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3,5-DIOXA-4-PHENYLTRICYCLO[5.1.0.0^{4,8}]OCTANE: A NOVEL HETEROCYCLIC CAGED SYSTEM

Bert Fraser-Reid, R. Li-jiun Sun and John T. Brewer

Department of Chemistry, University of Waterloo, Waterloo, Ontario, Canada.

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The tendency of carbenes to insert into sp^3 hybridised bonds has been utilised for construction of several caged molecules which, because of their rigid structures, command the attention of chemists interested in torsional strain and unusual reactivity associated therewith (1). This communication reports the construction of the tricyclic system, 3,5-dioxatricyclo[5.1.0.0^{4,8}]octane, whose novel skeleton immediately arouses interest since it is a structural heterocyclic equivalent of the highly reactive molecule semibullvalene (2). Of added significance is the fact that the new system furnishes a route to phenylcyclopropylketones, a class of molecules which have featured in recent studies on enolisation (3) and antiaromaticity (4). In this regard it is specially noteworthy that the ketones afforded are the thermodynamically unfavourable all cis-isomers, not readily obtainable by existing routes (5).

Treatment of cis-2-butene-1,4-diol with benzaldehyde and zinc chloride gave the viscous benzylidene derivative, 1,3-dioxa-2-phenyl-5-cycloheptene,(6) which reacted with dichlorocarbene (7) to yield in a highly selective manner 8,8-dichloro-4-phenyl-3,5-dioxabicyclo-[5.1.0]octane, **2**, m.p. 114-114.5°C. By analogy with the situation prevailing in cycloheptene, compound **1** should exist in a chair conformation (8) and of the various possibilities, the preferred conformer should be the one bearing the phenyl group in equatorial orientation. Suitably located oxygen atoms on occasions provide a powerful influence on the direction from which a carbene approaches a site of unsaturation (9). Comparable influence by the oxygen atoms of **1** should guide dichlorocarbene to the underside of the molecule thereby producing the anti-isomer, i.e. the 4-epimer of **2**. Conventional spectrometric techniques are incapable of distinguishing between these epimers, but the results to be disclosed below favour the syn-isomer (**2**) (10).

A solution of the dichloride (**2**) in ether was treated with a five fold excess of n-butyl lithium at -80°C for twenty hours and the reaction product (45% yield; m.p. 113-114.5) was isolated in the conventional manner. The infrared spectra showed absorptions at 4.71μ, 3.26μ, 2.26μ, and 1.62μ diagnostic of a cyclopropyl ring (11). The paramount feature in the

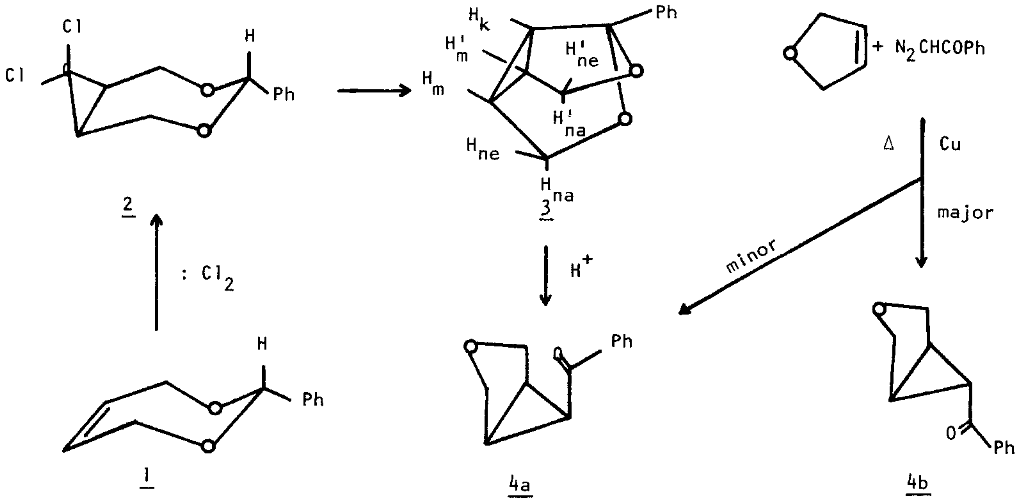

TABLE I

NMR PARAMETERS OF 3,5-DIOXA-4-PHENYLTRICYCLO[5.1.0.0^{4,8}] OCTANE IN CDCl$_3$ ^{a,b}

CHEMICAL SHIFTS^c(τ)			
H_k	H_m, H'_m	H_{ne}, H'_{ne}	H_{na}, H'_{na}
(H_8)	(H_1&H_7)	(H_2&H_6 equatorial)	(H_2&H_6 axial)
7.23	7.88	5.73	5.96
$J_{k,m(k,m')}=7.5$	$J_{k,m(k,m')}=7.5$	$J_{ne,m'(n'e,m)}=2.1$	$J_{na,m(n'a,m')}=0.0$
	$J_{m,n'e(m',ne)}=2.1$	$J_{ne,m(n'e,m)}=3.2$	$J_{na,ne(n'a,n'e)}=10.0$
	$J_{m,na}\,(m',n'a)=0.0$	$J_{ne,na(n'e,n'a)}=10.0$	
	$J_{m,ne}\,(m',ne)=3.2$		

a Spectra were run on a Varian 100MHz spectrometer.

b Coupling constants determined by double irradiation experiments.

c From internal TMS

spectrum of the substance in $CDCl_3$ was the absence of a signal around τ4.5 ascribable to the methine proton of the benzylidene moiety (12). The analytical data (6) indicated that the hydrogen content of 2 had been preserved during the reaction, and therefore, that the methine proton had been transferred to a different location in the new molecule. Information derived from the 100 MHz nmr spectrum of the material is presented in Table 1. Among the features are a triplet (1H) at τ7.23 and a multiplet at τ7.88 reminiscent of resonances found in semibullvalene (2), its dihydro (13a) and tetrahydro (13b) derivatives, all carbocyclic analogues of 3. The chemical shifts of the various protons and the coupling constants deduced from double irradiation experiments are in complete accordance with 3 as the structure of the reaction products (14). Independent affirmation was supplied by the mass spectra which showed principal fragments at m/e (relative intensity): 188 (4.5), 187(7.8), 157(100), 105(54), 77(50), 53(12), 39(17), 29(26) and 26(54). Although detailed discussion of the spectrum is reserved for the full paper, it may be noted here that the impressive pyrillium ion $[C_5H_4O\text{-}Ph]^+$ (m/e, 157) derivable from 3 by loss of H followed by expulsion of CH_2O forms the base peak of the spectrum.

A sample of 3 was warmed with dilute aqueous hydrochloric acid until it had just dissolved and the hydrolysate was extracted with chloroform. An oil was thereby obtained whose spectral properties (λ_{max}, mμ(ε) 244 (11,273), 278(791) in ethanol; λ_{max} mμ 3.27,5.92,9.77 in $CHCl_3$) were diagnostic of a phenylcyclopropylketone (11,15) and its elemental composition (m/e calcd. for $C_{12}H_{12}O_2$: 188.083724; found 188.083758) permitted elaboration to the structure 4 which by virtue of its genesis is necessarily the all cis-isomer, 4a. For a synthetic route which is subject to the constraints of thermodynamic factors, the major product ought to be 4b since it contains fewer serious non-bonded interactions than the isomer 4a. Accordingly, copper catalysed reaction (16) of diazoacetophenone and 2,5-dihydrofuran yielded material which contained two components in the ratio 8.3:1 (g.l.p.c. analysis). These were separated by preparative layer chromatography after which the major component judged to be 4b, crystallised (m.p. 62-63.5°C, M^+, 188). The minor component was an oil whose infrared, mass spectra and retention time on g.l.p.c. (10% S.E.-30 Silicone G.R. 10'x 1/4") were identical with the product from hydrolysis of 3.

The structure of 3 is therefore secure and its degradation to the otherwise inaccessible all cis-cyclopropylphenylketone (4a) has been demonstrated. Of special significance to those interested in enolisation of these ketones is the fact that the readily attainable 8-deuterio analogue of 3 (17) possesses the isotope at the site destined to become enolisable in the resulting ketone.

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