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SYNTHESIS AND STEREOSELECTIVE CHEMISTRY OF A NOVEL CYCLOPENTADIENYL SULPHONE

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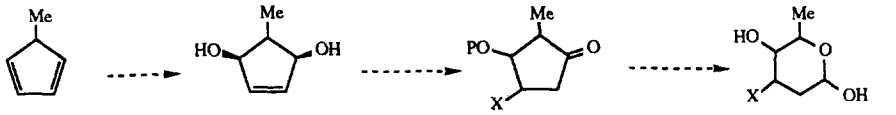
ABSTRACT: The synthesis of a novel cyclopentadienyl sulphone (3) has been achieved by two routes, one of which involves a previously unsuccessful alkylation of the sulphone carbanion (4), some preliminary chemistry of the new diene is also reported.

For some time we have been interested in the development of a general asymmetric route to the family of 6-deoxysugars, which would proceed *via* symmetrically substituted cyclopentenes such as (1), and ultimately to carbohydrate products using a Baeyer - Villiger ring expansion. This type of approach to carbohydrates is relatively unexplored,[1] and has the advantage of a high degree of flexibility, leading to several important targets, depending on the diastereomer of (1) used and the choice of groups introduced subsequently *via* a key asymmetric reaction (e.g. hydroboration), Scheme 1.

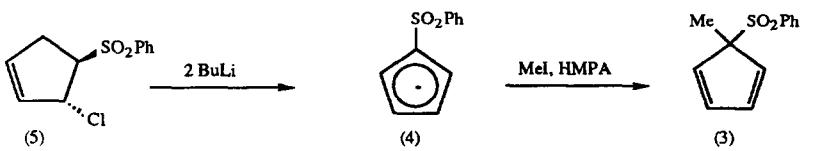


Scheme 1

e.g. X = NH_2 Daunosamine or Ristosamine
X = OH Olivose or Digitoxose

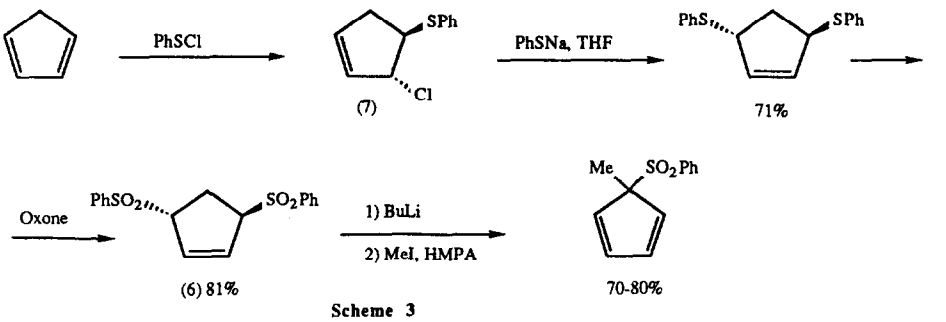
We expected that alkylation of cyclopentadiene to give the regio-unstable 5-methyl derivative (2),[2] and subsequent *in situ* singlet oxygen photooxygenation/endoperoxide workup would make available the desired symmetrical diol (1). In practice we found the preparation of workable quantities of product by this procedure extremely difficult,[3] and describe here a possible solution to this problem using a novel cyclopentadienyl sulphone.

Our hope was to replace the problematic 5-methylcyclopentadiene with a stable, storable equivalent, and to this end we chose to explore the chemistry of sulphone (3) which is potentially available by alkylation of the anion (4), Scheme 2.



Scheme 2

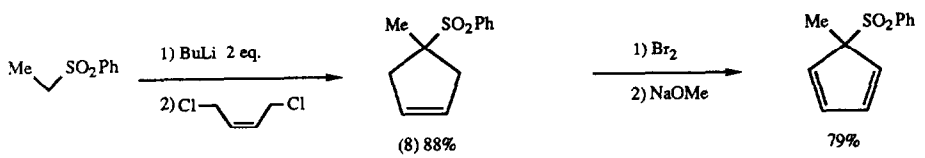
Previous attempts by Bridges and Fischer at alkylation of (4) generated from chlorosulphone (5) were largely unsuccessful, leading to poorly characterised dimeric products.[4] We have investigated an alternative approach to the sulphone (3) which is outlined in Scheme 3.



Scheme 3

Our synthesis of the *trans*-bis-sulphone (6) involved modification of the literature route,[5] and consisted of treating the chlorosulphide (7) with PhSNa in THF, followed by oxidation of the resulting bis-sulphide using oxone. Treatment of (6) in THF at -78°C with BuLi (2 eq.) followed by excess MeI/HMPA resulted in clean alkylation to give diene (3) as a white crystalline solid, m.p. 85-86°C, in 70-80% yield,[6] accompanied by small amounts of other isomers which were separated by chromatography. Attempts to alkylate the anion (4) with a range of other alkyl halides such as EtI or allyl bromide have so far been unsuccessful. We therefore decided to investigate an alternative route to dienes such as (3) in order to shorten the synthesis and to offer greater flexibility.

An improved three-step preparation of sulphone (3) was established using the reaction between the α,α-dianion of $PhSO_2Et$ and *cis*-1,4-dichlorobut-2-ene, Scheme 4.

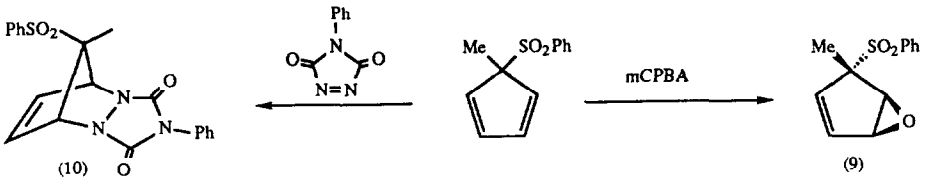


Scheme 4

Thus direct formation of the sulphonylcyclopentene (8), m.p.68-69°C was achieved in 88% yield by treatment of $PhSO_2Et$ with BuLi (2 eq.) in THF (-78 up to 0°C) followed by addition of the dichloride.[7] Subsequent reaction of (8) with bromine gave a dibromide, which was then treated with NaOMe (3 eq.) in THF to afford the diene (3) in 79% yield, identical in all respects to the product obtained by alkylation of (4).

We have subsequently investigated some of the chemistry of diene (3) which appears to be stable indefinitely if stored in a refrigerator. Disappointingly we have, to date, been unable to carry out successful singlet oxygen reactions with (3), which appears to be exceptionally unreactive even over prolonged reaction times.

However, epoxidation of (3) with mCPBA in CH_2Cl_2 at RT proceeded quantitatively to give a single mono-epoxide (9) with the stereochemistry shown.[8]



Further elaboration of this epoxide intermediate to give products suitable for carbohydrate synthesis is underway and will be reported in due course. Similarly, treatment of diene (3) in CH_2Cl_2 with a solution of 4-phenyl-1,2,4-triazoline-3,5-dione in CH_2Cl_2 resulted in immediate reaction, and the precipitation of the expected adduct (10), m.p. 190-192°C in 70% yield.[9] Again only one product was detected; the indicated stereochemistry is that expected by analogy with the epoxidation result, but has not yet been proven. We attribute the high degree of stereoselectivity in both these reactions to highly effective shielding of one face of the diene by the bulky sulphone group. Reaction of the diene with other, less reactive dienophiles under thermal conditions has been less rewarding, where isomerisation and dimerisation of the diene become predominant pathways.

Further study of dienes related to (3) and the products derived from them is underway, including the removal of the sulphone group, which is important if these compounds are to serve as stable equivalents of 5-alkylcyclopentadienes.

Acknowledgements

We would like to thank the SERC for financial support.

References and Footnotes

1. A Baeyer Villiger route to a deoxyaminosugar has recently appeared, see T. Kametani, Y. Suzuki, C. Ban, K. Kanada, and T. Honda, Heterocycles, 1987, 26, 1789, see also G.

Grethe, J.Sereno, T. H. Williams, and M. R. Uskokovic, J. Org. Chem., 1983, 48, 5315.

2. The *in situ* hydroboration of such 5 alkylcyclopentadienes is well known, see J. J. Partridge, N. K. Chadha, and M. R. Uskokovic, J. Am. Chem. Soc., 1973, 95, 532. Photooxygenation procedures are also known, see G. V. Bindu Madhaven and J. C. Martin, J. Org. Chem., 1986, 51, 1287, and references therein.
3. Even with bulky groups at the 5-position these compounds are known to be very difficult to handle, and the alkylation step usually necessitates the use of cyclopentadienyl thallium. With only a methyl group at the 5-position the volatility and thermal instability of the cyclopentadiene and its derived endoperoxide, coupled with the water solubility of the final diol product make the procedure even more difficult.
4. A. J. Bridges and J. W. Fischer, J. Chem. Soc., Perkin Trans. 1, 1983, 2359.
5. K. Hartke and H-U. Gleim, Justus Liebigs Ann. Chem., 1976, 716.
6. ^{1}H n.m.r. (250 MHz, $CDCl_3$) δ 1.70 (3H, s, CH_3), 6.14 (2H, m), 6.34 (2H, m), 7.25-7.78 (5H, m, C_6H_5). The olefinic region of the spectrum appears as a typical AA'BB' system. Found for (3): $(M+NH_4)^+$, 238.09047; C, 65.5; H, 5.69. $C_{12}H_{12}O_2S$ requires $(M+NH_4)^+$, 238.09018; C, 65.43; H, 5.49%.
7. For other cyclisations using α,α-dianions of sulphones see J. J. Eisch, S. K. Dua, and M. Behrooz, J. Org. Chem., 1985, 50, 3674; J. Vollhardt, H-J. Gais, and K. L. Lukas, Angew. Chem. Int. Ed. Engl., 1985, 24, 610. For similar annelations involving sulphones see A. F. Cunningham and E. P. Kundig, J. Org. Chem., 1988, 53, 1823; M. H. Nantz, X. Radisson, and P. L. Fuchs, Synth. Commun., 1987, 17, 55.
8. The relative stereochemistry indicated has been confirmed by an X-ray determination, for which we thank Prof. M. B. Hursthouse, Queen Mary College. Data for (9): ^{1}H n.m.r. (250 MHz, $CDCl_3$) δ 1.66 (3H, s), 3.56 (1H, br.m), 4.10 (1H, t, J 2.5Hz), 5.77 (1H, dt, J 2.5, 5Hz), 6.26 (1H, br.d, J 5Hz), 7.49-7.90 (5H, m). Found: $(M+NH_4)^+$, 254.08538; C, 60.9; H, 5.2. $C_{12}H_{12}O_3S$ requires $(M+NH_4)^+$, 254.08509; C, 61.0; H, 5.1%.
9. Data for (10): ^{1}H n.m.r.(250 MHz, $CDCl_3$) δ 1.70 (3H, s), 4.92 (2H, t, J 2Hz), 6.35 (2H, t, J 2Hz), 7.28-7.82 (10H, m). Found: C, 60.54; H, 4.51; N, 10.47. $C_{20}H_{17}N_3O_4S$ requires C, 60.75; H, 4.33; N, 10.63%.

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