Tetrahedron Letters,Vol.24,No.4,pp 405-408,1983 0040-4039/83/040405-04$03.00/0
Printed in Great Britain

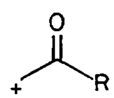
ALKENYL SULPHOXIDES AS PRECURSORS TO CYCLOPENTENONES AND PROSTANOID β-SIDE CHAINS

Peter J. Brown, D. Neville Jones,* M. Akram Khan, and Nicholas A. Meanwell

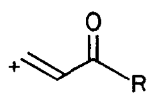
Department of Chemistry, The University, Sheffield S3 7HF

Summary Conjugate additions of enolate anions to α,β-unsaturated sulphoxides followed by sulphoxide-ketone transformations provided simple syntheses of cyclopentenones, and 2-phenylsulphinyloct-1-en-3-one provided a convenient electrophilic prostanoid β-side chain precursor.

Conjugate additions of stabilized carbanions,[1] organometallic compounds,[2] and heteroatomic nucleophiles[3] to α,β-unsaturated sulphoxides are finding increasing use in synthesis, but in contrast to the exploitation of ketene thioacetal monoxides in this role[4] the synthetic potential of the conversion of the sulphoxide group in the adducts into carbonyl functions has not been fully realized. In this letter we report that alkenyl sulphoxides, which are readily prepared from 1-alkynes,[5] provide synthons for the carbocations (A) and (B), which are useful respectively for the simple construction of 1,4-dicarbonyl compounds (and hence cyclopentenones)[6] and in providing an electrophilic precursor for the β-side chain in prostanoids.



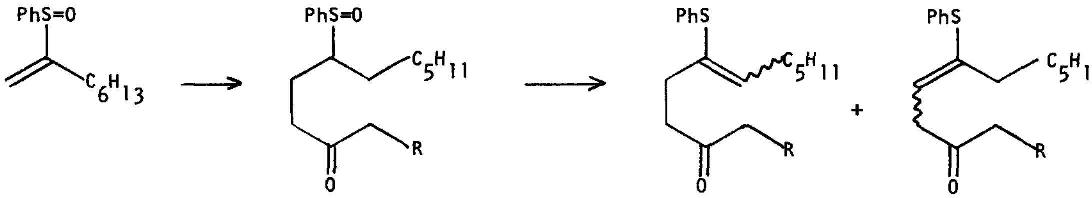
(A)



(B)

The lithio-enolate of acetone, generated by use of lithium tetramethylpiperidide in THF, reacted with 2-phenylsulphinyloct-1-ene (1)[5] (0.5 equiv.) at 20 °C for 12 h to give 5-phenylsulphinylundecan-2-one (2a) (63%).[7] Treatment of the keto sulphoxide (2a) with trifluoroacetic anhydride and pyridine in dichloromethane for 75 min gave, by way of a Pummerer rearrangement,[8] a mixture of keto alkenyl sulphides (3a)[9] and (4a) which was exposed to trifluoroacetic acid for 5 min at 20 °C to give undecan-2,5-dione (5a) (65% from 2a). Cyclization of this 1,4-diketone with aqueous ethanolic sodium hydroxide gave dihydrojasmone (6). This preparation of the perfume constituent compares favourably with numerous other methods in terms of convenience.[6]

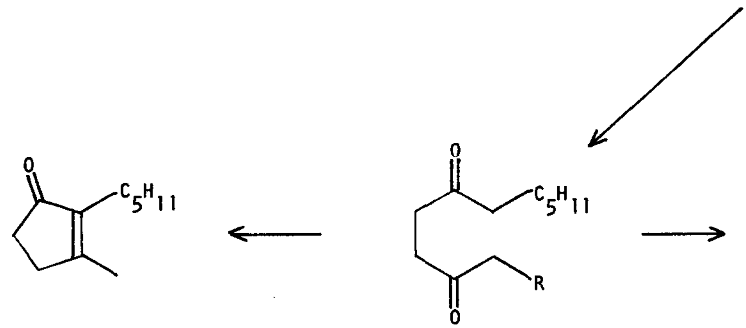
The lithio-sodio dianion from ethyl acetoacetate[10] added to 2-phenylsulphinyloct-1-ene (1) within 5 min at 0 °C in THF to give the adduct (2b) (89%), after the intermediate dianion (8) was quenched with aqueous ammonium chloride. Hydrolysis and decarboxylation of the adduct (2b) gave the keto sulphoxide (2a) (80%). When the intermediate dianion (8) was quenched with dimethyl disulphide the thioacetal monoxide derivative (9) was formed. That sulphenylation of the enolate part of the dianion (8) did not occur was expected.[11] The sensitive compound (9) was immiediately treated with trifluoroacetic acid in wet benzene for



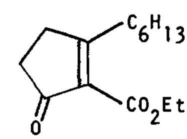
(1) (2) (3) (4)

a, R = H

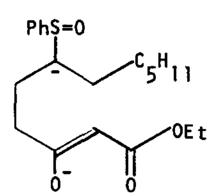
b, R = CO_2Et



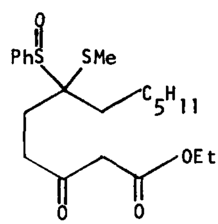
(6) (5)



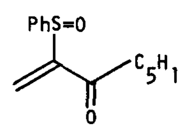
(7)



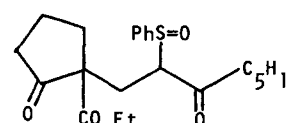
(8)



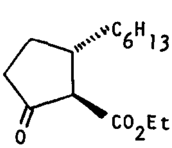
(9)



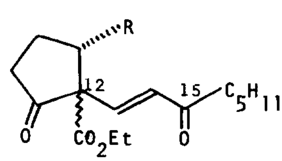
(10)



(11)



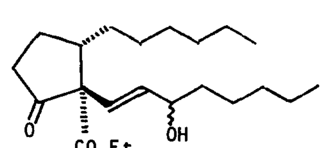
(12)



(13) a, R = H

b, R = C_6H_{13}, 12α-CO_2Et

c, R = C_6H_{13}, 12β-CO_2Et



(14) a, 15α-OH

b, 15β-OH

5 min to give the diketo ester (5b), which cyclized to 2-ethoxycarbonyl-3-hexylcyclopent-2-enone (7) on treatment of an ethereal solution for 10 min with dilute aqueous sodium hydroxide. In this way the alkenyl sulphoxide (1) was converted into the cyclopentenone derivative (7) rapidly in 62% yield after final chromatography, without isolation of intermediates. In an alternative procedure the adduct (2b) was treated with trifluoroacetic anhydride and pyridine in dichloromethane to give a mixture (83%) of isomeric unsaturated sulphides (3b) and (4b), and then with mercuric chloride and cadmium carbonate in aqueous acetonitrile[12] to effect hydrolysis to the product (5b) (65%).

The 'directed cyclization' of β,ε-diketo esters to give cyclopentenones [cf. (5b)→(7b)] has been exploited previously for prostanoid synthesis,[13] but the method described above for the construction of such diketo esters is significantly more concise.

Prompted by the reported biological activity of 9-deoxy- and 12-substituted prostaglandin analogues,[13 14] the cyclopentenone derivative (7) was converted into the prostanoid (14a), which is a constitutional isomer of 9-deoxy-PGD_1. This required an electrophilic precursor for the β-side chain, and in view of the inefficiency of the few precursors previously investigated,[15] we devised a new synthon, guided by the knowledge that γ-keto α,β-unsaturated sulphoxides are excellent Michael acceptors, and β-keto sulphoxides thermolyse readily and specifically to (E)-enones.[16]

Oxidation of 3-hydroxy-2-phenylsulphinyloct-1-ene[5] with Jones reagent provided 2-phenylsulphinyloct-1-en-3-one (10) (80%), the reactivity of which was confirmed by reaction with 2-ethoxycarbonylcyclopentanone (moist ether, catalytic trace K_2CO_3, 20 °C, 30 min) to give the adduct (11) (81%), which on thermolysis in boiling toluene for 30 min gave the (E)-enone 13a) (81%) [δ 6.94 and 6.16 (AB system, J_{AB} 16 Hz, vinyl protons)].

Reduction of the compound (7) with sodium cyanoborohydride[17] gave trans-2-ethoxycarbonyl-3-hexylcyclopentan-1-one (12) (54%), which on treatment with 2-phenylsulphinyloct-1-en-3-one (10) and subsequent thermolysis as before gave an inseparable mixture (89%) [ν_{max} ($CHCl_3$) 1755, 1730, 1670 and 1620 cm^{-1}] of 1-nor-11,15-dioxo-12α-ethoxycarbonylprost-13-ene (13b) [δ 7.05 and 6.19 (AB system, J_{AB} 15 Hz, vinyl protons)] and its 12β-isomer (13c) [δ 6.92 and 6.07 (AB system, J_{AB} 15 Hz)] in the ratio 8:1. Reduction of the mixture with sodium cyanoborohydride[18] gave a mixture of diastereoisomeric alcohols (73%) [ν_{max} ($CHCl_3$) 3590, 1750, and 1730 cm^{-1}] which slowly decomposed at room temperature, but from which the major constituents (14a) [δ 6.01 (1 H, d, J 15 Hz, -C*H*=CH-CH(OH)-), 5.62 (1 H, dd, J 7, 15 Hz, -CH=C*H*-CH(OH)-)] and (14b) [δ 5.97 (1 H, d, J 15 Hz), 5.65 (1 H, dd, J 7, 15 Hz)] were separated by chromatography. That these differed only in configuration at C-15, allocations of which depended only upon their relative chromatographic mobilities (cf, ref. 13), was confirmed by Jones oxidation of each isomer separately to the same enone (13b).

Reactions of 2-phenylsulphinyloct-1-en-3-one (10) with vinyl anions, and carbanions derived from sulphones, β-sulphonyl esters, and β-keto sulphides have been used to synthesize other prostanoids, and will be reported elsewhere. The ready availability of a variety of α,β-unsaturated sulphoxides from suitably substituted 1-alkynes,[5] and the demonstration that they add to simple enolates under aprotic conditions extends the potential synthetic utility of this class of compounds.

We thank the S.E.R.C. for Postgraduate Training Awards.

References and notes

1. G. Tsuchihashi, S. Mitamura, S. Inoue, and K. Ogura, Tetrahedron Lett., 1973, 323; G. Tsuchihashi, S. Mitamura, and K. Ogura, ibid., 1976, 855; K. Seki, T. Ohnuma, T. Oishi, and Y. Ban, ibid., 1975, 723; N. Ono, H. Miyake, A. Kamimura, N. Tsukui, and A. Kaji, ibid., 1982, 2957; G.A. Koppel and M.D. Kinnick, J. Chem. Soc., Chem. Commun., 1975, 473; N. Ono, I. Hamamoto, and A. Kaji, ibid., 1982, 821; D.H.R. Barton, I.H. Coates, P.G. Sammes, and C.M. Cooper, J. Chem. Soc., Perkin Trans. 1, 1974, 1459; R. Tanikaga, H. Sugihara, K. Tanaka, and A. Kaji, Synthesis, 1977, 299.
2. H. Sugihara, R. Tanikaga, K. Tanaka, and A. Kaji, Bull. Soc. Chem. Japan, 1978, **51**, 655; D.O. Spry, Tetrahedron Lett., 1980, 1293.
3. D.J. Abbott, S. Colonna, and C.J.M. Stirling, J. Chem. Soc., Perkin Trans. 1, 1976, 492; J.E. Mulvaney and R.A. Ottaviani, J. Polym. Sci., Polym. Chem. Ed., 1970, **8**, 2293; G. Tsuchihashi, S. Mitamura, and K. Ogura, Tetrahedron Lett., 1973, 2469; B.A. Trofimov, S.V. Amosova, N.K. Gusarova, and G.K. Musorin, Tetrahedron, 1982, **38**, 713.
4. J.L. Herrmann, G.R. Kieczykowski, R.F. Romanet, P.J. Wepplo, and R.H. Schlessinger, Tetrahedron Lett., 1973, 4711; J.L. Herrmann, G.R. Kieczykowski, R.F. Romanet, and R.H. Schlessinger, ibid., p. 4715; R.F. Romanet and R.H. Schlessinger, J. Am. Chem. Soc., 1974, **96**, 3701; G.R. Kieczykowski, C.S. Pogonowski, J. E. Richman, and R.H. Schlessinger, J. Org. Chem., 1977, **42**, 175; B. Cazes, C. Huynh, S. Julia, V. Ratovelomanana, and O. Ruel, J. Chem. Res. (S), 1978, 68.
5. R. Bell, P.D. Cottam, J. Davies, and D.N. Jones, J. Chem. Soc., Perkin Trans. 1, 1981, 2106.
6. R.A. Ellison, Synthesis, 1973, 397; T-L. Ho, Synth. Commun., 1977, **7**, 351; P-E. Sum and L. Weiler, Can. J. Chem., 1978, **56**, 2301, and references cited therein.
7. Analytical and spectroscopic data (NMR, IR, MS) for the new compounds were in accord with the structures allocated. All the compounds were racemic modifications.
8. H. Sugihara, R. Tanikaga, and A. Kaji, Synthesis, 1978, 881.
9. One of the isomers, (Z)-(3a), was obtained previously by a different method: R.C. Cookson and P.J. Parsons, J. Chem. Soc., Chem. Commun., 1976, 990.
10. S.N. Huckin and L. Weiler, Can. J. Chem., 1974, **52**, 2157.
11. M. Oki, W. Funakoshi, and A. Nakamura, Bull. Soc. Chem. Japan, 1971, **44**, 828; M.L. Quesada and R.H. Schlessinger, J. Org. Chem., 1978, **43**, 346.
12. E.J. Corey and R. Noyori, Tetrahedron Lett., 1970, 311.
13. N. Finch, J.J. Fitt, and I.H.S. Hsu, J. Org. Chem., 1975, **40**, 206.
14. P.A. Grieco, Y. Yokoyama, G.P. Withers, F.J. Okuniewicz, and C-L.J. Wang, J. Org. Chem., 1978, **43**, 4178, and references cited therein.
15. R.J.K. Taylor and I.T. Harrison, Tetrahedron Lett., 1976, 4793.
16. B.M. Trost, T.N. Salzmann, and K. Hiroi, J. Am. Chem. Soc., 1976, **98**, 4887.
17. R.O. Hutchins, D. Rotstein, N. Natale, J. Fanelli, and D. Dimmel, J. Org. Chem., 1976, **41**, 3328.
18. R.O. Hutchins and D. Kandasamy, J. Org. Chem., 1975, **40**, 2530.

(Received in UK 1 November 1982)