 1). The 4-chloro-3-nitrobenzyl derivative **13** was more rapidly photolyzed (Figure 1).

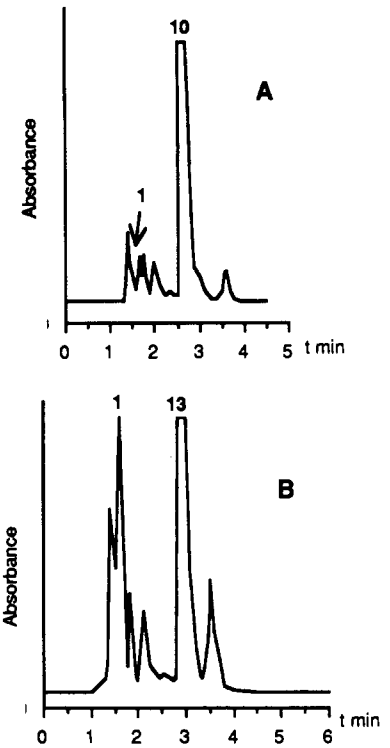


Figure 1. Chromatograms (HPLC) of the products from **10** (A) and **13** (B) after 2 h of photolysis. Conditions: column, Lichrosorb RP 18; eluent, MeOH–H_2O (80:20); flow rate, 1.5 mL min^{-1}.

N-(5-Amino-2-chlorobenzyl)isoproturon (**17**) gave quickly a product that had the same retention time as *N*-(3-aminobenzyl)-isoproturon (**14**), but on prolonged photolysis, a complex mixture containing isoproturon (**1**) was obtained, which was different from that observed from direct photolysis of compound **14** (Figure 2). The isomer **16** was photolyzed more slowly, giving also a complex mixture of products.

Quantum Yield Determination. The compounds **8**, **14**, **15**, and **18** were photolyzed at 20 °C in 10^{-3} M water–methanol (50:50) solutions in quartz tubes disposed in a carousel at the same distance of a 450-W medium-pressure mercury vapor lamp. The radiation at 313 nm was isolated by combining a Pyrex filter and a chemical filter (nickel sulfate, potassium chromate, and potassium hydrogenophthalate) (Murov, 1973). Potassium ferrioxalate was used as the actinometer. Isoproturon (**1**) produced was quantified by HPLC using internal standards. Measurements were done in the range 0–5% of isoproturon (**1**) produced.

Solar Light Photolysis. The photolysis of seven *N*-(arylmethyl)isoproturons was studied with sun as the light source (Table II). These compounds were selected because they both absorbed solar light significantly (upper limit of absorption spectra at $\lambda = 300$ nm) (Table I) and liberated isoproturon (**1**) in clean reactions. They were exposed to bright sun (early June), in 10^{-3} M water–methanol solutions (50:50) contained in Pyrex tubes. The amount of isoproturon (**1**) produced was measured by HPLC using internal standards. The times for production of 10% of isoproturon (**1**) from its arylmethyl precursors studied were determined to compare the rates of photolysis and are shown in Table II.

Compounds **8** and **18** were further studied in the above conditions, in parallel, in 1-octanol and in water–methanol solutions. The photolysis was completed within 2 h in 1-octanol solution, while 50% of the starting materials were still remaining in methanol–water (Figure 3). From both compounds, two new unidentified photoproducts were found from 1-octanol solutions, while the amount of isoproturon (**1**) produced was lower than expected.

RESULTS AND DISCUSSION

Syntheses. The *N*-arylmethyl derivatives of isoproturons **2–13** were prepared at ambient temperature, by

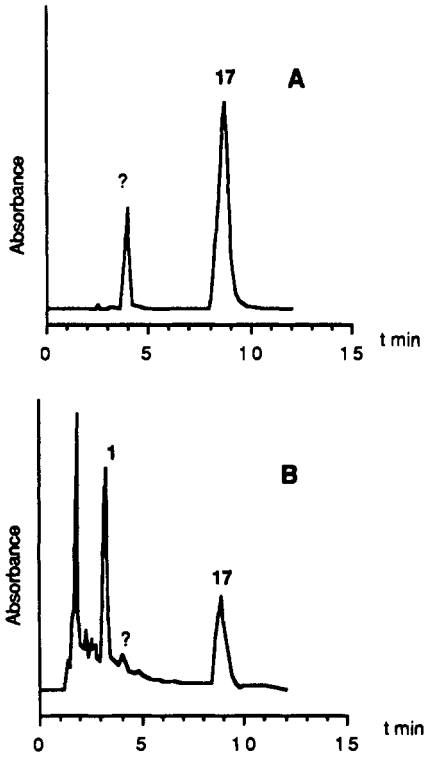
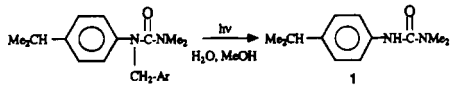
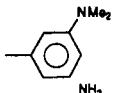
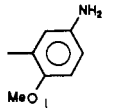
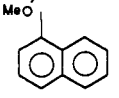
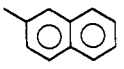
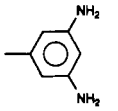
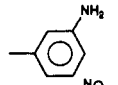
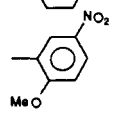


Figure 2. Chromatograms (HPLC) of the products from 17 after 10 min (A) and 40 h (B) of photolysis. Conditions: column, Lichrosorb RP 18; eluent, MeOH–H_2O–AcOH (69:30:1) plus sodium heptanesulfonate (0.005 M); flow rate, 1.5 mL min^{-1} (?, intermediate product).

Table II. Photolysis of *N*-(Arylmethyl)isoproturons



no.	Ar	t10%[a]	Ø%[b]
8		0.5 h	0.84
18		2 h	0.53
6		1 d	-
7		2 d	-
15		2 d	0.11
14		4 d	0.06
12		30 d	-

[a] Time needed to obtain a 10^{-4} M solution of 1 by solar irradiation of 10^{-3} M solutions of *N*-arylmethylisoproturons. [b] ϕ, moles of isoproturon/moles of absorbed photons [λ, 313 nm; sol 10^{-3} M in MeOH–H_2O (50:50)].

reacting the appropriate arylmethyl bromide with the aza anion of isoproturon (1) in THF. This aza anion was previously obtained by reaction of sodium hydride with

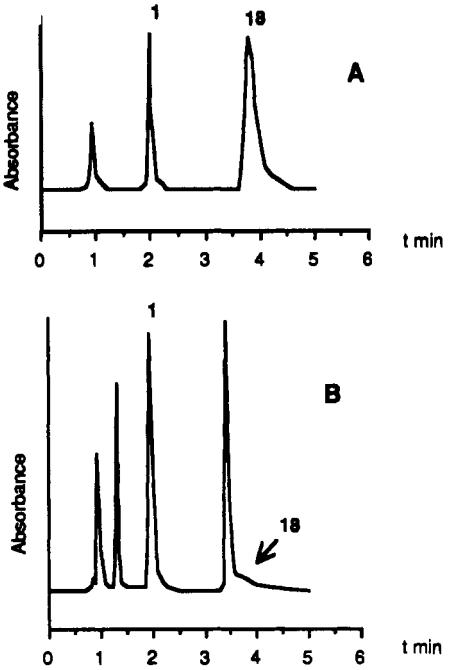
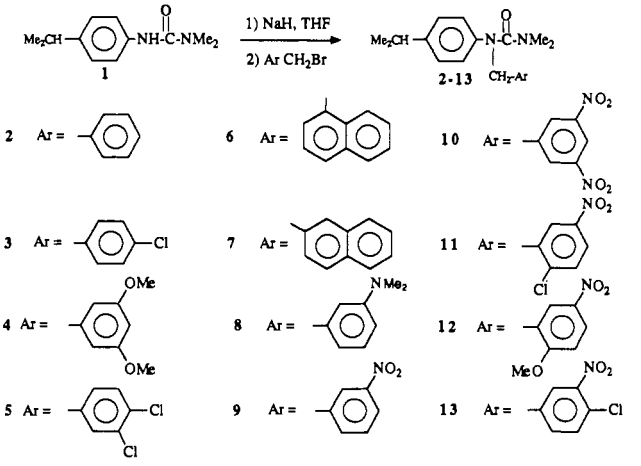


Figure 3. Chromatogram (HPLC) of the products from 18 in MeOH–H_2O (50:50) (A) and in 1-octanol (B). Conditions: column, Lichrosorb RP 18; eluent, MeOH–H_2O–AcOH (74:25:1) plus sodium heptanesulfonate (0.005 M); flow rate, 1.5 mL min^{-1}.

Scheme II



isoproturon (1) (Scheme II). Although reactions were driven almost to completion (>95%), moderate to low yields were obtained. The yields were sacrificed to purity at the recrystallization stage to completely remove the remaining starting material isoproturon (1) which might have interfered in biological assays. Chromatography on silica gel was sometimes necessary to reach this goal.

N-Arylmethylation (and not O-arylmethylation) of the trisubstituted urea 1 was proven by the observation in the IR spectra of compounds 2–13, of a characteristic absorption of tetrasubstituted ureas at 1660 cm^{-1} (Bellamy, 1958; Curtis, 1988), close to the value observed in isoproturon (1) itself. Figure 4 exhibits the spectra of 1 and of 2 as a typical example.

The aminoarylmethyl derivatives 14–18 were prepared by catalytic hydrogenation on Raney nickel of the corresponding nitro derivatives 9–13 (Scheme III).

UV Spectra. Absorption inside the solar emission spectrum area (λ > 290 nm) is the first requirement for a compound to be directly photoactivated by natural light. The data on UV absorption of compounds 2–18 (Table I) show that the benzyl derivative 2 and the chloro- or meth-

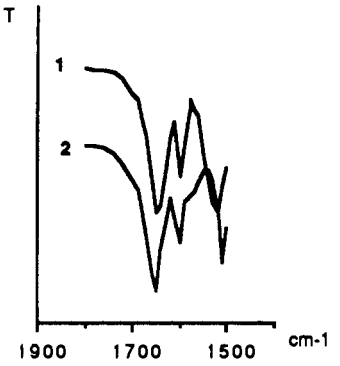
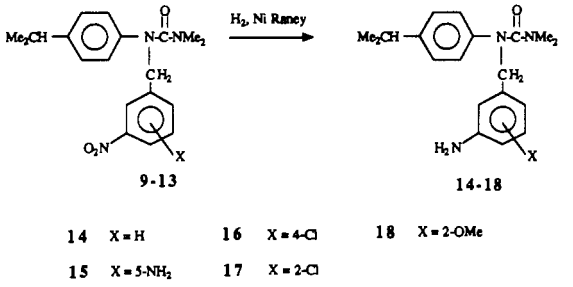
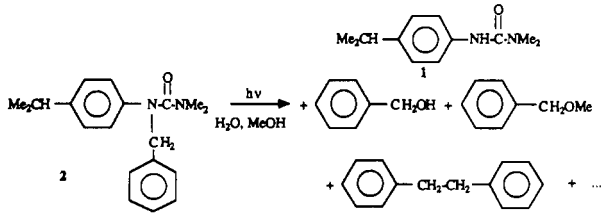


Figure 4. IR spectra of 1 and 2.

Scheme III



Scheme IV



oxy-substituted benzyl derivatives **3–5** whose spectra upper limit stands at 290 or 300 nm cannot absorb significantly solar light. On the other hand, the large bathochromic effects of the nitro and amino groups linked to the benzyl substituent allow the corresponding compounds **8–18** to fulfill that first requirement to be photolyzable. The naphthylmethyl derivatives **6** and **7** can moderately absorb solar light.

Photochemical Studies. Photolyses in water–methanol solutions of compounds **2–18** gave rise in most cases to isoproturon (**1**). The GC study of the other photolysis products of *N*-benzylisoproturon (**2**) (Scheme IV) revealed the formation of benzyl alcohol and benzyl methyl ether, the products expected from an ionic mechanism (Zimmerman and Sandel, 1963) (Scheme I), but we also detected a small amount of bibenzyl, a product obtained through the radical pathway. The photolysis of benzyl chloride in water–methanol mixtures also produced bibenzyl in a rate decreasing with decreasing methanol proportion (Hyomaki and Koskikallio, 1977).

The HPLC chromatograms that we obtained in the photolysis of most of the compounds **2–18** exhibited few peaks, attesting that simple mechanisms were involved, expectedly mainly photosolvolysis, with the following exceptions.

The nitrobenzyl derivatives **9–12**, in spite of the large absorbances of the tested solutions in the wavelength area used, were slowly photolyzed, with small amounts of isoproturon (**1**) produced. Figure 1 exhibits the chromatogram obtained after a 2-h photolysis time for (3,5-dinitrobenzyl)isoproturon (**10**). In the same conditions, the photolysis of (5-amino-2-methoxybenzyl)isoproturon (**18**), for example, was completed in no more than 1 h. Nitrobenzyl derivatives are not known to undergo photosolvolysis reactions. In this study, slow rates of photolysis indicate that nitro substituents exert a deactivating effect on the photocleavage of the C–N bond. Moreover, low yield of isoproturon (**1**) shows that photosolvolysis, if it effectively occurs, is a minor process in the photodecomposition of (nitrobenzyl)isoproturons **9–12**, which may be better explained by the complex photochemistry of the nitro group (Chow, 1982).

(4-Chloro-3-nitrobenzyl)isoproturon (**13**) was photolyzed more quickly than the other nitro compounds **9–12**, giving a complex mixture of products (Figure 1). This particular photoreactivity may be attributed to the presence of the 4-chloro substituent. In the photolysis of 4-chlorobenzyl chloride in polar solvents (methanol or water–acetonitrile), this substituent allows the generation of the photosolvolysis products and also products differing from those generally observed with meta- or ortho-substituted benzyl derivatives, some of them being photooxidation products (Choudhry et al., 1982).

The same influence of the *p*-chloro substituent was found in the photolysis of (3-amino-4-chlorobenzyl)isoproturon (**16**) which was photolyzed more quickly than its isomer **17**, giving a complex mixture of products. This latter compound **17** gave rise to a primary product which was further photolyzed to a complex mixture where isoproturon (**1**) was the main product but in weak amount (Figure 2). Moreover, these two compounds were photolyzed at least 10 times slower than (3-aminobenzyl)isoproturon (**14**), which produced isoproturon (**1**) in practically quantitative yield. Thus, at least when associated with an amino substituent, the chloro substituent, in ortho or para position, exerts an adverse effect both on the rate of photolysis and on the yield of isoproturon (**1**).

We did not attempt to characterize the secondary photoproducts observed from the nitrobenzyl (**9–13**) or the aminochlorobenzyl (**16–17**) derivatives of isoproturon. These compounds, despite their good ability to absorb solar light, produced isoproturon (**1**) either too slowly or in too small amount to allow them to be kept as good candidates for photoactivatable herbicides, and they were not further studied.

Photolysis under Solar Light. The six precursors (**6–8**, **14**, **15**, and **18**) of isoproturon that can appreciably absorb solar light (at $\lambda > 300$ nm) (Table I) and can also produce isoproturon (**1**) in appreciable rate, expectedly mainly by photosolvolysis, were finally selected as potential photoactivatable herbicides. They produced isoproturon (**1**) from 10^{-3} M water–methanol solutions irradiated with solar light, at rates distributed over a large scale ranging from 0.5 h (**8**) to 4 days (**14**) for 10% photolysis times (Table II). Thus, depending on the arylmethyl substituents of the precursors, the active material isoproturon (**1**) is liberated at variable rates compatible with the time scale of action of the herbicide. The study of (2-methoxy-5-nitrobenzyl)isoproturon (**12**) in the same conditions gave us confirmation of the low potentiality of releasing isoproturon (**1**) from the nitrobenzyl derivatives (Table II).

For penetrating into the plant, a herbicide has to travel through the lipophilic barrier of the cuticle. Thus, it was important to know the photochemical behavior of the (arylmethyl)isoproturons in a liphophilic environment. The two fastest reacting derivatives, **8** and **18**, were studied in parallel in water–methanol and 1-octanol solutions, this last solvent being chosen as a model of lipophilic medium. Figure 3 shows that compound **18** was about 50% photolyzed under solar irradiation within 2 h in water–methanol and almost 100% in the same time in 1-octanol.

However, two additional photoproducts appeared in this solvent, accounting for an observed slight reduction of yield of isoproturon (1). This result may be explained by a decrease of polarity of the solvent that favors the radical mechanism, the new photoproducts being obtained by radical coupling involving the isoproturon part of the precursors. Similar results were observed with compound 8. Thus, it is shown that isoproturon (1) may be expected to be photoproduced in lipophilic parts of the plants and not only in aqueous environment.

The four substituted benzyl derivatives (8, 14, 15, and 18) selected as potential photoactivatable herbicides bear *m*-amino substituents. These substituents, amino or dimethylamino, induce both a sufficient bathochromic shift in the UV spectra for allowing the benzyl nucleus to absorb solar light and activate the photolysis, giving mainly isoproturon (1) and photosolvolysis products. The absorption in the solar emission range increases slightly in the sequence 14 < 15 < 18 < 8 but can explain only partially the increase of the rate of photolysis, which is better correlated with the quantum yield of production of isoproturon (1) (Table II). This last factor accounts for the activating effects of the substituents of the benzyl ring. The comparison between the disubstituted derivatives 18 and 15 and the monosubstituted 14 shows clearly the influence of the second substituent: the *m*-amino group (in 15) is a less powerful activating substituent than the *o*-methoxy group (in 18). However, it should be pointed out that the dimethyl substitution of the amino group (in 8) dramatically increases the quantum yield. To our knowledge, the effect of the *m*-dimethylamino group on photolysis of a benzyl derivative is described here for the first time. The activation of the photolysis by the amino substituents is expected to originate from their electrodonating power acting at the level of the singlet excited state of the arylmethyl group, like with the methoxy substituent (Zimmerman and Sandel, 1963; Wan, 1985; Wan and Chak, 1986).

This concept of photoactivatable herbicide (or more generally pesticide) consisting in linking an appropriate arylmethyl group to an active molecule may be applied to a large range of compounds containing N-heterocycles or N-functional groups: amides, aromatic amines, carbamates, benzimidazoles, indoles, uraciles, etc. We have checked the ability of photoelimination of *N*-arylmethyl substituents from such N-functional groups, and we generally obtained positive results in most cases (Mohsinaly, 1987). However, the biological activity of the potential photoactivatable herbicide or pesticide will result not only from the release of the active molecule but also from many other phenomena which influence the pesticide action: plant penetration, transport, metabolism, chemical or photochemical degradation, etc. All of these properties are modified by the arylmethyl substitution of the active molecule in an unpredictable manner. Thus, only biological testing can account for the validity of the above concept of photoactivatable pesticide applied to any known active material. For the protection of industrial interests, the biological data concerning isoproturon derivatives 2–18 are not available.

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