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Synthesis of Fluoromonoterpenoids as Potential Suicide Substrates for Plant Cells

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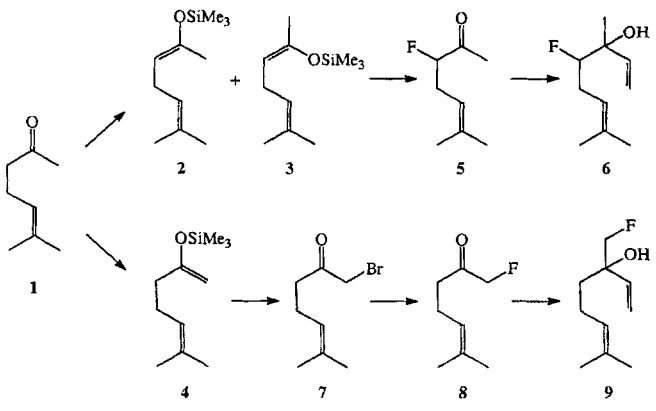
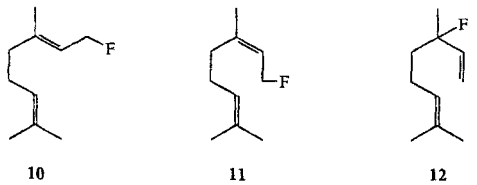
Suitably fluorinated monoterpenoids should act as suicide substrates if degraded to fluoroacetate by plant cell cultures. Consequently, such compounds could be of use to select for cloning those sub-populations of cells which accumulate rather than degrade endogenously or exogenously supplied monoterpenoids [1]. We describe here the synthesis of five such substituted monoterpenoids which, in turn, may be converted by standard procedures into numerous acyclic and alicyclic relatives. Our products should also prove useful in following the degradation processes *in vivo* using ^{19}F-NMR [*cf.* 2, 3].

Several fluorinated monoterpenoids have been previously reported: e.g.: 2-fluorogeraniol [4], 10-fluorogeraniol [5, 6], 2-fluoronerol and 2-fluorolinalool [4, 6, 7] and certain fluorinated chrysanthemic acids [8]; in addition to certain similarly-substituted sesquiterpenoids [9, 10]. The introduction of fluorine into organic compounds is not trivial [7, 11] and "most of the reagents have drawbacks of expense, toxicity and explosiveness – either alone or in combination" [12]. The multistep routes to these previously prepared compounds illustrate this and generally give poor (<10%) overall yields. We here report the preparation of 4- and 9- fluorolinalools **6** and **9** from 6-methylhept-5-en-2-one **1** as starting material. α-Fluorination of ketones has been applied to the synthesis of 2-fluorogeraniol in a several-step procedure using lithium trifluoroethene [4] and more generally using fluorine [13], perchloryl fluoride [7] or caesium fluoro- oxysulphate [14] *inter alia* and an indirect route to such substituted ketones involves treatment of oxiranes with hydrofluoric acid [11]. In contrast, we have devised simple routes that yield low overall yields (9; 3%) but nevertheless utilise relatively innocuous reagents. Thus the enols of **1** were trapped as the trimethylsilyl (TMS)-ethers **2**, **3** and **4** with TMS-iodide or ethyl- trimethylsilyl acetate. One isomeric pair (**2**/ **3**) was treated with N-fluoropyridinium triflate to yield ultimately the fluorinated ketone **5** in a sequence that had been previously applied to a few cyclic ketones [15–17]: in contrast, the other enol ether **4** was treated with N-bromosuccinimide to yield the isomeric fluoroketone **8**. Compounds **5** and **8** could then be coupled with vinylmagnesium bromide to give **6** and **9**. We also prepared geranyl, neryl and linaloyl fluorides **10**, **11**, **12** in yields 30, 31, 11%, respectively, from the corresponding alcohols by modified Corey–Kim chlorination followed by treatment with tetrabutylammonium fluoride. A previously recorded [9] route to these compounds involving treatment of the respective alcohol with methyllithium followed by reaction with *p*-tosyl fluoride and lithium fluoride plus a crown ether failed in our hands.





Some of the ^{19}F–^{13}C and ^{19}F–^{1}H couplings in the NMR spectra of certain intermediates and products are of interest. For example, $^{4}J_{HF}$ coupling could be detected in the spectra of ketones **5** and **8** and may be attributed to either conventional through-bond or to through-space effects [*cf.* 18, 19]. The latter can be analyzed by a convergent vector model [cf. 20] which predicts only one observable $^{4}J_{HF}$ splitting (to C_1–*H*) in **5**, as found. An alternative model ascribes the long-range effects to the presence of the oxygen atom [21]. Both $^{5}J_{HF}$

and $^5J_{CF}$ coupling were observed in the spectra of **10** and **11**, and here the vector model predicts that the interacting atoms are too far removed (>0.48 nm) for space effects to be important for any likely conformation. Presumably the C=C bond is necessary for the transmission in these examples. The measured couplings (see Experimental) were: $^2J_{HF}$ 47–50 Hz; $^3J_{HF}$ 8–20; $^4J_{HF}$ 3–5; $^5J_{HF}$ 5–7: and $^1J_{CF}$ 156–186; $^2J_{CF}$ 17–50; $^3J_{CF}$ 3–12; $^4J_{CF}$ 2–3; and $^5J_{CF}$ ca. 3. Not all the expected C–F couplings could be resolved: it has been stressed that such interactions may be complex and are difficult to predict on the basis of simple models [22, 23].

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Experimental

NMR spectra were measured on a Varian VXR 400 spectrometer at 399.5 MHz (^{1}H), 100.8 (^{13}C) and 376.3 (^{19}F). Solutions (10–20%) in $CDCl_3$ were used with TMS as standard for ^{1}H and ^{13}C spectra and $CFCl_3$ for ^{19}F; δ is given in ppm. FT-IR spectra were obtained with a Perkin-Elmer 983 instrument; MS with an AEI-MS9 spectrometer using EI (12eV), CI (NH_3) or FAB (glycerol matrix; argon); GC-MS with a VG-707H spectrometer (70eV) linked to a Pye 204 chromatograph fitted with an 0V-101 column (20×0.22 mm o. d.; injection 200 °C; 60–220 °C programme at 4 °C min^{-1}) interfaced with a Finnigan-Incos data system. All synthetic operations were carried out with flame-dried apparatus under argon: solids were heated *in situ* typically at 40 °C/0.1mm Hg for 24 to 48 hours, and all solvents and reactants were rigorously dried.

4-Fluorolinalool (6; 4-fluoro-3,7-dimethylocta-1,6-dien-3-ol) For general methods see refs. [15–17]

(a) endo-Trimethylsilyl enol ethers *of 6-methylhept-5-en-2-one (2, 3)*

6-Methylhept-5-en-2-one (**1**; 2.52g, 20 mmol) was mixed with hexamethyldisilazine (3.51g; 20 mmol) and pentane (250ml) at –20°C and after 10 minutes trimethylsilyl iodide (TMS-I ; 4.40g, 22mmol) was added. After stirring (30 min at ca. –10 °C) and allowing to warm to RT (ca. 2 hr), the reaction was quenched (saturated aq. $NaHCO_3$; 5 vols) extracted with pentane (2×25ml), the extract dried (Na_2SO_4), the solvent removed and the product passed through silica gel (70–230 mesh; 60×360mm) with hexane/EtOAc (85:15 v/v). The eluate was assayed by GC-MS and the TMS-enol ethers (**2** + **3**) purified by HPLC on silica gel (Nucleosil; 5μm: 4.6×250 mm) with hexane/EtOAc (90:10 v/v); yield 3.39 g (86%; **2**: **3**:**4** = 82:17:<1). – ^{1}H-NMR: δ 5.06 (m, 1H, H_5), *E*-isomer 4.38 (dt, 1H, H_3), *Z*-isomer 4.18 (dt, 1H, H_3), 2.65 (t, 2H, H_4), 1.74 (d, 6H, H_1), 1.66 (d, 3H, H_8), 1.60 (s, 3H, H_7), 0.21 (s, 9H, SiMe). – ^{13}C-NMR: δ 145.97 (C_2), 130.80 (C_5), 107.26 (C_3), 43.32 (C_{4Z}), 36.27 (C_{4E}), 26.54 (C_{1Z}), 25.27 (C_7), 24.05 (C_{1E}), 18.80 (C_8). – MS(EI): *m/z* = 198 (M^+, 18), 183 (40), 130 (15), 115 (20), 73 (100). MS reveals a population of interconverting distonic molecular ions (*cf.* fragmentation of the TMS enol ether of 2-heptanone [24, 25]). Reaction of **1** with TMS-Cl and Et_3N cf.[16, 26, 27] under a variety of conditions gave poor yields (< 20%) of the enol ethers.

(b) *3-Fluoro-6-methyl-5-en-2-one* (**5**)

N-Fluoropyridinium triflate (NFPT; 2.0 g, 10 mmol: *cf* [15]) was added to the mixture of **2** and **3** (1.60 g, 8.0 mmol) in CH_2Cl_2 (35 ml) and after stirring under reflux (24 hr), the hexane extract (3×25ml) was concentrated to ca. 1ml. This was prefractionated on silica gel (70–230 mesh; 60×360 mm) with hexane/EtOAc (85:15 v/v) followed by prep. HPLC [conditions as previously; 2 columns (10×200 mm) in series] to give **5**. Yield (0.30 g; 26%). – ^{1}H-NMR: δ 5.13 (m, 1H, H_5), 4.71 (m, 1H, H_3), 2.51 (dt$_1$ $^3J_{HF}$ = 19.43 Hz, 2H, H_4), 2.57 (m, $^4J_{HF}$ = 2.75, 3H, H_1), 1.70 (s$_1$ 3H, H_8), 1.60 (d, 3H, H_7). – ^{13}C-NMR: δ 136.33 (C_6), 116.48 (C_5; $^3J_{CF}$ = 3.50 Hz), 95.62 (C_3; $^1J_{CF}$ = 185.90 Hz), 30.76 (C_4; $^2J_{CF}$ = 50.04 Hz), 25.80 (C_7), 26.22 (C_1), 17.88 (C_8). MS (EI) : *m/z* = 144 (M^+ (2), 129 (8), 124 (55), 109 (100), 81 (70), 69 (85). – IR (KBr) ν 1675, 1049 (C–F) cm^{-1}. An unsuccessful route to **5** involved use of the 3-bromo derivative of **1** as an intermediate. Treatment of the mixture of **2** and **3** with N-bromosuccinimide or reaction of **1** with lithium diisopropylamide *cf.* [28] or trityllithium *cf.* [27], followed by reaction with N-bromosuccinimide in THF gave yields of 70 and 30%, respectively, of the 3-bromo compound, but attempts to convert the latter into **5** by treatment with fluoride or bifluoride ion led almost exclusively to elimination to form the conjugated diene.

(c) *4-Fluorolinalool* (**6**)

The fluoroketone **5** (0.50g, 3 mmol) in THF (2ml) was added to vinylmagnesium bromide (0.40 g, 3.6 mmol) in THF (20ml) at –25°C with rapid stirring. After warming to RT (1hr) the mixture was poured into aq. MeOH (20:80 v/v; 0.8 *l*) at 0 °C, extracted with Et_2O (3×25 ml), dried ($MgSO_4$) and after removal of solvent purified by HPLC on silica gel (Nucleosil, 5μm) with hexane/EtOAc (90:10 v/v) to give **6** yield 0.29 g, (40%), together with the 3-vinyl analogue of **6** (50%) and the nerol and geraniol isomers of **6** (10%). When aq. NH_4Cl was used to decompose the Grignard addition complex the yield of **6** was <2%. The purity (>99%) of **6** was assessed by analytical HPLC on silica gel with a variety of hexane/EtOAc and hexane/chloroform eluants. **6** had ^{1}H-NMR: δ 5.90 (q, 1H, H_2), 5.35 (d, 1H, H_1), 5.20 (m, 1H, H_6), 5.18 (d, 1H, H_1), 4.25 (m, $^2J_{HF}$ = 47.80Hz, 1H, H_4), 2.30 (m, 2H, H_5), 1.70 (s, 3H, H_{10}), 1.58 (s, 3H, H_8). – ^{13}C-NMR: δ 140.02 (C_2), 134.50 (C_7), 119.36 (C_6), 114.44 (C_1), 99.64 (C_4; $^1J_{CF}$ = 177 Hz), 74.69 (C_3; $^2J_{CF}$ = 21 Hz), 28.61 (C_5), 25.77 (C_9), 14.13 (C_8), 11.44 (C_{10}). – ^{19}F-NMR: δ –33.80(m). – MS (EI), *m/z* = 172 (M^+, 2), 129(8), 124(55), 109(100), 81(62), 69(78) – M^+(EI) = 172.1273, $C_{10}H_{17}OF$ requires 172.1264. $(M+1)^+$ (FAB, CI) = 173.1341; $C_{10}H_{18}OF$ requires 173.1342.

9-Fluorolinalool (9; 3-Fluoromethyl-7-methylocta-1,6-dien-3-ol) For general methods see Refs [29, 30].

(a) *exo-Trimethylsilyl enol ether of 6-methylhept-5-en-2-one* (**4**)

Ethyltrimethylsilyl acetate (7.05 g, 44 mmol) was stirred (10 min; –25°C) with tetrabutylammonium fluoride (TBAF; 4.01g,

15mmol) and **1** (5.00 g, 40mmol) was added over 5 mins. After further stirring (10 min), the mixture was allowed to warm to RT (1 hr), diluted with pentane (100ml), the TBAF removed by extraction with saturated aq. $NaHCO_3$ (5×50ml; 0 °C), the organic layer dried (($MgSO_4$) and the solvent removed. The product was chromatographed as for the (**2/3**) isomers but with hexane/EtOAc (70:30, v/v) as eluant to yield product (7.10 g; 98%) comprising a mixture of **4** and (**2** + **3**) in 93:7 proportion. Pure **4** was recovered by HPLC on silica gel (Nucleosil; 250×4.6mm) with hexane/EtOAc (99:1, v/v) when it eluted after **2** + **3**. – ^{1}H-NMR: δ 5.13 (m, 1H, H_5), 4.06 (m, 1H, H_{1E}), 4.05 (m, 1H, H_{1Z}), 2.05 (m, 2H, H_4), 1.69 (d, 3H, H_8), 1.62 (s, 3H, H_7), 0.21 (s, 9H, $Si-CH_3$). – ^{13}C NMR: δ 146.35 (C_2), 131.56 (C_6), 123.86 (C_5), 89.89 (C_1), 36.67 (C_3), 25.63 (C_7), 25.57 (C_4), 17.62 (C_8), 0.07 (Si–CH_3). – MS(EI), *m/z* = 198 (M^+, 8), 183(22), 155(30, 130(55), 115(57), 73(90), 69(100). The intense ions at 115 and 130 result from a *quasi* McLafferty rearrangement involving migration of H_5, [cf. 24].

(b) *1-Bromo-6-methylhept-5-en-2-one* (**7**)

The enol ether **4** (1.60 g, 8.0 mmol) was treated in the absence of solvent with N-bromosuccinimide (1.60 g, 9.0 nmol; 0.1 g aliquots) over 15 minutes at 4 °C and then stirred for two hours, following which the mixture was extracted with hexane (3 × 25ml). The extracts were concentrated to give a yellow oil which was purified on silica gel as before with hexane/EtOAc (83:15, v/v) to yield **7** (1.28 g; 78%). – ^{1}H-NMR: δ 5.05 (t, 1H, H_5), 4.61 (s, 2H, H_1), 2.63 (t, 2H, H_3), 2.25 (dt, 2H, H_4), 1.63 (d, 3H, H_8), 1.57 (s, 3H, H_7). – ^{13}C-NMR: δ 201.75 (C_2), 133.30 (C_6), 121.96 (C_5), 39.84 (C_1), 34.42 (C_3), 25.59 (C_7), 22.54 (C_4), 17.59 (C_8). – MS(EI), *m/z* = 204/6 (M^+, 10), 134/6(2), 125(90), 121/3(20), 69(100). **7** was also prepared by treatment of **1** with lithium diisopropylamide in THF followed by N-bromosuccinimide (yields 32, and 30%).

(c) *1-Fluoro-6-methylhept-5-en-2-one* (**8**)

The bromoketone **7** (0.54 g, 2.6 mol) was stirred with TBAF (2.05 g, 7.8 mmol) for 20 min at 40 °C in the absence of solvent, after which the product was extracted with MeOH (3×25ml), saturated aq. NaCl (50 ml, 0 °C) was added to the extracts and the mixture was extracted with hexane (100ml) and the organic layer washed twice with brine solution. The aqueous layer was then reextracted with hexane (3×25 ml), the combined organic fractions dried (K_2CO_3) and chromatographed on silica gel (70–230 mesh; 30×200mm) with hexane/EtOAc (85:15, v/v) to yield **8** (113 mg; 10%). – ^{1}H-NMR δ: 5.08 (m, 1H, H_5), 4.79 (d, $^2J_{HF}$ = 47.76 Hz, 2H, H_1), 2.57 (m, $^4J_{HF}$ = 2.57 Hz, 2H, H_3). 2.30 (dd, 2H, H_4), 1.68 (d, 3H, H_7), 1.62 (5, 3H, H_8). – ^{13}C-NMR: δ 133.37 (C_6),122.10 (C_5), 85.02 (C_1; $^1J_{CF}$ = 189.90 Hz), 38.44 (C_3), 31.59 (C_7), 22.66 (C_4), 14.12 (C_8). – MS (EI), *m/z* = 144 (M^+, 2), 111(10), 69(60), 41(100).

(d) *9-Fluorolinalool* (**9**)

8 was converted into **9** using the same procedure as for the preparation of **6** to yield a liquid (45 mg; 41%). – ^{1}H-NMR: δ 5.79 (m, 1H, H_2), 5.30 (dd, 1H, H_{1Z}), 5.20 (dd, 1H, H_{1E}), 4.10 (d, $^2J_{HF}$ = 53 Hz, 2H, C_1) 2.08 (m, 4H, $H_{4,5}$), 1.70 (s, 3H, H_{10}), 1.58 (s, 3H, H_8). – ^{13}C-NMR: δ 136.21 (C_1), 135.13 (C_7), 132.03 (C_2), 119.66 (C_8), 105 (C_9; $^1J_{CF}$ = 175 Hz), 92.14 (C_3), 33.78 (C_4), 29.45 (C_5), 14.55 (C_8), 11.05 (C_{10}). – ^{19}F-NMR: δ –36.20 (m). – MS(EI), *m/z* = 172 (M^+, 3), 154(29), 152(2), 139(40), 121(50), 111(70), 89(68), 71(28), 69(100). – M^+(EI) = 172.1276; $C_{10}H_{17}OF$ requires 172.1264. $(M+1)^+$ (FAB, CI) = 173.1336; $C_{10}H_{18}OF$ requires 173.1342.

Geranyl, Neryl and Linaloyl Fluorides (10 – 12)

The chlorides were prepared from the appropriate alcohols by a modified Corey–Kim procedure [31] in yields 83, 84 and 20%. respectively. Each chloride (3.90 g, 27 mmol) was then converted into the fluoride by stirring (6 hr; 40 °C) with tetrabutylammonium bifluoride (10.0 g; 36 mmol) in the absence of solvent. After the addition of sat. aq. NaCl (100ml) the products were extracted with pentane (5 × 25ml), dried ($MgSO_4$) and purified by chromatography on silica gel (70–230 mesh) with hexane/MeOH (85:15 v/v) followed by HPLC on silica gel (Nucleosil, 5 μm) with hexane/EtOAc (90:10, v/v). All products (>99% homogeneous by HPLC) were colourless mobile liquids.

(*a*) *1-Fluoro-3,7-dimethylocta-2E,6-diene* (**10**)

Yield 1.20 g (30%). – ^{1}H-NMR: δ 5.49 (m, $^3J_{HF}$ = 9.28 Hz, 1H, H_2), 5.10 (m,1H, H_6), 4.90 (d, $^2J_{HF}$ = 47.85 Hz, 2H, H_1), 2.10 (m, 4H, $H_{4,5}$), 1.72 (d, $^5J_{HF}$ = 4.73 Hz, 3H, H_9), 1.69 (d, 3H, H_{10}), 1.61 (d, 3H, H_8). – ^{13}C-NMR: δ 144.12 (C_3; $^3J_{CF}$ = 11.50 Hz), 131.92 (C_7), 123.59 (C_6), 118.90 (C_2; $^2J_{CF}$ = 16.90 Hz), 79.35 (C_1;$^1J_{CF}$ = 156.50 Hz), 39.51 (C_4; $^4J_{CF}$ = 2.60 Hz), 26.19 (C_5; $^5J_{CF}$ = 3.50 Hz), 25.64 (C_8), 17.65 (C_{10}), 16.43 (C_9; $^4J_{CF}$ = 3.10 Hz). – ^{19}F-NMR: δ –15.00 (m). – MS(E1) *m/z* = 156 (M^+,3), 141(3), 136(3), 113(10), 93(10), 69(10), 69(100). – M^+ (E1) = 156.1322; $C_{10}H_{17}F$ requires 156.1314; $(M+1)^+$ (FAB, CI) = 157.1396; $C_{10}H_{18}F$ requires 157.1392.

(*b*) *1-Fluoro-3,7-dimethylocta-2Z,6-diene* (**11**)

Yield 1.23 g (31%). – ^{1}H-NMR: δ 5.50 (m,$^3J_{HF}$ = 7.51 Hz, 1H, H_2), 5.08 (m, 1H, H_6), 4.86 (d, $^2J_{HF}$ = 47.88 Hz, 2H, H_1), 2.11 (m, 4H, $H_{4,5}$), 1.80 (d, $^5J_{HF}$ = 6.75 Hz, 3H, H_9), 1.69 (d, 3H, H_{10}), 1.60 (d, 3H, H_8). – ^{13}C-NMR δ: 144.25 (C_3; $^3J_{CF}$ = 11.50 Hz), 132.31 (C_7), 123.39 (C_6). 119.92 (C_2; $^2J_{CF}$ = 17.00 Hz), 79.03 (C_1; $^1J_{CF}$ = 1.56.21 Hz), 32.16 (C_4; $^4J_{CF}$ = 3.10 Hz), 26.72 (C_5; $^5J_{CF}$ = 3.30 Hz), 25.64 (C_8), 23.49 (C_9; $^4J_{CF}$ = 2.80 Hz), 17.61 (C_{10}). – ^{19}F-NMR: δ –15.01 (m).– MS(EI), *m/z* = 156 (M^+, 3), 141(3), 136(10), 93(10), 69(100), 41(80). M^+(EI) = 156.1316; $C_{10}H_{17}F$ requires 156.1314; $(M+1)^+$ (FAB, CI) = 157.1398; $C_{10}H_{18}F$ requires 157.1392.

(*c*) *3-Fluoro-3,7-dimethylocta-1,6-diene* (**12**)

Yield 0.42 g (11%); – ^{1}H-NMR: δ 5.89 (dq,$^3J_{HF}$ = 14.45, 1H, H_2), 5.46 (d, 1H, H_{1Z}), 5.30 (d, 1H, H_{1E}), 5.20 (m, 1H, H_6), 2.08 (m, 4H, $H_{4,5}$), 1.68 (d,3H, H_8), 1.60 (d, 3H, C_{10}), 1.40 (d, $^3J_{HF}$ = 21.67 Hz, 3H, H_9). – ^{13}C-NMR: δ 132.32 (C_7), 134.79 (C_1), 132.42 (C_2), 117.80 (C_6), 105 (C_3; $^1J_{CF}$ = 178.32 Hz), 40.27 (C_4; $^2J_{CF}$ = 28.17 Hz), 26.76 (C_5), 25.24 (C_9; $^2J_{CF}$ = 22.53 Hz), 13.24 (C_8), 12.42 (C_{10}). – ^{19}F NMR: δ –7.30 (m).– MS(E1), *m/z* = 156 (M^+, 21), 141 (3), 136 (36), 113 (10), 73 (2), 69 (100) 41 (80). – M^+(E1) = 156.1328; $C_{10}H_{17}F$

requires 156.1314. – $(M+1)^+$ (FAB, CI) = 157.1388; $C_{10}H_{17}F$ requires 157.1392.

References

[1] D. V. Banthorpe, Studies Nat. Prod. Chem. **7** (1990) 87
[2] J. J. M. Meyer, D. O'Hagan, Phytochemistry **31** (1992) 499
[3] J. J. M. Meyer, D. O'Hagan, Phytochemistry **31** (1992) 2699
[4] C. D. Poulter, J. C. Argyle, E. A. Mash, J. Biol. Chem. **253** (1978) 7227
[5] C. D. Poulter, P. L. Wiggins, T. L. Plummer, J. Org. Chem. **46** (1981) 1532
[6] H. Machleidt, R. Wessendorf, Liebigs Ann. Chem. **674** (1964) 1
[7] M. Schlosser, Tetrahedron **34** (1978) 3
[8] S. Cottens, M. Schlosser, Tetrahedron **44** (1978) 7127
[9] O. S. Park, H. J. Son, W. Y. Lee, Arch. Pharmacol. Res. **10** (1987) 239
[10] G. C. Briggs, G. R. Cayley, G. W. Dawson, D. C. Griffiths, E. D. M. Macaulay, J. A. Pickett, M. M. Pile, L. J. Wadhams, C. M. Woodcock, Pestic. Sci. **17** (1986) 141.
[11] S. Rozen, R. Filler, Tetrahedron **34** (1978) 3
[12] J. Mann, Chem. Soc. Rev. **16** (1987) 381
[13] S. T. Purrington, N. V. Lazaridis, C. L. Bumgardner, Tetrahedron Lett. **27** (1986) 2715
[14] S. Stavber, M. Zupan, J. Chem. Soc. Chem. Commun. **1981**, 795
[15] T. Umemoto, K. Kawada, K. Tomita, Tetrahedron Lett. **27** (1986) 4465
[16] T. Umemoto, E. Tomizawa, Bull. Chem. Soc. Jpn. **59** (1986) 3625
[17] R. D. Miller, D. R. McKean, Synth. Commun. **12** (1982) 319
[18] W. B. Smith, D. L. Devenport, A. M. Ihrig, J. Am. Chem. Soc. **94** (1972) 1959
[19] J. Hilton, L. H. Sutcliffe, Prog. Nucl. Magn. Reson. Spectrosc. **10** (1976) 27
[20] A. D. Cross, P. W. Landis, J. Am Chem. Soc. **84** (1962) 3784
[21] F. A. L. Anet, A. J. R. Bourn, P. Carter, S. Winstein, J. Am. Chem. Soc. **87** (1965) 5249
[22] J. W. Emsley, L. Phillips, V. Wray, Prog. Nucl. Magn. Reson. Spectrosc. **10** (1976) 83
[23] J. B. Grutzner, M. Jautelat, J. B. Dence, R. A. Smith, J. D. Roberts, J. Am. Chem. Soc. **92** (1970) 7107
[24] H. O. House, L. J. Czuba, M. Gall, H. D. Olmstead, J. Org. Chem. **34** (1969) 2324
[25] D. J. McAdoo, Org. Mass Spectrom. **23** (1988) 350
[26] G. Stork, P. F. Hudrlik, J. Am. Chem. Soc. **90** (1968) 4462
[27] P. Tomboulian, J. Org. Chem. **24** (1959) 229
[28] A. C. Cope,A. Trumbell, E. P. Trumbell, J. Am. Chem. Soc. **80** (1958) 2844
[29] E. Nakamura, M. Shimuzu, I. Kuwajima, Tetrahedron Lett. **1976**, 1699
[30] E. Nakamura, K. Hashimoto, I. Kuwajima, Tetrahedron Lett. **1978**, 2079
[31] E. J. Corey, C. U. Kim, M. Takeda, Tetrahedron Lett. **1972**, 4339

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