The Structure of a 3:2 Adduct from the Reaction of Dimethyl Acetylenedicarboxylate and Cyclohexyl Isocyanide

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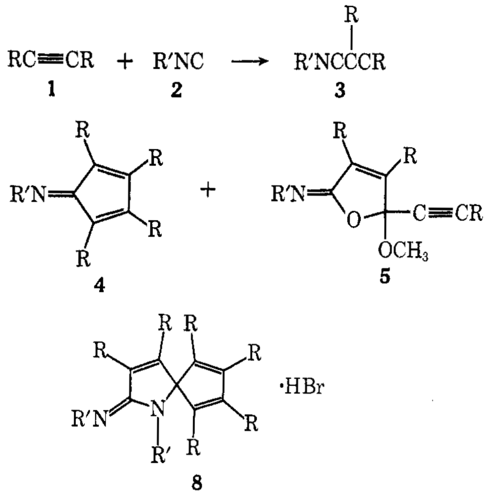
Reaction of dimethyl acetylenedicarboxylate (**1**) with organic isocyanides (**2**) usually yields a large number of products, although low temperatures and an excess of **2** apparently favor the formation of 2:1 adducts (**4** and **5**) derived from alternative additions of a second molecule of **1** to the initially formed 1:1 dipolar species **3**.[1]



$R = -CO_2CH_3$
$R' = C_6H_{11}^-$

Chemical information on the origin and structure of some of the other products was obtained in a recent study[2] of the reaction of **1** with cyclohexyl isocyanide (**2**, R' = C_6H_{11}–). A yellow 3:2 adduct **6** ($C_{32}H_{40}O_{12}N_2$, mp 155–156°) was isolated and found to undergo subsequent isomerization, upon heating at 130° in xylene, to a red isomer **7** (mp 136–137°) which, in turn, undergoes further thermal rearrangement to yet other isomers. Since 3:2 adducts had not been previously studied, we undertook a crystal structure analysis of the hydrobromide salt of **7**. Our results therefore establish simultaneously the molecular structure of a reactant and product of these complicated condensation reactions.[3]

The crystal data for the hydrobromide are $C_{32}H_{40}O_{12}N_2 \cdot HBr$; mp 155° dec; $a = 25.00 \pm 0.02$, $b = 10.98 \pm 0.02$, $c = 13.47 \pm 0.02$ Å, $\beta = 104.4 \pm 0.1°$; $Z = 4$; $\rho_{meas} = ca.\ 1.28$ g cm^{-3} and space group $P2_1/a$. Intensities from levels $h0l$–$h5l$ and $0kl$–$4kl$ were measured diffractometrically (Cu Kα) from two crystals (~0.15-mm cubes), converted to $|F|^2$ without correction for absorption, and merged to a common scale.

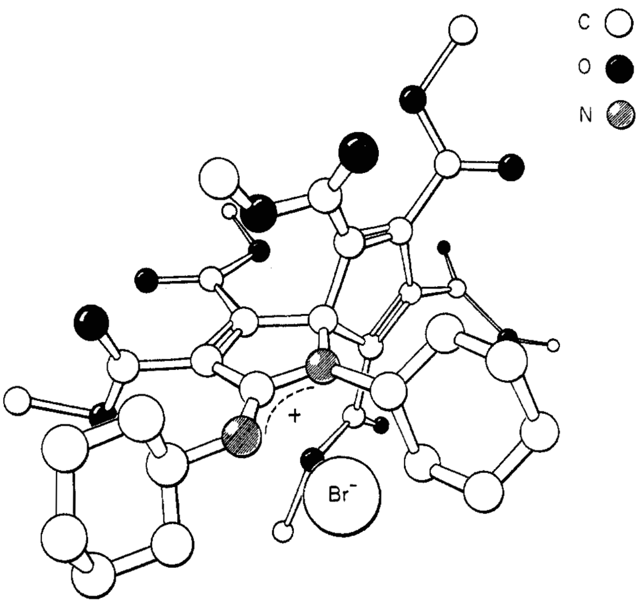


Figure 1.—The solid-state molecular structure and conformation of the hydrobromide salt **8**.

Although the three independent interbromine vectors were easily identified in a Patterson synthesis, their source could not be uniquely attributed to specific symmetry elements since the halogen was positioned on or very near the glide plane. An ambiguity thus arose between the location of the inversion centers and screw axes relative to the bromide ion. No independent structural information other than the chemical origin and atomic composition of **7** was available, and it was therefore not possible to resolve this ambiguity from additional considerations of the molecular packing requirements of possible trial structures. A Fourier map therefore was computed with phases from an arbitrary choice between the two possible bromine X coordinates ($R = 0.57$). Excessive caution in selecting trial molecular moieties near and across the false mirror planes in this map (symmetry $P2_1/m$) led us unknowingly to ignore the correct molecular structure which, in fact, was present along with many other false peaks. Chemical considerations of possible molecular structures for **7** eventually led to an interpretation of this map based on the nearly symmetric spiro structure **8** oriented with a close coincidence of the pseudo molecular mirror and the false Fourier mirror planes. Although successive Fourier syntheses were consistent with the spiro structure, the crystal structure based on all 47 nonhydrogen atoms could not be refined below $R \sim 0.25$. Since, in addition, several unreasonably short intermolecular distances were indicated across the inversion centers and screw axes, the entire hydrobromide structure was translated by $\vec{a}/4$ (6.25 Å) to the alternative unit cell site. This crystal structure and the *original* assignment of the molecular structure as **8** were verified completely through least-squares refinements of all coordinates and temperature parameters (only the Br$^-$ was refined anisotropically). The final agreement between the 2500 observed and calculated structure factors is $R = 0.11$.

The cyclopentadienyl and 3-pyrrolinyl rings are planar and mutually perpendicular within experimental error while the cyclohexane rings are in the chair conformation with equatorial nitrogen substituents (Figure 1).

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(1) E. Winterfeldt, *Angew. Chem.*, **78**, 757 (1966); *Angew. Chem., Int. Ed. Engl.*, **5**, 741 (1966).

(2) We wish to thank Professor M. V. George of the Department of Chemistry, Indian Institute of Technology, Kanpur, India, for calling our attention to his studies of this reaction and for providing crystals of the hydrobromide salt.

(3) Financial support by the U. S. Air Force Office of Scientific Research (Grant No. AFOSR-68-1509) is gratefully acknowledged.

The plane of the heterocycle (approximately coincident with the crystallographic glide plane) is nearly a mirror plane of each of the four rings. However, this molecular symmetry is violated by the essentially flat carbomethoxyl groups which are rotated unsymmetrically about the C–C bonds through various angles (in the pyrrolinyl ring, 87, 2°; adjacent in the cyclopentadienyl ring, 25, 40, 55, 4°) in order to relieve nonbonded steric interactions. The equal geminal C—N bond lengths (1.33 Å) and the coplanarity of all atoms bonded to the two nitrogen atoms suggest a delocalized amidine structure. Both cyclohexyl rings appear oriented so as to allow close approach of the protonated amidine to the bromide ion. The latter ion also lies essentially in the heterocyclic plane within hydrogen bonding distance (3.32 Å) of the exocyclic nitrogen atom which presumably bears the proton. The other Br^----N distance is 4.46 Å.

The structure of this 3:2 adduct can be formally derived by the addition of the dipolar 1:1 adduct **3** to the C═N bond of the 2:1 adduct **4**. However, in the absence of further chemical information, we cannot comment on the structure of its isomeric precursor **6**.

Registry No.—**1**, 762-42-5; **2** (R′ = C_6H_{11}), 931-53-3; **7**, 31528-92-4; **7** HBr, 31528-93-5.

Configuration and Conformation of the Dibromides Obtained from the Reaction of Bromine with 2-Ethoxy-5,6-dihydro-2*H*-pyran[1]

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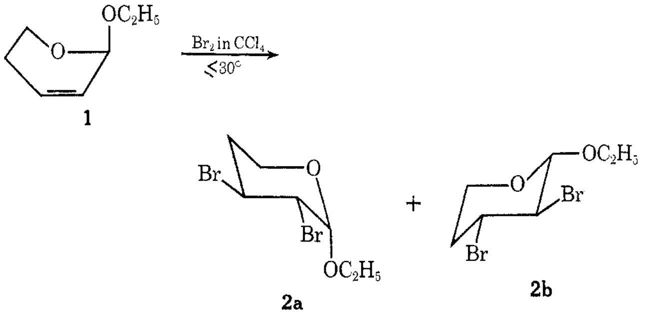
It has been reported[5] that the reaction of bromine with 2-ethoxy-5,6-dihydro-2*H*-pyran (**1**) produces a mixture of "two geometrical isomers of 2-ethoxy-3,4-dibromotetrahydropyran" (Scheme I). Although the separation of these isomers has been described,[5] no conformational assignment was made apart from the assumption that the two vicinal bromine atoms were mutually trans.[5] Our program of study of 2-alkoxydihydro- and tetrahydropyrans required a knowledge of the configurational and conformational details of these dibromides in order to determine their influence on the relative stability of the α and β anomers (the anomeric effect[6–8]) and on the course of the base-catalyzed dehydrohalogenation of the dibromides. This note reports our findings concerning the configuration and conformation of these dibromides.

Scheme I



Low-temperature (≤30°) bromination of **1** either in carbon tetrachloride or methylene chloride gave a mixture of dibromides in 71% yield (*cf.* 68%[5]). Bromination in methylene chloride at −80° or −40 to −45° provided a mixture in which the two isomers **2a** and **2b** were present in the approximate ratio 3:1, determined by the proton magnetic resonance (pmr) spectrum of the isolated crude mixture. An increase in reaction temperature to −30° changed the proportion to ~2:1. Bromination in carbon tetrachloride at either −45 or −30° gave **2a** and **2b** in the ratio ~2:1.

The minor constituent, **2b**, a solid, was separated in the pure state from the liquid mixture by crystallization as reported previously.[5] This did not give quantitative separation. However, most of the remainder of **2b** could be obtained from the residue left when the mother liquor was distilled. The major component, **2a**, a liquid obtained by vacuum fractional distillation of the mother liquor, was found to be contaminated by a small amount (<5%) of **2b** which extensive and careful fractional distillation failed to remove. However, subsequent gas–liquid chromatography (glc) of this distilled fraction did provide pure **2a**. Elemental analyses of the individual isomers agreed with that required for a dibromo-2-ethoxytetrahydropyran.

The configuration and conformation of the solid isomer **2b** was examined by pmr. The 100-MHz spectrum obtained in deuteriochloroform and referred to tetramethylsilane showed the anomeric proton signal as a doublet centered at τ 5.52 ($J_{2,3} \sim$ 7.0 Hz). In either acetonitrile or acetonitrile saturated with tetra-*n*-butylammonium bromide, the anomeric proton signal was found at τ 5.54 with $J_{2,3} \sim$ 7.8 Hz. The large coupling, as well as the change observed when acetonitrile was used as solvent, shows that the C-2 ethoxy group and the C-3 bromine atom are trans and equatorial.[9] By irradiation at appropriate frequencies, in spin decoupling experiments, it was possible to locate the signals for both H-3 and H-4. A first-order analysis showed a large coupling, $J_{3,4} \sim$ 9.8 Hz, indicating that these two protons are trans diaxially disposed and therefore that the two bromine atoms attached to C-3 and C-4 are trans and equatorial. The above information clearly shows that the solid isomer has the configuration shown by **2b** and that the preferred conformation of **2b** is that in which all the substituents are equatorial.

The 100-MHz pmr spectrum of the liquid isomer, **2a**, in deuteriochloroform possessed a doublet for the anomeric proton signal at τ 5.12 ($J_{2,3} \sim$ 2.8 Hz) which is nearly the same as that obtained in acetonitrile or ace-

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(1) In part from the thesis of F. Sweet, presented to the Faculty of Graduate Studies, University of Alberta, Edmonton, Alberta, Canada, in partial fulfillment of the requirements for the Ph.D. degree.

(2) Postdoctoral Fellow, 1968–1970.

(3) Postdoctoral Fellow, 1969–1971.

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