Facile Intramolecular Cyclization Reactions of Aromatic Ethers with Cationoids in Triptycene Systems

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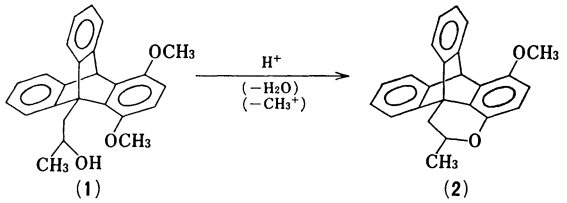
1,4-Dimethoxytriptycenes were found to give cyclic ethers with unusual ease when a substituent at the bridgehead bears a cationoid center. The easy reaction is attributed to the extreme proximity between the methoxyl group and the cationic center. Mechanisms involving a cyclic oxonium ion and subsequent attack by an anion to produce the cyclic ether and a methyl derivative are discussed.

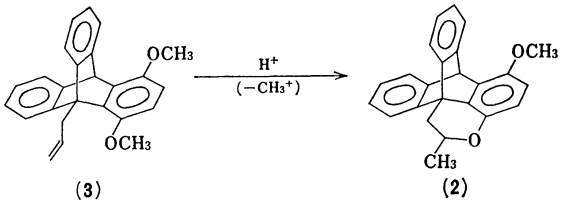
During the course of other study we have encountered a surprisingly facile ring formation of 1,4-dimethoxytriptycenes if a cationoid center is produced in the 2-position of a 9-substituent. This paper reports such findings and discusses the probable mechanisms of the reaction.

When oxidation of 9-(2-hydroxypropyl)-1,4-dimethoxytriptycene (**1**) was attempted with chromium(VI) oxide in the presence of sulfuric acid, a cyclic ether (**2**) was formed instead of the corresponding carbonyl compound. Expecting that the reaction was caused by the action of an acid which formed a cationoid center, we treated **1** with sulfuric acid and obtained **2** as expected.



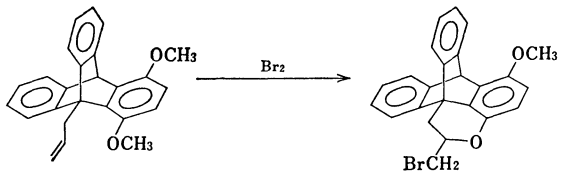
(1) (2)

The reaction is then regarded to proceed *via* an oxonium salt which is formed from the cationoid and the proximate methoxyl group in 1-position. The reaction occurs probably *via* both S_N1 and S_N2 mechanisms, because secondary alcohols undergo other substitution reactions in those fashions[1] and an electron-accepting group in the substituent at the bridgehead should interact strongly with the methoxyl group in the peri-position.[2] If the consideration is valid, 9-allyl-1,4-dimethoxytriptycene (**3**) should give the same product (**2**), when treated with an acid, since addition of a proton to the allyl moiety should produce a cationoid in the 2-position of the 9-substituent. In fact, treating **3** with trifluoroacetic acid gave **2**.



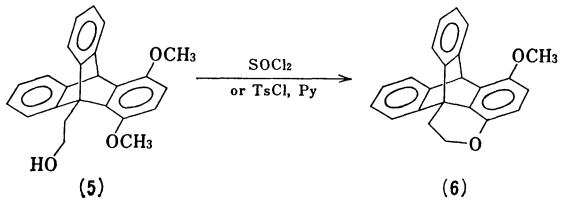
(3) (2)

Being encouraged by the extension, we then proceeded to cationoids which may be developed by a variety of methods. A variety of electrophilic additions to olefins are known to proceed *via* cationoids. We have taken addition of bromine to an olefin as an example.[3] 9-Allyl-1,4-dimethoxytriptycene (**3**) was treated with bromine and was found to give a cyclic ether (**4**).



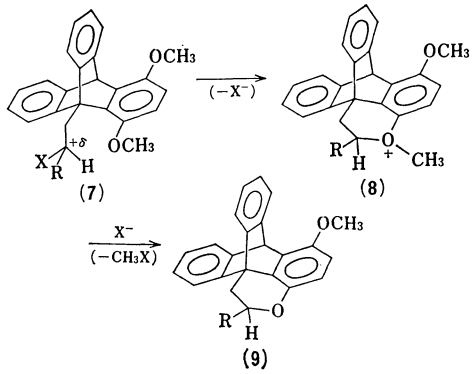
(3) (4)

The facile cyclization is not confined to the propyl derivatives carrying a cationoid in the 2-position. Treating 9-(2-hydroxyethyl)-1,4-dimethoxytriptycene (**5**) with thionyl chloride gave a cyclic ether (**6**). Since the reaction between alcohols and thionyl chloride is known to proceed *via* contact ion pairs,[4] the result was not a great surprise. To our surprise, however, a less cationic species, *p*-toluenesulfonate, cyclized as well: when **5** was treated with *p*-toluenesulfonyl chloride and pyridine at room temperature, the product was **6**. Thus weakly cationic species like sulfonates can react to form cyclic ethers.



(5) (6)

In order to discuss the mechanism of the reaction, the fate of the methyl group which had been in the methoxyl group must be explored. We ran the reaction of **5** with an excess of thionyl chloride in chloroform-*d* in a sealed tube, expecting that the product from the methyl group must be methyl chloride. The ^1H NMR spectrum of the reaction mixture clearly showed the presence of a sharp signal at δ 3.00 which is ascribable to methyl chloride. The formation of methyl chloride was further confirmed by addition of methanol to the mixture and observing the increase in the intensity of the signal at δ 3.00.



(7) (8) (9)

The mechanism of the reaction may be described now as follows. In the first step a cationoid species (**7**) is formed in the 2-position of the 9-substituent by an electrophilic addition to the olefin or by enhancing the leaving group ability of the substituent. In the second step it cyclizes to an oxonium ion (**8**) which is then attacked by an anion at the least hindered methyl to give the cyclic ether (**9**) and a substituted methane.

The reason for the facile cyclization must be proximate arrangement of the two groups. In other triptycene systems, the substituent in the 9-position and the peri-substituent are known to be well in the sum of the van der Waals radii[5,6] and some very weak interactions were detected.[2,7,8] Therefore, as soon as the cationic species is formed, it interacts very strongly with the methoxyl group in the peri-position, leading to the cyclic oxonium ion (**8**). This postulate is substantiated by the following facts. Although neighboring participation of oxygen[9] in bromination reactions is known to be stronger than that of bromine,[10] the yield of a cyclic ether is only 50—60% when 4-penten-1-ol is treated with bromine and, if it is a 6-membered ring, the yield of a cyclization product drops to 5—10%.[9] Since the cyclic ether formed here is 6-membered, the participation of the oxygen is unusually strong relative to the open-chain compounds, although the entropy factor may contribute to some extent.

The ^{13}C NMR spectrum of 9-allyl-1,4-dimethoxytriptycene (**3**) revealed that there were two detectable conformers at a low temperature. Since it will not be possible to observe conformers about the C_{sp^3}–C_{sp^2} bond in the allyl group, it is natural to assume that the conformers are those involving the restricted rotation about the C_9–C_{allyl} bond: the number of carbon atoms detected by the ^{13}C NMR conforms with this assignment. The competitive bromination of **3** with 9-allyltriptycene (**10**) revealed that a negligible amount of **10** reacted, while the color of bromine faded fast to give **4** as a sole product. This high reactivity of **3** cannot be explained if it reacts in the *ap* conformation because its steric environment is the same as **10** and no strong electronic effect is expected, if any. Rather it will be explained by the neighboring participation of the methoxyl group which facilitates the electrophilic attack.

We conclude that the unusually high reactivity of the methoxyl group toward cationoids is caused by the highly congested state in the triptycene system. The results suggest that the triptycene is a good system to find weak interactions which otherwise are not detectable.

Experimental

*9-Allyl-1,4-dimethoxytriptycene (**3**).* A solution of 2.2 g (0.01 mol) of 9-allylanthracene[11] and 1.1 g (0.01 mol) of *p*-benzoquinone in 10 mL of toluene was refluxed for 1 h. The reaction mixture was cooled. The resulting crystals were collected and washed with ether. The crystals in 20 mL of dioxane were treated with 1.0 g of sodium hydroxide in 10 mL of water and then with dimethyl sulfate under a nitrogen atmosphere. The process was repeated 2—3 times until coloration due to the enolate was not observable on addition of the alkali. The resulting mixture was poured into 500 mL of water. The precipitate was collected, dried, and recrystallized from hexane, mp 235—236 °C. The yield was 80%. Found: C, 84.50; H, 6.06%. Calcd for $C_{25}H_{22}O_2$: C, 84.92; H, 6.24%. ^1H NMR ($CDCl_3$, δ): 3.68 (3H, s), 3.78 (3H, s), 3.9—4.3 (2H, m), 5.0—5.7 (2H, m), 5.88 (1H, s), 5.9—6.4 (1H, m), 6.50 (2H, s), 6.8—7.7 (8H, m). ^{13}C NMR ($CDCl_3$, ppm from TMS): 32.9, 46.0, 54.3, 56.7, 57.1, 109.0, 109.7, 113.7, 122.6, 123.5, 123.8, 133.6, 136.6, 138.1, 145.2, 145.5, 147.2, 148.9.

The signals at 32.9 and 54.3 ppm and many at lower fields split into two peaks in a ^{13}C NMR spectrum at −32 °C. From these, the population ratio was calculated as 0.7. Altough it is not possible to tell which isomer is favored in the equilibrium, the ^1H NMR data suggest that the *ap* isomer is favored: the signal at δ 6.50 splits into two peaks at low temperatures and, if the peak at a higher field corresponds to the $\pm sc$ form as were other compounds of this series,[2] then the ratio $\pm sc/ap$ is 0.7.

*2-Methyl-6-methoxy-7,11b-o-benzeno-7,11b-dihydronaphtho[1,2,3-de]chroman (**2**).* *a)*: To a solution of 420 mg of 9-(2-hydroxypropyl)-1,4-dimethoxytriptycene, which had been prepared by the Grignard reaction of the corresponding aldehyde,[8] in 20 mL of acetone was added sulfuric acid (0.1 mL H_2SO_4 and 0.2 mL H_2O) and the mixture was stirred at 0 °C for 1 h. The solvent was removed *in vacuo* and the residue was washed with dilute alkali after addition of 30 mL of dichloromethane. The organic layer was evaporated after drying. The product was identical with the substance produced by the action of hydrochloric acid on an adduct from 9-allylanthracene and *p*-benzoquinone followed by methylation (see below).

b): A solution of 1.5 g of an adduct from 9-allylanthracene and *p*-benzoquinone in 50 mL of acetic acid was mixed with 10 mL of cencentrated hydrochloric acid and stirred for 24 h at room temperature. The mixture was poured into 1 L of water and the solid was collected. The solid was treated with aqueous sodium hydroxide and dimethyl sulfate under a nitrogen atmosphere, as was for the preparation of **3**. The product was recrystallized from benzene–hexane, mp 230.3—230.8 °C. Yield 82%. Found: C, 84.57; H, 5.95%. Calcd for $C_{24}H_{20}O_2$: C, 84.68; H, 5.92%. ^1H NMR ($CDCl_3$, δ): 1.65 (3H, d), 3.04 (2H, poorly resolved quartet), 3.73 (3H, s), *ca.* 4.3 (1H, m), 5.85 (1H, s), 6.50 (2H, s) 6.9—7.6 (8H, m).

c): To a solution of 20 mg of 9-allyl-1,4-dimethoxytriptycene (**3**) in 1.5 mL of $CDCl_3$ was added a few drops of trifluoroacetic acid. After standing overnight, the mixture was treated with 10% aqueous sodium hydrogencarbonate. The solvent was evaporated from the organic layer and the product was separated by TLC. The main product was identical with the compound described above.

A ^1H NMR spectrum of the mixture showed broadening of the signal due to dialkoxybenzo protons at δ 6.50, indicating rapid exchange between the aromatic protons and that of trifluoroacetic acid. Thus trifluoroacetic acid-*d* was used to see the exchange: the aromatic proton signal vanished during the reaction. After treatment with aqueous sodium hydrogencarbonate, the ^1H NMR spectrum of the product showed the presence of a deuterium in the methyl in 2-position (broad doublet at δ 1.64 in $CDCl_3$) and the signal due to the dialkoxybenzo protons had an intensity corresponding to one proton only. The position of the deuterium in the diakoxybenzo moiety is not known.

*6-Methoxy-7,11b-o-benzeno-7,11b-dihydronaphtho[1,2,3-de]chroman (**6**).* *a)*: A solution of 0.30 g (8.0 mmol) of

9-(2-hydroxyethyl)-1,4-dimethoxytriptycene (**5**)[2] in 30 mL of dichloromethane was stirred for 30 min with 0.3 mL (40 mmol) of thionyl chloride and then heated under reflux for 30 min. The mixture was treated with aqueous sodium hydroxide and the organic layer was evaporated. Chromatography followed by recrystallization, from benzene-hexane, of the product afforded a pure sample, mp 289.5—290.5 °C, in 95% yield. Found: C, 84.90; H, 5.37%. Calcd for $C_{23}H_{18}O_2$: C, 84.64; H, 5.56%. ^{1}H NMR ($CDCl_3$, δ): 3.15—3.40 (2H, m), 3.78 (3H, s), 4.20—4.50 (2H, m), 5.83 (1H, s), 6.50 (2H, s), 6.9—7.7 (8H, m).

b): A solution of 0.20 g (5.6 mmol) of the alcohol (**5**) in 10 mL of pyridine was mixed with 0.20 g (15 mmol) of *p*-toluenesulfonyl chloride and stirred for 24 h at room temperature. The mixture was mixed with 30 mL of dichloromethane and shaken with dilute hydrochloric acid. The product was identical with the above cyclic ether and was obtained in 92% yield after resrystallization from benzene-hexane. If the reaction was stopped at an incomplete stage, a mixture of **6** and the starting material (**5**) was obtained. The results indicate that the cyclization did not take place by the treatment of the alcohol with hydrochloric acid but it was the sulfonate ester which gave **6**.

*2-Bromomethyl-6-methoxy-7,11b-o-benzeno-7,11b-dihydronaphtho-[1,2,3-de]chroman (**4**).* To a solution of 35.4 mg (0.1 mmol) of **3** in 10 mL of chloroform was slowly added a solution of 15 mg (0.096 mmol) of bromine in 20 mL of chloroform at 0 °C. The reaction proceeded instantaneously as fading of the color indicated. After 1 h, the solvent was evaporated and the residue was purified by chromatography on silica gel, using hexane as an eluent. The product was recrystallized from hexane, mp 195—196 °C. The purity was checked by a ^{1}H NMR spectrum and the molecular constitution by high resolution mass spectroscopy. Found: M^+ 418.0545 and 420.0512. $C_{24}H_{19}O_2Br$ requires M^+ 418.05698 for ^{79}Br and 420.05501 for ^{81}Br. The relative intensities of the peaks were in good agreement with those calculated from the natural abundance of the isotopes. ^{1}H NMR ($CDCl_3$, δ): 2.7—3.6 (2H, m), 3.81 (2H, d), 3.79 (3H, s), 5.84 (1H, s), 6.51 (2H, s), 6.9—7.6 (8H. m).

Competitive Bromination of 9-Allyltriptycene and 9-Allyl-1,4-dimethoxytriptlycene. A solution of 15.5 mg (53 μmol) of 9-allyltriptycene and 18.8 mg (53 μmol) of **3** in 10 mL of chloroform containing 10.7 mg of hexachlorobenzene was treated with 8.4 mg (53 μmol) of bromine in chloroform as above. The disappearance of the starting material was checked by taking the internal standard (C_6Cl_6) in the high pressure liquid chromatography. The decrease in the amount of 9-allyltriptycene could not be detected, whereas **3** reacted completely as far as the detecting device could tell.

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References

1) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca (1953), pp. 306—418.
2) G. Izumi, G. Yamamoto, and M. Ōki, *Chem. Lett.*, **1980**, 969.
3) A neighboring participation by a chloro group was reported during the addition of bromine to allyltriptycenes: S. Hatakeyama, T. Mitsuhashi, and M. Ōki, *Bull. Chem. Soc. Jpn.*, **53**, 731 (1980).
4) D. J. Cram, *J. Am. Chem. Soc.*, **75**, 332 (1953).
5) M. Mikami, K. Toriumi, M. Konno, and Y. Saito, *Acta Crystallogr., Sect. B*, **31**, 2474 (1975).
6) N. Nogami, Ph. D. Thesis, The University of Tokyo (1978).
7) F. Suzuki and M. Ōki, *Bull. Chem. Soc. Jpn.*, **48**, 596 (1975).
8) M. Ōki, G. Izumi, G. Yamamoto, and N. Nakamura, *Chem. Lett.*, **1980**, 213.
9) D. L. H. Williams, E. B. Goetz, and J. E. Dubois, *J. Chem. Soc., B*, **1969**, 517.
10) E. B. Goetz, J. E. Dubois, D. W. Pearson, and D. L. H. Williams, *J. Chem. Soc., B*, **1970**, 1275.
11) D. Mosnaim, D. C. Nonhebel, and J. A. Russel, *Tetrahedron*, **25**, 3485 (1969).