Tetrahedron Letters, Vol.27, No.7, pp 845-846, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

BIS (ARYLSULFONYL)METHANE : A VERSATILE SYNTHON IN PHEROMONE SYNTHESIS

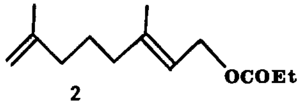
D. FERROUD; J.M. GAUDIN; J.P. GENET*

Laboratoire de Synthèse Organique et Organométallique
Associé au C.N.R.S.
Université Pierre et Marie Curie - 8 rue Cuvier - 75005 Paris(FRANCE).

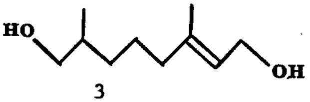
Abstract : (E)-9-oxo-2-decenoic acid (queen substance)(1);(E)-3,7-dimethyl-2,7-octadienyl propionate (2) and (E)-3,7-dimethyl-2-octene-1,8-diol (3)are easily synthesized via sequential alkylation of bis-(arylsulfonyl) methane 4 with 1,4-allylic substrates 7 and a second electrophile such as 4,4- ethylenedioxy)pentyl iodide and ethyl 2-methylallyl carbonate.

Queen substance, (E)-9-oxo-2 decenoic acid (1) ,is a well-known pheromone secreted by the queen honey bee. This compound inhibits ovary development in the worker bees and queen rearing within the colony.[1] (E)-3,7-dimethyl-2,7-octadienyl propionate (2),is a component of the San Jose Scale *Quadraspidiotus perniciosus* which is a serious worldwide insect pest.[2] (E)-3,7-Dimethyl-2-octene-1,8-diol (3) has been characterized as one of the major components of the secretion of the hairpencils of *Danaus chrysippus* (African Monarch butterfly).[3]

1

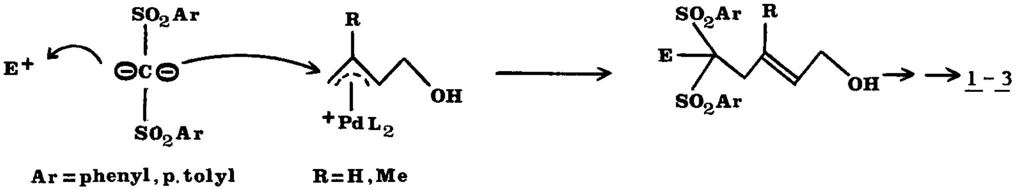


2



3

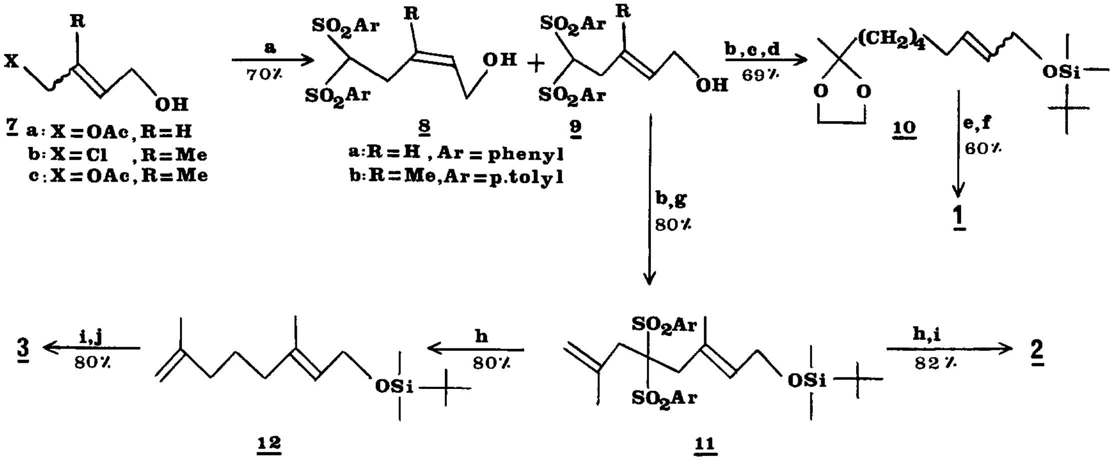
We have previously reported [4] that 1,4-bis allylic derivatives can be functionalized chemo and regioselectively in one allylic position via palladium η^3 -allyl intermediates such as 5. We now describe the application of this principle to syntheses of pheromones 1-3 .Sequential alkylation of bis-(arylsulfonyl)methane 4 with 5 and a second electrophile E^+ are the key steps of the synthetic approach to the carbon skeleton required. The choice of the two different electrophiles, 5 and E^+ , is the main problem for the successful utilisation of this strategy.



4 5 6

Synthesis of the queen bee substance 1 is outlined in scheme I. Palladium-catalyzed alkylation of the monoacetate of (Z)-2-butene-1,4-diol 7a with sodio derivatives of bis(phenylsulfonyl)methane gave a mixture of 9a and 8a : E/Z=83/17. Alcohols 8a and 9a were protected with t-butyldimethylsilyl chloride in DMF prior to a second alkylation with 4,4-ethylenedioxypentyl iodide to give 10. Hydrolysis of silyl and ketal groups (AcOH,THF,H_2O = 3:1:1) in 10 and oxidation with Jones reagent gave queen substance 1 (28% overall yield).[6,7]

Synthesis of 2 and 3 requires a properly functionalized C_5 isoprenoid unit such as 4-chloro-3-methyl-2-buten-1-ol (7b) or 4-acetoxy-3-methyl-2-buten-1-ol (7c).[8] (Scheme I). Alkylation of the bis(p.tolylsulfonyl)methane carbanion with a catalytic amount of Pd(dppe)$_2$ and either 7b or 7c (E/Z=70:30 mixture) gave 90-95 % of the (E) stereoisomer 9b.[9] Synthesis of the San Jose Scale pheromone[10] was readily achieved by protection of the hydroxyl group with t-BuMe$_2$SiCl in DMF and alkylation of the resulting silyl ether 12 under neutral conditions with Pd(dppe)$_2$ and ethyl 2-methylallyl carbonate to give 11 quantitatively.



Scheme I

(a) $NaCH(SO_2Ar)_2$; $Pd(dppe)_2$(5%),THF,2h(25°C) ;(b) $tBuMe_2SiCl$,Imidazole,DMF,2h(0°C) ;(c) $I-(CH_2)_3-\overset{\overset{\frown}{O\ O}}{C}-CH_3$ NaH(1.1eq)75h,(40°C) ; (d) Na/Hg,Na_2HPO_4,MeOH,0.5h(20°C) ; (e) AcOH/H_2O/THF,24h(25°C) ; (f) Jones reagent,10h(25°C) ; (g) $H_2C{=}C(CH_3)CH_2OCO_2Et$,$Pd(dppe)_2$,48h(25°C) ; (h) Na/Hg/MeOH,Na_2HPO_4,3h(-30°C) ;(i) $(nBu)_4N^+F^-$,THF,1.5h(25°C),C_2H_5COCl,NEt_3,2h(0°C) ; (j) 9-BBN,THF,0.5h(25°C),then H_2O_2/NaOH,2h(50°C).

Pheromone 2 was obtained in 46% yield from 7b by reductive cleavage with sodium amalgam, removal of the protecting group with $(n\ Bu)_4N^+\ F^-$ in THF,and acylation with propionyl chloride. Monarch butterfly pheromone 3 was obtained by hydroboration of the terminal double bond of 12,followed by deprotection of the primary hydroxyl group (35 % yield from 7b).[7]

In summary, we have demonstrated that bis-(arylsulfonyl) methyl alkylation using sequential introduction of various electrophiles is a simple and efficient process for the synthesis of natural products of biological interest.

References and notes

(1) a) A. Sannasi, and C.J. George, Nature, 237, 457 (1972) ; b) N.E. Gary, Science, 136, 773 (1962).

(2) M.J. Gieselmann, R.E. Rice, R.A. Jones and W.L. Roelofs, J.Chem.Ecol., 5, 891 (1979).

(3) a) J. Meinwald, W.R. Thompson, T. Eisner and D.F. Owen, Tetrahedron Lett., 3485 (1971) ; b) G. Bidan, J. Kossanyi, V. Meyer and J.P. Morizur, Tetrahedron, 33, 2193 (1977) ; c) T.Fuujisawa, T. Sato, T. Kawara and A. Noda, Tetrahedron Lett., 23, 3193 (1982) ; d) M. Julia and J.N. Verpeaux, Tetrahedron, 39, 3289 (1983) ; e) N.N. Joshi, V.R. Mandapur and M.S. Chadha, Ind.J.Chem., 238, (1982) ; e) P. Gramatica, G. Giardina, G. Speranza and P. Manitto, Chemistry Lett.in press.

(4) a) J.P. Genêt, F. Piau and J. Ficini, Tetrahedon Lett., 21, 3183, (1980) ; b) J.P. Genêt and F. Piau, J.Org.Chem., 46, 2414, (1981) ; e) J.E.Nyström, J.E. Bäckvall, J.Org.Chem., 48, 3947 (1983) ; f) J.P. Genêt, M. Balabane, J.E. Bäckvall and J.E. Nyström, Tetrahedron Lett., 24, 2745 (1983) ; d) J.E. Bäckvall, R.E. Nordberg and J.E.Nyström, Tetrahedron Lett., 23, 1617 (1982) ; J.Org.Chem., 48, 3947 (1983).

(5) For the first report of the use of bis (benzenesulfonyl) methane in palladium catalyzed reactions, see : B.M. Trost, T.R. Verhoeven and J.M. Fortunak, Tetrahedron Lett., 20, 2301 (1979).

(6) a) T. Fujisawa, T. Sato and T. Itoh, Chemistry Lett., 219, (1982) ; b) J. Villieras, M. Rambaud and M. Graff, Tetrahedron Lett., 26, 53 (1985) and references cited.

(7) All spectroscopic data IR; ^1H NMR, (80 MHz) of **1** - **3** were identical with those published. We thank J.P. Morizur for comparison of spectroscopic data with natural diol 3 (as its bis-trimethyldisilyl ether).

(8) Treatment of isoprene with NCS in acetic acid afforded 4-acetoxy-1-chloro-2-methyl-2-butene and 3-acetoxy-4-chloro-3methyl-1-butene in 60% and 12% yield, respectively : K. Sato, S. Inoue, S. Ota and Y. Fujita, J.Org.Chem., 37, 462 (1972). The 1,2 adduct is easily converted into the 1,4 isomer with $PdCl_2$ $(CH_3CN)_2$ in THF according to : L.E. Overmann and F.M. Knoll, Tetrahedron Lett., 20, 321 (1979). For the synthesis of 7c, see : M. Schmid, F. Gerber and G. Mirrth, Helv.Chim.Acta., 65, 3684 (1982).

(9) The two steroisomers were separated by chromatography on silica gel (eluent : ethyl acetate/hexane : 3/2).

9b (E) ^1H NMR (250 MHz, $CDCl_3$) : 7.88 ppm (d, 4H, J=8Hz) ; 7.42 (d, 4H, J=8Hz) ; 5.38 (t, 1H) ; 4.6 (t, 1H) ; 4.06 (t, 1H) ; 2.88 (d, 2H) ; 2.5 (s, 6H) ; 1.56 (s, 3H) ; IR (film) : 3700 to 3200, 2930, 1600, 1495, 1335 cm^{-1}.

8b (Z) ^1H NMR (250 MHz, $CDCl_3$) 7.88 ppm (d, 4H, J=8Hz) ; 7.42 (d, 4H, J=8Hz); 5.66 (t, 1H); 4.7 (t, 1H) ; 4.14 (d,2H) ; 3.02 (d, 2H) ; 2.5 (s, 6H) ; 1.64 (s,3H) ; IR (film) : 3700 to 3200, 2920, 1600, 1490, 1330 cm^{-1}.

(10) M. Alderdice, C. Spino and L. Weiler, Tetrahedron Lett., 25, 1643 (1984), and references cited.

(Received in France 15 December 1985)