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ACETOLYSIS OF *trans*-1,2-DIBROMOBENZOCYCLOBUTENE

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Abstract—Acetolysis of *trans*-1,2-dibromobenzocyclobutene (I) in the presence or absence of water gave *cis*-diol monoacetate (II) and *trans*-diacetate (VI), respectively. The corresponding *cis*- and *trans*-diols were obtained and NMR spectra of these 1,2-disubstituted benzocyclobutenes were recorded.

THE inertness of *trans*-1,2-dibromobenzocyclobutene (I) to solvolysis has been mentioned by Cava and Napier,[1] but crystalline *cis*-1-acetoxy-2-hydroxybenzocyclobutene (II) has now been obtained in 64% yield by the action of silver acetate on I in acetic acid containing 4% water.[2] Hydrolysis of II proceeded smoothly to give crystalline *cis*-1,2-dihydroxybenzocyclobutene (III). The *cis*-diol afforded an acetonide (IV) and a diacetate (V) which was also prepared by acetylation of the monoacetate (II). The same *cis*-diol and its dinitrate have very recently been obtained by Cava and others.[3]

When the acetolysis of I was carried out in a mixture of acetic acid and acetic anhydride in the presence of silver acetate, *trans*-1,2-diacetoxybenzocyclobutene (VI) was obtained under this anhydrous condition in 82% yield. Hydrolysis of VI gave crystalline *trans*-diol (VII), which was remarkably unstable upon heating and easily changed into a resinous material in contrast to the *cis*-isomer. The nature of this amorphous product is not yet certain.[4]

This highly stereospecific solvolysis of the dibromide (I) is best explained by the accompanying figures, involving cyclic bromonium (VIII) and acetoxonium (IX) ions.[2]

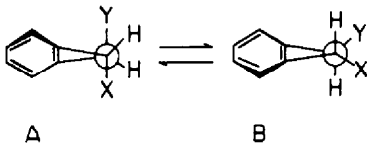
The possible conformational equilibrium of A and B forms of *trans*-1,2-disubstituted benzocyclobutenes, which is based on the assumption of a non-planar

[1] [a] M. P. Cava and D. R. Napier, *J. Amer. Chem. Soc.* **79**, 1701 (1957); [b] F. R. Jensen and W. E. Coleman, *J. Org. Chem.* **23**, 869 (1958).

[2] For a review of stereospecific displacements involving neighbouring group participation as studied by S. Winstein *et al.*, see [a] W. Lwowski, *Angew. Chem.* **70**, 483 (1958); [b] F. D. Gunstone in *Advances in Organic Chemistry* (Edited by R. A. Raphael, E. C. Taylor and H. Wynberg) Vol. I, p. 117. Interscience, New York (1960).

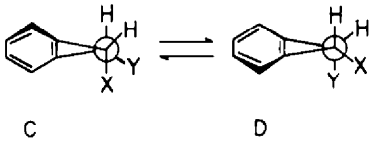
[3] M. P. Cava, D. R. Napier and R. J. Pohl, *J. Amer. Chem. Soc.* **85**, 2076 (1963); M. P. Cava, R. J. Pohl and M. J. Mitchell, *Ibid.* **85**, 2080 (1963).

[4] The IR spectrum of the amorphous polymer was fairly similar to the one of *trans*-diol (VII) and showed neither a carbonyl nor an olefinic band. According to this literature,[3] treatment of the *trans*-diol dinitrate with hydrazine in the presence of palladium gave a brown *gum*, while the same reaction with *cis*-diol dinitrate afforded the desired *cis*-diol (III).



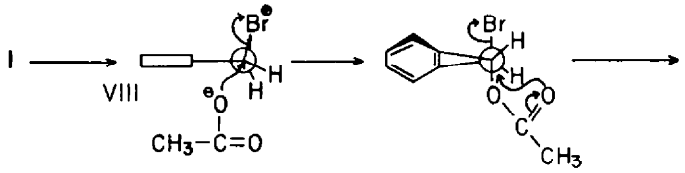
A B

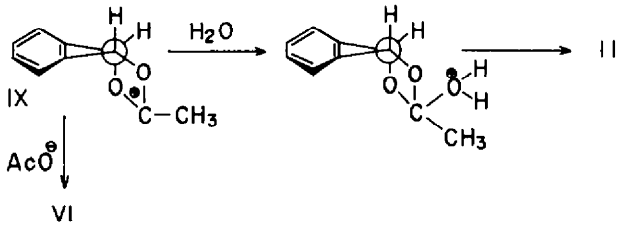
I X=Y=Br
VI X=Y=OCOCH$_3$
VII X=Y=OH



C D

II X=OH, Y=OCOCH$_3$
III X=Y=OH
IV X, Y= -O-C(CH$_3$)$_2$-O-
V X=Y=OCOCH$_3$





VI

cyclobutene ring,[5] has attracted our attention. Blomquist and Bottomley[6] apparently favoured the A conformation with "axial" substituents for *trans*-1-methyl-2-phenylbenzocyclobutene (A, X = methyl, Y = phenyl) on the basis of the coupling constant of 1,2-protons and the dihedral angle derived by applying the Karplus equation[7] to this system. In order to obtain further information on this conformational problem, NMR spectra of the compounds prepared were examined. The results are summarized in Table 1.

Although interpretation of the conformational equilibrium (A $\rightleftharpoons$ B or C $\rightleftharpoons$ D) based on the data is not possible, some points of interest may be mentioned. The methine proton of *trans*-1,2-disubstituted benzocyclobutenes, including those previously described,[6,8] appear at higher fields than those of the corresponding *cis*-isomers. The conformational exchange of *cis*-compounds (C $\rightleftharpoons$ D) does not affect the equal population of "axial" and "equatorial" protons, while aliphatic

[5] For the puckering of cyclobutane and trimethylene oxide rings, see [a] M. Takahashi, D. R. Davis and J. D. Roberts, *J. Amer. Chem. Soc.* **84**, 2935 (1962); [b] A. Danti, W. J. Lafferty, and R. C. Lord, *J. Chem. Phys.* **33**, 294 (1960); [c] S. I. Chan, J. Zinn, J. Fernandez, and W. D. Gwinn, *Ibid.* **33**, 1643 (1960). A planar cyclobutanone structure has, however, been claimed by A. Bauder, F. Tank and Hs. H. Günthard, *Helv. Chim. Acta* **46**, 1453 (1963).

[6] A. T. Blomquist and C. G. Bottomley, *Liebigs Ann.* **653**, 67 (1962).

[7] M. Karplus, *J. Chem. Phys.* **30**, 11 (1959).

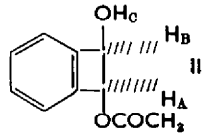
[8] L. A. Carpino, *J. Amer. Chem. Soc.* **84**, 2196 (1962).

protons of *trans*-disubstituted compounds are either both "equatorial" (A) or both "axial" (B). If the A conformation is the preferred one, as assumed by Blomquist and Bottomley,[6] this would favour the population of "diequatorial" protons. The conclusion might be that "equatorial" protons of benzocyclobutenes are *more shielded* than "axial" ones in contrast to the case of cyclohexane derivatives.[9,10]

TABLE 1. NMR DATA OF 1,2-DISUBSTITUTED BENZOCYCLOBUTENES[a]

Compound X	Y	δ-$(CH_3)_4Si$ p.p.m.	Wt.	Splitting	Assignment
Br	Br	7·4–7·0	2	A_2B_2	aromatic
trans (I)		5·32	1	singlet	methine
Br	Br	7·4–7·0	2	A_2B_2	aromatic
cis[b]		5·70	1	singlet	methine
AcO	AcO	7·27	2	singlet	aromatic
trans (VI)		5·67	1	singlet	methine
		2·04	3	singlet	acetoxy
AcO	AcO	7·27	2	singlet	aromatic
cis (V)		6·05	1	singlet	methine
		2·05	3	singlet	acetoxy
AcO	OH	7·31	4	singlet	aromatic
cis (II)[c]		6·06	1	doublet[d]	methine (A)[e]
		5·48	1	quartet[d]	methine (B)[e]
		2·90	1	doublet[d]	hydroxy (C)[e]
		2·10	3	singlet	acetoxy
OH	OH	7·29	2	singlet	aromatic
trans (VII)[c]		5·26	1	multiplet[f]	methine
		3·05	1	multiplet[g]	hydroxy
OH	OH	7·31	2	singlet	aromatic
cis (III)[c]		5·27	1	singlet	methine
		3·13	1	multiplet[g]	hydroxy

[a] All NMR spectra were taken on a Varian A-60 spectrometer at room temp. Unless otherwise stated, samples were dissolved in CCl_4.
[b] See M. P. Cava and K. Muth, *J. Org. Chem.* **27**, 757 (1962).
[c] Taken in deuteriochloroform solution.
[d] The coupling constants are J_{AB} 3·5 c.p.s. and J_{B0} 9·5 c.p.s.
[e] For notation see the attached formula.
[f] Apparent doublet poorly resolved.
[g] Poorly resolved, broad peak.



The coupling constant of methine protons of *cis*-diol monoacetate (II) was observed to be 3·5 c.p.s. The Karplus equation gave a calculated dihedral angle of about 50° for these protons, a value which would probably be too large to be rational in view of the large Baeyer strain of the cyclobutene ring. The application of the Karplus equation to the benzocyclobutene system appears to be highly questionable.[11]

[9] L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* p. 116. Pergamon Press, London (1959).
[10] If the magnetic anisotropy of the neighbouring benzene ring is operating, the "axial" protons in B form must absorb at higher fields than "equatorial" protons of A form. See, however, A. Nickon, M. A. Castle, R. Harada, C. E. Berkoff and R. O. Williams, *J. Amer. Chem. Soc.* **85**, 2185 (1963).
[11] For arguments on cyclobutane derivatives, see J. G. Atkinson, D. E. Ayer, G. Büchi and E. W. Robb. *J. Amer. Chem. Soc.* **85**, 2257 (1963) and references quoted.

The acetoxy methyl signals of *cis*- and *trans*-diacetates (V and VI) were observed at practically the same field value. This might imply that the two acetoxy groups of *trans*-diacetate (VI) are not fixed either at "diaxial" (A) or at "diequatorial" (B) conformation, but both A and B forms are present in a rapid equilibrium.

The hydroxy proton of the *cis*-diol monoacetate (II) was observed as a doublet with J 9·5 c.p.s. The splitting is ascribed to coupling with the adjacent methine proton. Addition of deuterium oxide to this solution resulted in complete removal of the hydroxy signal and the methine proton now appeared as a doublet separated by 3·5 c.p.s. This hydroxy proton splitting seemed exceptional, but could be rationalized by hydrogen bonding with the acetoxy carbonyl group. The oxygen-hydrogen stretching frequency was observed invariably at 3570 cm^{-1} in methylene chloride solutions of various concentration ranging from 0·01 to 0·5 molar, while the ester carbonyl frequency was observed at 1745 cm^{-1}. The *cis*- and *trans*-diols (III and VII) showed no appreciable signs of intramolecular hydrogen bonding.

EXPERIMENTAL

All temps are uncorrected. Microanalyses were performed by Miss K. Ogawa.

cis-1-*Acetoxy*-2-*hydroxybenzocyclobutene* (II). A mixture of 10·0 g (0·038 mole) *trans*-1,2-dibromobenzocyclobutene (I),[1b] 12·7 g (0·076 mole) silver acetate and 300 ml acetic acid containing 4% water was heated at 95–100° under stirring for 6 hr. After the precipitated solid was removed, the filtrate was concentrated *in vacuo*. The residue was treated with water and extracted with benzene. The combined extracts were washed, dried (Na_2SO_4) and evaporated *in vacuo*. Two recrystallizations of the residue (5·81 g) from benzene afforded 4·31 g (64% yield) colourless needles, m.p. 117·5–118°. The IR absorptions (nujol): 3470–3400, 1740, 1260, 1070 and 1055 cm^{-1}. (Found: C, 67·43; H, 5·70. $C_{10}H_{10}O_3$ requires: C, 67·40; H, 5·66%).

cis-1,2-*Dihydroxybenzocyclobutene* (III). A suspension of 3·05 g monoacetate (II) in 500 ml 5% Na_2CO_3 solution was stirred vigorously at room temp for 12 hr to give a clear solution, which was concentrated *in vacuo* and the residue was extracted with benzene. The combined extracts were washed with a small amount of water, dried (Na_2SO_4) and concentrated. Recrystallization of the residue (2·1 g) from benzene afforded 1·8 g (77%) colourless, feathery needles, m.p. 127·5–128°. The IR absorptions (nujol): ca. 3450 and 1080 cm^{-1}. (Found: C, 70·79; H, 6·06. Calc. for $C_8H_8O_2$: C, 70·57; H, 5·92%).

The acetonide of III (IV).[12] A solution of 0·26 g *cis*-diol (III) and 0·5 g *p*-toluenesulphonic acid dissolved in a mixture of 30 ml acetone and 10 ml benzene was heated at reflux for 5 hr. After concentration, the mixture was treated with water and extracted with benzene. The extracts gave 0·30 g crystalline crude product, which was recrystallized from n-hexane to afford 0·22 g (66% yield) an analytical sample, m.p. 91–91·5°. (Found: C, 74·82; H, 7·08. $C_{11}H_{12}O_2$ requires: C, 74·97; H, 6·86%).

cis-1,2-*Diacetoxybenzocyclobutene* (V). A mixture of 0·39 g II and 10 ml acetic anhydride containing 0·20 g *p*-toluenesulphonic acid was heated at 95–100° for 5 hr. Working up the reaction mixture, followed by distillation *in vacuo*, gave 0·26 g (54% yield) a colourless oil. b.p. (bath temp) 105–110°/0·4 mm, n_D^{25} 1·5090. The IR absorptions (neat): 1750 and 1260 cm^{-1}. (Found: C, 65·52; H, 5·83. $C_{12}H_{12}O_4$ requires: C, 65·44; H, 5·83%).

Acetylation of the *cis*-diol (III) gave the same diacetate (comparison of IR).

trans-1,2-*Diacetoxybenzocyclobutene* (VI). After refluxing a mixture of 200 ml glacial acetic acid and 50 ml acetic anhydride 30 min, 10·0 g (0·038 mole) dibromide (I) and 12·7 g (0·076 mole) silver acetate were added. The reaction mixture was heated at 95–100° for 6 hr with stirring and then the precipitated solid filtered off. Treatment of the filtrate, followed by distillation *in vacuo*, gave 6·9 g (82% yield) of a colourless oil, b.p. 99·5–102°/0·6 mm, which was redistilled before analysis, n_D^{25} 1·5070. The IR absorptions (neat): 1750 and 1240 cm^{-1}. (Found: C, 65·45; H, 5·59. $C_{12}H_{12}O_4$ requires: C, 65·44; H, 5·49%).

[12] For this procedure, see M. Sulzbacher, E. Bergmann and E. R. Pariser, *J. Amer. Chem. Soc.* **70**, 2827 (1948).

trans-1,2-*Dihydroxybenzocyclobutene* (VII). A suspension of 2·02 g *trans*-diacetate (VI) in 400 ml 5% Na_2CO_3 solution was stirred at room temp for 12 hr. The solution was subjected to continuous extraction with benzene. Concentration of the benzene extract *in vacuo* below 20° gave a mixture of cottony crystals and a resinous material. The crystals were collected and dissolved in methylene chloride. After standing 2 or 3 days at room temp, the solution deposited *trans*-diol (VII) as cottony crystals, m.p. 106–107° (dec). The IR absorptions (nujol): ca. 3400, 1080 and 1050 cm^{-1}. (Found: C, 70·78; H, 6·19. $C_8H_8O_2$ requires: C, 70·57; H, 5·92%).

The yields were variable and poor (less than 1%), as the diol (VII) was easily soluble in water and readily changed into an amorphous product in solutions even at 35°. This made the recrystallization difficult.

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