Serendipitous Synthesis of Diaxial 2,4-Diphenyl-3,7-dioxabicyclo[3.3.0]octane

Andrew Pelter^a, Robert S. Ward^a, Peter Collins^a, Revuru Venkateswarlu^b and Chakicherla Kamakshi^b

^{a)}Chemistry Department, University of Swansea, Singleton Park, Swansea SA2 8PP, U.K. ^{b)}Chemistry Department, Andhra University Postgraduate Centre, Nuzvid, 521201, India.

Abstract. Reduction of *cis*-3,4-dibenzoyltetrahydrofuran with BMS, very surprisingly yields diaxial 2,4-diphenyl-3,7-dioxabicyclo[3.3.0]octane in a reaction that contrasts sharply with processes involving equilibrating benzylic carbocations which yield the diequatorial isomer.

2,6-Diaryl-3,7-dioxabicyclo[3.3.0]octane lignans exist as diequatorial (1), equatorial-axial (2) and diaxial isomers (3).^{1,2} Equilibration, under acid conditions, *via* benzylic-carbocations, produces mixtures of (1), (2) and (3) containing less than 1% of the hindered diaxial isomers (3). Nevertheless, diaxial compounds do occur as natural products.^{1,2}



The chemistry of compounds of the 2,4-diaryl series is much less well documented. We have previously^{3,4} reported the reactions shown in equation (1), in which the cyclisation of diols (4) leads to the diequatorial isomer (5) as the only isolable product. Hence, as expected, this must be the thermodynamically favoured product of a process involving benzylic cations.



4361

We now report a second route (Scheme 1) leading either to (5) or the diaxial isomer (9).



Compound (6) was readily obtained by the photochemical cycloaddition of diphenylethyne so maleic anhydride,⁵ followed by hydrolysis. Reduction to the diol, m.p. 145°C was followed by cyclisation to yield (7), m.p. 60°C. Oxidative cleavage by $OsO_4/NaIO_4$ or ozone then gave the *cis*-diketone (8), m.p. 144°C, as a single isomer.

Reduction of (8) with sodium borohydride gave a mixture of diastereoisometric diols, which with methanolic HCl gave (5). This confirms that (5) is the thermodynamically favoured product.

In order to avoid basic conditions and possible epimerisations α - to the carbonyl groups, the diketone (8) was reduced with BMS in THF, followed by addition of methanol to destroy excess borane. This produced directly a sole product, m.p. 154°C (75% isolated yield) (m/z 266). Though clearly different from (5), its spectra (Table 1) indicated that it belonged to the cyclised series and that it was a symmetrical isomer of (5). The ¹³C shifts indicated that the phenyl groups we e axial.¹ The X-ray structure⁶ confirmed that the product was indeed the diaxial 2,4-diphenyl-3,7-dioxabicyclo[3.3.0]octane (9) (Figure). No trace of (5) was evidenced.



Figure

Table 1. ¹H and ¹³C nmr spectra of (5) and (9)*

	(5)	(9)		(5)	(9)
H - 1/5	2.87m	(3.28m(4H)	C - 1/5	55.44	49.91
H - 6/8	(3.50dd(8,5) (3.98d(8)	(3.45m(2H)	C - 6/8 C - 2/4	71.53 87.15	70.28 82.04
H - 2/4	4.54d(8)	5.14d(4)	Arom	141. 20	138.86
Arom.	7.2 - 7.5(m)	7.2 - 7.5(m)		128.58 127.87 126.17	128.33 127.30 126.09

CDCl₁ solutions.

This reaction was surprising in two ways: (i) a cyclised product was obtained directly and (ii) only one product, the one least favoured by carbocation equilibration processes, was isolated in excellent yield. A possible explanation for these unprecedented findings is presented below.

Models indicate that one favoured conformation of diketone (8) is (10), in which at least one carbonyl group is almost perpendicular to the five-membered ring. Addition of borane from the side away from the ring then gives (11) (Scheme 2).



It is known^{7,8} that benzylic carbonyl groups can be directly reduced by borane to benzyl groups, via hydride addition to benzylic carbocations produced as in equation (2).

$$ArCOR \rightarrow ArCH(OBH_2)R \rightarrow ArCHR \xrightarrow{+} H \rightarrow ArCH_2R$$
 (2)

In the case of (11), the "OBH₂" leaving group can be displaced in an S_N^2 type reaction by the adjacent carbonyl group to give cyclised ion (12), which then accepts hydride from its least hindered side to yield (9) (Scheme 3).



The ramifications of this process are being explored. Clearly it offers a simple entrance to difficultly accessible diaxial lignans of the 2,4-diaryl series, and possibly to other compounds.

Acknowledgement. We are grateful to Prof. M. Hursthouse (University College, Cardiff) for the X-ray determination.

References.

- 1. Pelter, A.; Ward, R. S. in "Chemistry of Lignans", Andhra University Press, Waltair, 1978 (Editor C. B. S. Rao).
- 2. Ayres, D. C.; Loike J. D., "Lignans", Cambridge University Press, Cambridge 1990.
- 3. Pelter, A.; Ward, R. S.; Watson, D. J.; Murray-Rust, P; Murray-Rust, J, Tetrahedron Lett., 1978, 19, 1509.
- 4. Pelter, A.; Ward, R. S.; Watson, D. J.; I. R. Jack, J. Chem. Soc. Perkin 1, 1982, 183.
- 5. Maier, G.; Hurton, H. G.; Sayrac, T, Angew. Chem., Int. Ed. Engl., 1976, 15, 226.
- 6. X-ray determination by Professor M. Hursthouse, SERC X-Ray Service, now at University College, Cardiff.
- 7. Kikugawa, Y., Chem. Pharm. Bull., 1979, 27, 2405.
- 8. Lane, C. F., Chem. Rev., 1976, 76, 773.

(Received in UK 1 May 1992)