methyl-8,9,10,11-tetrahydrobenz[a]anthracene as colorless rhombic crystals: mp 103–104 °C; NMR ($CDCl_3$) δ 1.68–2.15 (m, 4, $H_{9,10}$), 2.65–3.15 (m, 4, $H_{8,10}$), 2.90 (s, 3, $CH_3$), 7.33–8.00 (m, 6, aromatic), 8.60 (m, 1, $H_1$).

**(e) Dibenz[a,c]anthracene (10% Pt/C; 40 psig; 17 h; 1.0 g, 3.6 mmol; 200 mg; 30 mL).** The product isolated in essentially quantitative yield was identified as 10,11,12,13-tetrahydrodibenz[a,c]anthracene: mp 201–203 °C (benzene–hexane) (lit.[32] mp 198–199 °C); NMR ($CDCl_3$) δ 1.5–2.15 (m, 4, $H_{11,12}$), 2.81–3.21 (m, 4, $H_{10,13}$), 7.45–7.77 (m, 4, $H_{2,3,6,7}$), 8.25 (s, 2, $H_{9,14}$), 8.40–8.83 (m, 4, $H_{1,4,5,8}$).

**(f) Triphenylene ($PtO_2$; 35 psig; 48 h; 725 mg, 3.2 mmol; 260 mg; 20 mL).** The white solid product (730 mg) was separated by chromatography on a column of Florisil impregnated with 2% TNF.[15] Elution with hexanes gave 1,2,3,4,5,6,7,8,9,10,11,12-dodecahydrotriphenylene: 83 mg (12%); mp 233–234 °C (acetone–hexane) (lit.[34] mp 232–233 °C); NMR ($CCl_4$) δ 1.48–1.98 (m, 12, benzylic), 1.20–1.70 (m, 12, methylene). Further elution with hexanes gave 1,2,3,4,5,6,7,8-octahydrotriphenylene: 120 mg (16%); mp 127–129 °C (lit.[35] mp 129–130 °C); NMR ($CCl_4$) δ 1.40–2.15 (m, 8, $H_{2,3,6,7}$), 2.30–2.78 (m, 4, $H_{4,5}$), 2.80–3.18 (m, 4, $H_{1,8}$), 7.03–7.40 (m, 2, $H_{10,11}$), 7.60–7.90 (m, 2, $H_{9,12}$). Further elution with hexane gave 1,2,3,4-tetrahydrotriphenylene: 202 mg (28%); mp 118–120 °C (lit.[36] 120–121 °C); NMR ($CCl_4$) δ 1.72–2.17 (m, 4, $H_{2,3}$), 2.80–3.22 (m, 4, $H_{1,4}$), 7.25–7.56 (m, 4, $H_{6,7,10,11}$), 7.66–7.93 (m, 2, $H_{5,12}$), 8.30–8.60 (m, 2, $H_{8,9}$). Finally, elution with benzene gave recovered triphenylene (320 mg, 44%).

**(g) 5,6-Dihydrobenz[a]anthracene ($PtO_2$; 50 psig; 21 h; 315 mg, 1.4 mmol; 50 mg; 20 mL).** GLC and NMR analyses showed the product to consist of **2** (20%) and **5** (80%). The latter was collected from the GLC column as a colorless oil: NMR ($CCl_4$) δ 1.57–1.90 (m, 4, $H_{9,10}$), 2.7 (apparent s, 4, $H_{5,6}$), 2.55–2.98 (m, 4, $H_{8,11}$), 6.77–7.85 (m, 6, aromatic).

Analogous hydrogenation of **2** in the presence of 1% $FeCl_2 \cdot H_2O$ in concentrated HCl gave **5** (85%) and recovered **2** (15%) after only 2.5 h.

**(h) 5,6-Dihydro-7,12-dimethylbenz[a]anthracene ($PtO_2$; 50 psig; 24 h; 720 mg, 2.8 mmol; 100 mg; 10 mL + 10 mL of AcOH).** The sole product was 5,6,8,9,10,11-hexahydro-7,12-dimethylbenz[a]anthracene isolated in essentially quantitative yield as an oil: NMR ($CCl_4$) δ 1.62–1.93 (m, 4, $H_{9,10}$), 2.13 (s, 3, 7-$CH_3$), 2.39 (s, 3, 12-$CH_3$), 2.63 (s, 4, $H_{5,6}$), 2.50–2.82 (m, 4 $H_{8,11}$), 6.95–7.50 (m, 4, aromatic).

**(i) 4,5-Dihydrobenzo[a]pyrene ($PtO_2$; 50 psig; 24 h; 340 mg, 1.3 mmol; 45 mg; 10 mL + 10 mL of AcOH).** NMR analysis showed the product to consist of 4,5,7,8,9,10-hexahydrobenzo[a]pyrene (25%) and recovered unreacted dihydro compound. Chromatographic separation on a column of 2% TNF on Florisil[15] gave pure 4,5,7,8,9,10-hexahydrobenzo[a]pyrene: mp 87–88 °C; NMR ($CCl_4$) δ 1.9 (m, 4, $H_{8,9}$), 2.9 (m, 4, $H_{7,10}$), 3.25 (s, 4, $H_{4,5}$), 7.05–8.15 (m, 6, aromatic).

**Acknowledgment.** This research was supported by Grant No. CA 11968 and Research Contract No. CP 033385 from the National Cancer Institute, DHEW. We also wish to thank Ms. Cecilia Cortez for invaluable technical assistance.

**Registry No.** **1**, 56-55-3; **2**, 36914-99-5; **3**, 67064-62-4; **4**, 16434-59-6; **5**, 67064-61-3; **6**, 5981-10-2; **7**, 13090-93-2; **8**, 1610-39-5; **9**, 25486-92-4; benzo[a]pyrene, 50-32-8; 4,5-dihydrobenzo[a]pyrene, 57652-66-1; 3-methylcholanthrene, 56-49-5; 7,12-$Me_2$BA, 57-97-6; 5,6-$H_2$-7,12-$Me_2$BA, 35281-29-9; *cis*-7,12-$H_2$-7,12-$Me_2$BA, 24316-23-2; dibenz[a,h]anthracene, 53-70-3; 5,6-dihydrodibenz[a,h]anthracene, 153-34-4; 5,6,12,13-tetrahydrodibenz[a,h]anthracene, 153-31-1; pyrene, 129-00-0; 4,5-dihydropyrene, 6628-98-4; 4,5,9,10-tetrahydropyrene, 781-17-9; phenanthrene, 85-01-8; 9,10-diethylphenanthrene, 15810-14-7; 9,10-diethyl-1,2,3,4-tetrahydrophenanthrene, 73712-68-2; 9,10-diethyl-1,2,3,4,5,6,7,8-octahydrophenanthrene, 73712-69-3; 7,8,9,10-tetrahydrobenzo[a]pyrene, 17750-93-5; 4,5,7,8,9,10,11,12-octahydrobenzo[a]pyrene, 73712-70-6; 4,5,7,8,9,10-hexahydrobenzo[a]pyrene, 73712-75-1; 7,8,9,10,11,12-hexahydrobenzo[a]pyrene, 73712-71-7; 8,9,10,11-$H_4$-7,12-$Me_2$BA, 25486-91-3; 5,6,8,9,10,11-$H_6$-7,12-$Me_2$BA, 73712-72-8; *trans*-7,12-$H_2$-7,12-$Me_2$BA, 23660-33-5; 7-methylbenz[a]anthracene, 2541-69-7; 7-methyl-8,9,10,11-tetrahydrobenz[a]anthracene, 63020-38-2; 12-methylbenz[a]anthracene, 2422-79-9; 12-methyl-8,9,10,11-tetrahydrobenz[a]anthracene, 67099-80-3; 5,6,8,9,10,11-hexahydro-12-methylbenz[a]anthracene, 73712-73-9; 7,12-dihydro-12-methylbenz[a]anthracene, 73712-74-0; dibenz[a,c]-anthracene, 215-58-7; 10,11,12,13-tetrahydrodibenz[a,c]anthracene, 25486-89-9; triphenylene, 217-59-4; 9,10-dihydrophenanthrene, 776-35-2; chrysene, 218-01-9; 5,6-dihydrochrysene, 2091-92-1; 1,2,3,4-tetrahydrochrysene, 2091-90-9.

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(35) Rapson, W. S. *J. Chem. Soc.* **1941**, 15.
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# Rearrangement of 1-Aryl-2,2-dihalo-1-alkanones[1a]

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Reaction of 1-aryl-2,2-dichloro-1-alkanones with alkoxides in the corresponding alcohol afforded a mixture of 1-aryl-2,2-dialkoxy-1-alkanones and 1-aryl-1,1-dialkoxy-2-alkanones. The mechanism was shown to proceed via α-chloro-α′-alkoxy epoxides, which rearranged into 1-alkoxy-1-aryl-1-chloro-2-alkanones, the latter giving the final compounds via either another epoxide intermediate or a solvolysis mechanism. α,α-Dibromo- and α-bromo-α-chloroalkyl aryl ketones behaved analogously, but α-bromo-α-fluoro- and α-chloro-α-fluoroalkyl aryl ketones gave exclusively solvolysis of initially formed 1-alkoxy-1-aryl-1-fluoro-2-alkanones, resulting in rearranged 1-aryl-1,1-dialkoxy-2-alkanones. α,α-Difluoroalkyl aryl ketones did not rearrange but underwent reduction of the carbonyl function on treatment with sodium methoxide in methanol. The influence of varying factors, such as the steric requirements of the alkoxide and the substrate, the concentration of the alkoxide, the aromatic substituent, the temperature, and the halogens, was investigated and correlated to the mechanism involved.

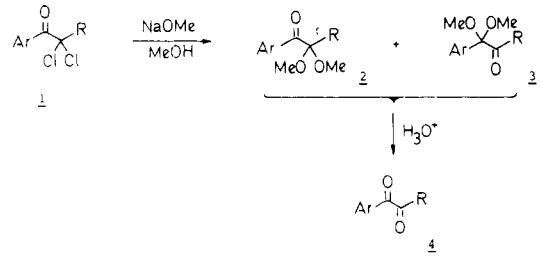
In a preliminary publication we reported on the synthesis of 1-aryl-1,2-alkanediones **4** by reaction of α,α-dichloroalkyl aryl ketones **1** with sodium methoxide in methanol and subsequent acidic hydrolysis of the resulting isomeric α,α-dimethoxy ketones **2** and **3** (Scheme I).[2] α,α-Dichloroalkyl aryl ketones **1** have not received much attention in the literature, but recently an increasing interest revealed several mechanistic and synthetic potentials for this class of compounds.[2-4] α,α-Dichloroaceto-

(1) (a) This paper was presented at the 1st European Symposium on Organic Chemistry, Aug 1979, Cologne, West Germany. (b) To whom correspondence should be addressed; Aangesteld Navorser of the Belgian Nationaal Fonds voor Wetenschappelijk Onderzoek.

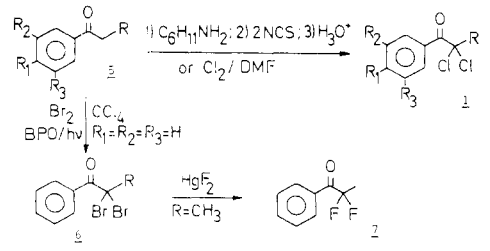
(2) N. De Kimpe, R. Verhé, L. De Buyck, and N. Schamp, *J. Org. Chem.*, **43**, 2933 (1978).

0022-3263/80/1945-2803$01.00/0 

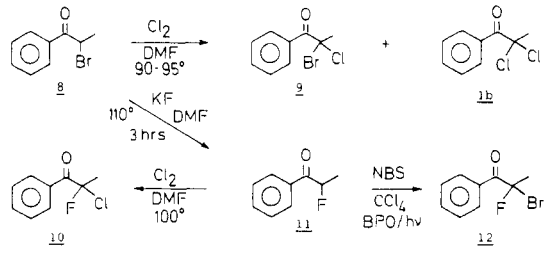
**Scheme I**



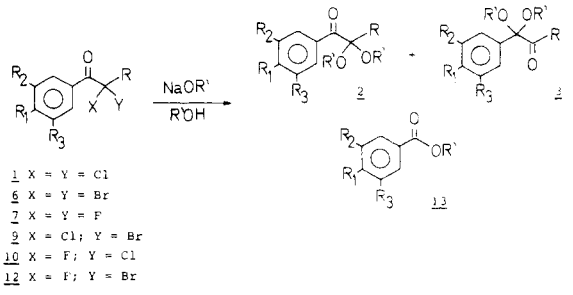
**Scheme II**



**Scheme III**



**Scheme IV**



phenones, e.g., **1** (R = H), were readily accessible according to literature reports, but higher homologues of **1** (R ≠ H) only recently became available.[5,6] Because of the fact that many controversies exist in the literature concerning the reactions of α,α-dihaloacetophenones (vide infra), we decided to investigate the reactions of α,α-dihaloacetophenones and their higher homologues with alkoxides in the corresponding alcohol in more detail. In this paper, several corrections and/or additions to literature reports will be made, and the fascinating mechanism is unraveled.

The synthesis of 1-aryl-2,2-dihalo-1-alkanones was accomplished as follows. 1-Aryl-2,2-dichloro-1-alkanones **1** were prepared by chlorination of the *N*-cyclohexyl imines, derived from the parent ketones **5**, with *N*-chlorosuccinimide and subsequent acidic hydrolysis[5] or by direct chlorination of the parent ketones **5** with chlorine gas in dimethylformamide[6] as reported previously (Scheme II). 2,2,3′-Trichloro-4′-methoxypropiophenone (**1i**; $R_1 = OCH_3$ and $R_2$ = Cl in **1**) was obtained by chlorination of 4′-methoxypropiophenone with chlorine in dimethylformamide[6] whereby also the aromatic nucleus was monochlorinated (yield 82%; mp 78 °C).[7] 2,2,3′-Trichloro-4′-methoxy-5′-nitropropiophenone (**1j**; R = $CH_3$, $R_1 = OCH_3$, $R_2$ = Cl, and $R_3 = NO_2$ in **1**) was synthesized by nitration of **1i** with fuming nitric acid. α,α-Dibromopropiophenone (**6**, R = $CH_3$) was prepared by bromination of propiophenone with bromine in carbon tetrachloride at reflux in the presence of benzoyl peroxide and under irradiation,[10] while α,α-difluoropropiophenone (**7**) was obtained from the reaction of α,α-dibromopropiophenone with mercuric fluoride.[11] α-Bromo-α-chloropropiophenone (**9**) was synthesized from α-bromopropiophenone (**8**) by chlorination with chlorine in dimethylformide at 90–95 °C, but the reaction mixture consisted of 58% α-bromo-α-chloropropiophenone (**9**) and 42% α,α-dichloropropiophenone (**1b**). Careful and repeated distillation over a 50-cm Vigreux column yielded the desired compound **9**. α-Bromo-α-fluoropropiophenone (**12**) was prepared from α-bromopropiophenone (**8**) by reaction with potassium fluoride in dimethylformamide at 100 °C, affording α-fluoropropiophenone (**11**), and subsequent photochemical bromination with *N*-bromosuccinimide. The corresponding α-chloro-α-fluoropropiophenone (**10**) was obtained similarly by chlorination of α-fluoropropiophenone (**11**) with chlorine in dimethylformamide (Scheme III).

## Results

α,α-Dihaloalkyl aryl ketones **1**, **6**, **7**, **9**, **10**, and **12** reacted very cleanly with sodium alkoxides in the corresponding alcohol to produce a mixture of isomeric α,α-dialkoxy ketones **2** and **3** in variable ratios (Table I). In some cases, small amounts of alkyl benzoates **13** were detected (Scheme IV).

α,α-Dichloro- and α,α-dibromoalkyl aryl ketones **1** and **6** gave rise to varying ratios of compounds **2** and **3**. The simplest member of the α,α-dichloro ketones, i.e., 2,2-dichloroacetophenone (**1a**; X = Y = Cl, and R = $R_1 = R_2 = R_3$ = H in **1**), and the bulky 2,2-dichloro-3,3-dimethyl-1-phenyl-1-butanone (**1e**; X = Y = Cl, R = *t*-Bu, and $R_1 = R_2 = R_3$ = H in **1**) also produced methyl benzoate (**13**; $R_1 = R_2 = R_3$ = H; R′ = $CH_3$) on reaction with sodium methoxide in methanol.

A complete breakdown reaction with formation of methyl benzoate was observed when 2,2-dichloro-1,2-diphenylethanone (**1f**; X = Y = Cl, $R_1 = R_2 = R_3$ = H, and R = $C_6H_5$ in **1**) was reacted with 1 N sodium methoxide in methanol. Reaction of sodium methoxide in methanol with 2-bromo-2-chloropropiophenone (**9**) also furnished a mixture of α,α-dialkoxy ketones **2** and **3**, but 2-chloro-2-

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(6) N. De Kimpe, L. De Buyck, R. Verhé, F. Wychuyse, and N. Schamp, *Synth. Commun.*, **9**, 575 (1979).

(7) It has been reported that the chlorination of 4′-methoxyacetophenone with chlorine in acetic acid afforded 2,2,3′-trichloro-4′-methoxyacetophenone.[8,9] Analogous to our reported method,[6] 4′-methoxyacetophenone was also converted into 2,2,3′-trichloro-4′-methoxyacetophenone with $Cl_2$ in DMF [85% yield; mp 102 °C (lit.[8,9] mp 101.5–103 °C)].

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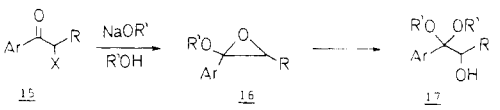
**Table I. Reactivity of 1-Aryl-2,2-dihalo-1-alkanones toward Alkoxides in Alcohol**

| entry | starting material | R | $R_1$ | $R_2$ | $R_3$ | OR′ | X | Y | reaction conditions[c] | % reaction products[a] 2 | 3 | other[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1a | H | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 1 h | 9 | 84 | 7% methyl benzoate |
| 2 | 1b | Me | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 1 h | 76 | 24 | |
| 3 | 1c | Et | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 1 h | 45 | 55 | |
| 4 | 1d | *n*-Pr | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 1 h | 43 | 57 | |
| 5 | 1e | *t*-Bu | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; Δ; 10 min | 0 | 38 | 62% haloform-type reaction |
| 6 | 1e | *t*-Bu | H | H | H | OMe | Cl | Cl | 1 N, 2.2 equiv; Δ; 30 min | 0 | 50 | 50% haloform-type reaction |
| 7 | 1e | *t*-Bu | H | H | H | OMe | Cl | Cl | 0.5 N, 2.2 equiv; Δ; 2 h | 0 | 60 | 40% haloform-type reaction |
| 8 | 1f | $C_6H_5$ | H | H | H | OMe | Cl | Cl | 1 N, 2.2 equiv; rt; 3 h | 0 | 0 | 100% haloform-type reaction |
| 9 | 1b | Me | H | H | H | OMe | Cl | Cl | 1 N, 2.2 equiv; rt; overnight | 75 | 25 | |
| 10 | 1b | Me | H | H | H | OEt | Cl | Cl | 1 N, 2.2 equiv; rt; overnight | 33 | 67 | |
| 11 | 1b | Me | H | H | H | O-*i*-Pr | Cl | Cl | 1 N, 2.2 equiv; rt; overnight | 0 | 67 | 7% 1-phenyl-1,2-propanedione |
| 12 | 1b | Me | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 1 h | 76 | 24 | |
| 13 | 1b | Me | H | H | H | OMe | Cl | Cl | 1 N, 2.2 equiv; rt; 1 h | 75 | 25 | |
| 14 | 1b | Me | H | H | H | OMe | Cl | Cl | 0.5 N, 2.2 equiv; rt; overnight | 75 | 25 | |
| 15 | 1b | Me | H | H | H | OMe | Cl | Cl | 0.1 N, 2.2 equiv; rt; overnight | 60 | 40 | |
| 16 | 1b | Me | H | H | H | OMe | Cl | Cl | 0.01 N, 2.2 equiv; rt; overnight | 27 | 73 | |
| 17 | 1b | Me | H | H | H | OMe | Cl | Cl | 10% methanolic soln; Δ; 3 days | 0 | 0 | 100% recovery |
| 18 | 1b | Me | H | H | H | OMe | Cl | Cl | 10% methanolic soln + 5 equiv of $Et_3N$; Δ; 7 days | 0 | 89 | 11% recovery |
| 19 | 1b | Me | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 1 h | 76 | 24 | |
| 20 | 1g | Me | Cl | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 1 h | 72 | 28 | |
| 21 | 1h | Me | Br | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 1 h | 66 | 34 | |
| 22 | 1i | Me | OMe | Cl | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 1 h | 60 | 40 | |
| 23 | 1j | Me | OMe | Cl | $NO_2$ | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; overnight | 56 | 44 | |
| 24 | 1b | Me | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; −30 °C; overnight | 0 | 0 | 100% recovery |
| 25 | 1b | Me | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; 0 °C; 1 h | 80 | 20 | |
| 26 | 1b | Me | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; 20 °C; 1 h | 76 | 24 | |
| 27 | 1b | Me | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; *b*; 10 min | 60 | 40 | |
| 28 | 1b | Me | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; 65 °C; 3 min | 50 | 50 | |
| 29 | 1b | Me | H | H | H | OMe | Cl | Cl | 2 N, 2.2 equiv; rt; 2 h | 76 | 24 | |
| 30 | 9 | Me | H | H | H | OMe | Cl | Br | 2 N, 2.2 equiv; rt; 2 h | 68 | 32 | |
| 31 | 6 | Me | H | H | H | OMe | Br | Br | 2 N, 2.2 equiv; rt; 2 h | 18 | 74 | 8% methyl benzoate |
| 32 | 12 | Me | H | H | H | OMe | F | Br | 2 N, 2.2 equiv; rt; 2 h | 0 | 100 | |
| 33 | 10 | Me | H | H | H | OMe | F | Cl | 2 N, 2.2 equiv; rt; 2 h | 0 | 100 | |
| 34 | 7 | Me | H | H | H | OMe | F | F | 2 N, 2.2 equiv; rt; 2 h | 0 | 0 | |
| 35 | 7 | Me | H | H | H | OMe | F | F | 2 N, 4 equiv; Δ; overnight | 0 | 0 | 100% 34 |

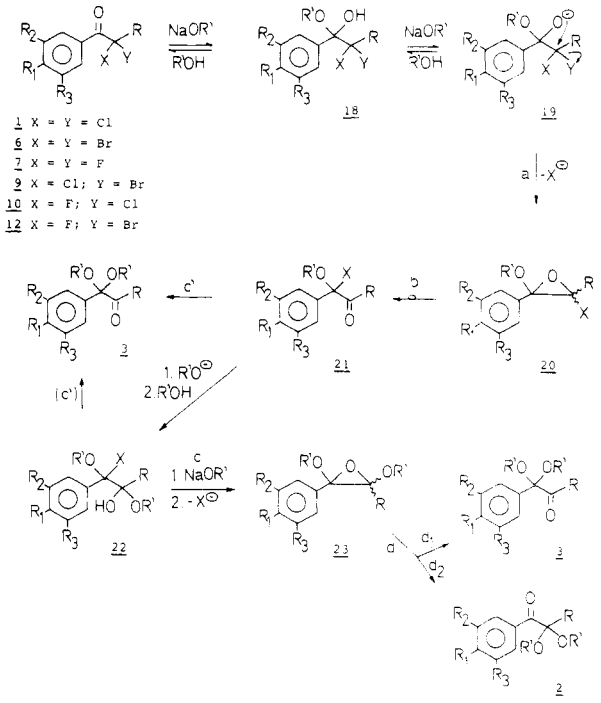
[a] The percentages of the reaction products listed in this table were obtained from GLC and NMR analysis. The total yield of the crude reaction mixture was nearly quantitative except as otherwise stated (the peak areas were used uncorrected for detector response). Distilled yields usually exceeded 90% of the theoretical amount. Compounds 2 and 3 gave satisfactory elemental analysis. [b] These conditions refer to an uncontrolled experiment in which the reactants were mixed rapidly at ambient temperature without cooling (exothermic reaction). [c] The designation 2 N, 2.2 equiv (etc.) indicates 2.2 equiv of NaOMe from a 2 N solution in methanol; Δ indicates heating; rt indicates room temperature.

Scheme V

Scheme VI



Scheme VII



fluoro- and 2-bromo-2-fluoropropiophenones (**10** and **12**, respectively) gave exclusively rearrangement to 1,1-dimethoxy-1-phenyl-2-propanone (**3b**) on reaction with the same reagent. On the contrary, 2,2-difluoropropiophenone (**7**) did not produce formal substitution products **2** or rearranged compounds **3** but yielded exclusively reduction of the carbonyl function by reaction with excess sodium methoxide in methanol at reflux.

Various factors influencing the distribution of products resulting from the reaction of $\alpha,\alpha$-dihaloalkyl aryl ketones with alkoxides in alcohol were studied (Table I). The influences of the steric requirements of the alkyl group R of the substrate (entries 1–8), the steric requirements of the nucleophile (entries 9–11), the concentration of the nucleophile (entries 12–18), the aromatic substituents (entries 19–23), the temperature (entries 24–28), and the halogen (entries 29–35) were investigated. These influences will be discussed thoroughly in the Discussion which describes the mechanistic rationale.

In general, a slight excess of nucleophilic reagent was used, and the reactions were monitored by regular sampling and by following the NMR analysis. The isomeric $\alpha,\alpha$-dialkoxy ketones **2** and **3** can be easily distinguished in the NMR spectrum of the reaction mixture, thus allowing accurate determination of the ratio of the reaction products. The percent composition was also verified by gas chromatographic analysis, which revealed good separation of isomeric compounds **2** and **3**. However, in some cases $\alpha,\alpha$-dialkoxyalkyl aryl ketones **2** lost one molecule of the alcohol under gas chromatographic circumstances and gave rise to $\alpha$-alkoxy $\alpha,\beta$-unsaturated ketones **14**, a phenomenon which is well-known in acetal chemistry (Scheme V).[12,13] As shown in Table I, a large variety of 2,2-dialkoxy-1-aryl-1-alkanones (**2**) and 1,1-dialkoxy-1-aryl-2-alkanones (**3**) were prepared and fully characterized; the physical and spectrometric data (NMR, IR, and mass spectra) are included as Tables II and III in the supplementary material.

## Discussion

The reactive behavior of aromatic $\alpha$-halogenated ketones is well documented in the literature. Especially phenacyl halides have been studied extensively mainly because of their very high $S_N2$ reactivity.[14,15] For instance, the relative rate of the nucleophilic substitution of phenacyl chloride by iodide ion in acetone is 105 000 as compared to the same reaction of 1-chlorobutane. Several mechanistic proposals have been formulated,[16–19] and it was recently shown that the rate enhancement is not a general process but is highly dependent upon the character of the nucleophile used.[20] However, the introduction of $\alpha$ substituents drastically reduced the reactivity due to the importance of steric effects. The relative reactivities of phenacyl chloride, 2-chloropropiophenone and $\alpha$-chloroisobutyrophenone varied from 1 over 0.006 to 0.000 003.[21] As a matter of fact, $\alpha$-bromopropiophenone (**15**; Ar = Ph, R = Me, X = Br)[22] and $\alpha$-chloropropiophenone (**15**; Ar = Ph, R = Me, X = Cl)[23] are known to react with sodium methoxide in methanol to give 1,1-dimethoxy-1-phenyl-2-propanol (**17**; Ar = Ph, R′ = R = Me). The formation of $\alpha$-hydroxy acetal **17** was explained by carbonyl attack, epoxide (**16**) production, and subsequent opening by the nucleophile (Scheme VI).

In general it is by now well recognized that $\alpha$-monohalogenated alkyl aryl ketones **15** react with alkoxides in the corresponding alcohol to produce nucleophilic addition at the aroyl moiety followed by intramolecular halide displacement and formation of an epoxide intermediate. The intermediate $\alpha$-alkoxy epoxides **16** have been isolated in less polar medium, e.g., diethyl ether,[22–25] but they were found to open to $\alpha$-hydroxy acetals **17** when alcohols were present in the reaction mixture.[22–26]

(12) G. M. Loudon, C. K. Smith, and S. E. Zimmerman, *J. Am. Chem. Soc.*, **96**, 465 (1974).
(13) Y. Chiang, W. K. Chwang, A. J. Kresze, L. H. Robinson, D. S. Sagatys, and C. I. Young, *Can. J. Chem.*, **56**, 456 (1978).
(14) J. B. Conant, W. R. Kirner, and R. E. Hussey, *J. Am. Chem. Soc.*, **47**, 488 (1925).
(15) A. Streitwieser, *Chem. Rev.*, **56**, 600 (1956).
(16) M. J. S. Dewar, "The Electronic Theory of Organic Chemistry", Clarendon Press, Oxford, 1948, p 73.
(17) R. G. Pearson, S. H. Langer, F. V. Williams, and W. J. McGuire, *J. Am. Chem. Soc.*, **74**, 5130 (1952).
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(19) P. D. Bartlett and E. N. Trachtenberg, *J. Am. Chem. Soc.*, **80**, 5808 (1958).
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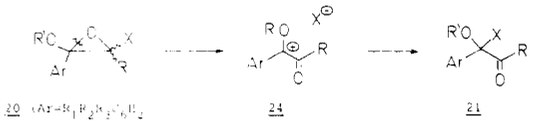
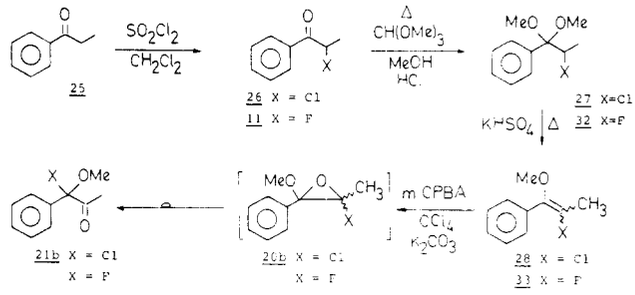
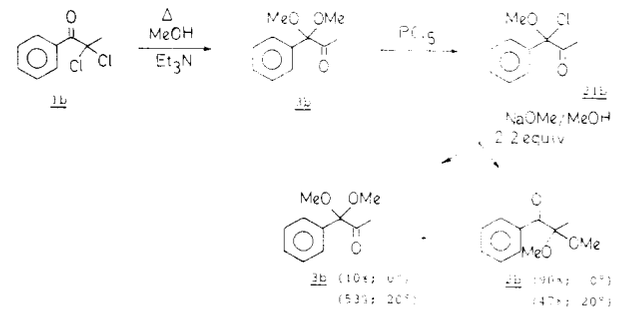
Scheme VIII



Scheme IX



Scheme X



The foregoing arguments clearly argue against the possibility of direct nucleophilic displacement of the halogens in 1-aryl-2,2-dihalo-1-alkanones as discussed in this paper. An $S_N1$ mechanism can be excluded because of the unfavorable influence (electrophilic nature) of the neighboring carbonyl group. Indeed, the positively induced carbonyl atom and the adjacent carbonium ion, occurring during nucleophilic substitution, exhibit repulsive effects, not allowing the latter reaction to take place. On the other hand, an $S_N2$ reaction is less favorable due to the fact that the starting material is a tertiary halide. This reasoning is substantiated by the lack of reaction when 2,2-dichloropropiophenone was refluxed with potassium iodide (2.2 equiv, 4 h) in acetone.

It is reasonable to believe that the title compounds, i.e., $\alpha,\alpha$-dihaloalkyl aryl ketones (X = Cl, Br) also give rise to nucleophilic addition and subsequent intramolecular nucleophilic attack (path a, Scheme VII), furnishing $\alpha$-halo-$\alpha'$-alkoxy epoxide intermediates **20** by halide displacement. Also $\alpha,\alpha$-dihalo aldehydes have been shown to rearrange via this route.[27]

The resulting $\alpha$-halo-$\alpha'$-alkoxy epoxide **20** is a very reactive species and will rapidly rearrange spontaneously to $\alpha$-halo-$\alpha$-alkoxy ketones **21** (path b, Scheme VII). It is indeed known that $\alpha$-halo epoxides easily undergo ring opening with migration of the halide anion to form an $\alpha$-halocarbonyl compound.[28,29] Kirrmann and co-workers extensively studied the thermal stability of $\alpha$-halo epoxides and concluded that the so-called "normal" ring opening, i.e., the opening at the $\alpha'$ position, occurred preferentially.[30-33] In the case of the intermediate epoxides studied here, it is expected that $\alpha$-halo-$\alpha'$-alkoxy epoxides **20** would even show an enhanced tendency to rearrange to the corresponding $\alpha$-halocarbonyl compounds because of the supplementary activating influence of the $\alpha'$-alkoxide group (Scheme VIII).

The normal opening of epoxide **20** at the $\alpha'$ position results in a stabilized carbonium ion **24**, which leads to $\alpha$-halo ether **21**. These $\alpha$-alkoxy-$\alpha$-halo ketones **21** can further give rise to $\alpha,\alpha$-dialkoxy ketones **3** by a direct route or via the hemiacetal **22** (path c', Scheme VII). Alternatively, the latter product can be deprotonated by the alkoxide, after which intramolecular nucleophilic substitution yields the $\alpha,\alpha'$-dialkoxy epoxide **23** (path c, Scheme VII). Diactivated epoxides such as **23** are then opened at both sides of the three-membered ring to produce the final isomeric $\alpha,\alpha$-dialkoxy ketones **2** and **3** (paths $d_1$ and $d_2$ in Scheme VII). We tried to substantiate the mechanistic rationale by the synthesis of an $\alpha$-halo-$\alpha$-alkoxy epoxide (Scheme IX). Monochlorination of propiophenone **25** with sulfuryl chloride in dichloromethane and subsequent acetalization with a large excess of trimethyl orthoformate and hydrogen chloride in methanol afforded $\alpha$-chloro acetal **27** in 60% isolated yield. The conversion into $\beta$-chloro enol ether **28** was accomplished by heating with potassium hydrogen sulfate. This functionalized olefin, **28**, was epoxidized with *m*-chloroperbenzoic acid in carbon tetrachloride at 0 °C in the presence of solid potassium carbonate, but the product which was isolated was 1-chloro-1-methoxy-1-phenyl-2-propanone (**21b**; X = Cl). This transformation supported the transient formation of $\alpha$-chloro-$\alpha'$-methoxy epoxide **20b** (X = Cl), which presumably rearranged spontaneously to $\alpha$-chloro ether **21b**. The latter compound was compared with an authentic sample, prepared by a reaction sequence involving rearrangement of $\alpha,\alpha$-dichloropropiophenone (**1b**; R = R' = Me and $R_1 = R_2 = R_3 = H$ in **1**) with refluxing methanol in the presence of triethylamine (vide infra), followed by conversion of the resulting acetal **3b** into $\alpha$-chloro ether **21** by phosphorus pentachloride treatment (Scheme X).[34]

According to the reaction mechanism presented in Scheme VII, $\alpha,\alpha$-dihaloalkyl aryl ketones rearrange in a straightforward manner to compounds which have undergone a transposition of the carbonyl function from the 1- to the 2-position, namely, 1-alkoxy-1-aryl-1-halo-2-alkanones, **21**. It is clear that these compounds hold a central position in the mechanism and that their reactivity completely determines the distribution of the isomeric $\alpha,\alpha$-dialkoxy ketones **2** and **3**. Analogously, as pointed out above for the synthesis of $\alpha$-chloro-$\alpha'$-methoxy epoxide **20** (R = R' = Me, X = Cl, $R_1 = R_2 = R_3 = H$), attempts were undertaken to synthesize $\alpha,\alpha'$-dimethoxy epoxide **23** (R = R' = Me, $R_1 = R_2 = R_3 = H$; see Scheme VII) via an epoxidation of the corresponding functionalized olefin. The reaction sequence involved carbonyl reduction of $\alpha,\alpha$-dimethoxy ketones **2b** and **3b**, methylation of the resulting alcohols with methyl iodide/dimsyl anion/$Me_2SO$, and subsequent acid-catalyzed methanol expulsion. These reactions have been carried out on the isolated keto acetals **2b** or **3b** as well as on the mixture, obtained from the

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(30) A. Kirrmann, P. Duhamel, and R. Nouri-Bimorghi, *Bull. Soc. Chim. Fr.*, 3264 (1964).
(31) A. Kirrmann and Nouri-Bimorghi, *Bull. Soc. Chim. Fr.*, 3213 (1968).
(32) R. Nouri-Bimorghi, *Bull. Soc. Chim. Fr.*, 2812 (1969).
(33) P. Duhamel, L. Duhamel, and J. Gralak, *Bull. Soc. Chim. Fr.*, 3641 (1970).
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alkoxide-induced rearrangement of α,α-dichloropropiophenone (**1b**). However, we could not induce methanol expulsion to the desired enediol ether on treatment with p-toluenesulfonic acid or potassium hydrogen sulfate. When the mixture of trimethoxy compounds was subjected to preparative GLC, the sole peak isolated consisted of a 1:1:2 mixture of 2,3-dimethoxy-3-phenylpropene and (*Z*)- and (*E*)-1,2-dimethoxy-1-phenylpropene.

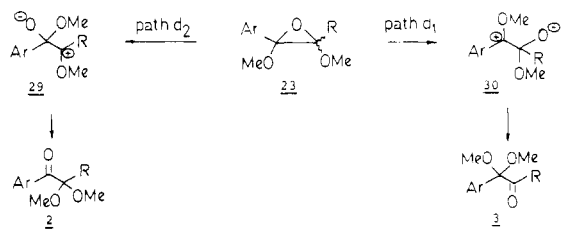
From the mechanistic rationale depicted in Scheme VIII, it is clear that the distribution of products **2** and **3** is completely determined by the reactive behavior of α-alkoxy-α-halo ketones **21**. This competitive phenomenon was verified by the reaction of authentic 1-chloro-1-methoxy-1-phenylacetone **21b** (X = Cl) with 1 N sodium methoxide in methanol (2.2 equiv) at different temperatures. At 0 °C the solvolysis of **21b** seemed to be suppressed by the reaction involving nucleophilic carbonyl attack and subsequent α,α′-dimethoxy epoxide formation. However, at 20 °C the ratio changed drastically to approximately 1:1 (Scheme X). With methanol or ethanol (10 min, room temperature), of course, the exclusive product was the alcoholysis product.

In order to obtain insight into the rearrangement discussed in this paper, we investigated the influence of various factors such as, among others, the steric requirements of the nucleophile (i.e., the alkoxide) and the alkyl group of the substrate, the concentration of the alkoxide, the type of aromatic substituent, the temperature, and the nature of the halogens.

**Factors Influencing the Distribution of Products. Steric Requirements of the Alkyl Group of the Substrate (Entries 1–8).** The reaction of α,α-dichloropropiophenone (**1b**) with 2.2 equiv of 2 N sodium methoxide in methanol at room temperature resulted in a mixture of 76% 2,2-dimethoxy-1-phenyl-1-propanone (**2b**) and 24% 1,1-dimethoxy-1-phenyl-2-propanone (**3b**). Homologation drastically changed the ratio from 3:1 to about 1:1 for the formal substitution products **2c,d** and the rearranged compounds **3c,d**. With the bulky α,α-dichloroneopentyl phenyl ketone (**1e**), not formal substitution product **2e** was found, but instead, 38% rearranged 1,1-dimethoxy-3,3-dimethyl-1-phenyl-2-butanone (**3e**) and 62% haloform-type reaction were observed. The latter breakdown reaction produced methyl benzoate (**13**; R′ = Me, $R_1 = R_2 = R_3$ = H) and 1,1-dichloro-2,2-dimethylpropane. The haloform-type reaction decreased with decreasing concentration of the alkoxide, and the 2:3 ratio of rearrangement to haloform-type reaction was reversed to a 3:2 ratio on going from 2 to 0.5 N sodium methoxide in methanol. For comparative reasons α,α-dichlorodeoxybenzoin was also treated with sodium methoxide in methanol, but in this case the exclusive reaction which occurred was the haloform-type reaction.

The above-mentioned results show that increasing steric hindrance in the substrate is related to increased rearrangement. A competitive haloform-type reaction in some cases occurs, especially when the R group exhibits anion-stabilization capacities. When R = *tert*-butyl, the same reaction is important, probably because of excessive steric crowding in the molecule. The influence of the concentration of sodium methoxide in this case is still unclear. The distribution of the isomeric α,α-dialkoxy ketones **2** and **3** can be explained by two simultaneously occurring processes (paths c and c′ of Scheme VII). In order to explain the formation of the formal substitution products **2**, one observes that the rearranged α-halo-α-alkoxy ketones **21** have to undergo another rearrangement, via α,α′-dialkoxy epoxides **23**, the opening of which can lead to the final

**Scheme XI**




isomeric α,α-dialkoxy ketones **2** and **3**. The other route involves a solvolysis of the α-halo ether **21** to the corresponding acetal **3**, most probably via the hemiacetal **22** because this reduces the less favorable influence of the aroyl moiety. It is clear that increased steric hindrance by the R group will negatively influence the addition at the carbonyl function, and this will decrease the overall reaction passing through α,α′-dialkoxy epoxide **23**. This reasoning is consistent with the extreme steric hindrance of the *tert*-butyl derivative **21e**, which does not allow reaction path c to take place due to the decreased affinity of the carbonyl to add nucleophiles (tertiary substitution at both sides). Accordingly, solvolysis of **21** is the preferred reaction but is accompanied by the haloform-type reaction. If path c leading to α,α′-dialkoxy epoxide **23** is followed, opening at the α or α′ position leads to two isomeric products **2** and **3**.

The variation of products of types **2** and **3** with the size of the alkyl group R may be explained as follows. Path $d_2$ (Scheme XI) leads to a carbonium ion **29** which is stabilized by one methoxy group and by R. When R = alkyl, carbonium ion **29** is much better stabilized than when R = H. Hence, path $d_2$ is less favorable for R = H, and **1a** gives mainly **3a** by path $d_1$ (vide infra). When R is larger (Et, Pr), nucleophilic attack at the carbonium ion is less efficient than when R is small (Me), and thus **1b** gives mainly **2b**, but **1c** and **1d** give more **3c** and **3d**. Additionally, decreasing steric hindrance of R results in a preferential opening at the alkyl side of **23** (path $d_2$). As mentioned already above, the simplest member in this series, α,α-dichloroacetophenone (**1a**; R = $R_1 = R_2 = R_3$ = H and X = Y = Cl in **1**), showed deviating results.

As only α,α-dihaloacetophenones are well-known in the literature, their reactivity was studied to some extent in the older literature. The reaction of α,α-dichloro- or α,α-dibromoacetophenone with methoxide or ethoxide in the corresponding alcohol was erroneously reported to give the formal substitution products, i.e., α,α-dialkoxyacetophenones **2** (R = H;[35-38] see structure in Scheme IV). This reaction was investigated again a decade ago,[39,40] and it was found that, in fact, the isomeric, rearranged 1,1-dialkoxy-1-phenylacetaldehyde **3** (R = H; see structure in Scheme IV) was produced as well as slight amounts of benzoates, while none of the formerly reported α,α-dialkoxyacetophenones was mentioned. These results did not fit well with our results with higher homologues, and, therefore, we duplicated these experiments and found that the main product of the reaction of sodium methoxide in methanol with α,α-dichloroacetophenone was indeed the

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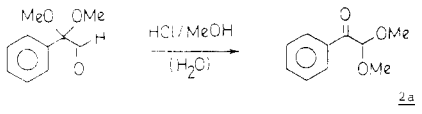
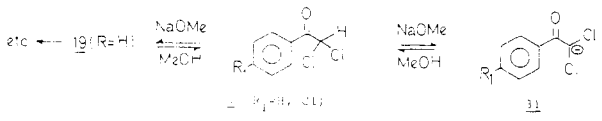
(36) J. Houben and W. Fischer, *Ber. Dtsch. Chem. Ges.*, **64**, 2636 (1931).
(37) W. Madelung and M. E. Oberwegner, *Justus Liebigs Ann. Chem.*, **490**, 201 (1931).
(38) G. Cavallini, *J. Med. Chem.*, **7**, 255 (1964).
(39) K. Henery-Logan and T. Fridinger, *Chem. Commun.*, **130** (1968).
(40) C. Raulet and E. Levas, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **269**, 996 (1969).

Scheme XII



Scheme XIII



rearranged 1,1-dimethoxy-1-phenylacetaldehyde (**3a**, 84%) but was accompanied by 7% methyl benzoate and 9% 2,2-dimethoxyacetophenone (**2a**). The latter compound was clearly identified by spectrometry, and the structure was unambigously proved by comparison with an authentic sample, obtained from acid-catalyzed isomerization of 1,1-dimethoxy-1-phenylacetaldehyde (**3a**) in the presence of trace amounts of water (Scheme XII).[41] A similar result was obtained with 2,2,4′-trichloroacetophenone (**1**; R = $R_2$ = $R_3$ = H, X = $R_1$ = Cl) which reacted with sodium methoxide in methanol (2.2 equiv, 1 N solution; 1 h of reflux) to produce 80% 2,2-dimethoxy-2-(4-chlorophenyl)acetaldehyde (**3**; R = $R_2$ = $R_3$ = H, $R_1$ = Cl, R′ = $CH_3$) and 20% 4′-chloro-2,2-dimethoxyacetophenone (**2**; R = $R_2$ = $R_3$ = H, $R_1$ = Cl, R′ = $CH_3$). The anomalous behavior of α,α-dichloroacetophenones can be explained by the above-mentioned considerations concerning the opening of epoxide **23** (R = H) and by the presence of an acidic α-hydrogen. In sodium methoxide/methanol, α,α-dichloroacetophenone probably exists in equilibrium with a fairly high concentration of the enolate ion **31**, because of stabilization of the latter by the carbonyl group and two halogens (Scheme XIII).

When 2,2,4′-trichloroacetophenone (1; R = $R_2$ = $R_3$ = H, X = $R_1$ = Cl) was added to a refluxing solution of sodium methoxide in methanol (2 equiv, 2 N solution) the amount of the α,α-dimethoxyacetophenone derivative **2** (R = H) came to 25%, next to the 75% of the dimethoxyacetaldehyde derivative **3** (R = H). The formation of more **2** (R = H) for the *p*-chloro derivative results from the less favorable opening of epoxide **23** (Ar = *p*-$ClC_6H_4$ and R = H in Scheme XI) by path $d_1$ due to the fact that the *p*-chloro carbonium ion **30** (Ar = *p*-$ClC_6H_4$, R = H) is not as stable as *p*-protio intermediate **30** (Ar = Ph, R = H). In this section on the influence of the alkyl group, it has to be pointed out that 2,2-dichloro-α-tetralone reacted in a different manner with sodium methoxide in methanol (2.2. equiv, 2 N solution; overnight at room temperature), as the only reaction product was 2-chloro-1-naphthol resulting from dehydrochlorination and subsequent double bond migrations.[42] The steric requirements of the α-tetralone moiety apparently do not permit epoxide formation and therefore lead to other reactions of cyclic ketones, e.g., elimination reactions.

**Steric Requirements of the Nucleophile (Entries 9–11).** The reaction of α,α-dichloropropiophenone (**1b**) with sodium methoxide in methanol (2.2 equiv, 1 N solution) at room temperature gave a 3:1 ratio of formal substitution product over rearranged compound. The use of sodium ethoxide in ethanol under similar conditions resulted in a drastic change in the ratio, namely, 1:2, while with sodium isopropoxide in 2-propanol only rearranged 1,1-diisopropoxy-1-phenyl-2-propanone (**3**; R = Me, R′ = *i*-Pr, $R_1$ = $R_2$ = $R_3$ = H) (67%) was isolated besides 7% 1-phenyl-1,2-propanedione and some unidentified compounds. These results are consistent with the aforementioned steric considerations concerning the competition between epoxide formation and solvolysis of α-halo-α-alkoxy ketones **21**. Here again an increased steric hindrance favors the reactions to proceed in the direction of solvolysis.

**Influence of the Concentration of the Nucleophile (Entries 12–18).** Another important factor on the distribution of the final products was the concentration of the nucleophile. This influence was studied on α,α-dichloropropiophenone (**1b**) with sodium methoxide in methanol at room temperature (2.2 equiv). Lowering the concentration of methoxide resulted in a slower reaction and an increase in rearranged α,α-dimethoxy ketone **2** (R = R′ = Me). Not much variation was noted for 0.5–2 N solutions, but more diluted solutions (0.1–0.01 N) reversed the ratio of the distribution. Methanol itself under reflux did not react with α,α-dichloropropiophenone (**1b**) even after a prolonged reflux period of 3 days. A slow exclusive rearrangement could be obtained by carrying out the reaction in the presence of excess triethylamine. A basic substance is apparently needed to generate a hemiacetal anion (conversion **18** ⇄ **19**), which then gives rise to intramolecular halide displacement with epoxide formation and the following reactions. With a lower concentration of base, the solvolysis of hemiacetal **22** becomes more important than the epoxide pathway since its kinetics are independent of base concentration.

**Influence of the Aromatic Substituent (Entries 19–23).** To a minor extent, the influence of the aromatic substituents on the distribution between the two isomeric α,α-dialkoxy ketones **2** and **3** was investigated. α,α-Dichloropropiophenones **1** (R = Me, X = Y = Cl; see structure in Scheme VII) were treated with a 10% excess of 2 equiv of sodium methoxide in methanol at room temperature for 1 h (Table I). All reactions proceeded rapidly, except for 2,2,3′-trichloro-4′-methoxy-5′-nitropropiophenone (**1j**; R = Me, X = Y = $R_2$ = Cl, $R_1$ = OMe, and $R_3$ = $NO_2$ in structure **1** of Scheme VII) which required an overnight period, as after 30 min only half of the conversion to the reaction products had occurred. There was a tendency for increased formation of rearranged carbonyl derivatives **3** when substituents with increasing electron-withdrawing properties were introduced. This phenomenon cannot be clearly interpreted in terms of the reaction pathway given in Scheme VII and demands additional research.

**Influence of the Temperature (Entries 24–28).** The results in Table I show that the temperature plays a determinative role in the distribution of the final products. The influence was studied on α,α-dichloropropiophenone (**1b**) with 2.2 equiv of sodium methoxide in methanol. At −30 °C no reaction occurred. The 4:1 ratio of **2b** to **3b** obtained at 0 °C was drastically changed into a 1:1 ratio when the substrate was dropped into a refluxing solution of sodium methoxide in methanol. It is clear that the rate of the reaction is very fast at temperatures above room temperature, but the distribution of products is determined by the temperature influence on the chemical behavior of α-chloro-α-methoxy-α-phenyl ketone **21** (R = R′ = Me, X = Cl, $R_1$ = $R_2$ = $R_3$ = H). At higher temperature, the competition between solvolysis of the latter α-chloro ether and nucleophilic attack at the carbonyl function and subsequent epoxide formation will be shifted to the solvolysis pathway because of the predictable, more important

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(42) C. L. Stevens, J. J. Beereboom, and K. G. Rutherford, *J. Am. Chem. Soc.*, 77, 4590 (1955).

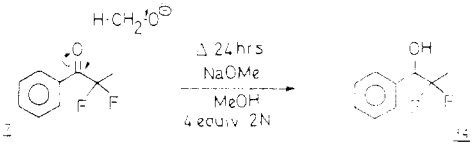
influence on the carbon–halogen bond breaking of the α-chloro ether. This results in a larger proportion of rearranged α,α-dimethoxy ketone **3** at the expense of the formal substitution product **2**.

**Influence of the Halogen (Entries 29–35).** These α,α-dihalopropiophenones were treated with 2.2 equiv of sodium methoxide (2 N solution in methanol). The α,α-dichloro derivative **1b** yielded a 3:1 ratio of α,α-dimethoxypropiophenone (**2b**) over 1,1-dimethoxy-1-phenylacetone (**3b**), while replacing one chlorine atom for a bromine atom resulted in a 2:1 ratio. With two α-bromo atoms the ratio dramatically changed in favor of 1,1-dimethoxy-1-phenylacetone (**3b**, 74%) while only minor amounts of α,α-dimethoxypropiophenone (**2b**, 18%) and methyl benzoate were isolated. The striking difference can be ascribed to the ease with which α-bromo ethers, such as **21** (R = R′ = Me, X = Br, $R_1$ = $R_2$ = $R_3$ = H), solvolyze. The α-bromo-α-chloro derivative **9** was converted mainly into the intermediate α-chloro ether **21** (R = R′ = Me, X = Cl, $R_1$ = $R_2$ = $R_3$ = H) and, therefore, its results were not very different from the α,α-dichloro analogue **1b**. The rearrangement of α,α-dibromopropiophenone (**6**, R = Me) is completely determined by the solvolytic behavior of α-bromo ether **21** (R = R′ = Me, X = Br, $R_1$ = $R_2$ = $R_3$ = H), which to a minor extent led to the carbonyl addition pathway. This result supports our proposal that the formal substitution products **2** are not a result of a direct displacement reaction.

α-Fluoro-α-halo ketones **10** and **12** showed remarkable mechanistic behavior toward methoxide in methanol in that they exclusively rearranged into 1,1-dimethoxy-1-phenylacetone (**3b**). No trace of any other compound was detected in this reaction. As fluoride anion is not readily displaced in substitution reactions, α-fluoro-α-halo ketones can be expected to result exclusively in the formation of α-fluoro-α′-methoxy epoxide **20** (R = R′ = Me, X = F, $R_1$ = $R_2$ = $R_3$ = H; see Scheme VII) which rearranges spontaneously into 1-fluoro-1-methoxy-1-phenylacetone (**21**; R = R′ = Me, X = F, $R_1$ = $R_2$ = $R_3$ = H). As the epoxide route by nucleophilic carbonyl attack of methoxide and then intramolecular nucleophilic fluoride expulsion is not a favorable route, the substitution reaction yielding 1,1-dimethoxy-1-phenylacetone (**3b**) remains the only plausible reaction.

Not much work has been undertaken in the literature in the field of the chemistry of α-fluoro epoxides. Only polyfluoro derivatives received some attention, and it was found that they readily undergo migration of the fluoride anion to afford an α-fluorinated carbonyl derivative.[28] In the early 1970's much progress was gained in this field by French research groups, who isolated and characterized more general members of the class of α-fluoro epoxides.[43-46] According to these results the activated α-fluoro-α′-methoxy epoxide **20** (R = R′ = Me, X = F, $R_1$ = $R_2$ = $R_3$ = H) rearranged into the corresponding α-fluoro-α-methoxy ketone **21** (R = R′ = Me, X = F, $R_1$ = $R_2$ = $R_3$ = H). This supposition was substantiated by an independent route leading to the rearrangement discussed here. As depicted from Scheme IX, α-fluoropropiophenone (**11**) was converted into the acetal **32** with a large excess of trimethyl orthoformate and hydrogen chloride in methanol. Distillation of α-fluoro acetal **32** over potassium hydrogen sulfate produced β-fluoro enol ether **33**. The latter was epoxidized with *m*-chloroperbenzoic acid in carbon tetrachloride at 0 °C to the highly reactive α-fluoro-α′-methoxy epoxide **20b** (X = F), which spontaneously rearranged by fluoro anion migration to α-fluoro ether **21b** (X = F).

Scheme XIV




The last rearrangement step is part of the entire mechanism of the conversion of α-fluoro-α-halo ketones **10** and **12** to keto acetal **3b**. Additionally, it was unambiguously proven that α-fluoro ether **21b** (X = F) was quantitatively transformed into keto acetal **3b** by treatment with sodium methoxide in methanol. On the other hand, α,α-difluoropropiophenone (**7**) did not react with 2 N sodium methoxide in methanol at room temperature. A reflux period of 4 h with the same reagent resulted in 66% conversion into 2,2-difluoro-1-phenyl-1-propanol (**34**) while the rest was unaltered material (Scheme XIV). The reaction could be completed by using an excess of a solution of 4 equiv of 2 N sodium methoxide in methanol under reflux for 24 h (92% isolated yield). This rather unusual reaction arises from the absence of any other plausible reaction, thus allowing less general reactions to occur. Methoxide is able to act as a reducing agent by delivering a hydride-like species and concomitantly producing formaldehyde (cf. Meerwein–Ponndorf–Verley reaction).

Finally, some efforts have been undertaken to rationalize the influence of the nature of the medium and the nucleophile on the reaction discussed in this paper. α,α-Dichloropropiophenone (**1b**) reacted exothermically with dry sodium methoxide in diethyl ether or dimethyl sulfoxide to afford dark reaction mixtures, in which only benzoic acid could be identified (haloform-type reaction). A similar observation was made for sodium hydroxide in water (reflux) or in aqueous dioxane (1:1, room temperature). When 5 equiv of sodium hydroxide in methanol (2 N solution; 10 min/50 °C) were reacted with **1b**, a 50:50 mixture of **3b** and **4b** was obtained. Also, less polar solvents were used, and it was found that α,α-dichloropropiophenone (**1b**) was converted cleanly into benzoic acid (more than 90% yield) when refluxed with powdered sodium hydroxide in xylene. The latter results contrast dramatically with the hydroxide-induced rearrangements of α,α-dichloroacetophenones[8,47] and α,α-dibromoacetophenones,[48] which were reported to yield α-hydroxyphenylacetic acid derivatives. From the data presented in Table I, it can be concluded that the reaction of α,α-dihaloalkyl aryl ketones with sodium alkoxides in the corresponding alcohol is greatly influenced by several factors. As mentioned before, α,α-dihalo aldehydes were reported to rearrange via a mechanism analogous to the one discussed here.[27] We are currently studying in more detail the reactivity of α,α-dihalo aldehydes since the results as reported up to now[27] lack details.

## Experimental Section

IR spectra were recorded with a Perkin-Elmer Model 257 spectrophotometer. NMR spectra were measured with a Varian T-60 apparatus, while mass spectra were obtained from a GC/MS

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coupling of a Pye-Unicam gas chromatograph (Model 104; 1.5% SE-30, 1.5-m column, He carrier gas) with an AEI MS-20 mass spectrometer. VPC analyses were performed with a Varian Model 920 gas chromatograph (5% SE-30, 3-m column, $H_2$ carrier gas). $\alpha,\alpha$-Dichloroalkyl aryl ketones 1, 6, 7, 9, 10, and 12 were obtained as described in the section dealing with the synthesis of the title compounds. Some unreported experimental procedures are given below.

**Synthesis of 2,2,3′-Trichloro-4′-methoxy-5′-nitropropiophenone (1j).** A mixture of 1.34 g (0.005 mol) of 2,2,3′-trichloro-4′-methoxypropiophenone (**1i**) and 4 mL of fuming nitric acid was kept at room temperature for 1 h. The homogeneous solution was then poured into 100 mL of water, extracted with carbon tetrachloride, washed three times with water, dried ($MgSO_4$), and evaporated to leave a clear light yellow oil (1.3 g, 84%), which was found to contain only one product by GC: NMR ($CCl_4$) $\delta$ 2.34 (3 H, s, $CH_3$), 4.13 (3 H, s, $OCH_3$), 8.41 (1 H, d, AB, $J$ = 1 Hz, 2′-CH=), 8.52 (1 H, d, AB, $J$ = 1 Hz, 6′-CH=); IR (NaCl) 1702 $cm^{-1}$ ($\nu_{C=O}$).

**Synthesis of 2-Fluoropropiophenone (11).** A solution of 13.4 g (0.1 mol) of propiophenone **25** in 300 mL of carbon tetrachloride was treated dropwise with 16.0 g (0.1 mol) of bromine at such a rate as to obtain a continuous discoloration. After the addition was complete (about 10 min), the mixture was evaporated in vacuo to yield a quantitative yield of 2-bromopropiophenone (**8**) [in some batches we observed 1–2% 2,2-dibromopropiophenone (**6**)], which was used as such in further experiments. Compound **8** thus obtained (21.3 g, 0.1 mol) was dissolved in 100 mL of dimethylformamide and treated with 29.0 g (0.5 mol) of dry potassium fluoride (freshly heated by a Bunsen burner flame in a porcelain vessel). The mixture was vigorously stirred and heated at 110 °C for 3 h, after which it was poured into excess 2 N aqueous hydrogen chloride. Extraction twice with carbon tetrachloride, washing once with 2 N HCl and twice with water, drying ($MgSO_4$), and evaporation in vacuo yielded crude 2-fluoropropiophenone. Distillation in vacuo afforded 9.2 g (60%) of pure **11**, bp 107–115 °C (15 mmHg) [lit.[49] bp 95–96 °C (12 mmHg)]. Several runs always yielded a large amount of unidentified residual tar. When potassium fluoride was not flame dried, distilled product **11** contained some 1-phenyl-1,2-propanedione.

**Synthesis of 2-Bromo-2-chloropropiophenone (9).** Chlorine gas was bubbled through a mixture of 21.3 g (0.1 mol) of 2-bromopropiophenone (**8**) and 36.5 g (0.5 mol) of dimethylformamide at 90–95 °C during 30 min. The reaction mixture was worked up by pouring it into excess 2 N aqueous hydrogen chloride and extracting the mixture with carbon tetrachloride. The organic phase was washed with 2 N HCl and water, dried ($MgSO_4$), and evaporated in vacuo to give a clear oil which consisted of 58% 2-bromo-2-chloropropiophenone (**9**) and 42% 2,2-dichloropropiophenone (**1b**). Careful distillation over a 50-cm Vigreux column yielded 9 g (37%) of pure compound **9**: bp 124–126 °C (12 mmHg); NMR ($CCl_4$) $\delta$ 2.51 (3 H, s, $CH_3$), 7.2–7.5 (3 H, m, meta and para protons), 8.1–8.4 (2 H, m, ortho protons); IR (NaCl) 1685 $cm^{-1}$ ($\nu_{C=O}$).

**Synthesis of 2-Chloro-2-fluoropropiophenone (10).** 2-Chloro-2-fluoropropiophenone (**10**) was prepared from 2-fluoropropiophenone (**11**) and chlorine in DMF (30 min/100 °C) as described in the forgoing experiment: yield 82%; bp 31–33 °C (0.015 mmHg); NMR ($CCl_4$) $\delta$ 2.16 (3 H, d, $J_{HF}$ = 20 Hz, $CH_3$), 7.3–7.6 (3 H, m, meta and para protons), 8–8.3 (2 H, m, ortho protons); IR (NaCl) 1700 $cm^{-1}$ ($\nu_{C=O}$); mass spectrum, $m/e$ (relative intensity) 186/188 ($M^+$, 1), 151 (4), 105 (100), 77 (68), 74 (4), 73 (6), 51 (24), 50 (8).

**Synthesis of 2-Bromo-2-fluoropropiophenone (12).** A solution of 3.04 g (0.02 mol) of 2-fluoropropiophenone (**11**) in 15 mL of carbon tetrachloride was treated with 4.27 g (0.024 mol) of *N*-bromosuccinimide and a trace amount of benzoyl peroxide and was refluxed under irradiation with a 300-W Philips ultraviolet lamp during 1 h. The reaction mixture was then cooled and filtered, and the filtrate was evaporated in vacuo to afford an oil. Distillation in vacuo gave 4.0 g (87%) of pure **12** as a pale yellow oil: NMR ($CCl_4$) $\delta$ 2.34 (3 H, d, $J_{HF}$ = 21 Hz, $CH_3$), 7.2–7.6 (3 H, m, meta and para protons), 8–8.4 (2 H, m, ortho protons); IR (NaCl) 1694 $cm^{-1}$ ($\nu_{C=O}$); mass spectrum, $m/e$ (relative intensity) 230/232 ($M^+$, 1), 151 (1), 123 (3), 105 (100), 77 (46), 74 (3), 73 (5), 51 (23), 50 (9).

**General Procedure for the Reaction of 2,2-Dihaloalkyl Aryl Ketones with Sodium Alkoxides in the Corresponding Alcohol.** The reaction of 2,2-dichloropropiophenone (**1b**) with sodium methoxide in methanol is representative of all other analogous experiments. To a magnetically stirred solution of sodium methoxide in methanol (33 mL, 2 N solution, 0.066 mol), equilibrated at a given temperature (see Table I) by means of a water bath, was added slowly and dropwise 6.18 g (0.03 mol) of 2,2-dichloropropiophenone (**1b**). Sodium chloride precipitated immediately, and the reaction mixture was further stirred for the time indicated in Table I (usually 1–2 h), after which methanol was evaporated in vacuo. The residual white slurry was taken up in water and carbon tetrachloride. The organic phase was isolated and the aqueous layer twice extracted with carbon tetrachloride. The combined extracts were dried ($MgSO_4$) and evaporated to leave a pale yellow oil. Distillation in vacuo afforded 5.5 g (94%) of a mixture of 2,2-dimethoxypropiophenone (**2b**) and 1,1-dimethoxy-1-phenylacetone (**3b**), bp 127–130 °C (12 mmHg) (the distribution of these compounds, obtained under various reaction conditions, is given in Table I). Compound **2b**: NMR ($CCl_4$) $\delta$ 1.50 (3 H, s, $CH_3$), 3.28 (6 H, s, $(OCH_3)_2$), 7.1–7.5 (3 H, m, meta/para $C_6H_5$ protons), 7.9–8.2 (2 H, m, ortho $C_6H_5$ protons); IR (NaCl) 1677 $cm^{-1}$ ($\nu_{C=O}$); mass spectrum, $m/e$ (relative intensity) no $M^+$, 163 (6), 151 (1), 135 (1), 105 (9), 89 (100), 77 (12), 57 (2), 51 (6), 43 (45). Compound **3b**: NMR ($CCl_4$) $\delta$ 2.06 (3 H, s, $CH_3CO$), 3.24 (6 H, s, $(OCH_3)_2$), 7.2–7.6 (5 H, m, $C_6H_5$); IR (NaCl) 1737 $cm^{-1}$ ($\nu_{C=O}$); mass spectrum, $m/e$ (relative intensity) no $M^+$, 163 (8), 151 (100), 105 (51), 91 (18), 77 (33), 59 (15), 51 (12), 43 (12). Analogous experiments with various starting materials, varying concentrations of the alkoxide, various alkoxides in alcoholic medium, and different temperatures were executed in a manner similar to that described (for detailed reaction conditions, see Table I). The respective spectral data are included in Tables II and III of the supplementary material.

**Synthesis of 2-Chloro-1,1-dimethoxy-1-phenylpropane (27).** To a mixture of 4.21 g (0.025 mol) of 2-chloropropiophenone (**26**),[50,51] 8 g (0.25 mol) of dry methanol, and 13.25 g (0.125 mol) of trimethyl orthoformate was added slowly drop by drop 15 g (0.125 mol) of thionyl chloride. (**Caution**: the production of hydrogen chloride in methanol by the addition of thionyl chloride to methanol is a highly exothermic reaction. It is recommended to work behind a safety shield.) The reaction mixture was heated under reflux for 30 min after which 4 g (0.125 mol) of dry methanol and 7.5 g (0.0625 mol) of thionyl chloride were added. After another reflux period of 20 min, 4 g (0.125 mol) of dry methanol and 7.5 g (0.0625 mol) of thionyl chloride were added, and the mixture was finally refluxed for 30 min. Evaporation in vacuo, trituration with 2 N aqueous sodium hydroxide, and extraction with carbon tetrachloride afforded, after drying ($K_2CO_3$), 3.2 g (60%) of **27** as a colorless oil: bp 63–67 °C (0.3 mmHg) (the product solidified on standing, mp <50 °C); NMR ($CCl_4$) $\delta$ 1.31 (3 H, d, $J$ = 6.5 Hz, $CH_3$), 4.32 (1 H, q, $J$ = 6.5 Hz, CHCl), 3.20 and 3.40 (6 H, 2 s, 3 H each, $(OMe)_2$), 7.2–7.6 (5 H, m, $C_6H_5$); IR (NaCl) 2830 $cm^{-1}$ ($\nu_{OCH_3}$); mass spectrum, $m/e$ (relative intensity) no $M^+$, 183/185 (10), 151 (100), 119 (1), 117 (2), 115 (3), 105 (26), 91 (10), 77 (25), 65 (2), 63 (3), 59 (11), 55 (2), 51 (8), 50 (2).

**Synthesis of 2-Chloro-1-methoxy-1-phenylpropene (28).** A mixture of 3.0 g (0.014 mol) of $\alpha$-chloro acetal **27** and 0.6 g of potassium hydrogen sulfate (1/5 w/w) was heated under vacuum (12 mmHg) in a distillation apparatus in an oil bath at 110 °C during 1 h. Further raising of the temperature resulted in distillation to yield 2.1 g (82%) of colorless 2-chloro-1-methoxy-1-phenylpropene (**28**), which was collected in a flask containing a little dry potassium carbonate; bp 121–127 °C (12 mmHg). The product consisted of a 1:1 mixture of *E* and *Z* isomers as revealed by NMR and VPC: NMR ($CCl_4$) $\delta$ 2.06 and 2.24 (3 H, 2 s, $CH_3$ of *Z* and *E* isomer, respectively), 3.37 and 3.40 (3 H, 2 s, $OCH_3$), 7.38 (5 H, m, $C_6H_5$); IR (NaCl) 2828 ($\nu_{OCH_3}$), 1650 $cm^{-1}$ (vw, $\nu_{C=C}$).

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Both *E* and *Z* isomers gave identical mass spectral fragmentations; the mass spectral data of the most volatile isomer (SE-30, VPC) is as follows: *m/e* (relative intensity) 182/184 ($M^+$, 90), 117 (67), 115 (48), 105 (39), 103 (41), 91 (34), 89 (25), 77 (100), 51 (55).

**Epoxidation of β-Chloro Enol Ether 28 with *m*-Chloroperbenzoic Acid.** To an ice-cooled stirred solution of 182 mg (0.001 mol) of **28** in 3 mL of dichloromethane, to which 276 mg (0.002 mol) of dry potassium carbonate was added, was added portionwise 213 mg of *m*-chloroperbenzoic acid (85% purity, 5% excess). After being stirred for 30 min, the mixture was filtered and carefully washed with dichloromethane, and the filtrate was evaporated at low temperature under vacuum. The remaining product was 1.6 g (80%) of pure 1-chloro-1-methoxy-1-phenylacetone (**21b**; X = Cl). A similar experiment was run in carbon tetrachloride during 5 min, and direct sampling indicated complete formation of **21b** (NMR analysis).

**Reaction of 1-Chloro-1-methoxy-1-phenylacetone (21b; X = Cl) with Methanol.** A 198-mg (0.001 mol) sample of **21b** was shaken with methanol for 2 min, after which evaporation under vacuum yielded quantitatively 1,1-dimethoxy-1-phenylacetone (**3b**).

**Rearrangement of 2,2-Dichloropropiophenone (1b) with Methanol in the Presence of Triethylamine.** A solution of 10.15 g (0.05 mol) of 2,2-dichloropropiophenone (**1b**) in 100 mL of dry methanol, containing 25 g of triethylamine (0.25 mol), was refluxed with stirring during 7 days. Sampling (by mixing 1 mL of the reaction mixture with 10 mL of water and 0.5 mL of $CCl_4$ and subsequent NMR analysis of the $CCl_4$ extract) indicated 89% conversion into 1,1-dimethoxy-1-phenylacetone (**3b**). The remaining starting material was further transformed into **3b** by the successive addition of 0.05 mol of triethylamine per day of reflux (repeated three times). The reaction mixture was then evaporated, and the residue was treated with water and extracted with carbon tetrachloride. After drying ($MgSO_4$) and evaporation in vacuo, the product was distilled to give 7.3 g (74%) of **3b**, bp 127–130 °C (12 mmHg).

**Synthesis of 1-Chloro-1-methoxy-1-phenylacetone (21b, X = Cl).** A mixture of 1.94 g (0.01 mol) of 1,1-dimethoxy-1-phenylacetone (**3b**) and 2.08 g (0.01 mol) of phosphorus pentachloride was left at room temperature until the vigorous reaction ceased. After being heated 5 min in an oil bath at 100 °C, the homogeneous yellow liquid was distilled in vacuo to afford 1.45 g (72%) of pure **21b** (X = Cl) as a colorless liquid; bp 80–81 °C (0.8 mmHg). The product is extremely sensitive to moisture and should be handled under an inert atmosphere: NMR ($CCl_4$) δ 2.23 (3 H, s, $CH_3$), 3.45 (3 H, s, $OCH_3$), 7.2–7.6 (5 H, m, $C_6H_5$); IR (NaCl) 2840 ($\nu_{OCH_3}$), 1737 $cm^{-1}$ ($\nu_{C=O}$); mass spectrum, *m/e* (relative intensity) no $M^+$, 163 (22), 145/147 (90), 105 (100), 91 (7), 89 (5), 77 (75), 51 (27), 50 (10), 43 (25).

**Reaction of 2b and 3b with Sodium Borohydride in Ethanol and Subsequent Methylation.** To a solution of 9.7 g (0.05 mol) of a mixture of 2,2-dimethoxypropiophenone (**2b**) and 1,1-dimethoxy-1-phenylacetone (**3b**), obtained from one of the various reactions of 2,2-dichloropropiophenone (**1b**) with sodium methoxide in methanol (Table I), in 100 mL of absolute ethanol was added 0.95 g (0.025 mol) of sodium borohydride. The mixture was stirred for 30 min and evaporated, water was added, and the mixture was extracted with dichloromethane. Drying ($MgSO_4$) and evaporation gave 9.6 g (96%) of a colorless mixture of 2,2-dimethoxy-1-phenyl-1-propanol and 1,1-dimethoxy-1-phenyl-2-propanol. The former gave the following spectral data: NMR ($CCl_4$) δ 0.94 (3 H, s, $CH_3$), 2.7 (1 H, br s, OH), 3.20 and 3.26 (2 s, 3 H each, 2 $OCH_3$), 4.69 (1 H, s, broadened, CHO), 7–7.6 (5 H, m, $C_6H_5$); IR (NaCl) 3600–3100 ($\nu_{OH}$), 2835 $cm^{-1}$ ($\nu_{OCH_3}$). The latter gave the following spectral data: NMR ($CCl_4$) δ 0.88 (3 H, d, *J* = 6 Hz, $CH_3$), 2.15 (1 H, br s, OH), 4.00 (1 H, q, *J* = 6 Hz, CHO), 3.16 and 3.38 (2 s, 3 H each, $OCH_3$), 7.1–7.5 (5 H, m, $C_6H_5$); IR (NaCl) 3600–3100 ($\nu_{OH}$), 2835 $cm^{-1}$ ($\nu_{OCH_3}$). VPC analysis of the mixture of alcohols afforded a mixture of 2-methoxypropiophenone[23,52] and 1-methoxy-1-phenylacetone.[52] Distillation of the alcohols resulted in decomposition. The mixture of alcohols, obtained as described above, was added to a mixture of 1.32 g of sodium hydride (55–60% mineral oil suspension, which was washed two times with pentane) in 100 mL of dimethyl sulfoxide. To this mixture was added 14.2 g (0.1 mol) of methyl iodide at once. The reaction mixture was left at ambient temperature for an overnight period and subsequently poured into 1 L of water. Extraction with pentane, drying ($MgSO_4$–$K_2CO_3$, 1:1), and evaporation gave 9.9 g (95%) of a colorless mixture of 1-phenyl-1,2,2-trimethoxypropane and 1-phenyl-1,1,2-trimethoxypropane. The former gave the following spectral data: NMR ($CCl_4$) δ 1.03 (3 H, s, $CH_3$), 3.25 and 3.27 (2 s, 3 H each, 2 $OCH_3$), 3.13 (3 H, s, Ph–C–$OCH_3$), 4.22 (1 H, s, CHO), 7–7.5 (5 H, m, $C_6H_5$); mass spectrum, *m/e* (relative intensity) no $M^+$, 178 (16), 148 (9), 147 (17), 121 (100), 105 (15), 77 (21). The latter gave the following spectral data: NMR ($CCl_4$) δ 0.89 (3 H, d, *J* = 6.5 Hz, $CH_3$), CHO covered by methoxy signals, 3.18, 3.25, and 3.43 (three methoxy signals), 7–7.5 (5 H, m, $C_6H_5$); mass spectrum, *m/e* (relative intensity) no $M^+$, 179 (9), 151 (100), 121 (13), 105 (22), 91 (7), 89 (28), 77 (12), 59 (8), 43 (13). Heating of the mixture of trimethoxy derivatives with a trace amount of *p*-toluenesulfonic acid in benzene under reflux for 30 min resulted mainly in 1-methoxy-1-phenylacetone. Similar observations were noted when these trimethoxy derivatives were heated neat with potassium hydrogen sulfate.

**Synthesis of 2-Fluoro-1,1-dimethoxy-1-phenylpropane (32).** A mixture of 4.56 g (0.03 mol) of 2-fluoropropiophenone (**11**), 15.9 g (0.15 mol) of trimethyl orthoformate, and 9.6 g (0.3 mol) of dry methanol was treated dropwise (**Caution!**) with 18 g (0.15 mol) of thionyl chloride. After the vigorous reaction ceased, the reaction mixture was evaporated in vacuo, and the residue was treated with 2 N aqueous sodium hydroxide followed by two extractions with carbon tetrachloride. After the extract was dried ($K_2CO_3$) and the solvent evaporated, the remaining oil was distilled to give 4.8 g (81%) of colorless **32**: bp 36–43 °C (0.03 mmHg); NMR ($CCl_4$) δ 1.06 (3 H, dd, $J_{HH}$ = 6 Hz, $J_{HF}$ = 24 Hz, $CH_3$); 4.83 (1 H, dq, $J_{HH}$ = 6 Hz, $J_{HF}$ = 48 Hz, CHF), 3.22 (3 H, s, $OCH_3$), 3.40 (3 H, d, $J_{HF}$ = 1 Hz, $OCH_3$), 7.2–7.6 (5 H, m, $C_6H_5$); IR (NaCl) 2832 $cm^{-1}$ ($\nu_{OCH_3}$); mass spectrum, *m/e* (relative intensity) no $M^+$, 167 (14), 151 (100), 105 (43), 91 (12), 77 (32), 59 (14), 51 (14), 50 (3), 47 (5).

**Synthesis of 2-Fluoro-1-methoxy-1-phenylpropene (33).** A mixture of 3.96 g (0.02 mol) of α-fluoro acetal **32** and 0.8 g of potassium hydrogen sulfate (1/5 w/w) was heated under vacuum (14 mmHg) in an oil bath at 130 °C for 2 h. Distillation afforded then 2.1 g (63%) of colorless **33**, bp 91–94 °C (12 mmHg). The product consisted of a 3:1 mixture of *E* and *Z* isomers: NMR ($CCl_4$) δ 1.98 and 2.13 (3 H, 2 d, *Z* and *E* isomers, respectively, $J_{HF}$ = 17 Hz, $CH_3$), 3.43 and 3.47 (3 H, 2 s, *E* and *Z* isomers, respectively, $OCH_3$), 7.1–7.5 (5 H, m, $C_6H_5$); IR (NaCl) 2830 $cm^{-1}$ ($\nu_{OCH_3}$); mass spectrum, *m/e* (relative intensity) 166 ($M^+$, 96), 165 (23), 135 (18), 123 (17), 105 (40), 103 (14), 91 (33), 77 (100), 73 (57), 51 (41).

**Epoxidation of β-Fluoro Enol Ether 33.** β-Fluoro enol ether **33** was epoxidized with *m*-chloroperbenzoic acid in the same manner as that described for β-chloro enol ether **28**. After 10 min at 0 °C, the reaction product was 1-fluoro-1-methoxy-1-phenylacetone (**21b**; X = F): NMR ($CCl_4$) δ 2.35 (3 H, s, $CH_3CO$), 3.33 (3 H, s, $OCH_3$), 7.2–7.6 (5 H, m, $C_6H_5$); IR (NaCl) 2835 ($\nu_{OCH_3}$), 1725 $cm^{-1}$ ($\nu_{C=O}$); mass spectrum, *m/e* (relative intensity) no $M^+$, 139 (100), 105 (68), 77 (50), 51 (20), 50 (8), 43 (22). Treatment of compound **21b** (X = F) with 1 N sodium methoxide in methanol at room temperature during 30 min gave complete conversion into 1,1-dimethoxy-1-phenylacetone (**3b**).

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**Registry No. 1a**, 2648-61-5; **1b**, 57169-51-4; **1c**, 66255-85-4; **1d**, 66255-86-5; **1e**, 71527-78-1; **1f**, 31315-51-2; **1g**, 57169-53-6; **1h**, 38868-79-0; **1i**, 73611-80-0; **1j**, 73611-81-1; **2** (R, $R_1$, $R_2$, $R_3$ = H; R′ = Me), 6956-56-5; **2** (R = Me; $R_1$, $R_2$, $R_3$ = H; R′ = Me), 38868-78-9; **2** (R = Et; $R_1$, $R_2$, $R_3$ = H; R′ = Me), 57205-27-3; **2** (R = *n*-Pr; $R_1$, $R_2$, $R_3$ = H; R′ = Me), 66255-87-6; **2** (R = Me; $R_1$, $R_2$, $R_3$ = H; R′ = Et), 73611-82-2; **2** (R = Me; $R_1$ = Cl; $R_2$, $R_3$ = H; R′ = Me), 32763-17-0; **2** (R = Me; $R_1$ = Br; $R_2$, $R_3$ = H; R′ = Me), 32763-18-1; **2** (R = Me; $R_1$ = OMe; $R_2$ = Cl; $R_3$ = H; R′ = Me), 73611-83-3; **2** (R = Me; $R_1$ = OMe; $R_2$ = Cl; $R_3$ = $NO_2$; R′ = Me), 73611-84-4; **3** (R, $R_1$, $R_2$, $R_3$ = H; R′ = Me), 19159-39-8; **3** (R = Me; $R_1$, $R_2$, $R_3$ = H; R′ = Me),

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57711-28-1; **3** (R = Et; $R_1$, $R_2$, $R_3$ = H; R′ = Me), 66255-88-7; **3** (R = *n*-Pr; $R_1$, $R_2$, $R_3$ = H; R′ = Me), 66255-89-8; **3** (R = *t*-Bu; $R_1$, $R_2$, $R_3$ = H; R′ = Me), 73611-85-5; **3** (R = Me; $R_1$, $R_2$, $R_3$ = H; R′ = Et), 73611-86-6; **3** (R = Me; $R_1$, $R_2$, $R_3$ = H; R′ = *i*-Pr), 73611-87-7; **3** (R = Me; $R_1$ = Cl; $R_2$, $R_3$ = H; R′ = Me), 64743-30-2; **3** (R = Me; $R_1$ = Br; $R_2$, $R_3$ = H; R′ = Me), 64743-31-3; **3** (R = Me; $R_1$ = OMe; $R_2$ = Cl; $R_3$ = H; R′ = Me), 73611-88-8; **3** (R = Me; $R_1$ = OMe; $R_2$ = Cl; $R_3$ = $NO_2$; R′ = Me), 73611-89-9; **6**, 2114-03-6; **7**, 703-17-3; **8**, 2114-00-3; **9**, 63017-05-0; **10**, 63017-20-9; **11**, 21120-36-5; **12**, 63017-06-1; **21b** (X = Cl), 73611-90-2; **25**, 93-55-0; **26**, 6084-17-9; **27**, 73611-91-3; (*E*)-**28**, 73611-92-4; (*Z*)-**28**, 73611-93-5; **32**, 73611-94-6; (*E*)-**33**, 73611-95-7; (*Z*)-**33**, 73611-96-8; **34**, 73611-97-9; sodium methoxide, 124-41-4; trimethyl orthoformate, 628-90-0; 2,2-dimethoxy-1-phenyl-1-propanol, 73611-98-0; 1,1-dimethoxy-1-phenyl-2-propanol, 73611-99-1; 1-phenyl-1,2,2-trimethoxypropane, 73612-00-7; 1-phenyl-1,1,2-trimethoxypropane, 73612-01-8; methyl benzoate, 93-58-3; 1-phenyl-1,2-propanedione, 579-07-7.

**Supplementary Material Available:** Yield and boiling point data for 1-aryl-2,2-dialkoxy-1-alkanones **2** and 1-aryl-1,1-dialkoxy-2-alkanones **3** (Table II) and spectrometric data for 1-aryl-2,2-dialkoxy-1-alkanones **2** and 1-aryl-1,1-dialkoxy-2-alkanones **3** (Table III) (5 pages). Ordering information is given on any current masthead page.

# Rearrangements of Tricyclo[3.2.1.$0^{3,6}$]octyl Systems

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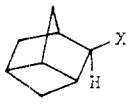
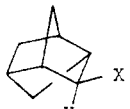
New 2,2-substituted derivatives of tricyclo[3.2.1.$0^{3,6}$]octane with the following sets of substituents were synthesized in a study designed to test their stability toward Wagner–Meerwein rearrangements: $CH_3$, OH; $CH_3$, Cl; $C_6H_5$, OH; Cl, Cl; Br, $CO_2H$. Epimerizations, but not skeletal rearrangements, were observed in some cases. The phenyl carbinol underwent self-reduction under vigorous conditions.

The first synthesis and some chemical studies of 2-substituted derivatives of the tricyclo[3.2.1.$0^{3,6}$]octyl system **1** were reported in 1963[1] at which time it was observed that



**1**



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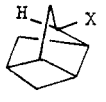

**3**

acetolysis of either the *exo*- or *endo*-2-tosylate resulted in clean formation of the *exo*-2-acetate. Similarly, no skeletal rearrangements were observed during deamination of the amine or during the transformation of the alcohol to the corresponding bromide with HBr–$ZnBr_2$.[2] We rationalized this behavior on the grounds that Wagner–Meerwein rearrangements[3] to systems **2** or **3** might be accompanied by an increase in ring strain. The facile rearrangement of derivatives of **2** to tricyclo[3.2.1.$0^{3,6}$]octanes[4,5] further supported our contention.

More recently, Freeman and co-workers[6] reported the results of two experiments which were believed to involve cationic rearrangements of **1** to system **3**: reaction of **1**-OH with thionyl chloride to give **3**-Cl and reductive solvolysis of **1**-OTs with lithium aluminum hydride to give **3**-H. In the former example, no direct evidence was given for the presence of **3**-Cl, but its presence was inferred since **3**-H was found among the hydrocarbon products after reduction with sodium in decane. Similarly, the reaction with lithium aluminum hydride produced a mixture of hydrocarbons which contained 27% **3**-H.

**Table I. Strain Energies of Hydrocarbons and Cations (kcal/mol)**

| compd | hydrocarbon (X = H) EAS[7] | SH[8] | GD[9] | 2-cation (X = +), SH[8] |
|---|---|---|---|---|
| 1 | 41.96 | 38.44 | 41.26 | 48.10 |
| 2 | 47.15 | 42.38 | 25.14[a] | 54.68 |
| 3 | 48.29 | | 47.46 | 51.71 |

[a] An "improved" estimate of this value was given as 35.72 kcal/mol by the authors, and it was stated that further extensions are in progress.[9]

From a theoretical point of view the calculation of strain energies in polycyclic molecules has been a continuing challenge, and several groups have utilized empirical methods to estimate heats of formation, geometries, and strain energies. The molecular mechanics studies of Schleyer[7] are particularly comprehensive in this context, and strain energies calculated for **1**, **2**, and **3** are given in Table I. Also included are the strain energies calculated by Smith and Harris[8] for the 2-cations and the results of a different method used by Gasteiger and Dammer.[9]

These calculations support the contention that skeletal rearrangements of **1** are both kinetically and thermodynamically unfavorable with respect to transformations to systems **2** and **3** owing to increases in strain energies of ca. 4–6 kcal/mol.

At this time we wish to report the results of extensive studies which were designed to probe the stability of derivatives of **1** toward cationic rearrangements and to com-

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