Nucleophilic Substitution Reactions at Chloro-Substituted Ozonides and at a Chlorinated Dimeric Peroxide

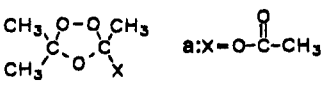
Karl Griesbaum* and Konrad Schlindwein

Engler-Bunte-Institut, Bereich Petrochemie, Universität Karlsruhe (TH), D-76128 Karlsruhe, Germany

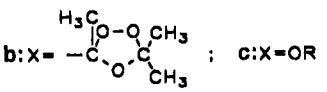
Received May 24, 1995[⊗]

Reactions of substituted 3-chloro- (**2a**–**4a**) and 3,5-dichloro-1,2,4-trioxolanes (**9a**, **10a**) with $AgBF_4$ in the presence of LiF gave the corresponding fluoro-substituted ozonides (**2b**–**4b** and **9b** and **10b**). Substitutions of some of these chlorinated ozonides by the methoxy and by the acetoxy groups, and of 3,6-dichloro-3,6-dimethyl-1,2,4,5-tetroxane (**22a**) with the acetoxy group have been achieved, too.

In previous work we had found that ozonides **1a** and **1b** can undergo nucleophilic substitution reactions with alcohols and with phenol to give the corresponding ozonides of type **1c**.[1] However, the fact that such



1



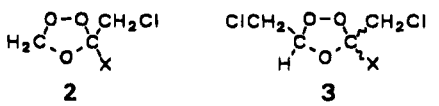
reactions occurred only at elevated temperatures of at least 40 °C limited their scope since thermal decompositions of the ozonides compete with the substitution reactions. Thus, attempts to extend the reaction to other acetoxy-substituted ozonides or other diozonides failed to give substitution products.

It appeared to us that reactions of chloro-substituted ozonides with silver ions in the presence of nucleophiles could be a better approach, since such reactions should occur at considerably lower temperatures. In order to test this hypothesis, we have tried the replacement of chlorine substituents in chloro-substituted ozonides by fluorine, methoxy, and acetoxy substituents. As substrates we used the monochloro substituted ozonides **2a**–**4a** and the dichloro-substituted ozonides **9a** and **10a**, which we had previously prepared as the first representatives of stable monocyclic chloro-substituted ozonides.[2]

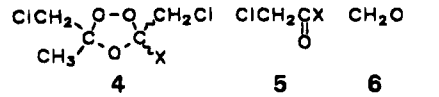
Treatment of ozonides **2a**–**4a** with ca. 1.2 molar equiv of $AgBF_4$ in the presence of ca. 10 molar equiv of LiF in ether at temperatures of 0–20 °C gave in spontaneous reactions the corresponding fluoro-substituted ozonides **2b**–**4b**, which were isolated in yields of 21%, 17%, and 26%, respectively. Ozonides **3b** and **4b** were mixtures of the corresponding *cis*- and *trans*-isomers, which could be individually isolated by HPLC separations. At room temperature, the neat ozonides **2b**–**4b** undergo gradual decomposition if they are kept in glass vials, whereas they are stable in Teflon vials.[3]

The structures of ozonides **2b**–**4b** and of the other ozonides mentioned below have been assigned on the basis of positive peroxide tests, their ^1H and ^{13}C NMR spectra, and their reduction with triphenylphosphine or with dimethyl sulfide to give the expected fragments, *viz.* **5b** + **6** from **2b**, **5b** + **7** from **3b** and **5b** + **8** from **4b**. The stereochemical assignments of **3b** and **4b**, and of the other stereoisomeric ozonides mentioned below, are based on the assumption that, in line with previous reports,[4] the compound with the longer chromatographic elution time is the *cis*-isomer. These assignments derive support from the fact that in the ^{13}C NMR spectra ^4J (C–F) couplings were only observed for the $ClCH_2$ groups of *trans*-**3b** and of *trans*-**4b**, and for the CH_3 group of *cis*-**4b**, i.e. when these groups were in *cis* position to the fluorine substituent. In all of these cases, the ^4J (C–F) coupling constants were larger than the corresponding ^3J (C–F) coupling constants, which indicates that the ^4J (C–F) coupling occurs through space and, hence, is due to the fact that the coupling substituents F and CH_2Cl or F and CH_3 are closer together in a *cis* than in a *trans* relationship.

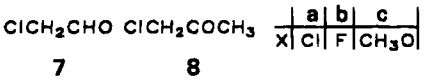
Treatment of ozonides **2a** and **4a** with methanol in the presence of potassium carbonate at ca. 5–20 °C gave the corresponding ozonides **2c**, *cis*-**4c**, and *trans*-**4c** even in the absence of silver ions. They were isolated in yields of 42%, 11%, and 3%, respectively, and they were stable at room temperature for several days. Their reductions gave **5c** + **6** from **2c** and **5c** + **8** from **4c**. The ^{17}O NMR spectrum of **2c** confirmed the ozonide structure.



2 **3**



4 **5** **6**



7 **8**

Treatment of ozonides **9a** and **10a** with ca. 2.5 molar equiv of $AgBF_4$ in the presence of ca. 10 molar equiv of

[⊗] Abstract published in *Advance ACS Abstracts,* November 1, 1995.

(1) Griesbaum, K.; Volpp, W.; Huh, T. S. *Tetrahedron Lett.* **1989,** *30,* 1511.

(2) Griesbaum, K.; Schlindwein, K.; Hilss, M. *Chem. Ber.* **1993,** *126,* 1843.

(3) For this reason, the ^1H and ^{13}C NMR spectra were recorded in Teflon tubes and elemental analyses of the more labile H-substituted ozonides **2b** and **3b** were not carried out.

(4) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, NY, 1978; Vol. I, p 52.

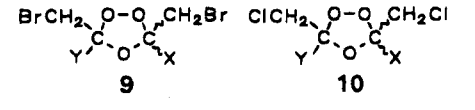
0022-3263/95/1960-8062$09.00/0

LiF in ether afforded the corresponding ozonides **9b** and **10b** in yields of 47% and 54%, respectively, along with the diacyl peroxides **11f** and **11a**, respectively. By HPLC separation, *cis*-**9b** (8%), *trans*-**9b** (28%), *cis*-**10b** (9%), and *trans*-**10b** (16%) have been isolated individually and stereochemically assigned. They are more stable than the monofluorinated ozonides **2b**–**4b**, and they could be kept in glass vials at room temperature without any noticeable decomposition. Reduction of **9b** with dimethyl sulfide in the presence of methanol gave **12g**; reduction of **10b** with triphenylphosphine gave **12c**.

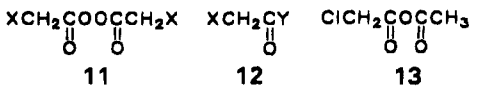
Treatment of ozonides **9a** and **10a** with deficient amounts of $AgBF_4$ in the presence of LiF in ether gave one stereoisomer each of **9c** and of **10c** in yields of 11% and 12%, respectively, along with the corresponding difluoro-substituted ozonides **9b** and **10b**, respectively. Ozonides **9c** and **10c** are tentatively assigned a *cis* configuration, since in the ^{13}C NMR spectra there were no through-space ^4J (C–F) couplings between fluorine and the respective halomethyl groups.

Treatment of **10a** with $AgBF_4$ and $NaOCH_3$ in methanol at 0 °C afforded *cis*- and *trans*-**10d**, which were isolated in yields of 6% and 10%, respectively. At room temperature they underwent slow decomposition. At 50 °C or at room temperature in the presence of anhydrous HCl, they underwent accelerated decomposition to give **12h**; reduction with dimethyl sulfide gave **12h**, too.

Treatment of **10a** with $AgBF_4$ in acetic acid at 15–25 °C gave a mixture of the stereoisomers of **10e**, from which enriched *cis*-**10e** and pure *trans*-**10e** have been isolated in yields of 1% and 46%, respectively. They were stable at room temperature, and the solid *trans*-**10e** melted at 94 °C without decomposition. Reduction of **10e** with dimethyl sulfide afforded anhydride **13**.



9 **10**

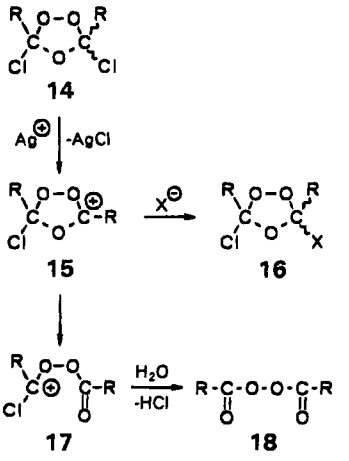


11 **12** **13**

	a	b	c	d	e	f	g	h
X	Cl	F	Cl	CH_3O	CH_3COO	Br	Br	Cl
Y	Cl	F	F	CH_3O	CH_3COO	F	CH_3O	CH_3O

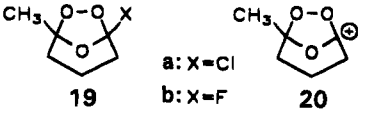
Whereas the first examples of substitution reactions at ozonides[1] **1a** and **1b** could have occurred by S_N1 or S_N2 mechanisms, the silver ion-mediated substitutions at chlorinated ozonides of type **14** are best interpreted as S_N1 reactions via ozonide cations of type **15** as intermediates. The formation of substitution products of type **16** in the presence of suitable nucleophiles of type X shows, that such ozonide cations have a finite lifetime. This is in contrast to the behavior of similarly generated epoxide cations, which could not be trapped but underwent spontaneous ring opening.[5] Apparently, ring-opening reactions also compete with the trapping of ozonide cations of type **15** by nucleophiles X. For, the occurrence of diacyl peroxides of type **18**, e.g. of peroxides **11f** and **11a** from ozonides **9a** and **10a**, respectively, is best interpreted by the reaction sequence **15** → **17** → **18**.

(5) Keul, H.; Pfeffer, B.; Griesbaum, K. *Chem. Ber.* **1984**, *117*, 2193 and references cited therein.



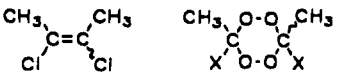
14 **15** **16** **17** **18**

The proposal of ozonide cation intermediates in silver ion-mediated substitutions of chloro ozonides is supported by the fact that, in contrast to the spontaneous reactions of the above-mentioned monocyclic chlorinated ozonides **2a**–**4a** and **9a** and **10a**, the bicyclic chlorinated ozonide **19a** reacted very slowly with silver ions: Equimolar amounts of **19a** and $AgBF_4$ in ether at room temperature gave a mixture containing 64% of unreacted **19a** and 36% of **19b** after 6 weeks of reaction.[6] This is ascribed to the difficulty which is associated with the formation of bridgehead cation **20**. Ozonide **19b** was isolated in 4% yield.



19 a: X=Cl b: X=F **20**

Preliminary results show, that the silver ion-mediated substitution of chlorine can also be applied to chlorinated dimeric peroxides: Reaction of **22a**, a product from the ozonolysis of **21**,[7] with $AgBF_4$ in acetic acid afforded in 41% yield the substitution product **22b** of unknown stereochemistry. In contrast to **22a**, which gave violent explosions,[7] peroxide **22b** could be heated to its melting point of 119 °C without decomposition. Reduction of **22b** with triphenylphosphine gave acetic anhydride.



21 **22**

a: X=Cl b: X=CH_3COO

The nucleophilic substitution reactions described in the foregoing represent further examples for the synthetic utility of reactions via peroxide cationic species, a field of research which attracts increasing interest.[8]

Experimental Section

General. ^1H, ^{13}C, ^{19}F, and ^{17}O NMR spectra were recorded on a 250 MHz and ^1H–^{19}F (BB) NMR spectra on a 500 MHz instrument. The ^1H and ^{13}C NMR spectra were obtained in $CDCl_3$ with TMS as internal reference. The ^{17}O NMR spectra were recorded in C_6D_6 with H_2O as external reference by a

(6) Greinert, R. Unpublished results.
(7) Griesbaum, K.; Hofmann, P. *J. Am. Chem. Soc.* **1976**, *98*, 2877.
(8) Dussault, P. H.; Lee, H.-J.; Niu, Q. N. *J. Org. Chem.* **1995**, *60*, 784 and references cited therein.

published procedure.[9] The ^{19}F NMR spectra were obtained in $CDCl_3$ with $CFCl_3$ as external reference. Chromatographic separations were carried out on silica gel by the method of flash chromatography.[10] HPLC separations were performed on an instrument equipped with a 3.2 × 25 cm column LiChrosorb Si 60. GLC analyses: 50 m capillary column SE 54, 50–180 °C at 7 °C/min. Preparative GLC separation: column 0.7 × 100 cm, 5% methylsilicone on Chromosorb G; 50 °C for 10 min, 50–180 °C at 10 °C/min.

Reaction of 2a with $AgBF_4$/LiF. A solution of 680 mg (4.3 mmol) of **2a** in 40 mL of pentane was dropwise added to a stirred suspension of 1.16 g (5.96 mmol) of $AgBF_4$ and 1.53 g (58.6 mmol) of LiF in 30 mL of ether at 20 °C. The mixture was decanted, the liquid was sequentially washed with aqueous solutions of NaCl and $NaHCO_3$, and dried with $MgSO_4$, and the solvent was distilled off at 10 °C at reduced pressure to leave 432 mg of a liquid residue. Chromatographic separation (pentane/ether, 12:1) gave 127 mg (21%) of **2b**.

3-(Chloromethyl)-3-fluoro-1,2,4-trioxolane (2b): colorless liquid; ^1H NMR[3] δ 3.92–3.93 (m, 2H), 5.20 (d, J = 7.5 Hz, 1H), 5.65 (s, 1H); ^{13}C NMR (BB)[3] δ 39.37 (d, J = 53.8 Hz), 96.41 (d, J = 2.4 Hz), 121.72 (d, J = 265.2 Hz).

Reduction of 2b. In a NMR tube, a solution of 10 mg (0.07 mmol) of **2b** in 0.6 mL of $CDCl_3$ was admixed with a solution of 10 μL of dimethyl sulfide in 0.1 mL of $CDCl_3$. ^1H NMR analysis immediately after the spontaneous reaction showed the presence of **5b** (δ 4.27, d, J = 0.8 Hz), **6** (δ 9.74, s), and dimethyl sulfoxide (δ 2.62, s) in approximately equimolar amounts.

Reaction of 3a with $AgBF_4$/LiF. With the procedure described for the reaction of **2a**, 875 mg (4.2 mmol) of **3a** in 15 mL of ether and a suspension of 920 mg (4.7 mmol) of $AgBF_4$ and 1.05 g (40.5 mmol) of LiF in 15 mL of ether at 20 °C gave 514 mg of a liquid residue. HPLC separation (pentane/ether 10:1) gave 14 mg (7%; elution time 38.6 min) of *cis*-**3b** and 21 mg (10%; elution time 33.6 min) of *trans*-**3b**.

***cis*-3,5-Bis(chloromethyl)-3-fluoro-1,2,4-trioxolane (*cis*-3b):** colorless liquid; ^1H NMR[3] ABX system, δ_A 3.76, δ_B 3.81, δ_X 5.62 (J_{AB} = 12.0, J_{BX} = 0.8, J_{XZ} = 8.2 Hz, 3 H), LM part of a LMXZ system, δ 3.83–3.97 (2 H), assignments confirmed by spin–spin-decoupling experiments; ^{13}C NMR (BB)[3] δ 39.14, 39.18 (d, J = 52.5 Hz), 105.08 (d, J = 2.5 Hz), 122.57 (d, J = 267.5 Hz); ^{19}F NMR Z part of a LMXZ system, δ_Z −69.25 (J_{LZ} = 3.3, J_{MZ} = 4.2, J_{XZ} = 8.1 Hz); CI-MS (*i*-C_4H_{10}) m/z (%) 175, 173, 171 (13, 77, 100) [M^+ − F].

***trans*-3,5-Bis(chloromethyl)-3-fluoro-1,2,4-trioxolane (*trans*-3b):** colorless liquid; ^1H NMR[3] ABX system, δ_A 3.61, δ_B 3.71, δ_X 5.90 (J_{AB} = 12.1, J_{AX} + J_{BX} = 2.2 Hz, 3H), 3.93 (d, J = 2.8 Hz, 2H); ^{13}C NMR (BB)[3] δ 38.15 (d, J = 52.7 Hz), 41.42 (d, J = 5.9 Hz), 104.31 (d, J = 1.8 Hz), 121.84 (d, J = 266.2 Hz); ^{19}F NMR δ −70.12 (t, J = 2.9 Hz).

Reduction of 3b. In a NMR tube 19 mg (0.10 mmol) of *cis*-**3b** in 0.6 mL of $CDCl_3$ was admixed with 30 mg (0.11 mmol) of triphenylphosphine in 0.2 mL of $CDCl_3$. ^1H NMR analysis immediately after the spontaneous reaction showed the presence of **5b** (δ 4.26, d, J = 1.1 Hz) and **7** (δ 4.05, d, J = 1.6 Hz, 2H) in equimolar amounts. Reduction of a 1:2 mixture of *cis*- and *trans*-**3b** gave the same result.

Reaction of 4a with $AgBF_4$/LiF. With the procedure described for the reaction of **2a**, 630 mg (2.9 mmol) of **4a** in 20 mL of ether and a suspension of 900 mg (4.6 mmol) of $AgBF_4$ and 1.19 g (46.0 mmol) of LiF in 20 mL of ether at 0 °C gave 484 mg of a liquid residue. Chromatographic separation (pentane/ether, 30:1) gave 230 mg (26%) of a mixture of *cis*- and *trans*-**4b** in a ratio of 1:3. HPLC separation (pentane/ether, 97:3) gave 38 mg (5%; elution time 24.8 min) of *cis*-**4b** and 109 mg (15%; elution time 21.6 min) of *trans*-**4b**.

***cis*-3,5-Bis(chloromethyl)-3-fluoro-5-methyl-1,2,4-trioxolane (*cis*-4b):** colorless liquid; ^1H NMR δ 1.71 (s, 3H), 3.77 (s, 2H), 3.87 (d, J = 4.0 Hz, 2H); ^{13}C NMR (BB) δ 20.41 (d, J = 4.2 Hz), 39.26 (d, J = 53.0 Hz), 44.79, 112.32 (d, J = 1.8 Hz), 122.81 (d, J = 265.3 Hz).

***trans*-3,5-Bis(chloromethyl)-3-fluoro-5-methyl-1,2,4-trioxolane (*trans*-4b):** colorless liquid; ^1H NMR δ 1.79 (s, 3H), AB system, δ_A 3.62, δ_B 3.74 (J = 11.9 Hz, 2H), 3.88 (d, J = 3.0 Hz, 2H); ^{13}C NMR (BB) δ 18.61, 38.45 (d, J = 52.9 Hz), 44.85 (d, J = 6.9 Hz), 112.01 (d, J = 2.1 Hz), 122.36 (d, J = 264.4 Hz); ^{19}F NMR δ −67.85 (t, J = 3.0 Hz). Anal. Calcd for $C_5H_7Cl_2FO_3$ (1:3 mixture of *cis*- and *trans*-**4b**): C, 29.19; H, 3.44. Found: C, 29.45; H, 3.44.

Reduction of 4b. One drop of **4b** (*cis*/*trans* = 1:3) in 0.6 mL of $CDCl_3$ was admixed with excess triphenylphosphine in a NMR tube. ^1H NMR analysis immediately after the spontaneous reaction showed the presence of equimolar amounts of **5b** (δ 4.24, d, J = 1.3 Hz) and of **8** (δ 2.31, s, 3H; 4.08, s, 2H).

Reaction of 2a with Methanol. A solution of 710 mg (4.5 mmol) of **2a** in 60 mL of pentane was dropwise added to a stirred suspension of 1.022 g (74 mmol) of K_2CO_3 in 6 mL of methanol at 4 °C within 25 min. The ensuing two phases were separated, and from the upper phase, the solvent was distilled off at 10 °C and reduced pressure to leave ca. 3 mL of a liquid residue. Chromatographic separation (pentane/ether, 8:1) gave 418 mg (42%) of **2c**.

3-(Chloromethyl)-3-methoxy-1,2,4-trioxolane (2c): colorless liquid; ^1H NMR δ 3.49 (s, 3H), AB system, δ_A 3.75, δ_B 3.77 (J = 12.44 Hz, 2H), 5.25 (d, J = 1.2 Hz, 1H), 5.50 (d, J = 1.0 Hz, 1H); ^{13}C NMR (BB) δ 43.60, 50.63, 96.26, 118.35; ^{17}O NMR δ 39.8, 104.1, 290.7; CI-MS (*i*-C_4H_{10}) m/z (%) 157, 155 (18, 54) [M^+ + 1]. Anal. Calcd for $C_4H_7ClO_4$: C, 31.09; H, 4.57. Found: C, 31.31; H, 4.42.

Reduction of 2c. One drop of **2c** in 0.6 mL of C_6D_6 was admixed with an excess of triphenylphosphine in a NMR tube. ^1H NMR analysis after the spontaneous reaction showed the presence of **5c** (δ 3.17, s, 3H; 3.41, s, 2H) and of **6** (δ 8.76), along with oligomers of **6** (δ 4.9–5.3).

Reaction of 4a with Methanol. A solution of 875 mg (4.0 mmol) of **4a** (*cis*/*trans* = 1:2; 92% purity) in 75 mL of pentane was dropwise added to a stirred suspension of 2.0 g (20 mmol) of K_2CO_3 in 5 mL of methanol at 20 °C. Workup as described for the reaction of **2a** gave 495 mg of a liquid residue. Sequential chromatographic (pentane/ether, 20:1) and HPLC separation (pentane/ether, 94:6) gave 148 mg (11%; elution time 38.8 min) of *cis*-**4c** and 41 mg (3%; elution time 35.8 min) of *trans*-**4c** of 92% purity.

***cis*-3,5-Bis(chloromethyl)-3-methoxy-5-methyl-1,2,4-trioxolane (*cis*-4c):** colorless liquid; ^1H NMR δ 1.75 (s, 3H), 3.52 (s, 3H), AB system, δ_A 3.66, δ_B 3.76 (J = 11.7 Hz, 2H), 3.75 (s, 2H); ^{13}C NMR (BB) δ 18.22, 42.49, 45.41, 51.57, 110.32, 118.91; CI-MS (*i*-C_4H_{10}) m/z (%) 221, 219, 217, (0.3, 1.5, 2.1) [M^+ + 1]. Anal. Calcd for $C_6H_{10}Cl_2O_4$: C, 33.20; H, 4.64. Found: C, 33.27; H, 4.54.

***trans*-3,5-Bis(chloromethyl)-3-methoxy-5-methyl-1,2,4-trioxolane (*trans*-4c):** colorless liquid; ^1H NMR δ 1.66 (s, 3H), 3.56 (s, 3H), AB system, δ_A 3.70, δ_B 3.76 (J = 12.0 Hz, 2H), 3.74 (s, 2H); ^{13}C NMR (BB) δ 20.30, 43.97, 46.02, 51.07, 110.17, 120.47; CI-MS (*i*-C_4H_{10}) m/z (%) 221, 219, 217 (0.1, 0.2, 0.4) [M^+ + 1].

Reduction of Ozonide 4c. A solution of 20 mg (0.09 mol) of **4c** (*cis*/*trans* = 3:1) in 0.5 mL of $CDCl_3$ was admixed with an excess of triphenylphosphine. ^1H NMR analysis after 8 h showed the presence of **5c** (δ 3.80, s, 3H; 4.09, s, 2H) and of **8** (δ 2.32, s, 3H; 4.08, s, 2H) in equimolar amounts.

Reaction of 9a with Excess $AgBF_4$/LiF. With the procedure described for the reaction of **2a**, 250 mg (0.76 mmol) of **9a** (*cis*/*trans* = 4:1) in 6.5 mL of ether and a suspension of 365 mg (1.88 mmol) of $AgBF_4$ and 210 mg (8.1 mmol) of LiF in 6.5 mL of ether at ca. 10 °C gave 227 mg of a liquid residue. Upon addition of pentane, 67 mg (32%) of peroxide **11f** precipitated and was filtered off. The solvent was distilled from the filtrate at rt and reduced pressure to leave 157 mg of a liquid residue, from which 106 mg (47%) of a mixture of *cis*- and trans-**9b** was isolated by chromatography (pentane/ether, 19:1). HPLC separation (pentane/ether, 19:1) of this mixture afforded 18 mg (8%; elution time 32.0 min) of *cis*-**9b** and 62 mg (28%; elution time 26.0 min) of *trans*-**9b**.

***cis*-Bis(bromomethyl)-3,5-difluoro-1,2,4-trioxolane (*cis*-9b):** colorless liquid; ^1H NMR δ 3.68–3.82 (m); ^1H–^{19}F (BB)

(9) Hock, F.; Ball, V.; Dong, Y.; Gutsche, S.-H.; Hilss, M.; Schlindwein, K.; Griesbaum, K. *J. Magn. Reson.* **1994**, *A111*, 150.
(10) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1977**, *43*, 2923.

NMR AB system, δ_A 3.72, δ_B 3.76 (J = 12.0 Hz); ^{13}C NMR (BB) δ 24.88 (dd, J = 47.1 and 1.6 Hz), 124.34 (d, J = 274.1 Hz); ^{19}F NMR δ −71.41 to −71.48 (m); EI-MS m/z (%) 300, 298, 296 (0.3, 0.6, 0.3) M^+.

***trans*-3,5-Bis(bromomethyl)-3,5-difluoro-1,2,4-trioxolane (*trans*-9b):** colorless liquid; ^1H NMR 3.70−3.82 (m); $^1H-^{19}F$ (BB) NMR δ 3.75 (s); ^{13}C NMR (BB) X part of ABX system, δ_X 23.85 ($J_{AX} + J_{BX}$ = 42.9 Hz), 123.06 (d, J = 275.2 Hz); ^{19}F NMR δ −72.23 to −72.29 (m); ^{17}O NMR δ 156.8, 302.2; EI-MS m/z (%) 300, 298, 296 (1, 2, 1) M^+. Anal. Calcd for $C_4H_4Br_2F_2O_3$: C, 16.13; H, 1.35. Found: C, 16.38; H, 1.37.

Bis(bromoacetyl)peroxide (11f): ^1H NMR δ 3.96 (s); IR (CCl_4) 1821, 1798, 870, 847 cm^{-1}; lit.[11] IR 1818, 1786, 877, 862 cm^{-1}.

Reduction of 9b in the Presence of Methanol. A solution of 15 mg of **9b** (*cis/trans* = 1:4) and one drop of methanol in 0.5 mL of $CDCl_3$ was admixed with an excess of dimethyl sulfide. ^1H NMR analysis after 2 d showed the presence of methyl bromoacetate (**12g**) (δ 3.80, s, 3H; 3.86, s, 2H) and dimethyl sulfoxide (δ 2.65, s) in a molar ratio of 2:1.

Reaction of 10a with Excess $AgBF_4$/LiF. With the procedure described for the reaction of **2a**, a solution of 670 mg (2.77 mmol) of **10a** (*cis/trans* = 1.5:1) in 25 mL of ether and a suspension of 1.15 g (5.9 mmol) of $AgBF_4$ and 0.66 g (25.4 mmol) of LiF in 15 mL of ether gave 600 mg of a liquid residue. It was dissolved in 1 mL of ether, admixed with 4 mL of pentane and cooled to −30 °C for 16 h. The precipitated peroxide **11a** (25 mg; 5%) was filtered off, and the filtrate was concentrated at rt to leave 600 mg of a liquid residue. Separation by chromatography (pentane/ether, 30:1) gave 310 mg (54%) of a 1:4 mixture of *cis*- and *trans*-**10b**. HPLC separation (pentane/ether, 9:1) gave 49 mg (9%; elution time 24.2 min) of *cis*-**10b** and 91 mg (16%; elution time 21.8 min) of *trans*-**10b**.

***cis*- and *trans*-3,5-Bis(chloromethyl)-3,5-difluoro-1,2,4-trioxolane (10b):** CI-MS (i-C_4H_{10}) m/z (%) 193, 191, 189, (9, 66, 100) [M^+ − F]. Anal. Calcd for $C_4H_4Cl_2F_2O_3$: C, 22.99; H, 1.93. Found: C, 22.98; H, 1.96.

***cis*-3,5-Bis(chloromethyl)-3,5-difluoro-1,2,4-trioxolane (*cis*-10b):** colorless liquid; ^1H NMR δ 3.85−4.00 (m); $^1H-^{19}F$ (BB) NMR AB system, δ_A 3.90, δ_B 3.95 (J = 13.3 Hz); ^{13}C NMR (BB) δ 39.51 (dd, J = 48.9 and 1.5 Hz), 124.63 (dd, J = 274.9 and 1.0 Hz); ^{19}F NMR δ −73.40 to −73.45 (m).

***trans*-3,5-Bis(chloromethyl)-3,5-difluoro-1,2,4-trioxolane (*trans*-10b):** colorless liquid; ^1H NMR 3.95−3.97 (m); $^1H-^{19}F$ (BB) NMR δ 3.95 (s); ^{13}C NMR (BB) X part of ABX system, δ_X 38.80 ($J_{AX} + J_{BX}$ = 45.1 Hz), 123.43 (d, J = 275.9 Hz); ^{19}F NMR δ −74.17 to −74.21.

Reduction of 10b. A solution of one drop of **10b** (*cis/trans* = 1:4) in 0.6 mL of $CDCl_3$ was admixed with an excess of triphenylphosphine. ^1H NMR analysis after the spontaneous reaction showed the presence of **12c** (δ 4.25; d, J = 1.0 Hz) as the sole product of reduction.

Reaction of 9a with a Deficient Amount of $AgBF_4$. A solution of 107 mg (0.55 mmol) of $AgBF_4$ in 10 mL of ether was dropwise added to a stirred suspension containing 152 mg (0.46 mmol) of **9a** (*cis/trans* = 4:1) and 120 mg (4.6 mmol) of LiF in 15 mL of ether, kept at 0 °C. After 1 h, the liquid phase was decanted and sequentially washed with aqueous solutions of NaCl and $NaHCO_3$, dried with Na_2SO_4, and concentrated at rt and reduced pressure to leave 120 mg of a liquid residue. Chromatographic separation (pentane/ether, 9:1) gave 50 mg of a mixture of **9a**, **9b**, and **9c** in relative proportions of 10%, 42%, and 48%. HPLC separation (pentane/ether, 19:1) gave 20 mg (11%) of **9c**.

3,5-Bis(bromomethyl)-3-chloro-5-fluoro-1,2,4-trioxolane (9c): colorless liquid; ^1H NMR AB part of ABX system, δ_A 3.779, δ_B 3.781 ($J_{AX} + J_{BX}$ = 17.3 Hz, 2 H), 4.07 (s, 2 H); ^{13}C NMR (BB) δ 24.12 (d, J = 42.5 Hz), and partly overlapping signals at δ 30.03, 120.77, 120.82, 125.23.

Reaction of 10a with a Deficient Amount of $AgBF_4$. With the above described procedure for the reaction of **9a**, 710 mg (3.65 mmol) of $AgBF_4$ in 60 mL of ether and 686 mg (2.84 mmol) of **10a** (*cis/trans* = 4:1) and 610 mg (23.5 mmol) of LiF in 20 mL of ether, kept at −10 °C one obtained 560 mg of a liquid residue. HPLC separation (pentane/ether, 95:5) gave 40 mg (7%) of *cis*-**10b**, 90 mg (15%) of *trans*-**10b** and 75 mg (12%) of **10c**.

3,5-Bis(chloromethyl)-3-chloro-5-fluoro-1,2,4-trioxolane (10c): colorless liquid; ^1H NMR AB part of ABX system, δ_A 3.98, δ_B 3.99 (J_{AB} = 13.1, $J_{AX} + J_{BX}$ = 13.0 Hz, 2 H), AB system, δ_A 4.19, δ_B 4.21 (J = 13.4 Hz, 2 H); ^{13}C NMR (BB) δ 39.01 (d, J = 44.4 Hz), 44.13, 121.52 (d, J = 2.6 Hz), 123.33 (d, J = 277.7 Hz); ^{19}F NMR δ −72.21 (t, J = 6.6 Hz). Anal. Calcd for $C_4H_4Cl_3FO_3$: C, 21.31; H, 1.79. Found: C, 21.18; H, 1.65.

Reaction of 10a with $AgBF_4$ in Methanol. A solution of 200 mg (0.83 mmol) of **10a** (*cis/trans* = 1.5:1) in 2 mL of methanol was dropwise added to a stirred suspension of 330 mg (1.74 mmol) of $AgBF_4$ and 87 mg (1.62 mmol) of sodium methoxide in 1 mL of methanol at 0 °C. Stirring was continued for 30 min at 0 °C, the solvent was distilled off at 0 °C and reduced pressure, and the solid residue was leached with ether. The extract was washed with an aqueous solution of NaCl, dried over $MgSO_4$, and concentrated at rt and reduced pressure to leave 100 mg of a residue. The experiment was repeated with 575 mg (2.37 mmol) and 464 mg (1.92 mmol) of **10a**, and the corresponding amounts of $AgBF_4$ and sodium methoxide. Chromatographic separation (pentane/ether, 10:1) of the combined residues (670 mg) gave 94 mg of *trans*-**10d** and 113 mg of a mixture of *cis*-**10d**, *trans*-**10d**, and ester **12h** in relative proportions of 70%, 20%, and 10%. Chromatographic separation (pentane/ether, 20:1) of this mixture gave 61 mg (6%; elution time 16.4 min) of *cis*-**10d** and 22 mg (together with the 94 mg from above 10%; elution time 9.2 min) of *trans*-**10d**.

***cis*-3,5-Bis(chloromethyl)-3,5-dimethoxy-1,2,4-trioxolane (*cis*-10d):** colorless liquid; ^1H NMR δ 3.58 (s, 6H), AB system, δ_A 3.76, δ_B 3.82 (J = 12.5 Hz, 4H); ^{13}C NMR (BB) δ 42.14, 51.85, 120.72; CI-MS (i-C_4H_{10}) m/z (%) 237, 235, 233 (0.1, 0.3, 0.4) [M^+ + 1].

***trans*-3,5-Bis(chloromethyl)-3,5-dimethoxy-1,2,4-trioxolane (*trans*-10d):** colorless solid; mp 69 °C; ^1H NMR δ 3.56 (s, 6H), 3.84 (s, 4H); ^1H NMR (C_6D_6/TMS) δ 3.06 (s, 6H); AB system, δ_A 3.39, δ_B 3.44 (J = 12.1 Hz, 4 H); ^{13}C NMR (GD) δ 43.00 (t, J = 152.8 Hz), 51.28 (q, J = 145.5 Hz), 120.08 (m); CI-MS (i-C_4H_{10}) m/z (%) 237, 235, 233 (0.1, 0.4, 0.5) [M^+ + 1]. Anal. Calcd for $C_6H_{10}Cl_2O_5$: C, 30.92; H, 4.33. Found: C, 30.96; H, 4.21.

Thermal Decomposition of 10d. A solution of 17 mg (0.07 mmol) of *trans*-**10d** in 0.6 mL of $CDCl_3$ was kept in a NMR tube at rt. ^1H NMR analysis showed the presence of ester **12h** (δ 3.81, s, 3 H; 4.08, s, 2 H) in ca. 25% after 3 d and in ca. 40% after 6 d. In a second experiment, anhydrous HCl was introduced into a solution of 10 mg (0.04 mmol) of **10d** in 0.5 mL of $CDCl_3$ at rt. ^1H NMR analysis showed the presence of ester **12h** in ca. 72% after 1 d.

Reduction of 10d. A solution of 13 mg (0.06 mmol) of *trans*-**10d** in 0.6 mL of $CDCl_3$ was admixed with an excess of dimethyl sulfide. ^1H NMR analysis after 5 d showed that ester **12h** (δ 3.81, 4.08) was formed as the sole product of reduction. Reduction of *cis*-**10d** gave the same result.

Reaction of 10a with $AgBF_4$ in Acetic Acid. A solution of 610 mg (2.52 mmol) of **10a** (*cis/trans* = 1.5:1) in 4 mL of acetic acid was dropwise added to a stirred solution of 1.10 g (5.65 mmol) of $AgBF_4$ in 6 mL of acetic acid at 24 °C. The rate of addition was adjusted such that the temperature of the mixture, which was cooled in an ice bath, did not supersede 28 °C. Ether (30 mL) was added, the liquid was decanted from the solid precipitate and sequentially washed with 10 mL, each, of a 10% aqueous NaCl solution and water. The organic phase was separated, neutralized with an aqueous solution of $NaHCO_3$, dried over $MgSO_4$, and concentrated at rt and reduced pressure to leave 520 mg of solid residue. Chromatographic separation (pentane/ether, 700 mL at a ratio of 6:1, 300 mL at a ratio of 2:1) gave 177 mg of *trans*-**10e** and 206 mg of a mixture of *cis*- and *trans*-**10e** in the relative proportions of 7% and 93%. Chromatographic separation of this

(11) Cadogan, J. I. G.; Hey, D. H.; Hibbert, P. G. *J. Chem. Soc.* **1965**, 3950.

mixture (pentane/ether, 2:1) gave 160 mg of *trans*-**10e** (together with the 177 mg from above 46%; elution time 8.8 min) and 10 mg (ca. 1%; elution time 14.0 min) of a mixture containing 84% of *cis*-**10e** and 16% of *trans*-**10e**.

***cis*-3,5-Diacetoxy-3,5-bis(chloromethyl)-1,2,4-trioxolane (*cis*-10e, in Admixture with 16% of *trans*-10e):** colorless liquid; ^{1}H NMR: δ 2.19 (s, 6 H), AB system, δ_A 4.16, δ_B 4.19 (J = 12.7 Hz, 4 H); ^{13}C NMR (BB) δ 21.21, 41.36, 119.77, 167.08.

***trans*-3,5-Diacetoxy-3,5-bis(chloromethyl)-1,2,4-trioxolane (*trans*-10e):** colorless solid; mp 94 °C; ^{1}H NMR δ 2.16 (s, 6 H); AB system, δ_A 4.23, δ_B 4.27 (J = 12.8 Hz, 4 H); ^{13}C NMR (GD) δ 21.33 (q, J = 130.6 Hz), 40.24 (t, J = 155.7 Hz), 118.94 (t, J = 4.5 Hz), 167.56 (q, J = 7.2 Hz). Anal. Calcd for $C_8H_{10}Cl_2O_7$: C, 33.24; H, 3.49. Found: C, 33.16; H, 3.25.

Reduction of 10e. A solution of 25 mg (0.09 mmol) of *trans*-**10e** in 0.5 mL of $CDCl_3$ was admixed with an excess of dimethyl sulfide. ^{1}H NMR analysis after 1.5 h showed anhydride **13** (δ 2.29, s; 4.20, s) as the sole product of reduction.

Reaction of 19a with $AgBF_4$. A solution of 628 mg (3.80 mmol) of **19a** in 25 mL of ether was admixed with a solution of 800 mg (3.9 mmol) of $AgBF_4$ in 25 mL of ether and stirred at rt. GLC analysis after 6 weeks showed the presence of **19a** (t_R = 13.8 min) and of **19b** (t_R = 10.4 min) in relative proportions of 64% and 36%. The mixture was treated with an aqueous solution of NaCl; the organic phase was dried over Na_2SO_4, filtered, and concentrated at rt and reduced pressure to leave 430 mg of a colorless liquid residue. Sequential separation of the residue by chromatography (pentane/ether, 20:1) and by preparative GLC gave 22.5 mg (4%) of **19b**.

1-Fluoro-5-methyl-6,7,8-trioxabicyclo[3.2.1]octane (19b): colorless liquid; ^{1}H NMR δ 1.58 (s), 1.79–1.96 (m), 2.02–2.23 (m); ^{13}C NMR (GD) δ 18.0 (t, m, J = 135.0 Hz), 20.3 (q, J = 129.0 Hz), 30.1 (t, d, m, J = 135.2 and 33.1 Hz), 33.1 (t, m, J = 130.5 Hz), 112.8 (s, m), 126.8 (d, m, J = 271.1 Hz); CI-MS (CH_4) m/z (%) 149 (100) [M^+ + 1].

Reduction of 19b. A solution of 20 mg (0.1 mmol) of **19b** in 0.5 mL of $CDCl_3$ was admixed with one drop of ethanol and an excess of triphenylphosphine. GLC analysis by coinjection of an authentic sample (t_R = 15.9 min) showed the presence of ethyl-5-oxohexanoate as the sole reduction product.

Reaction of 22a with $AgBF_4$ in Acetic Acid. A solution of 392 mg (2.08 mmol) of **22a**[7] (*cis*/*trans* = 1:2) in 4 mL of acetic acid was dropwise added to a stirred solution of 876 mg (4.5 mmol) of $AgBF_4$ in 4 mL of acetic acid at 12 °C. Then, 40 mL of ether was added; the liquid was decanted and sequentially washed with aqueous solutions of NaCl and $NaHCO_3$, dried over $MgSO_4$, and concentrated by distillation of the solvent at rt and reduced pressure to leave 292 mg of a solid residue. A second experiment starting from 280 mg (1.53 mmol) of **22a** afforded 198 mg of a solid residue. Chromatographic separation (pentane/ether, 2.5:1) of the combined residues afforded 345 mg (41%) of **22b**.

3,6-Diacetoxy-3,6-dimethyl-1,2,4,5-tetroxane (22b): colorless solid; mp 119 °C; ^{1}H NMR δ 1.86 (s), 2.19 (s); ^{13}C NMR (GD) δ 19.73 (q, J = 132.7 Hz), 21.46 (q, J = 130.3 Hz), 116.61 (q, J = 5.8 Hz), 167.23 (q, J = 7.1 Hz); ^{17}O NMR (30 °C) δ 197.6 (O—Ac), 258.1 (O—O), 383.0 (C=O); IR (CCl_4) 1778 cm^{-1} (C=O); CI-MS (i-C_4H_{10}) m/z (%) 237 (4.5) [M^+ + 1]. Anal. Calcd for $C_8H_{12}O_8$: C, 40.68; H, 5.12. Found: C, 40.72; H, 5.20.

Reduction of 22b. A solution of 4 mg (0.02 mmol) of **22b** in 0.6 mL of $CDCl_3$ was admixed with 13 mg (0.05 mmol) of triphenylphosphine. ^{1}H NMR analysis showed the presence of **22b** (δ 1.88) and of acetic anhydride (δ 2.24) in a molar ratio of 3:1 after 90 min and the presence of acetic anhydride and of acetic acid (δ 2.05) in a molar ratio of 3:1 after 4 d.

Acknowledgment. Support of this work by the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

JO950947X