Tetrahedron Letters No.43, pp. 3861-3867, 1965, Pergamon Press Ltd.
Printed in Great Britain.

BROMINATION OF TRICYCLO[4.2.2.0^{2,5}] DECA-3,7-DIENES. DEPRESSION OF TRANSANNULAR DOUBLE BOND PARTICIPATION BY THE PRESENCE OF ELECTRONEGATIVE SUBSTITUENTS.

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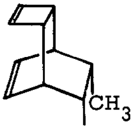
(Received 26 July 1965; in revised form 3 September 1965)

Neighboring group participation by a double bond in carbonium ions is now a well known phenomenon.[1] We wish to report preliminary results on a series of compounds in which the geometrical disposition of the double bond and the reacting site remains essentially the same, while the availability of the π electrons of the participating double bond is decreased by the introduction of electronegative groups far from the reacting site. In this series, double bond participation decreases very markedly as evidenced by reaction rates and product analyses. A related, though less subtle effect has been observed by Bird, Cookson and Crundwell.[2]

The compounds selected for study were the dienes 1 through 5. Compounds 1, 2 and 4 were prepared by previously reported methods.[3,4] Compound 3 was prepared by partial reduction of 4 with lithium aluminum hydride in tetrahydrofuran at room temperature.** Compound 5*** was prepared



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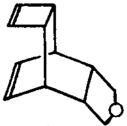

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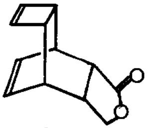

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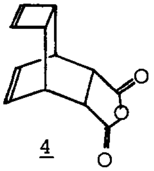

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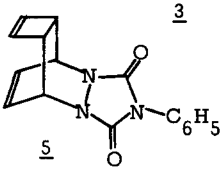

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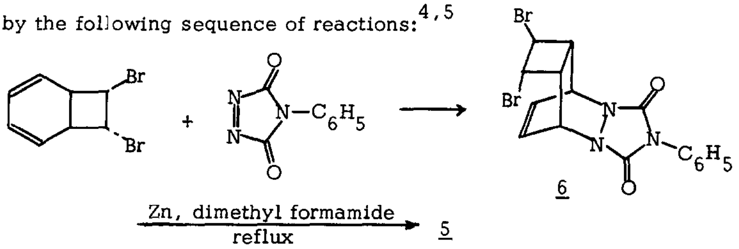
** M.p. 122.5-123.5°. Found: C, 76.47; H, 6.53. λ_{max} 5.68μ. Partial n.m.r. τ4.14 (2H, triplet), 4.27 (2H, singlet), 5.80 (1H, quartet).

*** M.p. 216-217°. Found: C, 68.13; H, 4.77; N, 15.06. λ_{max} 5.84, by the following sequence of reactions:[4,5]



The reactions of this series of compounds with bromine in chloroform showed a striking progression in both reactivity and products formed. Thus, compound 2 reacted with one equivalent of bromine instantly at 25°. Thin layer chromatography (TLC) revealed the presence of one minor and two major components. Integration through the vinyl region of the n.m.r. spectrum suggested the presence of about 5-10% of a component with two olefinic hydrogens (τ^{CCl_4} 3.78, multiplet). The olefinic component, m.p. 174.5-176.0°, (Found: C, 43.19; H, 4.29; Br, 47.98), could be isolated in 9% yield by crystallization from ether, and was identified as the minor component of the thin layer chromatogram. The n.m.r. spectrum of this product was entirely consistent with its formulation as the cis dibromide 7. The two equivalent vinyl hydrogens appeared as a clean triplet centered at τ3.64, while the methylene protons on the intact tetrahydrofuran ring appeared as an unsymmetrical triplet at τ6.25 and an unsymmetrical quartet at τ6.67, quite similar to those at τ6.38 and 6.82 in the starting diene 2. The equivalent hydrogens α to the bromines appeared at τ5.81 (doublet), while the remainder appeared at 7.3 (4H, multiplet) and 7.80 (2H, multiplet). Further confirmation of the structure of the cis dibromide 7 was found in the isolation of the trans dibromide 8, m.p. 104.5-105.5° (Found: C, 42.97; H, 4.18; Br, 47.67) in less than 1% yield* by chromatography. This substance was identified by independent synthesis as indicated in Chart 1.[4] The n.m.r. spectrum of the trans-dibromide differed from that of the cis,

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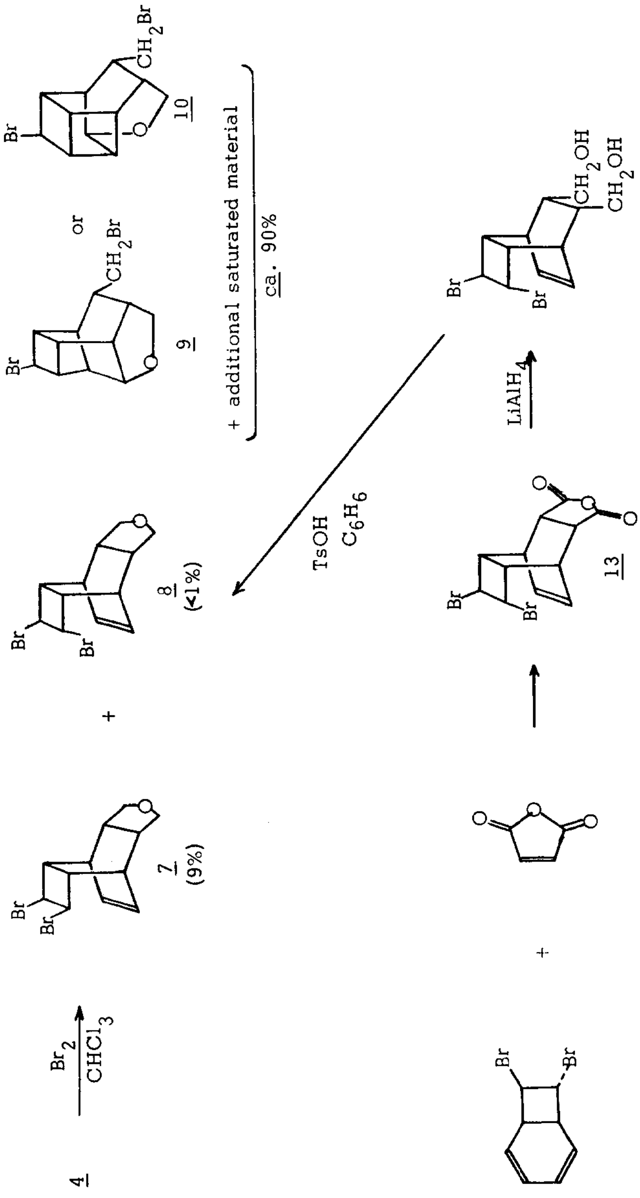
6.18, 6.22µ. N.m.r.: τ2.59 (5H, broad), 3.80 (3H, triplet), 3.99 (2H, singlet), 4.95 (2H, quartet), 6.65 (2H, doublet).

* The cis-dibromide was shown to be stable to the reaction and work-up conditions.

CHART 1


4
Br2
CHCl3
Br
7
(9%)
+
8
(<1%)
TsOH
C6H6
9
or
CH2Br
10
+ additional saturated material
ca. 90%
+
13
LiAlH4
CH2OH
CH2OH

in that the vinyl hydrogens were now non-equivalent, appearing as two triplets at τ3.47 and 3.81. Similarly, the hydrogens *alpha* to the bromines appeared as two quartets at τ5.31 and 5.82. The remainder of the spectra were quite similar, the *trans* exhibiting resonance at τ6.25 (2H, triplet), 6.80 (2H, quartet), 7.15 (4H, multiplet) and 7.77 (2H, multiplet).

Crystallization of the chromatographic fractions afforded one of the major components of the reaction mixture, m.p. 76.5-77° in 15% yield. It was identified as a saturated dibromide, possibly 9 or 10,* by its analysis (Found: C, 43.33; H, 4.23; Br, 47.87) and n.m.r. spectrum, which was transparent in the vinyl proton region, but exhibited resonance at τ6.17 (5H, multiplet), 6.48 (1H, overlapping triplet), 6.78 (1H, multiplet), 7.52 (3H, multiplet), and 7.60-8.50 (4H, multiplet). The remainder of the product had no vinyl proton absorption in its n.m.r. spectrum.

The course of the reaction of 2 with bromine is summarized in Chart 1.

The reaction of the maleic anhydride adduct 4 with one equivalent of bromine in chloroform required more than 30 minutes at room temperature for completion. A crystalline precipitate consisting of a 37% yield of *cis*-dibromide 11, m.p. 255-260°, was isolated directly from the reaction mixture. The compound was identified by its analysis (Found: C, 39.72; H, 2.84; Br, 43.65), i.r. spectrum (λ_{max}^{KBr} 5.35, 5.60μ), and n.m.r. spectrum (τ, dimethyl sulfoxide solvent: 3.46 (2H, triplet), 5.10 (2H, multiplet), 5.65 (2H, multiplet)). The *cis* nature of the bromines was again evident by the equivalence of the vinyl hydrogens at τ3.46 and the *alpha* hydrogens at τ5.10. Further confirmation of the structure was obtained by reduction of 11 to the known diene-diol 12[3] with lithium aluminum hydride for 12 hours in boiling tetrahydrofuran.

The remainder of the bromination product (total yield, including iso-

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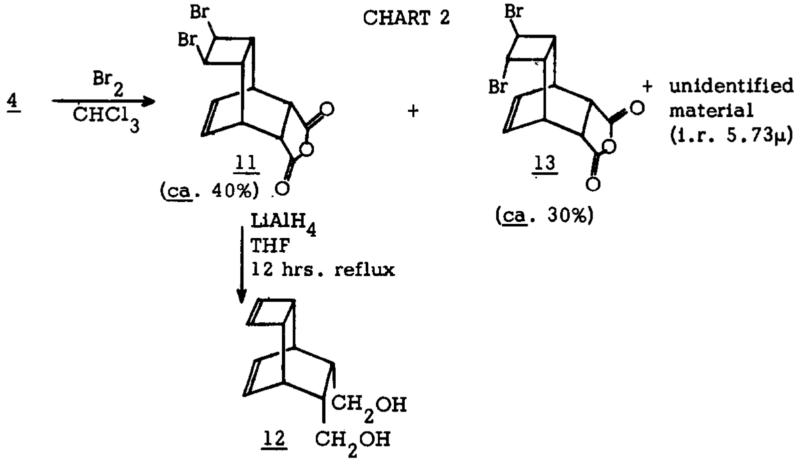
* It should be noted that the n.m.r. spectrum clearly indicates the destruction of the original tetrahydrofuran nucleus with its methylene resonances near τ6.3 and 6.7. Similarly the i.r. absorption near 9.0 and 9.6μ observed for 2, 7 and 8 was absent in the saturated dibromide. There are several structures which can be derived by reasonable mechanistic paths. Structures 9 and 10 are representative.

lated *cis*-dibromide, of 96%) appeared to be a mixture of *trans*-dibromide 13 (about 50%), *cis*-dibromide 11 (about 10%) and a component with infrared absorption at 5.73μ (remainder), as judged by i.r. spectroscopy. The pure *trans*-dibromide 13, identical with a synthetic sample,[4] could be isolated in low yield by crystallization.

The course of the reaction of the maleic anhydride adduct, 4, with bromine is summarized in Chart 2.

CHART 2



The N-phenylurazole diene 5 required 5 1/2 hours at reflux for the decoloration of one equivalent of bromine. Even under these conditions, starting diene was recovered from the reaction mixture in about 40% yield by extraction of the crude product with carbon tetrachloride. The carbon tetrachloride insoluble material consisted of a near quantitative yield of a 2:1 mixture of *trans*-dibromide 6 and what is probably the *cis*-dibromide 14. Thus, TLC of the crystalline solid resolved it into a minor component and a major component exhibiting an Rf value identical with that of authentic *trans*-dibromide 6 (see above).* The i.r. spectrum of the material was nearly identical with that of pure 6 save for relative intensity differences of a few peaks in the 9.0-9.5, 11.0-12.0 and 12.8-15.0μ regions. The

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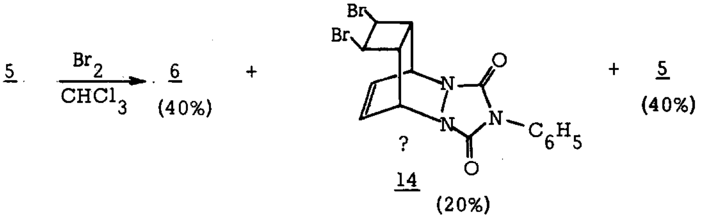
* M.p. 253.5-257.5° (dec.), (Found: C, 43.89; H, 3.31; N, 9.62; Br, 36.42).

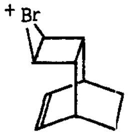
n.m.r. spectrum exhibited the characteristic broad multiplet of the nonequivalent vinyl hydrogens of 6 from $\tau 3.0$-3.6. Superimposed upon this was a relatively sharp triplet centered at $\tau 3.3$ identical with that observed for the *cis*-dibromides 7 and 11. An accurate quantitative analysis was not possible but approximately one-third the vinyl proton area was accounted for by the sharp triplet.

The reaction of the N-phenylurazole diene 5 is summarized in Chart 3.

CHART 3



The increasing amount of olefinic dibromide and increasing *trans*-*cis* ratio observed in comparing the products from the action of bromine on 2, 4, and 5 can be interpreted as the result of decreasing participation of the double bond in a cationic bromination proceeding through either the bromonium ion 15 or a rearranged cation such as 16 or 17. As the availability of the electrons of the participating double bond is decreased by the introduction of electronegative substituents, more of the reaction will be forced through the bromonium ion 15, leading to simple *trans*-bromination. It is not entirely clear whether the rearranged cation should be written as 16 or with full bond formation, as in 17. It is clear, however, that the essentially non-participating double present in 5 presents severe hindrance to *trans*-bromination without facilitating *cis*-bromination, while the participating double bond present in 2 markedly facilitates both *cis*-bromination and rearrangement.



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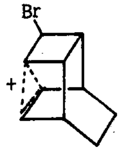

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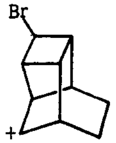

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Preliminary results on the remaining dienes 1 and 3 fit quite neatly into this scheme. Thus, 1 decolorized one equivalent of bromine instantly to give a product mixture containing 5% olefinic product as evidenced by n.m.r. spectroscopy. The ether oxygen of 2 is, therefore, not necessary for double bond participation. The lactone 3 decolorized bromine at a rate intermediate between that of 2 and 4 to give a product containing 40-50% olefin as evidenced by n.m.r. analysis.

Acknowledgement.- We are grateful for support of this work by the National Science Foundation (Grant GP 1944).

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