468 J. Org. Chem. 1994, 59, 468–471

Study of I-Strain Relief in the Intermediate When Forming Spiro Ketones from Unsymmetrical Cycloalkylidenecycloalkanes, Their Dibromides, and Their Pinacols

Richard D. Sands

Department of Chemistry, Alfred University, Alfred, New York 14802

Received May 17, 1993[●]

Three unsymmetrical intercyclic olefins, their dibromides, and their pinacols were prepared, each so the two carbons involved at the functional group were part of a different sized ring. The pinacols were reacted with 25% sulfuric acid and with boron trifluoride etherate, the dibromides with silver nitrate, and the olefins with mercuric acetate and with trifluoroperacetic acid. The predominant spiro ketone found in each product mixture was used to determine which carbon, and hence which size ring, could better undergo the sp^2 to sp^2 or the sp^2 to sp^3 transition. The findings were consistent with Brown's observations on ring strain.

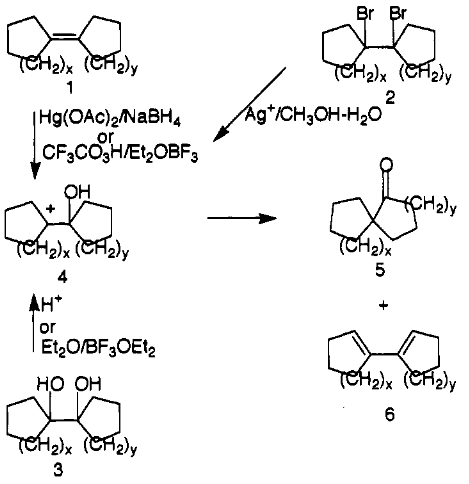
The object of the present study was to use the reactions in Scheme 1 to show which of two carbons better undergoes an sp^3 to sp^2 or an sp^2 to sp^3 transition when each is part of a different sized ring.

The expectation was that the intermediate in each reaction would form according to Brown's observation[1,2] that relief of strain when a ring carbon goes from sp^2 to sp^3 hybridization is greater in a six- than in a five- and greater in a five- than in a seven-membered ring. With a few exceptions (because the reactivities involving the five- and seven-membered rings are similiar), the strain decreases, in the reverse order, for reactions where a ring carbon goes from sp^3 to sp^2 hybridization.[3]

The idea is that when either transition takes place on a ring carbon, the angles from that carbon to the other ring carbons must change. That, in turn, affects the interaction of attached hydrogen atoms and changes the internal- or I-strain of the ring. The size of the ring of which it is a part will determine which carbon better undergoes the sp^3 to sp^2 or the sp^2 to sp^3 transition in the reactions of Scheme 1. That will determine which isomeric structure 4 is the intermediate and which isomeric spiro ketone is the product.

The mercuric acetate reaction, a reaction which normally gives Markovnikov hydration of unsymmetrical olefins,[4] should put an HgOAc group on one of the sp^2 carbons of the intercyclic olefin 1 and an OH group on the other. Reduction should then give one of two possible alcohols depending on which end of the double bond gets the HgOAc in Scheme 2. The trifluoroperacetic acid reaction with olefins, a reaction that converts olefins to ketones,[5] should form an intermediate structure 4, Scheme 3, possibly via an epoxide.[5] The reaction of the pinacol bromides with silver ion in aqueous methanol, a reaction that converts dibromides to ketones,[6] would be expected to give an intermediate structure 4 as in Scheme 4. Finally, the pinacol pinacolone rearrangement of each of the diols, Scheme 5, should also go by way of a structure 4 by loss of one of the two OH groups. In all cases intermediate 4 would be expected to rearrange to a spiro ketone.

Scheme 1



a x=1; y=1
b x=1; y=2
c x=1; y=3
d x=1; y=4
e x=2; y=1
f x=2; y=2
g x=2; y=3
h x=2; y=4
i x=3; y=1
j x=3; y=2
k x=3; y=3
l x=3; y=4

Results

The reactions of mercuric acetate/sodium borohydride with the unsymmetrical intercyclic olefins **1b**, **1c**, and **1g** are summarized in Table 1. It is to be noted that none of the intercyclic olefins reacted well and that none gave alcohols as expected. Spiro ketones, however, did form in each case, indicating an intermediate structure 4.

The reactions of trifluoroperacetic acid/boron trifluoride etherate with unsymmetrical intercyclic olefins **1b**, **1c**, and **1g** are summarized in Table 2. As expected, they formed spiro ketones, which must have formed from intermediates with structure 4.

The reactions of symmetrical, **2a** and **2f**, and unsymmetrical, **2b**, **2c**, and **2g**, cyclic dibromides with silver nitrate are summarized in Table 3. Elimination to a diene was a serious competing reaction, but spiro ketones usually did form.

The reactions of symmetrical, **3a**, **3f**, **3k**, and unsymmetrical, **3b**, **3c**, and **3g**, pinacols with refluxing 25%

[●] Abstract published in *Advance ACS Abstracts*, January 1, 1994.

(1) Brown, H. C.; Fletcher, R. S.; Johannesen, R. B. *J. Am. Chem. Soc.* **1951**, *73*, 212.

(2) Brown, H. C.; Brewster, J. H.; Shechter, H. *J. Am. Chem. Soc.* **1954**, *76*, 467.

(3) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; p 268.

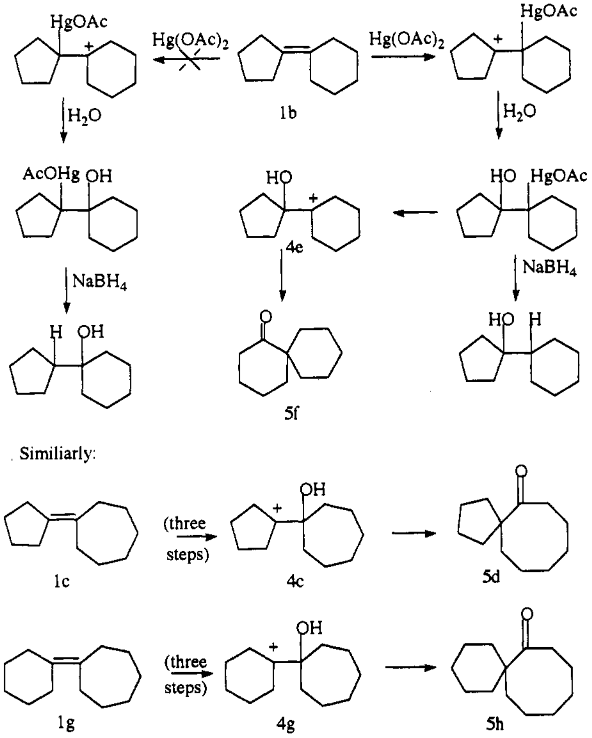
(4) Brown, H. C.; Georghegan, P., Jr. *J. Am. Chem. Soc.* **1967**, *89*, 1522.

(5) Hart, H.; Lerner, L. R. *J. Org. Chem.* **1967**, *32*, 2669.

(6) Kakis, F. J.; Brace, D.; Oshima, A. *J. Org. Chem.* **1971**, *36*, 4117.

0022-3263/94/1959-0468$04.50/0

Scheme 2



Scheme 3

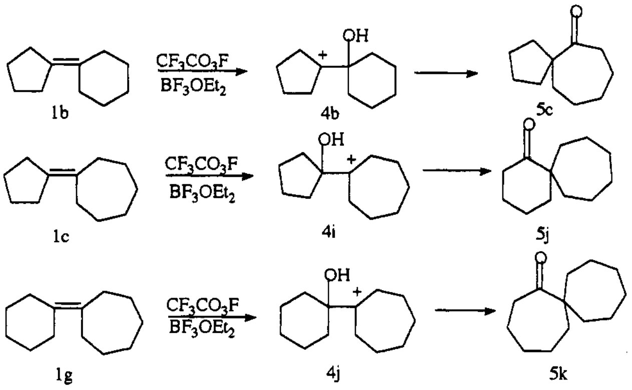


Table 1. Spiro Ketones from Reaction of Intercyclic Olefins with Mercuric Acetate/NaBH$_4$

olefin	presumed intermed	spiro ketone (%)
1b	**4e**	**5f** (47.3)
1c	**4c**	**5d** (9.5)
1g	**4g**	**5h** (23.0)

Table 2. Spiro Ketones from Reaction of Intercyclic Olefins with Trifluoroperacetic Acid/Boron Trifluoride Etherate

olefin	presumed intermed	spiro ketone (%)
1b	**4b**	**5c** (48.0); **5f** (6.3)
1c	**4i**	**5j** (67.9); **5d** (6.0)
1g	**4j**	**5k** (33.5)

sulfuric acid and with cold boron trifluoride etherate are summarized in Table 4. The intermediates were clearly of structure 4 type. The use of boron trifluoride etherate practically eliminated the competing diene formation.[7]

Table 3. Spiro Ketones from Reactions of Cyclic Pinacol Bromides with Silver Nitrate

dibromide	presumed intermed	ketones (%)	dienes (%)
2a	*a*	**5b** (89.1)	
2f	*a*		**6f** (100)
2b	**4e**	**5f** (20.9)	**6b** (74.6)
2c	**4i**	**5j** (27.5); **5d** (3.1)	
2g			**6g** (63.2)

[a] There is no choice of intermediate with the symmetrical diols.

Table 4. Spiro Ketones from Reactions of Cyclic Pinacols with 25% Sulfuric Acid (A) and with Boron Trifluoride Etherate (B)

pinacol	reagent	presumed intermed	ketones (%)	diene (%)
3a	A	*a*	**5b** (85)	**6a** (15)
3f	A	*a*	**5g** (5.9)	**6f** (90.0)
3k	A	*a*	**5l** (4.4)	**6k** (95.6)
3b	A	**4e**[b]	**5f** (10.8); **5c** (0.3)	**6b** (88.9)
3c	A	**4i**	**5j** (73.1)	**6c** (26.9)
3g	A	*a*		**6g** (100)
3a	B	*a*	**5b** (100)	
3f	B	*a*	**5g** (89.4)	**6g** (10.6)
3k	B	*a*	**5l** (100)	
3b	B	**4b**	**5c** (73.9); **5f** (14.7)	**6b** (11.1)
3c	B	**4i**	**5j** (100)	
3g	B	**4j**	**5k** (92.8)	**6g** (7.2)

[a] Only one intermediate could form. [b] See discussion.

Discussion

In the mercuric acetate reaction the intercyclic olefins were mainly recovered unreacted, but small amounts of spiro ketones did form. While hydration of olefins with mercuric acetate/sodium borohydrate normally involves addition of $^+$HgOAc, hydroxylation by water, and reduction,[4] the intercyclic olefins apparently lose the mercury salt to form ions of structure 4. The spiro ketone formed, by expansion of the ring of ion 4 that has the OH group, is the indication of which way the addition took place. Scheme 2 shows the steps by which **1b** is converted to **4e**. Similarly, **1c** and **1g** are converted to **4c** and **4g**, respectively. Scheme 3 shows the conversion of **1b**, **1c**, and **1g** to **4b**, **4i**, and **4j**, respectively, either by the addition of the OH cation or from an initially formed epoxide.[5]

The intermediates, identified by which spiro ketones formed in the greater abundance, have the plus charge and OH reversed in the mercuric acetate and trifluoroperacetic acid reactions even though both reactions require an electron-seeking group to attack the same carbon.

It should be clear from Schemes 2 and 3 that the initial sp^2 to sp^3 change occurs at the six-membered ring instead of the five-membered ring, at the six-membered ring instead of the seven-membered ring, and at the five-membered ring instead of the seven-membered ring. In short, for the sp^2 to sp^3 transition the favored ring size is six > five > seven.

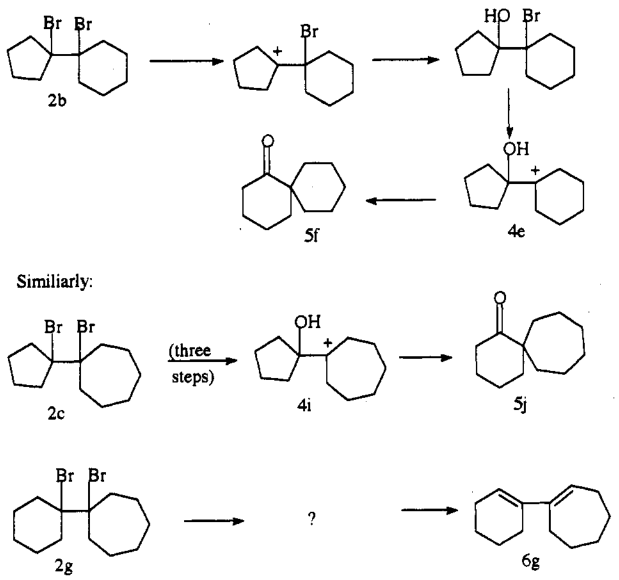
Also in the trifluoroperacetic acid reaction, the two intercyclic olefins having six-membered rings, **1b** and **1g**, formed fair amounts of byproducts that appear to have resulted from isomerization of the double bond into one of the rings. These products were not pursued further.

In the reactions of chloroform solutions of structure 2-type dibromides with silver nitrate in aqueous methanol, elimination competes seriously with rearrangement especially when either ring is six-membered. The Kakis mechanism for the conversion of olefins to ketones[6] via dibromides, applied to dibromides of structure 2, is shown in Scheme 4, where it can be seen that initial loss of a bromide ion from the carbon whose ring is better able to support the sp^3 to sp^2 transition leads to the structure 4

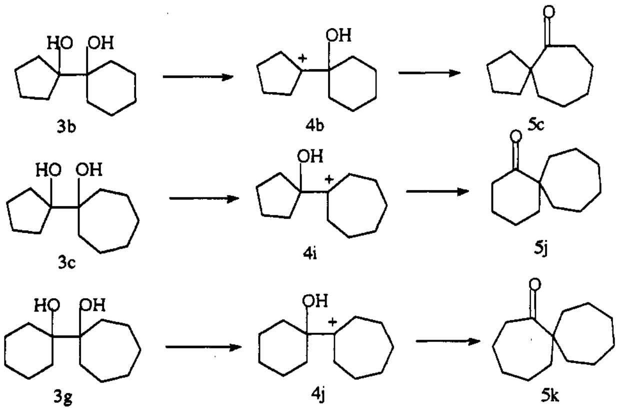
---

(7) Sands, R. D. *J. Chem. Educ.* **1992**, *69*, 667.

Scheme 4



Scheme 5



that gives the spiro ketone formed in the greater quantity. In the case of the dibromides, the preference is five > six and (unexpectedly) five > seven. Six vs seven could not be determined because no spiro ketone was formed from **2g**.

In the pinacol pinacolone rearrangement of the unsymmetrical diols a hydroxide ion is removed initially to give an ion **4**. The hydroxide is removed from the carbon whose ring size can better accommodate the sp^3 to sp^2 transition. Again, the spiro ketone formed indicates which carbon that is.

In the reaction of **3b** with refluxing 25% sulfuric acid, **4e** seems to be the favored intermediate, but when so much diene is formed, it could be argued that **4b** is the favored ion and that the **4b** formed mainly diene, under the rather severe conditions, instead of spiro ketone. The much milder conditions used in the boron triflouride etherate reactions not only gave more rearrangement in all cases but made it clear that **4b** is indeed the favored intermediate.[7] Scheme 5 shows a seven > five > six preference for the sp^3 to sp^2 transition.

Conclusion

In the reaction of mercuric acetate/$NaBH_4$ and in the reaction of trifluoroperacetic acid/$BF_3{\cdot}OEt_2$ with intercyclic olefins the sp^2 to sp^3 transition is easier for carbons that are part of six-membered rings than for those that are part of five-membered rings and easier for carbons that are part of five-membered rings than for carbons that are part of seven-membered rings.

The ease of the sp^3 to sp^2 transition for carbons that are part of rings, with the exception of the reaction of dibromide **2c** with silver nitrate in aqueous methanol, goes in the opposite direction.

Dibromide **2c** involves both a five- and a seven-membered ring. Early work by Brown and others[3] showed the two rings to exhibit similiar reactivity in the sp^3 to sp^2 transition, sometimes better with the five-membered ring, sometimes better with the seven-membered ring. In the pinacol rearrangement of **3c**, however, there is little question that the seven-membered ring is better able to undergo the sp^3 to sp^2 transition than is the five-membered ring. The results, therefore, are consistent with Brown's I-strain observations in that the reactions studied follow the course that gives the greatest relief of ring strain, which is six > five > seven for sp^2 to sp^3 and seven > five > six for sp^3 to sp^2.

Experimental Section

Boron Trifluoride Etherate Treatment of Diols.[7] The diol, 3.0 g, was dissolved in 50 mL of methylene chloride, stirred at room temperature under nitrogen with 1.0 g of anhydrous magnesium sulfate for 1 h, cooled in an ice bath, treated with 0.5 mL of boron trifluoride etherate, and stirred for another hour. Then 2.5 g of sodium carbonate was added, and stirring under nitrogen was continued until the ice melted. The mixture was then filtered and evaporated.

Sulfuric Acid Treatment of the Diols.[8] The diol was heated under reflux with 25% sulfuric acid for 2 h, cooled, taken up in ether, washed with bicarbonate solution and water, dried, and then evaporated.

Bromine/Silver Nitrate Treatment of Olefins.[6] The olefin (5.58 mmol) was dissolved in 25 mL of chloroform in an ice bath on a magnetic stirrer. A solution of 5 mL of bromine in 95 mL of chloroform was added in a thin stream until a slight color remained. Then 50 mL of an ice-cold solution of silver nitrate saturated in 90% methanol/10% water was added. The mixture was stirred in the ice bath overnight while the ice melted. The silver bromide was filtered off and washed with chloroform. The chloroform solution was evaporated in the rotovap to give a clear residue.

Trifluoroperacetic Acid/Boron Trifluoride Etherate Reaction.[5] Trifluoroperacetic anhydride (10.02 g, 47.7 mmol), 10 mL of methylene chloride, and 1.00 g (8.82 mmol) of 30% hydrogen peroxide were mixed at 0 °C. The peracid solution and boron trifluoride etherate (1.24 g, 8.82 mmol) were added simultaneously, dropwise, to a stirred solution of 8.43 mmol of the olefin in 10 mL of methylene chloride at 0–8 °C. The mixture was stirred for 15 min at 0 °C and then treated with 20 mL of water.

The organic layer was washed twice each with 20 mL of water, three times each with 20 mL of sodium bicarbonate, and twice each with 20 mL of water. It was then dried over sodium sulfate, filtered, and evaporated.

Mercuric Acetate/Sodium Borohydride Reaction.[4] THF (7 mL) was added to a solution of mercuric acetate (2.033 g, 6.38 mmol) in 7 mL of deionized water. After the yellow solution was stirred at room temperature for 15 min, the olefin (6.33 mmol) was added. Stirring was continued for several hours. The mixture was cooled in an ice bath and treated with 7 mL of 3 M sodium hydroxide with stirring. Then 7 mL of 3 M sodium hydroxide containing sodium borohydride (0.13 g, 4.68 mmol) was added, and the mixture was left to stir for another 3 h. The liquid was poured off the mercury. The water layer was saturated with salt and extracted with ether. The ether layer was dried over sodium sulfate, filtered, and evaporated.

---

[8] Sands, R. D.; Botteron, D. G. *J. Org. Chem.* **1963**, *28*, 2690.

Analysis. Two drops of each washed, dried, and concentrated product mixture was dissolved in 10 mL of ether. A 1-μL sample of the ether solution was injected into the GC/MS. The injector temperature was 250 °C, and the solvent delay was 1 min. The initial oven temperature was 100 °C, and that was increased by 20° per min to 250 °C. The column was 12 m × 0.2 mm and contained methylsilicone gum. Ions with masses between 50 and 250 were tabulated.

The areas under the GC peaks were machine-integrated and printed as percentages. The percent compositions reported are those of the product mixtures (with unreacted starting material subtracted in the case of the mercuric acetate reactions) and do not represent isolated products.

The three intercyclic olefins were prepared by the method Krapcho[9] used to prepare **1b** and a number of other cycloalkylidenecycloalkanes: preparation of a β-hydroxy acid, and then its lactone, and pyrolysis of the lactone to give the olefin.

a. Cyclopentylidenecyclohexane, 1b, was formed in 79% yield from 1-(1-hydroxycyclopentyl)cyclohexanecarboxylic acid lactone: bp 105 °C/25 mm; $N^{19}{}_{D}$ 1.5020. Its FT-IR had all the peaks given by Christol[10] and none between 3000 and 3200 cm^{-1}. **b. Cyclopentylidenecycloheptane, 1c.** 1-(1-Hydroxycycloheptyl)cyclopentanecarboxylic acid was formed in 80% yield from cyclopentanecarboxylic acid: mp 86–87 °C. Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.03; H, 9.73. Found: C, 69.22; H, 9.54. 1-(1-Hydroxycycloheptyl)cyclopentanecarboxylic acid lactone was formed in 44% yield from the hydroxy acid: mp 88 °C. Anal. Calcd for $C_{13}H_{20}O_2$: C, 75.00; H, 9.62. Found: C, 75.34; H, 9.59. Cyclopentylidenecycloheptane was formed in 83% yield from the lactone, bp 107–109 °C/12 mm; $N^{11}{}_{D}$ 1.5063, FT-IR 1449, 1350, 1141, 1027 cm^{-1} and no peaks between 3000 and 3200 cm^{-1}. Anal. Calcd for $C_{12}H_{20}$: C, 87.80; H, 12.20. Found: C, 87.48; H, 12.36. **c. Cyclohexylidenecycloheptane, 1g**: 1-(1-Hydroxycycloheptyl)cyclohexanecarboxylic acid was formed in 93% yield from cyclohexanecarboxylic acid: mp 156–157 °C. Anal. Calcd for $C_{14}H_{24}O_3$: C, 70.00; H, 10.00. Found: C, 69.75; H, 10.21. 1-(1-Hydroxycycloheptyl)cyclohexanecarboxylic acid lactone was formed in 62% yield from the hydroxy acid: mp 107–108 °C. Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.68; H, 9.91. Found: C, 75.84; H, 9.86. Cyclohexylidenecycloheptane was formed in 81% yield from the lactone: bp 132–135 °C/22 mm; $N^{18}{}_{D}$ 1.5109; FT-IR 1444, 1349, 1234, 1012, 850 cm^{-1} and no peaks between 3000 and 3200 cm^{-1}. Anal. Calcd for $C_{13}H_{22}$: C, 87.64; H, 12.36. Found: C, 87.65; H, 12.28.

1,1′-Dibromo-1,1′-bicyclopentane, **2a**, and 1,1′-dibromo-1,1′-bicyclohexane, **2f**, were prepared from the respective diols, **3a** and **3f**, by stirring with 48% hydrobromic acid saturated with hydrogen bromide at −20 °C.[11] Dibromides **2b**, **2c**, and **2g** were formed by reaction of olefins **1b**, **1c**, and **1g** with bromine in chloroform solution as described above and treated with the silver nitrate solution without isolation.

The symmetrical pinacols **3a**, **3f**, and **3k** were prepared from the cyclic ketones by pinacol reduction with aluminum turnings.[12] The unsymmetrical pinacols were prepared in the same way using an equal number of moles of the two different cyclic ketones.[13] It was not considered necessary to separate the symmetrical diols from the unsymmetrical diols. The symmetrical diols gave single GC peaks. The compositions of the unsymmetrical diols used, as determined from their automatically integrated GC spectra were as follows: (a) **3b**: 7.3% **3a**, 48.6% **3b**, 44.1% **3f**; (b) **3c**: 27.0% **3a**, 36.9% **3c**, 36.1% **3k**; and (c) **3g**: 28.9% **3f**, 53.3% **3g**, 17.8% **3k**.

Dienes **6a**, **6b**, and **6f** were isolated from pinacol rearrangement mixtures, both as their maleic anhydride adducts and as the pure dienes after removing the spiro ketones as their semicarbazones. The GC retention times and the mass spectra of dienes **6c**, **6g**, and **6k** were obtained from rearrangement mixtures, and those of the other dienes were obtained from pure compounds.

Spiro ketones **5b**, **5c**, **5g**, and **5j** were isolated from rearrangement mixtures. Spiro ketones **5c**, **5d**, **5f**, **5h**, and **5k** were synthesized from the cyclic ketones and the necessary α–ω dibromides in the presence of potassium *tert*-butoxide by the method of Christol.[14] The GC retention times and mass spectra of all the pure ketones were determined and tabulated. The retention time and the mass spectrum of **5l** were determined from the pinacol rearrangement mixture.

---

[9] Krapcho, A. P.; Jahngen, E. G. E., Jr. *J. Org. Chem.* **1974**, *39*, 1650.

[10] Christol, H.; Arnal, C.; Vanel, R.; Bessierem, J. M. *Bull. Soc. Chim. Fr.* **1967**, 2458.

[11] Criegee, R.; Vogel, E.; Hoger, H. *Chem. Ber.* **1952**, *85*, 144.

[12] Qudrat-i-Khunda *J. Indian Chem. Soc.* **1939**, *16*, 525.

[13] Sands, R. D. *Tetrahedron* **1965**, *21*, 887.

[14] Mousseron, M.; Jacquier, R.; Christol, H. *C. R. Acad. Sci. Paris* **1954**, *239*, 1805.