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TRANSANNULAR O-HETEROCYCLIZATION OF TWELVE AND THIRTEEN MEMBERED TRIENES BY METHOXYBROMINATION PROCEDURE [1]

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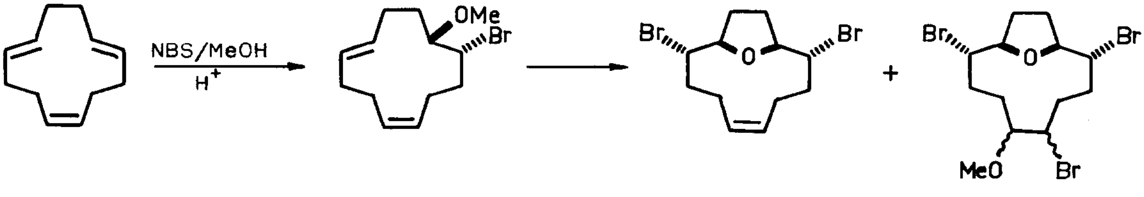
Summary: The reaction of (E,E,Z)-cyclododeca-1,5,9-triene (1) with NBS and methanol gives bicyclic tetrahydrofuran derivatives (3) and (4) as well as usual 1,2-addition products while the related reaction with (Z,E,Z)-cyclotrideca-1,5,9-triene (7) leads to the bicyclic tetrahydropyran derivative (6), in both cases like O-heterocyclization products as the result of transannular participation of a methoxy group.

Under the conditions of the hydroxybromination or methoxybromination with N-bromosuccinimide (NBS) from cyclohepta-1,4-diene and (Z,Z)-cycloocta-1,5-diene dibromo-oxa-bicycloalkanes were formed by transannular participation of the oxygen containing functional group [2], while the reaction of (Z,Z)-cyclonona-1,5-diene gave only 3% of an oxabicyclic product [3]. The main process is the π-cyclization which is the sole pathway in the case of (E,Z)-cyclodeca-1,5-diene [4]. Starting from the isomeric large ring dienes (E,E)- and (E,Z)-cyclododeca-1,5-dienes under the same conditions the formation of two isomeric 2,9-dibromo-13-oxa-bicyclo[8.2.1]tridecanes was observed [5].

Now we describe that the reaction of (E,E,Z)-cyclododeca-1,5,9-triene (1) with NBS (molar ratio 1:2) and methanol in the presence of catalytic amounts of sulfuric acid gives endo,endo-2,9-dibromo-13-oxa-bicyclo[8.2.1]tridec-5-(Z)-ene (3) [6] (m.p. 102,5 - 103,5°C) in 38% isolated yield and one consecutive product (4) [6](m.p. 156 - 158°C) in 11% isolated yield in addition to the usual 1,2-addition products such as 2.

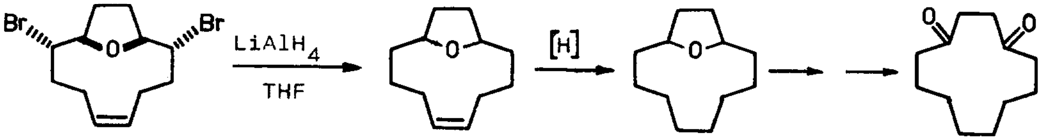


1 2 3 4

These products are formed by methoxybromination of one trans double bond of the triene in the first step and transannular participation of the methoxy group on the cation which is formed from the other trans double bond by the attack of an additional bromonium species in a second step (cf. [2]).

Such transannular O-heterocyclizations are characteristic reactions for electrophilic additions to (Z,Z)-cycloocta-1,5-diene in solvents like water or alcohols [2,7], but they are unusual with large rings.

The structures of (3) and (4) are derived from spectroscopic data [6] and chemical transformation. The presence of the tetrahydrofuran ring was established e.g. by the following chemical transformation. The reduction of (3) with LiAlH$_4$ in THF and subsequent hydrogenation gave 13-oxa-bicyclo[8.2.1]-tridecane (5) which was converted to cyclododecan-1,4-dione (6) by NOZAKI's procedure [9]. The identity of the 1,4-diketone was shown by comparison with an authentic sample [10].



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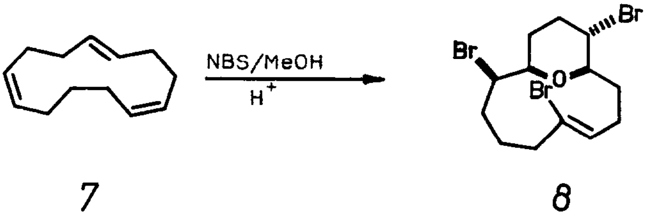
The related reaction of (Z,E,Z)-cyclotrideca-1,5,9-triene (7) [11] with NBS and methanol by the above-mentioned conditions gave simple 1,2-addition products and the 2,6,11-tribromo-14-oxa-bicyclo[8.3.1]tetradec-6(E)-ene (8) [6] (m.p. 143 - 144°C) in 22% isolated yield.



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The structure of this product could not be established by the usual spectroscopic methods (MS: m/e 428, M$^+$; ^{1}H-NMR: δ 5.76 (q, 1H), 3.78 (m, 2H), 3,50 (m, 2H), 2.6-1.2 (m, 14H); ^{13}C-NMR: δ 130.5, 126.1, 84.2, 74.6, 57.4, 51.1, 42,6, 36.5, 34.1, 33.6, 31.5, 30.6, 23.3).

The true constitution and stereochemistry of this compound was proven by X-ray crystallographic analysis [12]. The following figure shows the molecular structure of the molecule.

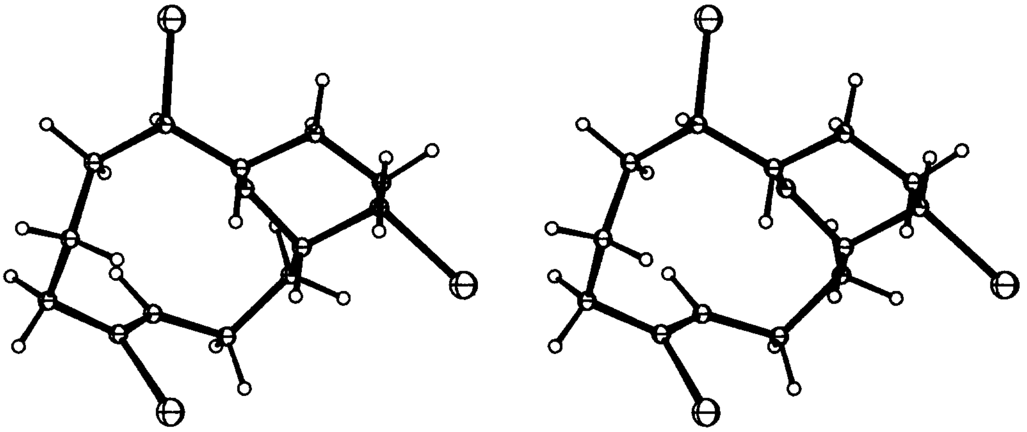

Figure 1: Molecular structure of 2,6,11-tribromo-14-oxa-bicyclo-[8.3.1]tetradec-6(E)-ene (8) (stereopair)

This is the first example of a transannular O-heterocyclization of a thirteen-membered unsaturated ring by electrophilic addition procedure.

Contrary to the related twelve-membered triene (1) and the isomeric cyclododeca-1,5-dienes [5] in the case of the thirteen membered triene (7) a tetrahydropyran ring was formed from one trans- and one cis-double bond of the 1,5-diene system instead of a tetrahydrofuran ring as it was obtained in the reaction of (E,Z)-cyclododeca-1,5-diene under the same conditions [5]. This different reaction pathway seems to be caused not only by the different configurations of (1) and (7) but mainly by the conformation of the intermediate leading to the transannular cyclization. A conclusive interpretation of this fact cannot be given yet. Further experiments are in progress.

Acknowledgement

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References and Notes

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6. Satisfactory elemental analyses, MS, IR, and ^{1}H NMR spectra were obtained for all new compounds. Carbon-13-NMR spectra (22,63 MHz, TMS, $CDCl_3$):
   3: δ 128.2 (C-5,C-6), 85.6 (C-1,C-10), 54.9 (C-2,C-9), 37.6 (C-3,C-8), 31.5 (C-4,C-7), 26.2 (C-11,C-12);
   4: δ 81.7, 81,2, 80.6, 58.1, 57.4, 55.1, 50.2, 35.1, 31.5, 30.5, 27.5 (double intensity), 27.0[8].

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