and **16** was $F_1 = F_2 = 1300$ Hz, and $F_1 = F_2 = 1208.5$ Hz for **15c**. With a recycle delay $t_2 = 4.5$ s and $\Delta = 1 \times 10^{-5}$ s the acquisition time was 10 h in each case. Phase cycling for quadrature detection in both dimensions was used.

The NOESY spectra were recorded by using the pulse sequence $90°-t_1-90°-\tau_m-90°-\text{FID}(t_2)$ with $\tau_m = \tau_m + t_1\kappa$.[25] The mixing times were $\tau_m = 2.7$ s (**15a**), 2.5 s (**15b**), 3.8 s (**15c**), and 1.85 s (**16**), and $\kappa$ was 0.15. The values of the other parameters were equivalent to those used in the measurements of the COSY spectra.

5-Chloro-1,3-cycloheptadiene (**10**) was prepared from cycloheptatriene and HCl as described previously.[15b] The sample used in the following reactions was contaminated by some 6-chloro-1,3-cycloheptadiene, which is inert under these conditions.[15b] Zinc chloride/ether was prepared according to ref 26.

**5-Chloro-1,3-cycloheptadiene (10) and 1-Phenylpropyne (11).** A solution of **11** (2.32 g, 20.0 mmol) in $CH_2Cl_2$ (30 mL) was added dropwise (1.5 h) to a cooled solution (-78 °C) of **10** (2.06 g, 16.0 mmol) and $ZnCl_2$ (3.22 g)/$Et_2O$ (2.7 mL) in 35 mL of $CH_2Cl_2$. After stirring at -78 °C for 4.5 h, the solution was washed with 25% aqueous $NH_4Cl$ solution and dried over $CaCl_2$, and the solvent was evaporated. Distillation gave a forerun of unreacted **11** and 1.65 g (42%) of **12a** and **12b** (≈10:1 estimated from the NMR signals of the bridgehead protons) with bp 100-105 °C (bath) (0.1 mbar) and 2.10 g of nonvolatile residue.

**(1*R**,9*S**)-9-Chloro-7-methyl-8-phenylbicyclo[4.2.1]nona-2,7-diene (12a):** $^1$H NMR ($CDCl_3$) δ 1.79-1.91 (m, 1 H, 5-H), 1.93 (mc, 3 H, $CH_3$), 2.03-2.32 (m, 3 H, 4-$H_2$, 5-H), 2.85 (br t, $J$ = 6.7 Hz, 1 H, 6-H), 3.45 (br t, $J$ = 6.7 Hz, 1 H, 1-H), 4.65 (br t, $J$ = 6.7 Hz, 1 H, 9-H), 5.65-5.77 (m, 1 H, 2-H), 5.86-5.98 (m, 1 H, 3-H), 7.31 (mc, 5 H); $^{13}$C NMR ($CDCl_3$) δ 13.50 (q, $CH_3$), 25.21, 26.79 (2 t, C-4,5), 52.62, 52.99 (2 d, C-1,6), 62.44 (d, C-9), 126.74 (d, C-para), 127.89, 128.14 (2d, C-ortho, meta), 128.20, 133.33 (2 d, C-2,3), 136.48, 136.75, 136.89 (3 s, C-7,8, C-ipso). Anal. Calcd for $C_{16}H_{17}Cl$ (244.8): C, 78.51; H, 7.00. Found: C, 78.37; H, 7.08.

**9-Chloro-8-methyl-7-phenylbicyclo[4.2.1]nona-2,7-diene (12b)** is assumed to be the minor component of the mixture because of $^1$H NMR absorptions at δ 3.12-3.27 (m, 1,6-H) and 4.70 (br t, $J$ = 6.7 Hz, 9-H). The relation of these protons was ascertained by spin-decoupling experiments. $^{13}$C NMR ($CDCl_3$) δ 15.01 (q, $CH_3$), 25.45, 27.14 (2 t, C-4,5), 51.55, 54.60 (2 d, C-1,6), 62.52 (d, C-9), 126.89 (d, C-para), 128.00, 128.31 (2d, C-ortho, meta), 127.34, 133.93 (2 d, C-2,3), 133.26, 135.76, 136.79 (3 s, C-7,8, C-ipso).

**5-Chloro-1,3-cycloheptadiene (10) and 1-Methoxy-2-methylpropene (13).** A solution of **13** (4.30 g, 50.0 mmol) in 30 mL of $CH_2Cl_2$ was added dropwise (0.5 h) to a rapidly stirred solution of **10** (5.14 g, 40.0 mmol) and $ZnCl_2$ (5.04 g)/$Et_2O$ (4.20 mL) in 60 mL of $CH_2Cl_2$ (-78 °C). After 1 h the reaction mixture was washed with 50 mL of 25% aqueous $NH_4Cl$ solution and dried with $CaCl_2$. The solvent was evaporated, and the yellow residue was distilled to give 1.29 g of **10** (bp 20-30 °C (bath) (0.4 mbar)), 5.09 g of the 1:1 products **14-16**, and 1.27 g of a nonvolatile residue. Separation of 1.00 g of the 1:1 product mixture by MPLC (silica gel, 15-25 μm, hexane:ether = 98.5:1.5) yielded 153 mg of (1*S**,4*R**,6*S**)-4-chloro-6-methoxy-7,7-dimethylbicyclo[3.2.2]-non-2-ene (**15a**), 81 mg of (1*S**,4*R**,6*R**)-4-chloro-6-methoxy-7,7-dimethylbicyclo[3.2.2]non-2-ene (**15b**), 189 mg of (1*S**,4*S**,6*R**)-4-chloro-6-methoxy-7,7-dimethylbicyclo[3.2.2]-non-2-ene (**15c**), 54 mg of (1*S**,4*R**,7*S**)-4-chloro-7-methoxy-6,6-dimethylbicyclo[3.2.2]non-2-ene (**16**), and 393 mg of 2-(2,6-cycloheptadienyl)-2-methylpropanal (**14**) (77% total yield with respect to reacted **10**).

NMR data: Tables I and II. Mass spectrum (70 eV) of **15c**: $m/z$ (rel intensity) 216, 214 (0.5%, 1.9%, $M^+$), 147 (3), 135 (2), 121 (3), 105 (4), 97 (12), 93 (15), 91 (11), 86 (100). Anal. Calcd for $C_{12}H_{19}ClO$ (214.7): C, 67.12; H, 8.92. Found for **15a**: C, 67.56; H, 9.31. Found for **15b**: C, 67.89; H, 8.97. Found for **15c**: C, 67.02; H, 8.78. Spectroscopic data of **14**: see ref 15b.

**Acknowledgment.** We thank R. Lammers for experimental assistance, Dr. E. Bäuml and Dr. Ch. Wolff for discussions, and the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

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# Photocycloaddition of 1,4-Dioxene to 3-Methylcyclohex-2-en-1-one: Conformational Analysis, X-ray Crystal Structures, and Acid-Catalyzed Rearrangement of the Photoadducts

Jean-Marie Bernassau, Anne Bouillot, Marcel Fêtizon,* Issam Hanna, and Elaine Rose Maia

*Laboratoire de Synthèse Organique, Ecole Polytechnique, 91128 Palaiseau, Cedex, France*

Thierry Prangé

*L.U.R.E., Université de Paris-Sud, Bâtiment 209 D, 91405 Orsay, Cedex, France*

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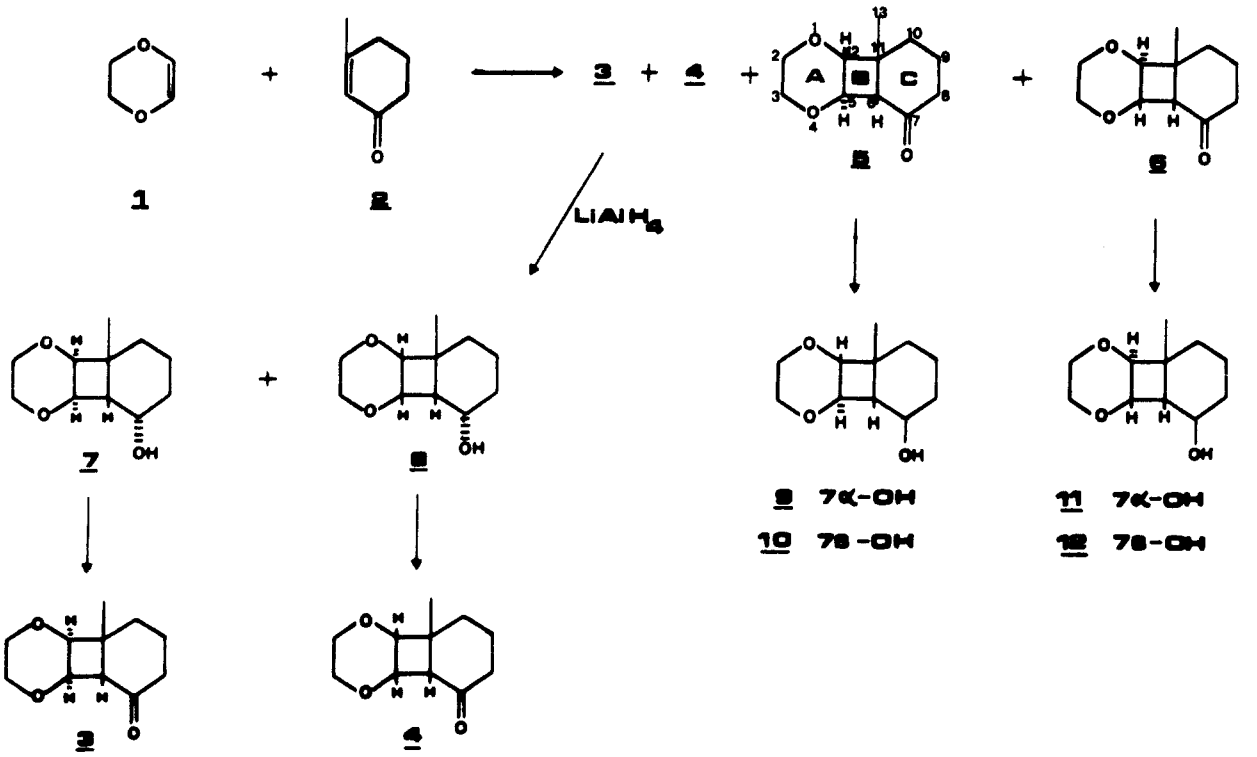
Photochemical cycloaddition of 1,4-dioxene to 3-methylcyclohex-2-en-1-one leads to a mixture of four 11-methyl-1,4-dioxatricyclo[6.4.0.0.$^{6,11}$]dodecan-7-one isomers **3-6**. Their structures have been established by X-ray diffraction and $^{13}$C NMR, and their conformational properties have been studied by force field calculations. They only differ by the stereochemistry of the cyclobutane-dioxane junction, which is found to have a pronounced influence upon the conformation of the molecules. The four-membered rings are strongly distorted in all cases. These cyclobutane photoadducts undergo an unusual acid-catalyzed rearrangement, affording compounds **19-21**. The structures of two of them, **19** and **20**, have been established by X-ray diffraction. The formation of these rearranged products can be rationalized in terms of a common cationic intermediate **23** stabilized by oxygens.

The photocycloaddition of cyclic α,β-unsaturated ketones to alkenes has been extensively studied. It has become an important tool in the arsenal of the synthetic organic chemist, leading to versatile intermediates that can be subsequently used in a number of ways. For example, the cyclobutane intermediates smoothly undergo an acid-catalyzed rearrangement, providing useful precursors of many natural products.[1]

0022-3263/87/1952-1993$01.50/0 

Scheme I




As part of our work on the use of dihydro-1,4-dioxin (1,4-dioxene, 1) in the synthesis of polyfunctionalized compounds,[2] we have examined the [2+2] photocycloaddition of this electron-rich substrate to 3-methylcyclohex-2-enone (2) and the subsequent acid-catalyzed rearrangement of the photoadducts. This paper describes the reactions and characterization of these cyclobutane derivatives based on X-ray diffraction analysis, $^{13}C$ NMR, and force field calculations. We report also the structure of the products of acid-catalyzed rearrangement and suggest a reasonable mechanism to account for these results.

## Results and Discussion

**Photochemical Cycloaddition.** Irradiation of 3-methylcyclohex-2-enone (2) with a 10-fold excess of dioxene (1) in dichloromethane at 0 °C using Pyrex-filtered light from a medium-pressure Hg lamp gave a mixture of photoadducts that were separated by flash column chromatography.

The less polar component, isolated in 51.6% yield, was found to be a mixture of two stereoisomers, 3 and 4, in 3:1 ratio according to $^1H$ and $^{13}C$ NMR spectra. Treatment of the mixture with sodium methoxide in methanol did not result in epimerization according to NMR data.

Two other crystalline [2+2] photoadducts, 5 and 6, were isolated in 31% and 17.4% yields, respectively. Neither of these substances epimerized under the aforementioned conditions. We therefore deduced that the four isomers 3–6 have the same stereochemistry at the cyclobutane–cyclohexane ring junction.

Since spectral data did not allow the unambiguous determination of the structure of the compounds, 5 and 6 were submitted to X-ray crystallographic studies; the results are shown in Figure 1.

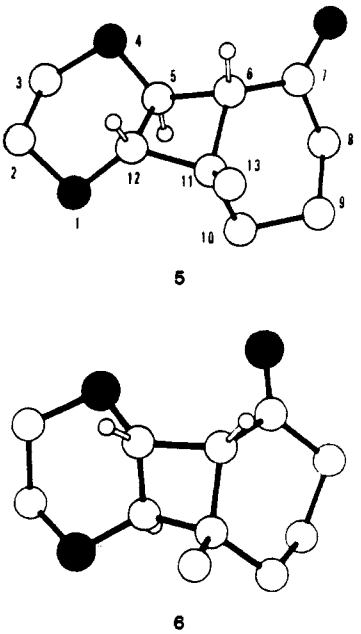



**Figure 1.** View of the two photoproducts 5 and 6 with oxygens as black circles and with the numbering used in the Discussion.

Taking advantage of our knowledge of the structures of 5 and 6, we next examined the stereochemistry of the other photoadducts, keeping in mind that they should only differ at the cyclobutane–dioxane junction.

Since ketones 3 and 4 could not be separated by chromatography, their isolation was achieved through reduction, separation of the corresponding alcohols, and reoxidation. Thus, lithium aluminum hydride reduction gave a mixture of *only two alcohols* in a 3:1 ratio, which were separated by flash chromatography. These results indicated that the reduction of each ketone proceeded in a highly stereoselective manner. As expected, the approach of the hydride reducing agents takes place from the least

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**Table I. Carbon Chemical Shifts[a] of Some of the Compounds Used in the Text**

| | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|
| C(2) | 63.5[b] | 62.8[b] | 68.2[b] | 68.5[b] | 63.8[b] | 63.1[b] | 68.1 | 68.1 | 69.0[b] | 68.4[b] |
| C(3) | 60.8[b] | 62.2[b] | 67.9[b] | 67.9[b] | 60.6 | 61.5[b] | 68.1 | 68.1 | 68.2[b] | 68.2[b] |
| C(5) | 67.5 | 69.7 | 76.4 | 77.4 | 67.3 | 72.5 | 73.2 | 75.3 | 77.2 | 75.4 |
| C(6) | 54.3 | 52.7 | 54.6 | 53.5 | 45.4 | 42.2 | 48.3 | 48.7 | 46.6 | 51.3 |
| C(7) | 210.4 | 210.1 | 208.0 | 208.8 | 63.2 | 67.7 | 66.2 | 65.1 | 65.0 | 67.1 |
| C(8) | 38.8 | 41.4 | 38.6 | 40.7 | 32.9 | 33.7 | 27.4 | 27.6 | 33.6 | 32.8 |
| C(9) | 21.5 | 20.8 | 22.6 | 20.8 | 20.8 | 20.5 | 20.4 | 14.0 | 14.2 | 20.5 |
| C(10) | 32.3 | 29.1 | 27.2 | 32.3 | 31.2 | 29.4 | 30.2 | 29.4 | 29.6 | 31.7 |
| C(11) | 39.1 | 43.4 | 47.6 | 45.6 | 36.7 | 46.4 | 43.6 | 40.4 | 40.9 | 44.1 |
| C(12) | 76.2 | 76.7 | 82.1 | 76.1 | 76.9 | 73.4 | 82.9 | 83.1 | 76.9 | 77.4 |
| C(13) | 19.9 | 27.9 | 26.3 | 20.8 | 19.9 | 27.4 | 26.4 | 27.8 | 22.7 | 22.3 |

[a] In ppm with respect to $Me_4Si$, using $CDCl_3$ as an internal standard. [b] Numbers can be interchanged inside a column.

hindered side of the molecule, i.e. anti to the cyclobutyl ring, leading to the endo stereoisomers. Oxidation of the alcohols by $CrO_3$–DMP complex led to the pure photoadducts **3** and **4** (Scheme I).

Reduction of ketones **5** and **6** was less stereoselective. Thus, treatment of **5** with lithium aluminum hydride gave a mixture of alcohols **9** and **10** in a 70:5 ratio. The major isomer was assigned structure **9** on the basis of the spectral data, confirming the expected approach of the reducing reagent from the least hindered side of the molecule. In the same way, the photoadduct **6** afforded a mixture of **11** and **12** in 46:7 ratio.

The stereochemical assignments of alcohols **7–12** were based on $^{13}C$ NMR.

**$^{13}C$ NMR.** The $^{13}C$ NMR spectra of all the compounds coming from the cycloaddition were recorded, and the results are gathered in Table I.

Interpretation of the spectra was considerably simplified by the knowledge of the structures of compounds **5** and **6**. In agreement with the equilibration experiments on basic medium, the B/C ring junction was found to be the same in all compounds. This is supported by the fairly consistent chemical shifts found around the C ring. The stereochemistry of the A/B junction was unambiguously determined by the $C_{10}/C_{13}$ chemical shifts: when the oxygen is cis to one of these carbons, it is shielded by ca. 5 ppm.

From the known structure of the ketones, the spectra of the corresponding alcohols can easily be interpreted, the stereochemistry at position 7 being determined by the chemical shift of carbon 9.

Finally, the conformational nature of the A ring is found to differ in **3** and **4** from that of **5** and **6**. The C(2) and C(3) carbons exhibit a ca. 6 ppm downfield shift on going from the former to the latter. As supported by force field studies, this effect may be assigned to a transition from boat to chair forms. The dioxane ring adopts a chair conformation when the A/B junction is trans and a boat conformation when this junction is cis.

**Force Field Calculations.** In the course of the preceding spectroscopic work, inspection of molecular models showed that the conformational properties of the compounds were by no means simple. We therefore undertook a careful molecular mechanics study in order to ascertain the preferred energy conformations of the various substances. The knowledge of these conformations was of course of great help in the $^{13}C$ study but also provided some rationalization of the experimental observations.

The 1,4-dioxane molecule has its most stable conformation in the chair form, the boat form being destabilized by 5.69 kcal·mol$^{-1}$.

When a fused cyclobutane moiety is added in position 5,6 of the dioxane, the conformational properties of the resulting bicyclic compounds depend on the junction stereochemistry. The cis junction is favored by ca. 7 kcal·mol$^{-1}$ over the trans junction. In the former case however, the dioxane ring can be found in two conformations, chair and boat, the chair form being favored only by ca. 0.7 kcal·mol$^{-1}$. When the junction is trans, then only one conformer exists with the dioxane ring in the chair form. Figure 2 summarizes these findings.

Addition of a cis-fused cyclohexanone and a methyl group to the preceding compounds results in molecules **3–6**. Here again, the cis cyclobutane–cyclohexanone junction provides the six-membered ring with two alternate conformations, chair and boat, the energy difference between the two (0.5 kcal·mol$^{-1}$) being insufficient to discard the high-energy conformer. This property of cis 4,6-membered ring junctions yields a rather complex conformational situation in the case of compounds **3** and **4**. Notice that in the cis–syn–cis case (compound **4**) the boat form of the dioxane ring is favored over the chair form. Figure 3 summarizes the results obtained. When the dioxane–cyclobutane junction is trans, however, only one conformer exists, the others being of a much higher energy. In all the compounds, the cyclobutane rings are severely distorted with a dihedral C–C–C–C angle ranging from 28.73 to −30.0°.

Finally, the alcohols corresponding to the previous ketones were studied. In this case, the situation is simplified with respect to the previous one since the cyclohexanol ring cannot assume a boat conformation. The results presented in Figure 4 are therefore easily interpreted in light of the previous observations. It will be noted that the computed conformations of compounds **10** and **11** perfectly rationalize the observed $^{13}C$ chemical shifts at position 9, $\gamma$ effect of the axial oxygen shielding this position by ca. 5 ppm.

**Acid-Catalyzed Rearrangement.** The mechanism of acid-catalyzed rearrangements of cyclobutane photoadducts is well documented, and important contributions of Cargill and others have helped to clarify the course of these reactions.[3] Thus, under acidic conditions, bicyclo[4.2.0]octan-2-one derivatives **13** undergo cyclobutane ring expansion, affording compounds **15** or **16** according to the mechanism shown in Scheme II.

The protonated ketone **14** can give rise to either fused (path a) or bridged (path b) carbocations. Although one would expect a preference for bridged migration on the basis of maximum continuous orbital overlap, both kinds of migration are in fact observed.[3,4]

With this as background, we examined the acid-catalyzed rearrangement of photoadducts **3–6** under various conditions.

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(4) Pirrung, M. C. *J. Am. Chem. Soc.* **1981**, *103*, 82 and references therein.

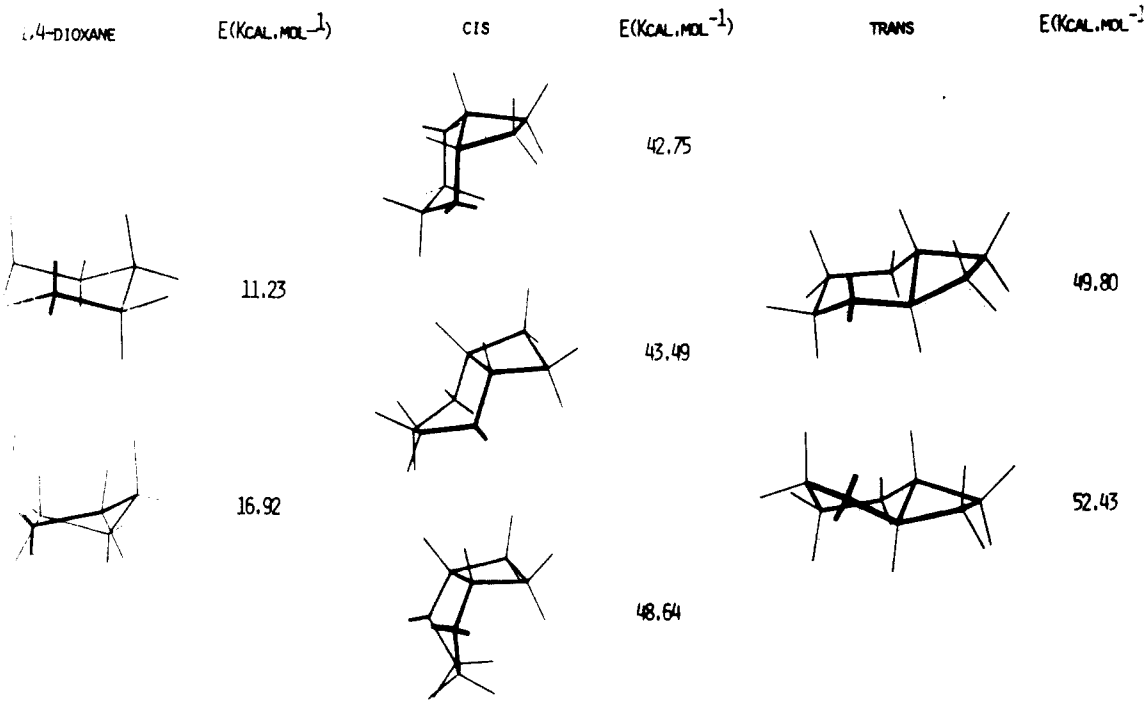



**Figure 2.** Computed conformations of 1,4-dioxane and 1,4 dioxabicyclo[4.2.0]octane and their steric energies.

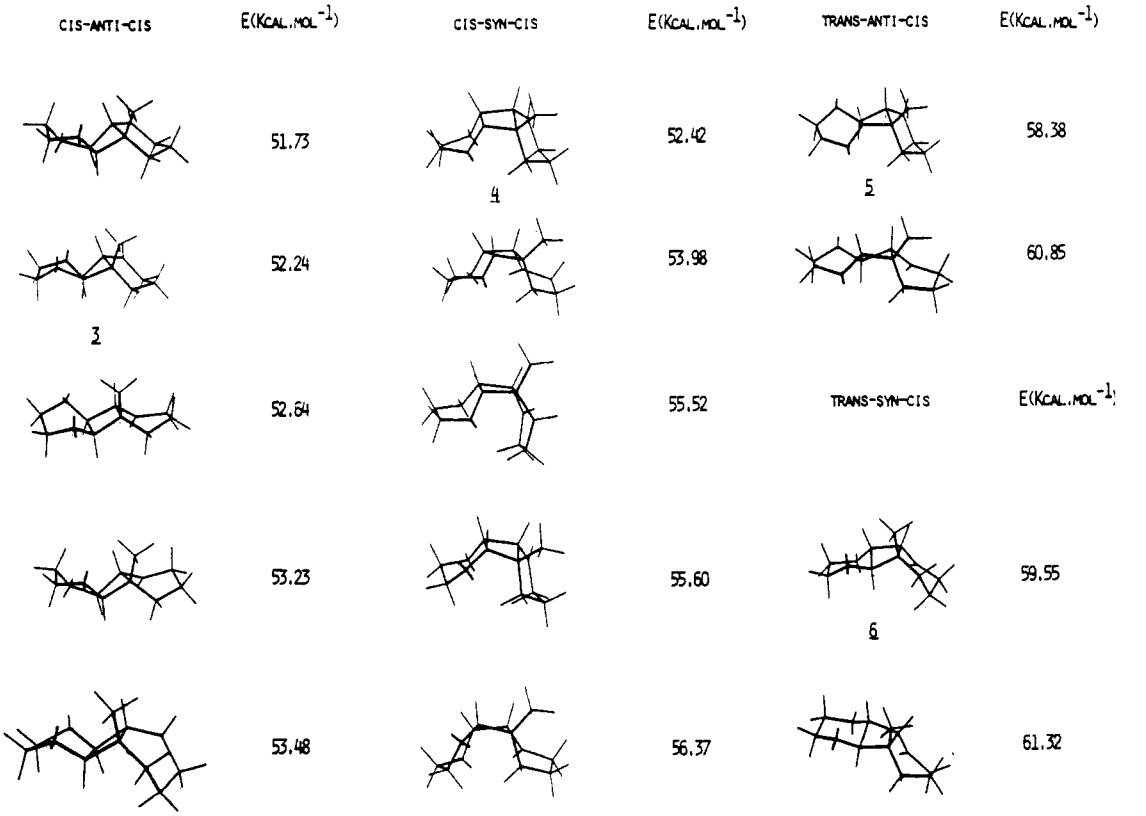



**Figure 3.** Computed conformations of 11-methyl-1,4-dioxatricyclo[6.4.0.0$^{6,11}$]dodecan-7-one stereoisomers and their steric energies.

Treatment of pure ketone **5** with an equal weight of *p*-toluenesulfonic acid in refluxing benzene provided a mixture of three products A–C, which were separated by flash chromatography.

Spectral data of the major component A (26% yield), which is a crystalline compound, do not fit any of the rearranged products **17** or **18** (Scheme III) as expected on the basis of the general mechanism shown in Scheme II. In particular, the mass spectrum showed a molecular peak at $m/z$ 240 (instead of $m/z$ 196 for **17** or **18**), and no carbonyl band absorption was observed in the IR spectrum. In addition, the $^{13}C$ NMR spectrum contains eight resonances for carbons bonded to oxygen ($\delta$ between 57 and 96).

The two other products, B and C, both of which are crystalline, have been found to be structural isomers with a molecular peak at $m/z$ 196. The minor product C (8% yield) possesses an IR absorption band at 1755 cm$^{-1}$ while B (obtained in 20% yield) displays a band at 1765 cm$^{-1}$. Although these data could be in agreement with the expected rearranged compounds, $^{13}C$ NMR spectra were consistent neither with **17** nor with **18**. Specifically, each

Scheme II

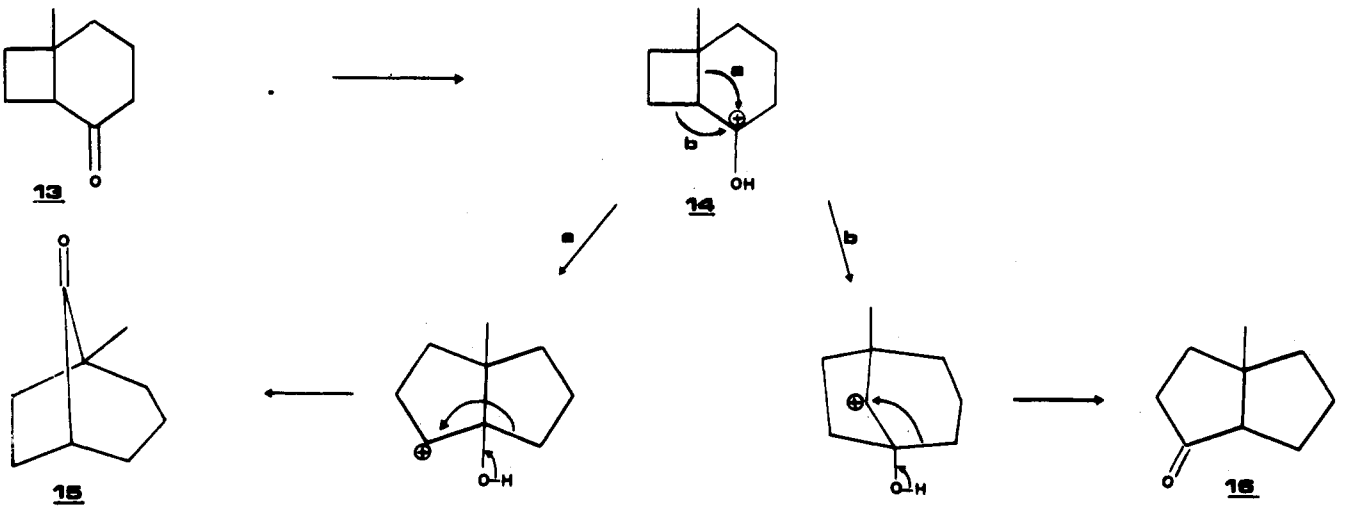



Table II. Crystallographic Details for the Cyclobutane Derivatives 5 and 6 and for the Rearranged Products 19 and 20

| | 5 | 6 | 19 | 20 |
|---|---|---|---|---|
| formula | $C_{11}H_{16}O_3$ | $C_{11}H_{16}O_3$ | $C_{13}H_{20}O_4$ | $C_{11}H_{16}O_3$ |
| cryst syst | orthorhombic | monoclinic | monoclinic | orthorhombic |
| space gp | *Pbca* | $P2_1/c$ | $P2_1/c$ | *Pbca* |
| unit cell param | | | | |
| $a$, Å | 14.280 (2) | 10.378 (3) | 13.446 (2) | 22.279 (4) |
| $b$, Å | 13.232 (2) | 8.449 (2) | 10.792 (3) | 10.726 (3) |
| $c$, Å | 10.666 (2) | 11.565 (3) | 8.250 (2) | 8.416 (2) |
| $\beta$, deg | | 92.5 (5) | 89.02 (8) | |
| $Z$ | 8 | 4 | 4 | 8 |
| $d_{calcd}/d_{measd}$ | 1.28/1.27 | 1.29/1.29 | 1.25/1.26 | 1.28/1.29 |
| $F_o$ (>2 SD) | 1360 | 1395 | 1631 | 1269 |
| $\theta_{max}$, deg | 65 | 63 | 62 | 65 |
| $R = \sum\|\|F_o\| - \|F_c\|\|/\sum\|F_o\|$, % | 8.4 | 7.8 | 7.4 | 4.7 |
| final max in $F_o - F_c$ map, e Å$^{-3}$ | 0.25 | 0.3 | 0.25 | 0.2 |

compound gave resonances for six secondary and only two quaternary carbons.

Interestingly, pure ketone **6** as well as the mixture **3** and **4** afforded, under standard conditions of acid catalysis, the mixture A, B, and C, although the yields differed (see the Experimental Section).

On the other hand, treatment of these photoadducts with boron trifluoride etherate in refluxing benzene led to a mixture of A and B along with 3-methylcyclohexen-2-one. Compound C was formed as traces (TLC) and could not be isolated.

Since the mechanism of the acid-catalyzed rearrangement evidently differs from the documented cases, we felt that structure determination should be unambiguous. The crystalline compounds A and B were therefore submitted to X-ray crystallographic studies, giving structures **19** and **20**, respectively (Figure 5). Structure **21** was assigned to compound C on the basis of the spectral data. Specifically, the $^{13}C$ NMR spectrum of **21** contains resonances for three secondary and one quaternary $sp^3$ carbon ($\delta$ 63.6, 66.3, 67.1, 83.4) in agreement with the dioxane ring. In addition, the shielded methyl group ($\delta$ 14.0) fits 1-methylbicyclo-[2.2.1]heptane bearing a *gem*-dimethyl group at C-7.

**X-ray Structures.** The final structures and relative configurations at ring junctions in **5** and **6** were definitively settled by single-crystal X-ray diffraction techniques. Both compounds crystallized in large prisms on evaporation of a methanolic solution.

The corresponding crystal data for **5** and **6** as well as **19** and **20** are listed in Table II. Coordinates, bond lengths, bond angles, and thermal parameters are given in the supplementary material.

Table III. Torsional Angles in Four- and Six-Membered Rings, as Deduced from X-ray Data (Esd's in Parentheses)

| ring | atoms | 5 | 6 |
|---|---|---|---|
| | C(12)–O(1)–C(2)–C(3) | 52.2 (5) | 54.0 (6) |
| | O(1)–C(2)–C(3)–O(4) | −53.1 (6) | −57.0 (7) |
| A | C(2)–C(3)–O(4)–C(5) | 51.9 (5) | 55.8 (7) |
| | C(3)–O(4)–C(5)–C(12) | −60.8 (5) | −62.3 (6) |
| | O(4)–C(5)–C(12)–O(1) | 72.2 (5) | 71.7 (6) |
| | C(5)–C(12)–O(1)–C(2) | −60.1 (5) | −60.8 (6) |
| | C(12)–C(5)–C(6)–C(11) | 27.7 (5) | 25.9 (7) |
| | C(5)–C(6)–C(11)–C(12) | −26.5 (5) | −25.0 (6) |
| B | C(6)–C(11)–C(12)–C(5) | 27.9 (6) | 26.1 (7) |
| | C(11)–C(12)–C(5)–C(6) | −28.6 (6) | −26.8 (7) |
| | C(6)–C(7)–C(8)–C(9) | −44.3 (6) | −44.2 (7) |
| | C(7)–C(8)–C(9)–C(10) | 60.6 (6) | 58.1 (7) |
| | C(8)–C(9)–C(10)–C(11) | −62.9 (6) | −56.2 (7) |
| C | C(9)–C(10)–C(11)–C(6) | 45.8 (5) | 38.6 (6) |
| | C(10)–C(11)–C(6)–C(7) | −30.9 (5) | −23.2 (6) |
| | C(11)–C(6)–C(7)–C(8) | 30.7 (5) | 26.7 (6) |

In compounds **5** and **6**, the four-membered rings are found strongly distorted, as deduced from Table III, which contains the dihedral angle values (ca. 26°). These values are relevant of polysubstituted cyclobutane with hindered substituents or polyhalogenated cyclobutanes.[5] The two six-membered rings are in the normal chair (ring A) and half-chair (ring C) conformations.

**Mechanism.** The absence of expected products (**17**, **18**) from the acid-catalyzed rearrangement of photoadducts **3**–**6** can be explained by the presence of the oxygens of the dioxane ring. Scheme IV shows plausible mechanism ra-

(5) Bellechini-Ferrari, M.; Gasparri-Fava, M.; Pellinghelli, M. A. *Cryst. Struct. Commun.* **1973**, *2*, 511.

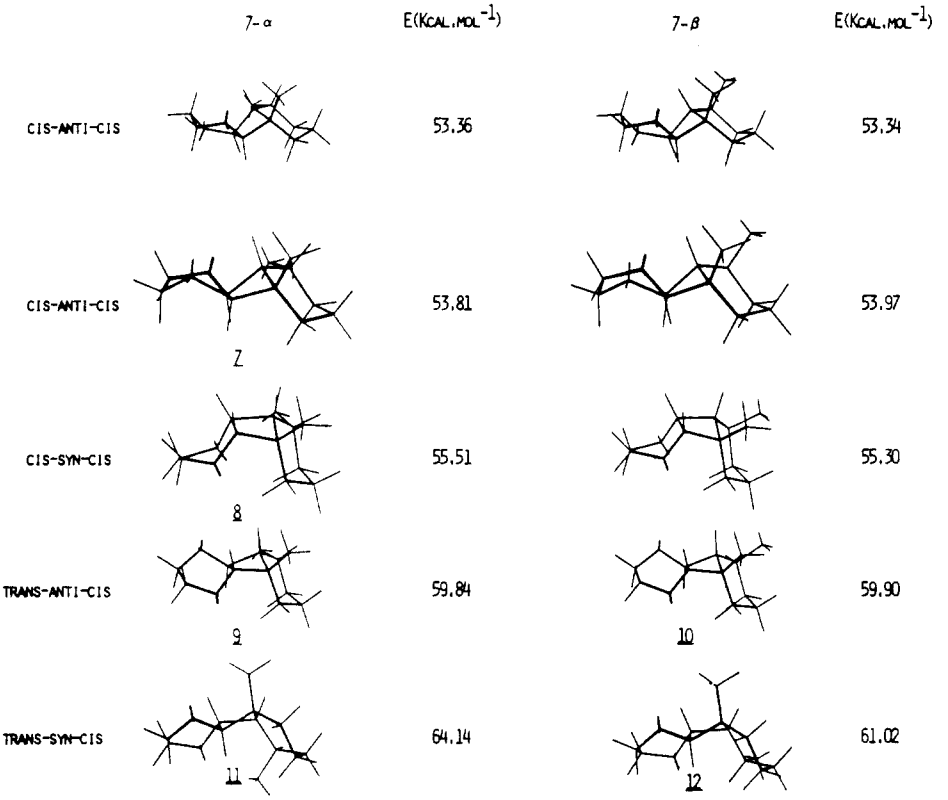
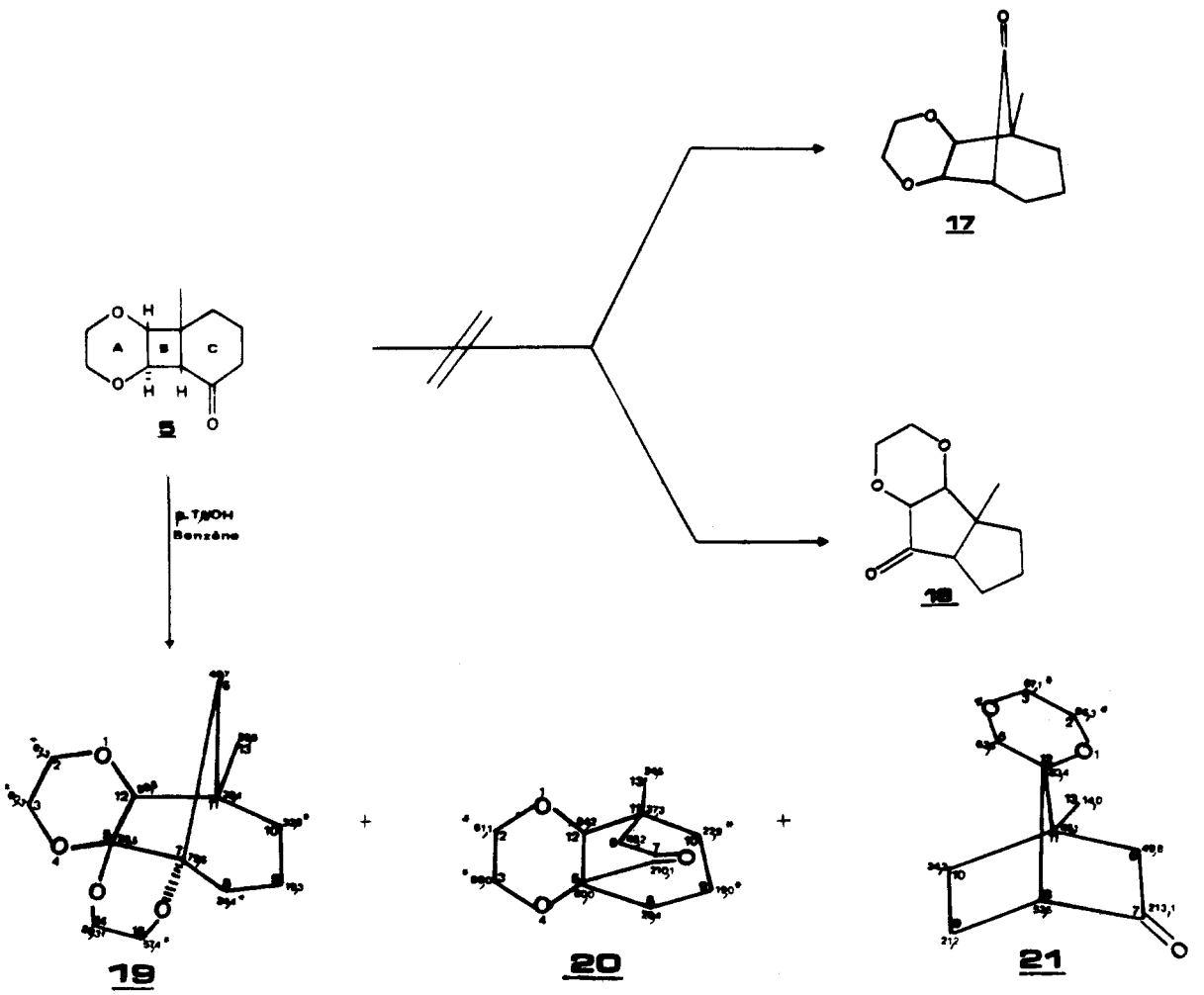
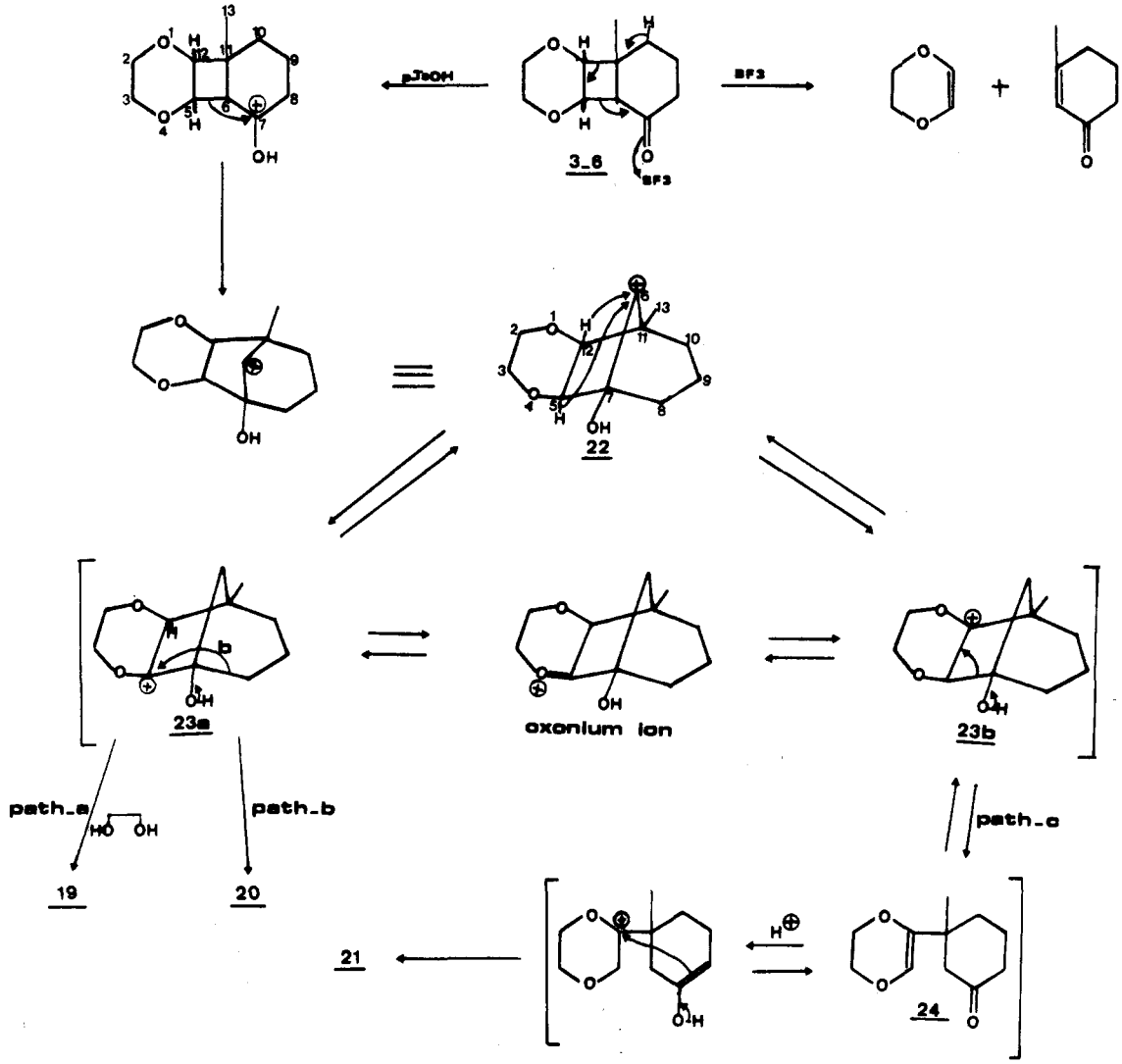



**Figure 4.** Computed conformational of alcohols 7–12 and their steric energies.

**Scheme III**



Scheme IV




tionalizing the formation of **19–21**.

The skeletal rearrangement was preferentially initiated by bridged-mode migration that allows overlap of the migrating bond, namely C(5)–C(6), with the p orbital of the carbinyl center. Examination of models of the bridged cations **22** indicates that the vacant orbital at C(6) and the *exo*-C(5H) [or the *exo*-C(12H)] bond are parallel. The 1,3 hydride shift from C(5) [or C(12)] leading to **23** is therefore readily understood. Moreover, positive charge that is developing at C(5) [or C(12)] is stabilized as an oxonium cation.

At this stage, the formation of **19** could be explained by nucleophilic attack of ethylene glycol followed by dehydration–cyclization (path a). In order to confirm this hypothesis, ketone **5** was subjected to the acidic rearrangement conditions in the presence of an excess of ethylene glycol. Compound **19** was isolated exclusively in 60% yield.

Although this mechanism is in agreement with the formation of **19**, the formation of ethylene glycol under standard acidic rearrangement conditions cannot be easily rationalized.

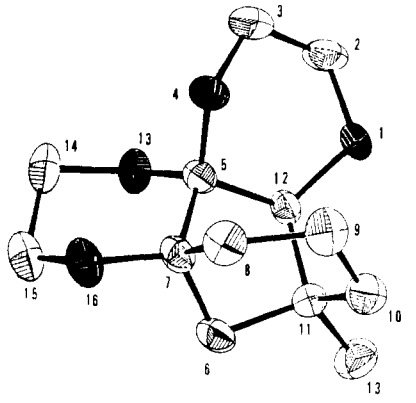
The hypothetical cation **23** is probably the key intermediate in the formation of the ketone **20**. Thus, the C(7)–C(8) bond is favorably disposed for 1,3-shift regenerating the ketone (path b) and affording **20**. On the other hand, the formation of the third compound of probable structure **21** is slightly more involved. We propose that its formation is via two steps from the cationic intermediate **23b**, as shown in Scheme IV.

## Conclusion

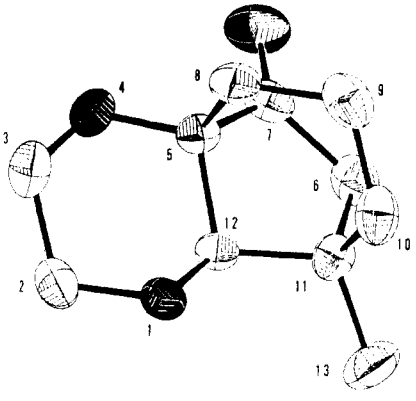
The photocycloaddition of 1,4-dioxene to 3-methylcyclohex-2-en-1-one is not stereoselective. However, the products differ only by the stereochemistry of the dioxane–cyclobutane ring junction. The cyclohexane–cyclobutane ring junction was found to be cis, and this configuration is the thermodynamically favored arrangement as confirmed by equilibration studies.

The conformational properties of the photoadducts were studied by molecular mechanics because of the rather unusual shape of the compounds. When the dioxane–cyclobutane junction is cis, the dioxane ring adopts a boat conformation. Conversely, when the junction is trans, it is found in the chair form. Several compounds were subjected to X-ray crystallography in order to ascertain their structure. This was particularly important for the rearranged compounds. The molecular geometries found by the two techniques are in good agreement, as examplified by the dihedral angles of the distorted cyclobutane ring.

Under acid-catalyzed conditions, the photoadducts undergo an unusual rearrangement leading to three different compounds. Their structure was determined by X-ray crystallography for two of them, the third one being determined on the basis of $^{13}C$ NMR spectroscopy. The formation of these compounds can be rationalized in terms



19



20

**Figure 5.** ORTEP diagram of the two acid-catalyzed rearranged compounds **19** and **20**. The ellipsoids (in black for oxygens) are drawn at the 50% density level.

of an intermediate cation stabilized by oxygen.

## Experimental Section

Melting points were taken on a Reichert hot-stage microscope apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 399 spectrophotometer as solution in $CCl_4$. $^1H$ NMR spectra of $CDCl_3$ solutions were recorded on Bruker W.P. 200 and Bruker W.M. 400 spectrometers. $^{13}C$ NMR spectra of $CDCl_3$ solutions were recorded on Varian XL 100 and Bruker W.P. 200 instruments. Mass spectra were recorded on a ZAB.2F.Vg micromass spectrometer using electron impact at 70 eV. TLC was performed with Merck precoated 0.2-mm silica gel 60 (F254) plates and flash column chromatography on 40–63-$\mu$m (400–230-mesh) silica gel 60.

The force field calculations were performed on a NAS 9080 computer. The program used is based on Allinger's MM2 version[6,7] interfaced with input and output subroutines allowing modification and visualization of the structures.

All the X-ray diffraction data were recorded on a Philips PW 1100 automatic four-circle diffractometer, operating with the Cu K$\alpha$ radiation, monochromatized by graphite.

The orientation of the crystals was deduced from least-squares refinements of the angular values of 25 randomly distributed reflections between $10 < \theta < 25$.

Reflections were recorded up to $\theta = 63°$ at a speed of 0.04°/s. over a range of 1.2°. Backgrounds were obtained from stationary counts on both sides of the reflections, and the $\sigma$ values were estimated from the counting statistics. The number of reflections obtained in each case is given in Table I.

The structures were solved by direct methods, using the multisolution techniques[8] and refined by least-squares procedures with anisotropic thermal factors. In all the structures, hydrogens were located on Fourier difference maps and included in the subsequent refinement cycle with a fixed isotropic thermal factor equal to the mean, recalculated, isotropic $\langle U \rangle$ factor of the bonded carbon.

The final agreement factors are reported in Table II.

**Photoadducts of 1,4-Dioxene and 3-Methylcyclohex-2-enone.** A solution of 3-methylcyclohex-2-enone (**2**; 1.0 g, 9 mmol) and a large excess of 1,4-dioxene (**1**; 10.0 g, 0.12 mol) in dichloromethane (70 mL) was irradiated under argon through a Pyrex filter with a 150-W medium-pressure mercury lamp (Hanau TQ 150) at 0 °C. After 7 h, TLC (ethyl acetate–petroleum ether, 1:3) indicated consumption of enone. After evaporation of the solvent and the excess of 1,4-dioxene under reduced pressure, the residual oil (2.1 g) was flash chromatographed (ethyl acetate–petroleum ether, 1:3) to yield three fractions in 90% combined yield. The less polar component (840 mg) was a colorless oil and gave a single spot by TLC ($R_f$ 0.5). The IR spectrum showed a broad carbonyl absorption band at 1705 $cm^{-1}$, and $^1H$ NMR contained two singlets at $\delta$ 1.16 and 1.23 corresponding to a mixture of **3** and **4** in 3:1 ratio. The next fraction was the pure crystallized **5**: 506 mg; mp 117–118 °C (petroleum ether); IR, $\nu$ 1715, 1155, 1110, 1060 $cm^{-1}$; $R_f$ 0.35 (AcOEt–petroleum ether, 1:3); $^1H$ NMR (400 MHz) $\delta$ 1.31 (s, 3 H), 1.66 (m, 1 H), 1.76 (tt, 1 H, $J$ = 15 and 4 Hz), 2.07 (m, 2 H), 2.38 (m, 2 H), 2.49 (td, 1 H, $J$ = 15 and 6 Hz), 3.16 (d, 1 H, $J$ = 9 Hz), 3.90 (m, 5 H). The more polar component was the pure crystallized **6**: 283 mg; mp 81–82 °C (petroleum ether); IR, $\nu$ 1715, 1170, 1095, 1030 $cm^{-1}$; $R_f$ 0.15 (AcOEt–petroleum ether, 1:3); $^1H$ NMR (400 MHz) $\delta$ 1.33 (s, 3 H), 1.48 (m, 1 H), 1.96 (m, 4 H), 2.43 (m, 1 H), 2.78 (d, 1 H, $J$ = 9 Hz), 3.38 (d, 1 H, $J$ = 9 Hz), 3.79 (m, 5 H).

**$LiAlH_4$ Reduction of Photoadducts 3–6. General Procedure.** To a stirred suspension of 120 mg of $LiAlH_4$ in 10 mL of dry ether was added dropwise a solution of 300 mg (1.5 mmol) of ketone in 5 mL of ether. The mixture was stirred for 2 h at room temperature and then cooled in an ice–water bath. The excess hydride was destroyed by dropwise addition of 10% aqueous HCl. The reaction mixture was subjected to continuous extraction with ether, yielding an only crude product mixture that was separated by flash chromatography.

**Reduction of the Mixture 3 and 4.** Alcohols **7** and **8** were isolated in 84.1% combined yield. The more polar product **7** ($R_f$ 0.21, ethyl acetate–petroleum ether 2:3, two elutions) isolated in 65.7% yield was an oily compound: IR, $\nu$ 3620, 3470, 1130, 1105, 1050 $cm^{-1}$; $^1H$ NMR (200 MHz) $\delta$ 0.95 (s, 3 H), 1.50 (m, 6 H), 2.28 (br s, 1 H), 2.88 (dd, 1 H, $J$ = 9 and 5 Hz), 3.58 (m, 5 H), 3.90 (m, 1 H), 4.09 (dd, 1 H, $J$ = 9 and 5 Hz). The minor alcohol **8** (18.4% yield, $R_f$ 0.29) was isolated as a colorless oil: IR, $\nu$ 3595, 3490, 1155, 1050 $cm^{-1}$; $^1H$ NMR (200 MHz) $\delta$ 1.03 (s, 3 H), 1.40 (m, 5 H), 1.93 (m, 3 H), 2.23 (td, 1 H, $J$ = 14 and 3 Hz), 3.65 (m, 4 H), 4.08 (m, 1 H), 4.33 (t, 1 H, $J$ = 5 Hz).

**Reduction of 5** afforded two separable alcohols: the 7$\alpha$- and 7$\beta$-hydroxy isomers **9** and **10**, respectively. The major alcohol **9**, which is more polar ($R_f$ 0.32, ethyl acetate–petroleum ether, 3:1), was isolated in 69.5% yield as pure crystalline compound: mp 66–68 °C (pentane); IR, $\nu$ 3610, 3460, 1055, 1030 $cm^{-1}$; $^1H$ NMR (200 MHz) $\delta$ 0.82 (s, 3 H), 1.18 (m, 6 H), 1.63 (m, 1 H), 2.66 (d, 1 H, $J$ = 9 Hz), 2.91 (br s, 1 H), 3.20 (t, 1 H, $J$ = 9 Hz), 3.45 (m, 5 H). The less polar isomer ($R_f$ 0.42) isolated in 5% yield is an oily compound. IR $\nu$ 3630, 3480, 1170, 1090, 1065 $cm^{-1}$; $^1H$ NMR (200 MHz) $\delta$ 1.25 (s, 3 H), 1.43 (m, 6 H), 2.28 (m, 1 H), 2.93 (d, 1 H, $J$ = 8 Hz), 3.28 (t, 1 H, $J$ = 9 Hz), 3.66 (m, 5 H), 4.09 (s, 1 H).

**Reduction of 6** gave two separable crystalline alcohols: the 7$\alpha$- and 7$\beta$-hydroxy epimers **11** and **12**, respectively. The major compound **11**, which was isolated in 60.5%, is the less polar ($R_f$ 0.65, ethyl acetate–petroleum ether, 2:3): mp 49–51 °C (pentane); IR, $\nu$ 3540, 1030, 1095 $cm^{-1}$; $^1H$ NMR (200 MHz) $\delta$ 1.05 (s, 3 H), 1.08 (m, 3 H), 1.71 (m, 3 H), 2.13 (m, 1 H), 3.15 (m, 1 H), 3.81 (m, 6 H), 4.25 (m, 1 H). The more polar isomer ($R_f$ 0.21) was isolated in 11.2% yield: mp 95–97 °C (pentane); IR, $\nu$ 3610, 3440, 1120, 1090, 1040 $cm^{-1}$; $^1H$ NMR (200 MHz) $\delta$ 1.20 (s, 3 H), 1.36

(6) Allinger, N. L. *Adv. Phys. Org. Chem.* **1976**, *13*, 1.
(7) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127.
(8) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. A: Cryst. Phys., Diffr., Theor. Gen. Crystallogr.* **1971**, *27*, 368.

(m, 7 H), 2.03 (t, 1 H, $J$ = 8 Hz), 2.63 (m, 1 H), 3.40 (d, 1 H, $J$ = 9 Hz), 3.81 (m, 5 H).

**Oxidation of Pure Alcohols 7 and 8. Pure Photoadduct 3.** To a stirred suspension of 0.85 g of dry chromium trioxide in 8 mL of dry dichloromethane at −20 °C under argon was added rapidly 0.80 g of 3,5-dimethylpyrazole (DMP). After 15 min, a solution of 140 mg of **7** in 2 mL of $CH_2Cl_2$ was added dropwise. The mixture was stirred at −20 °C for 1 h, 3.5 mL of 5 N aqueous NaOH was added, and stirring was continued for 1 h at 0 °C. The organic layer was successively washed with 10% HCl aqueous solution, saturated $NaHCO_3$, and saturated NaCl and dried. The crude product was purified by flash column chromatography using ethyl acetate–petroleum ether (3:7) as eluting solvent to give 106 mg (76.5% yield) of pure oily ketone **3**: IR, $\nu$ 1710, 1195, 1190, 1150, 1115, 1100 $cm^{-1}$; $^1H$ NMR (200 MHz) $\delta$ 1.02 (s, 3 H), 1.63 (m, 4 H), 2.26 (m, 2 H), 3.15 (d, 1 H, $J$ = 9 Hz), 3.53 (m, 3 H), 3.83 (d, 1 H, $J$ = 5 Hz), 3.88 (m, 1 H), 4.21 (dd, 1 H, $J$ = 9 and 5 Hz).

**Pure Photoadduct 4.** Oxidation of the alcohol **8** with $CrO_3$–DMP as described above, afforded pure ketone **4** as a colorless oil in 66% yield: IR 1715, 1180, 1150, 1140 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 1.22 (s, 3 H), 1.49 (m, 1 H), 1.72 (m, 1 H), 2.1 (m, 1 H), 2.35 (m, 3 H), 2.55 (d, 1 H, $J$ = 8 Hz), 3.54 (m, 2 H), 3.8 (m, 1 H), 3.85 (dd, 1 H, $J$ = 5 Hz and 1.5 Hz), 3.94 (m, 1 H), 4.41 (dd, 1 H, $J$ = 8 Hz and 5 Hz).

**Rearrangement of 5 with *p*-TsOH.** A solution of 0.25 g of **5** and 0.2 g of *p*-toluenesulfonic acid monohydrate in 12 mL of benzene was refluxed for 24 h. The cooled reaction mixture was poured into 5% sodium bicarbonate solution. After separation, the aqueous phase was extracted with ether, and the combined organic layers were washed with saturated NaCl solution and dried. The solvent was evaporated, and flash column chromatography of the crude product easily separated three compounds.

**Compound 19**, which is less polar ($R_f$ 0.64, AcOEt–petroleum ether, 1:4), was isolated in 26% yield (65 mg): mp 66–68 °C (petroleum ether); IR, $\nu$ 1170, 1115, 1105, 1080, 1050, 990, 940 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 1.10 (s, 3 H), 1.82 (m, 6 H), 3.07 (s, 1 H), 3.70 (m, 8 H); $^{13}C$ NMR $\delta$ 19.0 (t), 26.6 (q), 33.6 (t), 34.2 (t), 39.2 (s), 40.5 (t), 57.2 (t), 59.1 (t), 60.1 (t), 61.1 (t), 79.4 (s), 88.6 (d), 96.3 (s); mass spectrum, $m/z$ 240 ($M^{\bullet+}$).

**Compound 21**, which is the minor product ($R_f$ 0.53), was obtained in 8% yield (20 mg): mp 114–115 °C (petroleum ether); IR, $\nu$ 1755, 1140, 1130, 1095, 1080 $cm^{-1}$; $^1H$ NMR (200 MHz) $\delta$ 0.98 (s, 3 H), 1.35 (m, 2 H), 1.93 (m, 4 H), 3.03 (d, 1 H, $J$ = 4 Hz), 3.59 (m, 6 H); $^{13}C$ NMR $\delta$ 14.6 (q), 34.3 (t), 46.1 (s), 49.8 (t), 53.6 (d), 63.6 (t), 66.3 (t), 67.1 (t), 83.4 (s), 213.1 (s); mass spectrum, $m/z$ 196 ($M^{\bullet+}$).

**Compound 20**, which is more polar ($R_f$ 0.28), AcOEt–petroleum ether, 1:4), was obtained in 20% yield: mp 95 °C (ether–petroleum ether); IR, $\nu$ 1765, 1140, 1120, 1095 $cm^{-1}$; $^1H$ NMR $\delta$ 1.07 (s, 3 H), 1.43 (m, 5 H), 1.90 (d, 1 H, $J$ = 20 Hz), 2.16 (d, 1 H, $J$ = 20 Hz), 2.43 (m, 1 H), 3.28 (s, 1 H), 3.75 (m, 4 H); $^{13}C$ NMR $\delta$ 19.1 (t), 23.0 (t), 24.5 (q), 29.4 (t), 37.4 (s), 48.2 (t), 61.2 (t), 68.1 (t), 80.0 (s), 84.2 (d), 210.2 (s); mass spectrum, $m/z$ 196 ($M^{\bullet+}$).

**Acid-Catalyzed Rearrangement of 5 in the Presence of Ethylene Glycol.** To a solution of 150 mg of **5** and 0.20 g of *p*-TsOH in 8 mL of benzene was added 0.5 mL of ethylene glycol. The mixture was refluxed for 45 min and allowed to cool to room temperature. Normal workup followed by flash chromatography afforded 110 mg (60.1%) of pure crystallized **19**, in all respects identical with the previously isolated material.

**Rearrangement of Pure 6 with *p*-TsOH.** The acidic treatment of **6** as described above afforded **19** in 27.6% yield (81 mg), **21** in 3.75% yield (9 mg), and **20** in 11.3% yield (27 mg).

**Rearrangement of the mixture 3 and 4 with *p*-TsOH** afforded **19** in 10.9% yield (20 mg) and **20** in 34% yield (51 mg).

**Rearrangement with $BF_3$–$Et_2O$. General Procedure.** To a solution of ketone (1 mmol) in 15 mL of benzene was added 0.03 mL of $BF_3$–$Et_2O$, and the mixture was refluxed for 30 min. After being cooled to room temperature, the reaction solution was poured into 5% $NaHCO_3$ and diluted with ether, and the layers were separated. The organic layer was washed with brine and dried with magnesium sulfate; removal of the solvent afforded the crude product mixture, which was separated by flash column chromatography.

The pure ketone **5** gave **19** in 16.7% yield (40 mg), **20** in 7.6% yield (15 mg), and 3-methylcyclohex-2-enone in 27.3% yield (30 mg).

The pure ketone **6** gave **19** in 17.5% yield (42 mg), **20** in 10.7% yield (21 mg), and 3-methylcyclohex-2-enone in 15.5% yield (17 mg).

The mixture **3** and **4** gave **19** in 20.8% yield (50 mg), **20** in 15.3% yield (30 mg), and 3-methylcyclohex-2-enone in 18.2% yield (20 mg).

**Registry No.** **1**, 543-75-9; **2**, 1193-18-6; (±)-**3**, 107200-97-5; (±)-**4**, 107296-95-7; (±)-**5**, 107296-96-8; (±)-**6**, 107296-97-9; (±)-**7**, 107200-98-6; (±)-**8**, 107296-98-0; (±)-**9**, 107296-99-1; (±)-**10**, 107297-00-7; (±)-**11**, 107297-01-8; (±)-**12**, 107297-02-9; (±)-**19**, 107200-99-7; (±)-**20**, 107201-01-4; (±)-**21**, 107201-00-3; (±)-**22**, 107201-04-7; (±)-**23a**, 107201-02-5; (±)-**23b**, 107201-03-6.

**Supplementary Material Available:** Description of the unit cell and tables of positional parameters and isotropic thermal parameters for non-hydrogen and hydrogen atoms, anisotropic thermal parameters for non-hydrogen atoms, bond distances, and bond angles for compounds **5**, **6**, **19**, and **20** (8 pages). Ordering information is given on any current masthead page.