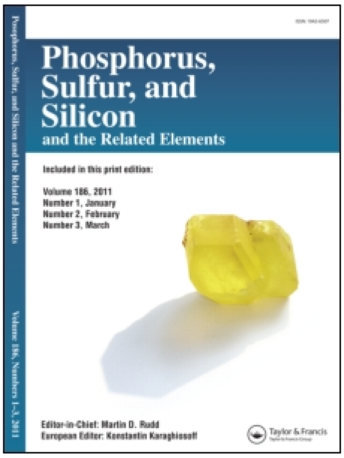

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SYNTHESIS OF NONIONIC AROXYLSULFONYL CARBAMATES

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Novel aroxylsulfonyl carbamates containing polar head or core type were synthesized from the action of aroxysulfonylisocyanate on oligooxyethylmonomethylated ethers or glycols without solvent. At room temperature the reaction occurs rapidly with satisfactory yields. The synthetic pathway of isocyanate derivatives is achieved in a one-pot reaction in order to use low price commercially available compounds such as phenolic derivatives and chlorosulfonylisocyanate as starting materials. This new class of nonionic compounds contains one aromatic part and one polar part. All these compounds are monodisperse, that is, they include a perfectly defined number of oxyethylene units. The synthesis and characterization of these new series of carbamates are described.

Keywords: Aroxylsulfonylisocyanate; aroxylsulfonylcarbamate; glycol; nonionic carbamates

INTRODUCTION

Since the discovery of chlorosulfonyliscyanate,[1] numerous works[2] have been done due to its exceptional reactivity. This industrial raw material has two electrophilic sites for attack by nucleophilic reagent, which are the carbonyl carbon and the sulfur of the sulfonyl chloride moiety.[3] Furthermore, cycloadditions to the double bond carbon-nitrogen of the cumulative function can occur.[4] The presence of the chlorosulfonyl moiety inside this bifunctional molecule greatly increases the electrophilic

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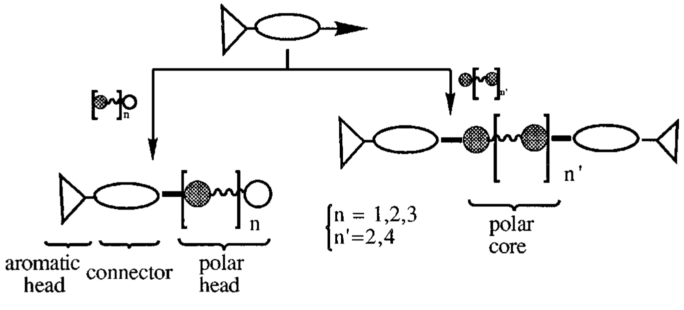
power of the isocyanate function. The main compounds developed from this raw material are of the aroxysulfonyl isocyanates type. The high reactivity of these monofunctionalized isocyanates leads to numerous compounds, not only within the hydrocarbon series but also within the fluorinated series, by the action of different kinds of compounds: amine,[5] alcohol,[6] or thiol,[7] each highly fluorinated. It is worth noting that due to their low toxicity, oxosulfonyl ureas[8–10] as well as carbamates[11–13] allow us to consider interesting properties for agricultural treatment. It is in the biologiocal field that carbamates lead to numerous activities.[14–16] However, the presence of a nonionic oligo(oxyethylated) part is required in some biological applications involving a great compatibility with cellular functioning.[17–18] From these results, the aim of this work is to extend the reaction of aroxysulfonyl isocyanate with polar nonionic nucleophic agents. The resulting compounds involving the following main structural segment:

- an aromatic head and a polar head bonding through a connector (corresponding to the oxosulfonyl carbamate moiety)
- or two aromatic head groups bonding to the rigid core by the same connector as above.

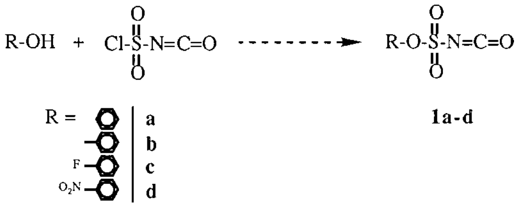
The molecular shape of the compounds synthesised is described in Scheme 1.



SCHEME 1 Molecular shape of synthesized compounds.

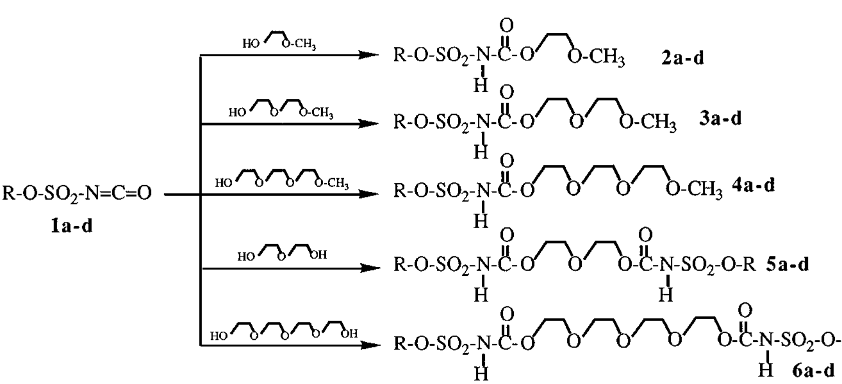
RESULTS AND DISCUSSION

The preparation of aroxysulfonylisocyanates is described in Scheme 2. The reaction of chlorosulfonyl isocyanate with phenols (a–d) at room temperature or slightly elevated temperatures leads to the corresponding carbamates. But, by heating above about 100°C this reaction can



SCHEME 2 Reaction pathway for the synthesis of **1a–d**.

give a new type reaction by the production of aryloxysulfonyl isocyanates (**1a–d**). Two different mechanisms are proposed.[19–20] The possibility to obtain this second reaction type is in connection with the ability of the former group to move on. In fact this reaction is not directly applicable to unsaturated alcohols since the formation of carbamate in the first step is not reversible in these conditions. In this case, as a general consideration, the possibility to obtain the second type reaction is governed by the ability, that a leaving group of the nucleophilic compound is involved in the first attack. Hence aroxylate but also perfluorinated alcoholate[21] moieties can satisfy this condition. The synthetic intermediate (**1a–d**) is obtained with high yields.[19,22] Hence, it is easy to obtain isocyanate in a one-pot reaction. The preparation of nonionic compounds is described in Scheme 3. We can obtain, with satisfactory yield, these compounds by the action of monomethylated glycol (compound **2a–d** to **4a–d**) or by the action of glycol (compounds **5a–d** to **6a–d**). Physico-chemical results are reported in Table I. The compounds prepared are monodisperse, that is, they have a well-defined number of ethoxylated groups in the polar moiety. This synthetic pathway allows us to obtain nonionic N-sulfonyl carbamates with high yields. The



SCHEME 3 Reaction pathway for the synthesis of **2a–d** to **6a–d**.

TABLE I Preparation of **2a–d** to **6a–d** Nonionic Aryloxysulfonylcarbamates

Cpd no	Yield[a]	Yield[b]	m.p.°C (b.p./mmHg)	$n_{20°C}$
2a	98	91	64	
2b	96	88	101	
2c	91	84	79	
2d	98	92	128	
3a	97	90		1.4980
3b	95	88		1.4850
3c	95	88		1.4795
3d	94	87	88	
4a	91	83	(105/0.01)	
4b	89	81	(136/0.1)	
4c	88	80	(141/0.02)	
4d	96	88	(122/0.015)	
5a	94	87		1.4995
5b	98	91		1.4982
5c	96	88		1.3602
5d	93	87		1.5034
6a	93	87		1.5118
6b	92	86		1.4877
6c	97	91		1.3754
6d	88	84		1.5127

[a] Yield from the last step.
[b] Yield from phenyl derivatives.

resulting compounds have to be evaluated in order to compare their biological activity with homologs previously described.[7]

EXPERIMENTAL

Methods

IR spectra were recorded at room temperature with a Perkin Elmer 681 1000 FT-IR spectrometer as films for the neat liquids. ^{1}H-NMR (chemical shifts measured in deuterated solvents are given in ppm from TMS) spectra were recorded with a Bruker AC 200 MHz spectrometer, using $CDCl_3$ solutions (5–10 wt%). HRMS were run on a Mat SBE apparatus. Distillations were performed with a Kugelrohr Aldrich with an Alcatel pump 2004 A.

Synthesis

The synthesis of aroxylsulfonyl isocyanates, compounds **1a–d** in Scheme 2, are described elsewhere.[19,22]

***General Procedure for Compounds** 2a–d **to** 6a–d*

To a freshly prepared solution of 0.02 mmol of aroxysulfonylisocyanates, **1a–d**, was added dropwise, under nitrogen atmosphere, 0.02 mol of 2-(methoxy)ethanol, 2-(2-(methoxy)ethoxy)ethanol or 2-(2-(2-methoxyethoxy)-ethoxy)ethanol for the polar head compounds or 0.01 mol. of 2-(2-(hydroxy)ethoxy)ethanol of 2-(2-(2-(2-hydroxyethoxy) ethoxy)-ethoxy)ethanol in order to obtain the polar core compounds. After the complete addition without solvent, the resulting mixture was left at room temperature for 0.5 h. The reaction was followed by gas phase chromatography until removal of alcoholic raw material. The residue was purified either by recrystallization in ethanol, or by distillation under reduced pressure or colomn chromatography using ether-petroleum ether (7:3) as eluent. In this case the evaporation after drying of the organic phase gives the desired pure colorless product. Compounds are in good agreement with MS recording. Molecular weights are obtained systematically.

(2-Methoxyethyl)-N-(phenoxysulfonyl)carbamate ***2a***. IR (ν (cm^{-1}), $CHCl_3$): 3618 (ν_{NH}) 1176–1364 (ν_{SO2}); 1709 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 9.0 (s, 1H, NH); 7.22–7.40 (s, 5H, C_6H_5); 4.3 (t, 2H, CH_2—O—CO, $^3J_{H-H}$ = 8.5 Hz); 3.7 (t, 2H, CH_2, $^3J_{H-H}$ = 8.5 Hz) 3.2 (s, 3H, CH_3—O).

(2-Methoxyethyl)-N-(4-methylphenoxysulfonyl)carbamate ***2b***. IR (ν (cm^{-1}), $CHCl_3$): 3380 (ν_{NH}) 1168–1391 (ν_{SO2}); 1766 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.22–7.3 (s, 4H, C_6H_4); 4.3 (t, 2H, CH_2—O—CO, $^3J_{H-H}$ = 8 Hz); 3.7 (t, 2H, CH_2, $^3J_{H-H}$ = 8 Hz); 3.2 (s, 3H, CH_3—O); 2.3 (s, 3H, CH_3). HRMS calc. For $C_{11}H_{15}NO_6S$: 289.306; found: 289.0517.

(2-Methoxyethyl)-N-(4-fluorophenoxysulfonyl)carbamate ***2c***. IR (ν (cm^{-1}), $CHCl_3$): 3378 (ν_{NH}) 1170–1391 (ν_{SO2}); 1768 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 8.8 (s, 1H, NH); 7–7.62 (m, 4H, C_6H_4, $^3J_{H-F}$ = $^3J_{H-H}$ = 8.6 Hz, $^4J_{H-F}$ = 4.5 Hz). 4.4 (t, 2H, CH_2—O—CO, $^3J_{H-H}$ = 8.1 Hz); 3.7 (t, 2H, CH_2) 3.2 (s, 3H, CH_3—O) ^{19}F NMR (d (ppm), $CDCl_3/C_6F_6$): 48.2 (m, 1F, $^3J_{H-F}$ = 8.6 Hz, $^4J_{H-F}$ = 4.5 Hz).

(2-Methoxyethyl)-4-(N-(nitrophenoxysulfonyl)carbamate ***2d***. IR (ν (cm^{-1}), $CHCl_3$): 3376 (ν_{NH}) 1168–1350 (ν_{SO2}); 1768 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 9.0 (s, 1H, NH); 7.22–7.40 (s, 4H, C_6H_4); 4.3 (t, 2H, CH_2—O—CO, $^3J_{H-H}$ = 8.5 Hz); 3.7 (t, 2H, CH_2, $^3J_{H-H}$ = 8.5 Hz) 3.4 (s, 3H, CH_3—O).

(2-[2-Methoxyethoxy]ethyl)-N-(phenoxysulfonyl)carbamate ***3a***. IR (ν (cm^{-1}), $CHCl_3$): 3338 (ν_{NH}) 1176–1363 (ν_{SO2}); 1714 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 10.2 (s, 1H, NH); 7.22–7.4 (m, 5H, C_6H_5); 4.3

(t, 2H, CH_2—O—CO, $^3J_{H-H} = 8$ HHz); 3.6 (m, 6H, $3xCH_2$); 3.2 (s, 3H, CH_3—O).

(2-[2-Methoxyethoxy]ethyl)-N-(4-methylphenoxysulfonyl)carbamate de ***3b***. IR (ν (cm^{-1}), $CHCl_3$): 3370 (ν_{NH}) 1168–1391 (ν_{SO2}); 1761 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.0 (s, 4H, C_6H_4); 4.1 (m, 2H, CH_2—O—CO); 3.5 (m, 2H CH_2); 3.4 (m, 2H, CH_2); 3.3 (m, 2H, CH_2); 3.1 (s, 3H, CH_3—O); 2.1 (s, 3H, CH_3). HRMS calc. For $C_{13}H_{19}NO_7S$: 333.359; found: 333.07038.

(2-[2-Methoxyéthoxy]ethyl)-N-(4-fluorophenoxysulfonyl)carbamate ***3c***. IR (ν (cm^{-1}), $CHCl_3$): 3410 (ν_{NH}) 1176–1363 (ν_{SO2}); 1759 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 10.4 (s, 1H, NH); 6.2–7.1 (m, HH, C_6H_4, $^3J_{H-F} = {}^3J_{H-H} = 8.7$ Hz, $^4J_{H-F} = 4.6$ Hz); 4.1 (t, 2H, CH_2—O—CO; $^3J_{H-H} = 8$ Hz); 3.4 (m, 2H, CH_2); 3.3 (m, 2H, CH_2); 3.2 (m, 2H, CH_2); 3 (s, 3H, CH_3—O). ^{19}F NMR (d (ppm), $CDCI_3/C_6F_6$): 48.55 (m, 1F, $^3J_{H-F} = 8.7$ Hz, $^4J_{H-F} = 4.6$ Hz).

(2-[2-Methoxyethoxy]ethyl)-N-(4-nitrophenoxysulfonyl)carbamate ***3d***. IR (ν (cm^{-1}), $CHCl_3$): 3442 (ν_{NH}) 1151–1351 (ν_{SO2}); 1760 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.5–8.3 (m, 4H, C_6H_4); 4.3 (t, 2H, CH_2—O—CO; $^3J_{H-H} = 7.5$ Hz); 3.7 (m, 2H, CH_2); 3.5 (m, 2H, CH_2); 3.4 (m, 2H, CH_2); 3.2 (s, 3H, CH_3—O).

[2-(2-[2-Methoxyethoxy]ethoxy)ethyl]-N-(Phenoxysulfonyl)carbamate ***4a***. IR (ν (cm^{-1}), $CHCl_3$): 3349 (ν_{NH}) 1166–1361 (ν_{SO2}); 1715 (ν_{CO}) ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 6.9–7.2 (m, 5H, C_6H_5); 4.2 (t, 2H, CH_2—O—CO, $^3J_{H-H} = 8.7$ Hz); 3.6 (m, 2H, CH_2); 3.5 (m, 4H, $2xCH_2$); 3.4 (m, 4H, $2xCH_2$); 3.3 (s, 3H, CH_3—O).

[2-(2-[2-Methoxyethoxy]ethoxy)ethyl]-N-(4-methylphenoxysulfonyl) carbamate ***4b***. IR (ν (cm^{-1}), $CHCl_3$): 3429 (ν_{NH}) 1170–1362 (ν_{SO2}); 1718 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.1 (s, 4H, C_6H_4); 4.1 (m, 2H, CH_2—O—CO); 3.5 (m, 2H, CH_2); 3.4 (m, 4H, $2xCH_2$); 3.3 (m, 4H, $2xCH_2$); 3.1 (s, 3H, CH_3—O); 2.1 (s, 3H, CH_3).

[2-(2-[2-Methoxyethoxy]ethoxy)ethyl]-N-(4-fluorophenoxysulfonyl) carbamate de ***4c***. IR (ν (cm^{-1}), $CHCl_3$): 3265 (ν_{NH}) 1176–1368 (ν_{SO2}); 1756 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 6.2–7.1 (m, HH, C_6H_4, $^3J_{H-F} = {}^3J_{H-H} = 8.7$ Hz, $^4J_{H-F} = 4.6$ Hz); 4.1 (m, 2H, CH_2—O—CO); 3.4 (m, 2H, CH_2); 3.3 (m, 4H, $2xCH_2$); 3.2 (m, 4H, $2xCH_2$); 3.3 (s, 3H, CH_3—O). ^{19}F NMR (d (ppm), $CDCl_3/C_6F_6$): 48.55 (m, 1F, $^3J_{H-F} =$ 8.7 Hz, $^4J_{H-F} = 4.6$ Hz).

[2-(2-[2-Methoxyethoxy]ethoxy)éthyl]-N-(4-nitro-phenoxysulfonyl) carbamate ***4d***. IR (ν (cm^{-1}), $CHCl_3$): 3386 (ν_{NH}) 1151–1386 (ν_{SO2}); 1719 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.2–7.4 (m, HH, C_6H_4,

$^3J_{H-H} = 8.7$ Hz, 4.1 (t, 2H, CH_2—O—CO); 3.4 (m, 2H, CH_2); 3.3 (m, 4H, 2xCH_2); 3.2 (m, 4H, 2xCH_2); 3 (s, 3H, CH_3—O).

7-(N-phenoxysulfonylamino)-7-oxo-3,6-dioxahept-1-yl-N-(phenoxysulfonyl)carbamate ***5a***. IR (ν (cm^{-1}), $CHCl_3$): 3618 (ν_{NH}) 1176–1364 (ν_{SO2}); 1720 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.2 (s, 10H, C_6H_5); 4.3 (t, 4H, 2xCH_2—O—CO, $^3J_{H-H} = 8$ Hz); 3.6 (t, 4H, 2xCH_2; $^3J_{H-H} = 8$ Hz).

7-(N-4-methylphenoxysulfonylamino)-7-oxo-3,6-dioxahept-1-yl-N-(4-methylphenoxysulfonyl)carbamate ***5b***. IR (ν (cm^{-1}), $CHCl_3$): 3440 (ν_{NH}) 1172–1381 (ν_{SO2}); 1760 ((ν_{CO})). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.2 (s, 8H, 2xC_6H_4); 3.4 (t, 4H, 2xCH_2—O—CO); 3.3 (t, 4H, 2xCH_2); 2.3 (s, 6H, 2xCH_3).

7-(N-4-fluorophenoxysulfonylamino)-7-oxo-3,6-dioxahept-1-yl-N-(4-fluorophenoxysulfonyl)carbamate ***5c***. IR (ν (cm^{-1}), $CHCl_3$): 3271 (ν_{NH}) 1167–1366 (ν_{SO2}); 1704 ((ν_{CO})). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7–7.62 (m, 8H, 2xC_6H_4, $^3J_{H-F} = {}^3J_{H-H} = 8.7$ Hz, $^4J_{H-F} = 4.7$ Hz). 3.4 (t, 4H, 2xCH_2—O—CO, $^3J_{H-H} = 8.1$ Hz); 3.2 (t, 4H, 2xCH_2). ^{19}F NMR (d (ppm), $CDCl_3/C_6F_6$): 48 (m, 2F, $^3J_{H-F} = 8.7$ Hz, $^4J_{H-F} = 4.7$ Hz).

7-(N-4-nitrophenoxysulfonylamino)-7-oxo-3,6-dioxahept-1-yl-N-(4-nitrophenoxysulfonyl)carbamate ***5d***. IR (ν (cm^{-1}), $CHCl_3$): 3332 (ν_{NH}) 1168–1337 (ν_{SO2}); 1759 ((ν_{CO})). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.22–7.40 (s, 8H, 2xC_6H_4); 4.2 (t, 4H, 2xCH_2—O—CO, $^3J_{H-H} = 8$ Hz); 3.7 (t, 4H, 2xCH_2).

13-(N-phenoxysulfonylamino)-13-oxo-3,6,9,12-tetraoxatridec-1-yl-N-(phenoxysulfonyl)carbamate ***6a***. IR (ν (cm^{-1}), $CHCl_3$): 3459 (ν_{NH}) 1168–1386 (ν_{SO2}); 1749 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.3 (s, 10H, C_6H_5); 4.2 (t, 4H, 2xCH_2—O—CO, $^3J_{H-H} = 8$ Hz); 3.7 (m, 12H, 6xCH_2).

13-(N-4-methyl-phenoxysulfonylamino)-13-oxo-3,6,9,12-tetraoxatridec-1-yl-N-(4-methyl-phenoxysulfonyl)carbamate ***6b***. IR (ν (cm^{-1}), $CHCl_3$): 3440 (ν_{NH}) 1172–1381 (ν_{SO2}); 1763 (ν_{CO}). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7.1 (m, 8H, 2xC_6H_4); 4.2 (t, 4H, 2xCH_2—O—CO, $^3J_{H-H} = 8$ Hz); 3.5 (m, 12H, 6xCH_2); 2.2 (s, 6H, 2xCH_3).

13-(N-4-fluorophenoxysulfonylamino)-13-oxo-3,6,9,12-tetraoxatridec-1-yl-N-(4-fluoro-phenoxysulfonyl)carbamate ***6c***. IR (ν (cm^{-1}), $CHCl_3$): 3262 (ν_{NH}) 1165–1368 (ν_{SO2}); 1756 ((ν_{CO})). ^{1}H NMR (δ (ppm), $CDCl_3$/TMS): 7–7.7 (m, 8H, 2xC_6H_4, $^3J_{H-F} = {}^3J_{H-H} = 8.6$ Hz, $^4J_{H-F} = 4.6$ Hz). 4.2 (t, 4H, 2xCH_2—O—CO, $^3J_{H-H} = 8.1$ Hz); 3.5 (t, 12H, 6xCH_2) ^{19}F NMR (d (ppm), $CDCl_3/C_6F_6$): 48 (m, 2F, $^3J_{H-F} = 8.6$ Hz, $^4J_{H-F} = 4.6$ Hz).

13-(N-4-nitro-phenoxysulfonylamino)-13-oxo-3,6,9,12-tetraoxatridec-1-yl-N-(4-nitro-phenoxysulfonyl) carbamate ***6d***. IR (ν (cm^{-1}), $CHCl_3$): 3330 (ν_{NH}) 1168–1337 (ν_{SO2}); 1760 (ν_{CO}). ^1H NMR (δ (ppm), $CDCl_3$/TMS): 7.22–7.35 (s, 8H, 2xC_6H_4), 4.2 (t, 4H, 2xCH_2—O—CO, $^3J_{H-H} = 8$ Hz); 3.4 (m, 12H, 6xCH_2).

REFERENCES

[1] R. Graf, *Chem. Ber.*, **89,** 1071 (1956).
[2] D. N. Dhar and K. S. K. Murthy, *Synthesis*, 437 (1986).
[3] J. K. Rasmussen and A. Hassner, *Chem. Rev.*, **76**(3), 389 (1976).
[4] A. G. M. Barrett, M. J. Betts, and A. Fenwick, *J. Org. Chem.*, **50,** 169 (1985).
[5] M. El Kateb, M. Beji, and A. Baklouti, *J. Fluorine Chem.*, **94,** 119 (1999).
[6] M. El Kateb, M. Beji, and A. Baklouti, *J. Fluorine Chem.*, **81,** 139 (1997).
[7] M. Beji, H. Sbihi, A. Baklouti, and A. Cambon, *J. Fluorine Chem.*, **99,** 17 (1999).
[8] P. J. Houghton, J. Sosinsky, J. H. Thakar, G. B. Boder, and G. B. Grindey, *Biochem. Pharmacol.*, **49,** 661 (1995).
[9] J. Sosinski, J. H. Thakar, G. S. Germain, P. Dias, F. C. Harwood, J. F. Kutesch, and P. J. Houghton, *Mol. Pharmacol.*, **45,** 962 (1994).
[10] G. Hamprecht, H. Mayer, K. O. Westphalen, and H. Walter, Fluorine in Agriculture Conference, University of Manchester, UK, **12,** 1 (1995).
[11] R. Andree, M. W. Drewes, A. Merhold, H. J. Santel, and M. Dollinger, *Ger Offen.* DE 4, 412, 079 (Cl.C07D239/54), 23 Feb. 1995.
[12] D. B. Kallander, *Diss. Abstr. Int. B*, **54**(11), 5495 (1994).
[13] L. H. Machemer and M. Pickel, *Toxicology*, **91,** 29 (1994).
[14] F. Bennett, V. M. Girijavallabhan, and N. M. Patel, PCT Int. Appl. WO 94 17, 096 (Cl.CO7K5/06), 4 Aug. 1994.
[15] M. N. R. Arasaki, H. Ishitsuka, I. Kuruma, M. M. C. Miwa, N. Shimma, and U. Isao, Imperial Higashihak, *Eur. Pat. Appl.* EP 602, 454 (Cl.CO7H19/067), 22 June 1994.
[16] J. A. Picard, P. M. O'Brien, D. R. Sliskovic, M. K. Anderson, R. F. Bousley, K. L. Hamelehle, B. R. Krause, and R. L. Stanfield, *J. Med. Chem.*, **39,** 1243 (1996).
[17] N. Mureau, H. Trabelsi, F. Guittard, and S. Geribaldi, *J. Colloid Interface Sci.*, **229,** 440 (2000).
[18] F. Guittard, E. Taffin de Givenchy, and A. Cambon, *J. Colloid Interface Sci.*, **177,** 101 (1996).
[19] G. Lohaus, *Chem. Ber.*, **105,** 2791 (1972).
[20] A. Warm and G. Bernardinelli, *J. Org. Chem.*, **59,** 3540 (1994).
[21] S. Saidi, F. Guittard, S. Geribaldi, M. Beji, and A. Baklouti, manuscript in preparation.
[22] M. Hedayatullah and J. F. Brault, *C. R. Acad. Sci.*, **C285,** 153 (1977).