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THE ADDITION OF PHENYLSULFENYL CHLORIDE TO 5-METHYLENE-2-NORBORNENE SYNTHESIS OF TRICYCLO-*EKA*-SANTALOL

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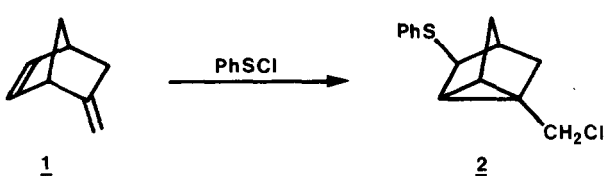
ABSTRACT : *Phenylsulfenyl chloride adds to 5-methylene-2-norbornene to give 1-chloromethyl-3-nortricyclyl phenyl sulfide in good yield. This reaction is used in a tricyclo-*eka*-santalol synthesis.*

The addition of sulfenyl chlorides to unsaturated compounds has long been known and has received considerable attention (2). The reaction with bridged bicyclic olefins has been reported. In the case of norbornadiene, no nortricyclenic products derived from homoconjugative addition were observed, when treated with p-toluenesulfenyl chloride (3). However a mixture of such products has been obtained when 2,4-dinitrophenylsulfenyl chloride in acetic acid was used (4). We wish to describe here the reaction of phenylsulfenyl chloride with 5-methylene-2-norbornene, a compound which is known to undergo homoconjugative additions with electrophilic reagents (5).

Freshly distilled phenylsulfenyl chloride (1 molar equivalent) (6) in methylene chloride was slowly added to a solution of 5-methylene-2-norbornene 1 in methylene chloride at 0°C. The orange color of the sulfenyl chloride was discharged immediately upon addition. After completion of the reaction, the crude NMR spectrum showed no vinylic protons and was consistent with structure 2. The yield was *ca* 85 %.



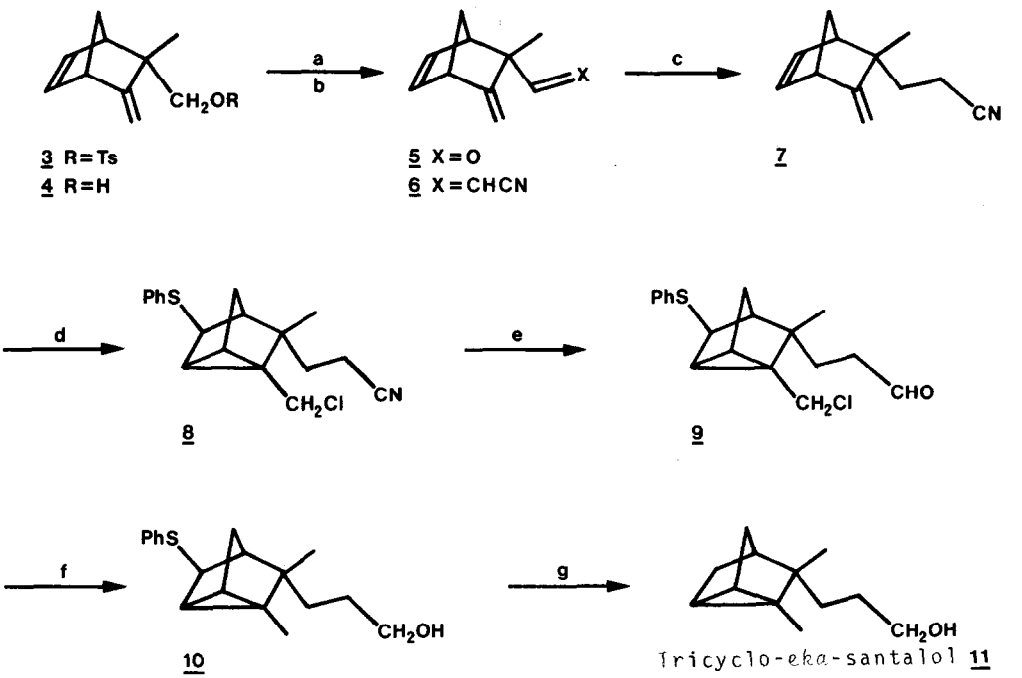
1 2

1-chloromethyl-3-nortricyclyl phenyl sulfide 2
IR (CCl_4) : 3070, 3000, 2960, 1590, 1485, 1445, 1290 cm^{-1}
NMR δ ($CDCl_3$) : 1,28-1,68 (m, 5H) ; 1,92 and 2,10 (2 broad s, 2H) ; 3,36 (broad s, 1H, >CH-S-) ; 3,78 (s, 2H, $-CH_2Cl$) ; 7,15-7,58 (m, 5H, Ph).
MS : M^+ = 250 and 252.

This reaction can be used in the synthesis of tricyclenic natural products (7). As an illustration of this approach, we report a total synthesis of tricyclo-*eka*-santalol, a minor constituent of East Indian sandalwood oil (*Santalum album* L) (8).

The bicyclic tosylate 3, obtained in four steps from citraconic anhydride and cyclopentadiene (5d), was converted to the alcohol 4 in 80 % yield by treatment with dimsyl sodium (sodium methylsulfinylmethide) (9) in dimethyl sulfoxide at 70°C for 3 hr. Collins oxidation (10) of the alcohol 4 afforded the aldehyde 5 (96 % yield). Subjection of the latter to a Wittig-Emmons reaction (11) using diethyl cyanomethylphosphonate in the presence of dimsyl sodium in dimethyl sulfoxide (9) gave the α,β-unsaturated nitrile 6 (94 % yield) which was selectively reduced to the nitrile 7 with magnesium in methanol (96 % yield) (12). The nitrile 7 was then treated with phenylsulfenyl chloride in methylene chloride at 0°C to afford the tricyclic compound 8 in 85 % yield. Reduction of 8 with diisobutylaluminum hydride in benzene furnished the aldehyde 9 (78 % yield) (13) which was reduced to compound 10 with lithium triethylborohydride in tetrahydrofuran (94 % yield) (14). Raney nickel desulfurization of 10 produced quantitatively the alcohol 11 which was identified (IR, NMR, MS) as tricyclo-*eka*-santalol (15).

Further synthetic work, taking advantage of the chloro - or of the phenylthio - substituent of the tricyclene system, is underway.



3 R=Ts
4 R=H

5 X=O
6 X=CHCN

7

8

9

10

Tricyclo-*eka*-santalol 11

a) Collins reagent (yield : 96 %); b) $(EtO)_2P(O)CHNaCN$, DMSO, (94 %); c) Mg, MeOH (96 %); d) PhSCl, CH_2Cl_2, 0°C (85 %); e) 1) $(i\text{-}Bu)_2AlH$, benzene; 2) 10 % H_2SO_4 (78 %); f) $LiBHEt_3$, THF (94 %); g) Raney nickel, EtOH (100 %).

Spectral and Physical Data

The IR spectra were determined in CCl_4 and the NMR spectra in $CDCl_3$.

Alcohol 4 : F = 98-99°C ; IR : 3640, 3420, 3070, 1655 cm^{-1} ; NMR δ : 1,30 (s, 3H,-CH_3) ; 3,30 (s, 2H,-CH_2-OH) ; 4,66 and 4,96 (2s, 2H, >C=CH_2) ; 6,18 (dAB, J = 5,5Hz, J' = 3Hz, 2H, -CH=CH-) ; MS : M^+ = 150.

Aldehyde 5 : IR : 3080, 2830, 2730, 1720, 1655 cm^{-1} ; NMR δ 1,32 (s, 3H, -CH_3) 4,72 and 5,08 (2s, 2H, >C=CH_2) ; 6,24 (dAB, J = 5,5Hz, J' = 3Hz, 2H, -CH=CH-); 9,18 (s, 1H,-CHO).

α,β-Unsaturated Nitrile 6 : IR : 3080, 2230, 1655, 1630 cm^{-1} ; NMR δ : 1,35 (s, 3H, -CH_3) ; 4,62 and 5,10 (2s, 2H, >C=CH_2) ; 5,30 (d, J = 16Hz, 1H, -CH=); 6,12 (m, 2H, -CH=CH-) ; 6,58 (d, J = 16Hz, 1H, =CH-CN).

Nitrile 7 : F = 44-45°C ; IR : 3070, 2250, 1655 cm^{-1} ; NMR δ : 1,22 (s, 3H, -CH_3) ; 2,20-2,50 (m, 2H, -CH_2CN) ; 4,65 and 4,98 (2s, 2H, >C=CH_2) ; 6,18 (m, 2H, -CH=CH-) ; MS : M^+ = 173.

Nitrile 8 : IR : 3070, 2260, 1590 cm^{-1} ; NMR δ : 1,04 (s, 3H, -CH_3) ; 3,55 (s, 1H, >CH-S-) ; 3,72 (AB, J = 12Hz, 2H, -CH_2Cl) ; 7,15-7,52 (m, 5H, Ph) ; MS : M^+ = 317 and 319.

Aldehyde 9 : IR : 3070, 2820, 2720, 1730, 1590 cm^{-1} ; NMR δ : 1,02 (s, 3H, CH_3) ; 3,58 (s, 1H, >CH-S-) ; 3,76 (s, 2H, -CH_2Cl) ; 7,15-7,55 (m, 5H, Ph) ; 9,75 (t, J = 1,5Hz, 1H, -CHO).

Alcohol 10 : IR : 3640, 3420, 3070, 1590 cm^{-1} ; NMR δ : 0,88 (s, 3H, -CH_3) ; 1,04 (s, 3H, -CH_3) ; 3,60 (m, 3H, -CH_2-OH and >CH-S-) ; 7,12-7,48 (m, 5H, Ph); MS : M^+ = 288.

Alcohol 11 : see ref. 8.

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