ing the procedure in part G of the standard Favorskii reaction conditions. After chromatography 0.20 g of product was shown by vpc peak enhancement, ir, and nmr to be identical with methyl 2-methyl-3-(*m*-nitrophenyl)propionate except tha tthe nmr spectrum showed the integral of the multiplet from δ 2.5 to 3.2 to be 1.6 instead of 3.0 protons. Isotopic analysis showed 1.38 ± 0.04 atoms of deuterium incorporated (two analyses).

Reaction of 1-Chloro-1,3-diphenylpropan-2-one (5) in 0.05 *M* Sodium Methoxide in Methanol. The reaction of 1.00 g (4.09 mmol) of **5** in 164 ml (8.18 mmol) of 0.05 *M* sodium methoxide was carried out as previously described in part A of the standard Favorskii reaction conditions. A 0.95-g of sample of crude products was chromatographed on a 2 × 30 cm column of silica gel using 3% ether in hexane as eluent. Fractions (250 ml) 4–8 yielded 0.25 g (26%) of methyl 2,3-diphenylpropionate (**6**): λ_{max}^{film} 5.77 μ (C=O) 8.59 (C—O), 13.30 and 14.30 (Ph); $\delta_{TMS}^{CCl_4}$ 3.08 (d, 2, CH_2, J = 6.5 Hz), 3.43 (3, OCH_3), 3.76 (t, 1, CH, J = 7.0 Hz), 7.17 (m, 5, Ph), 7.27 (m, 5, OPh); $n^{25}D$ 1.5508.

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.84; H, 6.77.

Fractions 10–15 gave 0.35 g (36%) of 1-methoxy-1,3-diphenylpropan-2-one (**7**): λ_{max}^{film} 5.80 μ (C=O), 9.12 (C—O), 13.15 and 14.30 (Ph); $\delta_{TMS}^{CDCl_3}$ 3.21 (3, OCH_3), 3.68 (2, CH_2), 4.63 (1, CH), 7.12 (m, 5, Ph); 7.30 (m, 5, OPh); $n^{25}D$ 1.5509.

After fraction 17 the ether content was gradually increased to 50%. Fractions 25–32 yielded 0.35 g of a solid (mp 125–132°) which was not identified.[29]

Reaction of 1-Chloro-1,3-diphenylpropan-2-one (5) with 2.0 *M* Sodium Methoxide in Methanol. The reaction of 1.00 g (4.09 mmol) of **5** with 25 ml of 2.0 *M* sodium methoxide solution was carried out as described in part C of the Favorskii reaction procedure. After work-up the 1.00 g of crude product was chromatographed on a 1 × 30 cm silica gel column eluted with 3% ether in hexane. The first seven 250-ml fractions contained 3% ether in hexane and thereafter the ether content was increased to 20%. Fractions 5–7 contained 0.38 g (39%) of oil identified by nmr, ir, and vpc peak enhancement as methyl ester **6**. Fractions 12–16 yielded 0.60 g of solid which could not be identified. No methoxy ketone **7** was present.

Reaction of 1-Chloro-1,3-diphenylpropan-2-one (5) with 0.05 *M* Sodium Methoxide, Inverse Addition Procedure. A 0.05 *M* solution of sodium methoxide in methanol (100 ml, 4.2 mmol) was added dropwise over a period of 8 hr to 1.00 g (4.09 mmol) of **5** in 100 ml of methanol following the directions in part D of the Favorskii reaction procedure. After work-up the 0.98 g of product was identified by ir, nmr, and vpc peak enhancement as the methoxy ketone **7**. The yield was quantitative.

Acknowledgment. This work was supported by the National Science Foundation (GP 7065).

(29) The product probably rearranges during chromatography. The nmr of the recrystallized solid contained several peaks not present in the nmr of the crude reaction products prior to chromatography.

Favorskii Rearrangements. V. Mechanisms for α-Alkoxy Ketone Formation[1]

F. G. Bordwell and M. W. Carlson

Contribution from the Department of Chemistry, Northwestern University, Evanston, Illinois 60201. *Received November 6, 1969*

Abstract: Reaction of $PhCHClCOCH_2CH_3$ (**7**) with 0.05 *M* NaOMe–MeOH gave the same products and nearly the same distribution of products, $PhCH_2CH(CH_3)CO_2Me$ (**10**, 70%) and $PhCH_2COCH(OMe)CH_3$ (**11**, 30%), as was obtained earlier[3] from its isomer, $PhCH_2COCHClCH_3$ (**8**). The following parallelisms were noted for acid-catalyzed and base-catalyzed solvolyses of **7**, **8**, and $PhCH_2COCHClPh$ (**9**): (a) **7** formed the same (rearranged) methoxy ketone (**11**) in either acid-catalyzed or base-catalyzed methanolysis, (b) **8** formed **11** in either acid-catalyzed or base-catalyzed solvolyses in 50% (v/v) H_2O–MeOH to the exclusion of the corresponding hydroxy compound (**12**), despite the presence of 70 mole % water, (c) **8** formed a nearly constant ratio of **11** (*ca.* 75%) and **12** (*ca.* 25%) for acid-catalyzed and a variety of base-catalyzed solvolyses in 75% (v/v) H_2O–MeOH (Table I), (d) **9** gave methoxy ketone [$PhCH_2COCH(OMe)Ph$] to the exclusion of the corresponding hydroxy ketone in acid-catalyzed and base-catalyzed solvolyses in 50% (v/v) H_2O–MeOH, and (e) **9** gave the same ratio of ethoxy and hydroxy ketones (70:30) in acid-catalyzed and base-catalyzed solvolyses in 50% (v/v) H_2O–EtOH. It is proposed that both the acid-catalyzed and base-catalyzed solvolyses proceed by the same mechanism, solvolysis of an intermediate enol allylic chloride. A striking and unprecedented selectivity for reaction with methanol or ethanol, rather than with water, is exhibited during these reactions. Reactions of sodium phenoxide in methanol were consistent with the proposed mechanism. It is suggested that the alkoxy ketones formed as by-products in many Favorskii rearrangement reactions are derived from solvolysis of enol allylic chlorides.

Alkoxy ketones are common by-products in Favorskii rearrangements. With certain α-halo ketones they can become the predominant or even exclusive product.[2,3] At least eight mechanisms have been suggested to account for their formation. These include: (1) SN1, (2) SN2,[4] (3) SN2′,[5] (4) cleavage of an allene oxide,[6] (5) rearrangement of an epoxy ether,[4a-c,6a] (6) reaction of a dipolar ion[7] or (7) cyclopropanone[6,7c] intermediate with (alcohol) solvent, and (8) alcoholysis

(1) For a preliminary account, see F. G. Bordwell and M. W. Carlson, *J. Am. Chem. Soc.*, 91, 3951 (1969).

(2) (a) A. W. Fort, *ibid.*, 84, 2620 (1962); (b) A. W. Fort, *ibid.*, 84, 2625 (1962).

(3) F. G. Bordwell and M. W. Carlson, *ibid.*, 92, 3370 (1970).

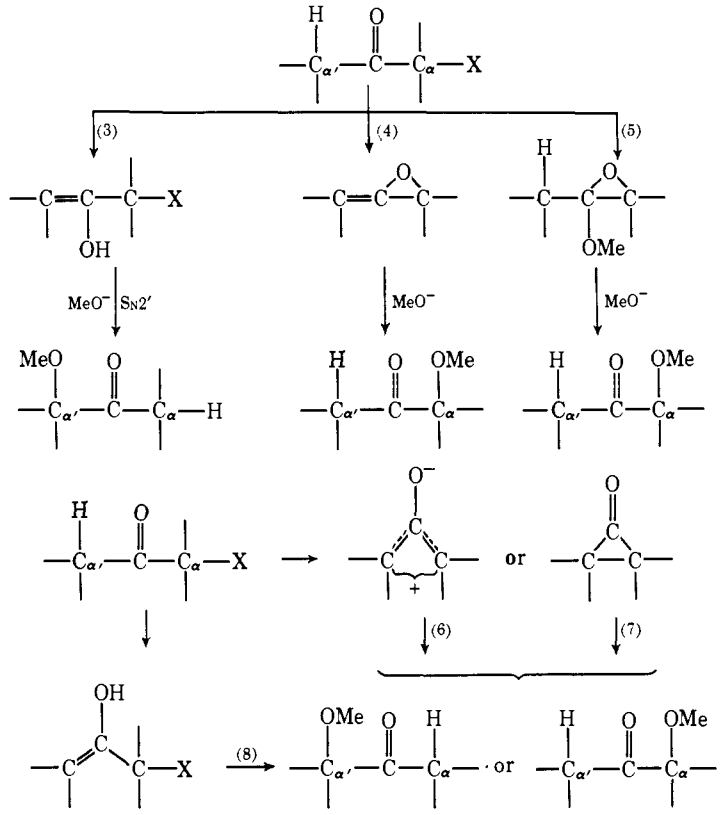
(4) (a) J. G. Aston, J. T. Clark, K. A. Burgess, and R. G. Greenburg, *ibid.*, 64, 300 (1942); (b) M. Kopp-Mayer and M. J. Troéfouël, *Compt. Rend.*, 240, 1115 (1955); (c) E. J. Smissman, T. J. Lemke, and O. Kristiansen, *J. Am. Chem. Soc.*, 88, 334 (1966); (d) M. Mousseron, R. Jacquier, and A. Fontaine, *Bull. Soc. Chim. Fr.*, 19, 767 (1952).

(5) J. S. G. Cox, *J. Chem. Soc.*, 4508 (1960).

(6) (a) H. O. House and G. A. Frank, *J. Org. Chem.*, 30, 2948 (1965); (b) R. C. Cookson and M. J. Nye, *J. Chem. Soc.*, 2009 (1965); (c) R. C. Cookson, M. J. Nye, and G. Subrahmanyam, *ibid.*, c, 473 (1967); (d) N. J. Turro, R. B. Gagosian, C. Rappe, and L. Knutson, *Chem. Commun.*, 270 (1969).

(7) (a) H. O. House and H. W. Thompson, *J. Org. Chem.*, 28, 164 (1963); (b) N. J. Turro and W. B. Hammond, *J. Am. Chem. Soc.*, 87, 3258 (1965); (c) W. B. Smith and C. Gonzalez, *Tetrahedron Lett.*, 5751 (1966).

Scheme I



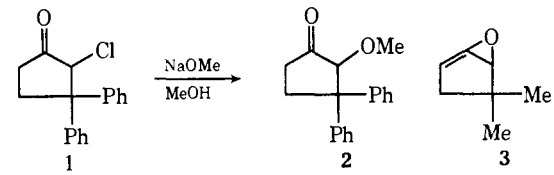
of an intermediate enol allylic chloride.[3] Pathways 3–8 are illustrated in Scheme I.

Although SN2 displacement α to carbonyl is known to be greatly accelerated in some instances relative to displacement with alkyl halides, alkoxide nucleophiles do not appear to be able to effect such displacements at rates fast enough to compete with attack by these reagents at the carbonyl group or at an α' proton (leading to the Favorskii rearrangement). Thus, reaction of NaOMe–MeOH with $PhCOCHClPh$ has $k_2 = 2.18 \times 10^{-2}\ M^{-1}\ sec^{-1}$ at 25° (*ca.* 1.9×10^{-3} at 0°).[8] This is *ca.* 3000-fold slower than the Favorskii rearrangement of $PhCH_2COCHClPh$.[3] Furthermore, the product from $PhCOCHClPh$ is a methoxy epoxide, which indicates that the SN2 reaction must be occurring at yet a 100-fold or more slower rate. The rate and product data for $PhCOCHClPh$ agree well with that for $PhCHClCOCH_3$ for which $k_2 = 3.1 \times 10^{-3}\ M^{-1}\ sec^{-1}$ for reaction at 0° with NaOMe–MeOH.[9] Here the product is 87% methoxy epoxide (isolated as the hydroxy ketal) and 13% Favorskii ester.[9] With $CH_3CHClCOCH_2Ph$ under these conditions $k_2 = 6.7\ M^{-1}\ sec^{-1}$. Here the product is 61% Favorskii ester and 39% α-methoxy ketone, but the latter disappears at higher methoxide ion concentrations (which is inconsistent with an SN2 mechanism).[3] These kinetic data make it evident that the SN2 displacement has little chance of competing with other pathways, at least in protic solvents. The SN2 mechanism has been discounted for valid reasons in other systems.[2,6a]

The SN2′ mechanism has been invoked to explain the appearance of the alkoxy group at the α' position.[5] Inasmuch as the SN2′ process has never been found capable of competing with the SN2 reaction with alkoxide nucleophiles, and there is good reason to question the very existence of concerted SN2′ reactions,[10] we can also eliminate this as a mechanistic possibility.

Most α-halo ketones undergo SN1 solvolysis in alcohol or aqueous alcohol solutions at rates far slower than the competing base-catalyzed reactions (see, *e.g.*, ref 3). Even in favorable instances, such as with $Ph_2CClCOCH_3$, methanolysis of the chloro ketone accounts for only a small part of the products obtained in basic medium.[11]

Formation of α-alkoxy ketones by solvolysis of allene oxide intermediates[6a] is, in our opinion, unlikely. A major disadvantage of this mechanism is that it cannot account for α-alkoxy ketone formation from α-halo cyclic ketones and these by-products are common in such systems.[2b,4c,5,6a,7a,c] A particularly striking example is the reaction of 2-chloro-3,3-diphenylcyclopentanone (**1**) with sodium methoxide in methanol which gives exclusively 2-methoxy-3,3-diphenylcyclopentanone (**2**).[11] Allene oxides from α-halo cyclic ketones (*e.g.*, **3**) would appear to be too highly strained to be reasonable as intermediates in this and analogous reactions.



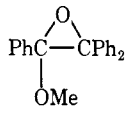
(8) V. S. Karavan and T. I. Temnikova, *Zh. Org. Khim.*, **2** (8), 1410 (1966); *Chem. Abstr.*, **66**, 54849*g* (1967).

(9) F. G. Bordwell and R. G. Scamehorn, *J. Am. Chem. Soc.*, 90, 6751 (1968).

(10) F. G. Bordwell and D. A. Schexnayder, *J. Org. Chem.*, 33, 3240 (1968); F. G. Bordwell, *Accounts Chem. Res.*, in press.

(11) R. G. Scamehorn, Ph.D. Dissertation, Northwestern University, 1968.

Although epoxy ethers are known to rearrange to α-alkoxy ketones under acid catalysis ($MgBr_2$ in Et_2O[12a] or HCl in MeOH[12b]) or during work-up,[6d] Stevens has shown that compounds of this type are often surprisingly stable in solution or on heating with bases. For example, **4** failed to react when refluxed in methanol for 2 days,[12b] **5** was recovered after heating with sodium methoxide at 250° for 5 min,[12b] and **6** failed to react with sodium methoxide at 200° in 1 hr.[12c] There is little reason to believe, therefore, that such rearrangements will occur under conditions of Favorskii rearrangements in methanolic sodium methoxide since these reactions occur rapidly even at 0°.[3]



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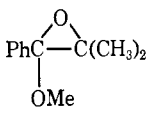

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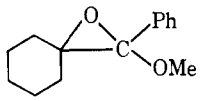
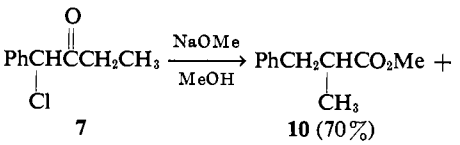


6

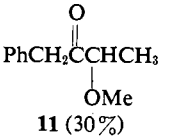
Through a recent elegant labeling experiment in which α-phenoxycyclohexanone-1,2,6-^{14}C was formed by the action of sodium phenoxide in phenol on α-chlorocyclohexanone-1,2-^{14}C Smith and Gonzalez ruled out SN1, SN2, and SN2′ pathways for this reaction;[7c] their data also rule out rearrangement of an epoxy ether or cleavage of an allene oxide. This result requires that the α-phenoxy ketone be formed from a symmetrical intermediate such as a cyclopropanone or dipolar ion.[7c] The present paper will present evidence for an enol allylic carbonium ion (or ion pair) as a likely precursor for α-alkoxy ketones in this and many other systems.

Results

Methoxide-Catalyzed Methanolysis of $PhCHClCOCH_2CH_3$ (7). In the previous paper evidence was presented to show that the formation of α-methoxy ketones from $PhCH_2COCHClCH_3$ (**8**) and $PhCH_2COCHClPh$ (**9**) at low methoxide ion concentrations occurred by methanolysis of enol allylic chloride intermediates.[3] It was of interest to see how chloride **7**, which is an isomer of **8**, would behave under these conditions. Reaction of **7** with 0.05 *M* sodium methoxide in methanol gave 70% of Favorskii ester **10** and 30% of methoxy ketone **11**. These are the same products and nearly the same distribution of products as was obtained from **8**.[3]



7 **10** (70%)



11 (30%)

The product distribution from **7** was dependent on the methoxide concentration, just as was observed with **8**.[3] With 2 *M* NaOMe–MeOH **10** was the sole product, while under inverse addition concentrations (*ca.* 10^{-5} *M* NaOMe) the product was almost entirely **11**.

(12) (a) C. L. Stevens, M. L. Weiner, and R. C. Freeman, *J. Am. Chem. Soc.*, 75, 3977 (1953); (b) C. L. Stevens and J. J. DeYoung, *ibid.*, 76, 718 (1954); (c) C. L. Stevens and S. J. Dykstra, *ibid.*, 75, 5975 (1953).

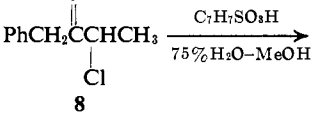
In the absence of a catalyst **7** failed to undergo methanolysis in 24 hr. But in the presence of 1 *M* 2,6-lutidine or 0.5 *M* *p*-toluenesulfonic acid **7** underwent slow methanolysis to give **11**. No **8** was present when these reactions were interrupted prior to completion. On the other hand, some **8** was observed in an incomplete methanolysis catalyzed by hydrogen chloride. Also, **7** rearranged to **8** to the extent of about 20% on standing under refrigeration for 6 months. Appreciable rearrangement of **7** to **8** apparently occurs at room temperature during chlorination since chlorination of ethyl benzyl ketone with sulfuryl chloride at −20° gave **7**, but at room temperature the product was *ca.* a 50–50 mixture of **7** and **8**.

In 2 *M* NaOMe–MeOD **7** formed an ester (**10**) which had incorporated 1.8 deuterons. Since exchange of one hydrogen is required in the overall reaction, this result indicates an 80% exchange of the α-hydrogen prior to reaction.[13]

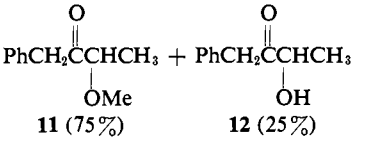
Rate measurements with **7** gave $k = 1.15 \times 10^{-1}$ M^{-1} sec^{-1} at 0°. This is a 58-fold slower rate than was observed with **8**.[3]

Reactions of 8 and 9 in Aqueous Methanol and Aqueous Ethanol. The acid-catalyzed solvolysis of α-halo ketones to form α-alkoxy ketones is almost certain to proceed by solvolysis of the enol allylic chloride. These reactions can then serve as models for this mechanism. For example, the product distribution between hydroxy ketone and methoxy ketone observed for an acid-catalyzed solvolysis of **8** or **9** in aqueous methanol should be the same as that obtained in a comparable base-catalyzed solvolysis if both reactions are proceeding by the same mechanism. Tests of this type were carried out.

In 50% (v/v) H_2O–MeOH (*ca.* 70 mol % H_2O) acid-catalyzed (3 *M* or 6 *M* *p*-toluenesulfonic acid) solvolysis of **8** gave methoxy ketone **11** and no more than a trace of the corresponding hydroxy ketone, $PhCH_2COCHOHCH_3$ (**12**). Even in 75% (v/v) H_2O–MeOH (*ca.* 90 mol % water) more **11** (*ca.* 75%) than **12** (*ca.* 25%) was obtained.



8



11 (75%) **12** (25%)

A very similar product distribution was obtained for base-catalyzed solvolysis of **8**. Using 35% (v/v) 2,6-lutidine in 50% (v/v) aqueous methanol **8** gave **11** with less than 1% of **12**. With 0.05 *M* NaOMe–NaOH in 50% (v/v) H_2O–MeOH the products were **11** (64%) and ester **10** (36%). The distribution of products from acid-catalyzed and base-catalyzed solvolyses in 75% (v/v) H_2O–MeOH is summarized in Table I.

Methanolysis of **9** to give $PhCH_2COCHOMePh$ (**13**) occurs slowly under acid catalysis.[2] Solvolysis of **9** in 50% (v/v) H_2O–MeOH catalyzed by *p*-toluenesulfonic acid was found to give a nearly quantitative

(13) Nmr analysis does not exclude the possibility of prior exchange at the α′ hydrogen atom, but this seems highly unlikely.

Table I. Relative Yields of Solvolysis Products from 3-Chloro-1-phenylbutan-2-one (**8**) in 75% (v/v) H_2O–MeOH[a]

Conditions	% methoxy ketone (**11**)	% hydroxy ketone (**12**)
6 *M* *p*-$MeC_6H_4SO_3H$	77	23
3 *M* *p*-$MeC_6H_4SO_3H$	74	26
2,6-Lutidine buffer[b]	73	27
1 *M* 2,6-lutidine	77	23
Inverse addition of NaOMe–NaOH	78	22
0.02 *M* NaOMe–NaOH[c]	78	22
0.05 *M* NaOMe–NaOH[d]	84	16
0.10 *M* NaOMe–NaOH[e]	87	13

[a] Total yields ranged from 84 to 95%, except where noted; reaction times varied from 2 hr to 3 days. [b] 0.05 *M* each in 2,6-lutidine and 2,6-lutidinium tosylate. [c] 1% ester **10** was formed. [d] 24% ester **10** and 8% of the corresponding acid were formed. [e] 36% ester **10** and 8% of the corresponding acid were formed.

Table II. The Effect of Phenol (and Sodium Phenoxide) on the Distribution of Products Formed from Reactions of $PhCHClCOCH_2CH_3$ (**7**) and of $PhCH_2COCHClCH_3$ (**8**) with 0.05 *M* Sodium Methoxide in Methanol at 0°

Chloro ketone	[PhOH], *M*	% ester (**10**)[a]	% MeO ketone[b] (**11**)	% PhO ketone (**14**)	% PhO ketone (**15**)
7	None	70	30		
8	None	61	39		
7	0.05	21	79	0	0
8	0.05	25	75	0	0
9	0.50	0	93	1	6
8	0.50	0	93	1	6
7	2.0[c]	28	12	6	54
8	2.0[c]	28	12	6	54

[a] Contains some phenyl ester; the phenyl ester is converted to methyl ester under these conditions. [b] The phenoxy ketones are not converted to methoxy ketones under these conditions. [c] 2 *M* NaOPh in MeOH.

yield of **13** with no more than 1% of the corresponding hydroxy compound. Solvolysis of **9** in 50% (v/v) H_2O–MeOH catalyzed by 2,6-lutidine gave an identical result.

Solvolysis of **9** in 50% (v/v) H_2O–EtOH catalyzed by 0.5 *M* *p*-toluenesulfonic acid gave 70% $PhCH_2COCHOEtPh$ and 30% $PhCH_2COCHOHPh$. The same product distribution was obtained when the reaction was catalyzed by 2,6-lutidine.

Solvolysis of 7 and 8 in the Presence of Sodium Phenoxide. Reaction of **7** with sodium phenoxide in phenol has been reported to give 70% $PhCH(OPh)COCH_2CH_3$ (**14**) and 30% ester $PhCH_2CH(CH_3)CO_2Ph$.[4b] With sodium phenoxide in dioxane equal amounts of these same two products were said to be obtained.[4b] In our hands reaction of **7** with 0.05 *M* sodium phenoxide in phenol gave 18% **14** and 82% the isomeric phenoxy ketone $PhCH_2COCH(OPh)CH_3$ (**15**). Under inverse addition conditions the results were identical. A similar result was also obtained in a reaction with **8** and 1 *M* sodium phenoxide in phenol, 11% **14** and 89% **15** being formed. Reaction of **8** with 1.5 *M* NaOPh in dioxane gave 7% **14** and 93% **15**. The structures of **14** and **15** are clearly established by their nmr spectra.[14]

$$\underset{\text{Cl}}{\text{PhCHCOCH}_2\text{CH}_3}\ \xrightarrow[\text{PhOH}]{\text{NaOPh}}\ \underset{\text{OPh}}{\text{PhCHCOCH}_2\text{CH}_3} + \underset{\text{OPh}}{\text{PhCH}_2\text{COCHCH}_3}$$

7 **14** (18%) **15** (82%)

The marked effect of phenol and sodium phenoxide on the distribution of products from **7** and **8** is brought out in Table II.

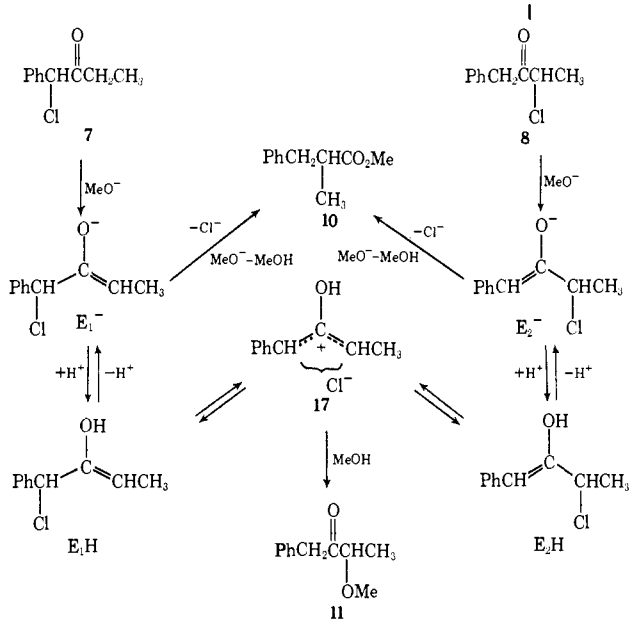
A few experiments were carried out in order to compare the behavior of $ArCH_2COCH_2Cl$ (**16**) type chloro ketones with that of **7** and **8**. It has already been established that **16** (Ar = Ph or *m*-ClC_6H_4) gives a quantitative yield of ester even at low methoxide ion concentrations (inverse addition).[15] The *m*-NO_2 and *m*-Cl derivatives of **16** failed to react when they were refluxed in methanol containing 10% (v/v) 2,6-lutidine. When the *m*-CH_3 derivative of **16** reacted with 0.05 *M* base in methanol containing 0.5 *M* phenol it was converted completely to a mixture of methyl and phenyl Favorskii esters ($PhCH_2CH_2CO_2R$, R = Me or Ph).

Discussion

Formation of the same products and in nearly the same distribution from the reaction of either **7** or **8** with 0.05 *M* sodium methoxide in methanol is suggestive of a common intermediate, such as ion pair **17**.

According to Scheme II α-methoxy ketone **11** arises

Scheme II



from ion pair **17** derived from either of the two enols (E_1H or E_2H). Ester **10** is pictured as arising from the two enolate ions (E_1^- and E_2^-). The slight (but real) difference in product distribution (**10**/**11** = 70/30 from **7** and **10**/**11** = 62/38 from **8**) would then be interpreted as indicating that the methanolysis rate of E_1^- relative to E_1H is slightly greater than that of E_2^- relative to E_2H.

The 58-fold slower rate of reaction of **7**, as compared to **8**, is about the order of magnitude expected for abstraction of a methylene hydrogen ($PhCHClCOCH_2CH_3$) *vs.* a benzylic hydrogen ($PhCH_2COCHClCH_3$). The 37-fold faster k_{obsd} for **7**, as compared to PhCHCl-

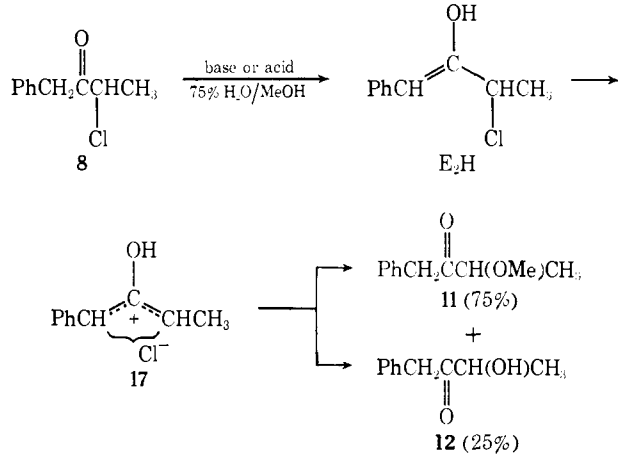
(14) No evidence was provided by Kopp-Mayer and Troéfouël for their structure assignments.[4b]

(15) F. G. Bordwell, R. G. Scamehorn, and W. R. Springer, *J. Am. Chem. Soc.*, 91, 2087 (1969).

$COCH_3$, is explained by the differences in rate-limiting steps for the two reactions. For **7** proton abstraction (k_1) is rate limiting and $k_{obsd} = k_1$; for $PhCHCl-COCH_3$ proton abstraction is reversible and $k_{obsd} = k_1k_2/(k_{-1}[MeOH] + k_2)$,[9] where k_2 is the rate of halide release from the enolate.

The enol chlorides (E_1H and E_2H) are allylic chlorides bearing β-hydroxy substituents. The rearrangement of **7** to **8** and the formation of a methoxy ketone with rearranged structure (**11**) from **7** thus have ample precedent in allylic rearrangements.[16] For example, $PhCH{=}CHCH(OCOC_6H_4NO_2\text{-}p)CH_3$ rearranges on methanolysis to give *ca.* 40% of $PhCH(OMe)CH{=}CH-CH_3$.[16c]

The close similarity of the product distribution in basic media from **7** or **8** with that observed for solvolysis in acidic media provides convincing evidence for comparable mechanisms operating under the two sets of conditions. Since the solvolyses in the acidic media no doubt proceed by an enol mechanism this mechanism must also be operative in the basic media. The parallelism of product distribution may be summarized as follows: (a) **7** forms the same (rearranged) methoxy ketone (**11**) in either acid-catalyzed or base-catalyzed methanolysis, (b) **8** forms **11** in either acid-catalyzed or base-catalyzed solvolyses in 50% (v/v) H_2O–MeOH to the exclusion of the corresponding hydroxy ketone (**12**), despite the presence of 70 mol % water, (c) **8** forms a nearly constant ratio of **11** (*ca.* 75%) to **12** (*ca.* 25%) for acid-catalyzed and a variety of base-catalyzed solvolyses in 75% (v/v) H_2O–MeOH (Table I), (d) **9** forms methoxy ketone [$PhCH_2COCH(OMe)Ph$] to the exclusion of the corresponding hydroxy ketone in acid-catalyzed and base-catalyzed solvolyses in 50% (v/v) H_2O–MeOH, and (e) **9** gives the same ratio of ethoxy and hydroxy ketones (70:30) with 50% (v/v) H_2O–EtOH in reactions catalyzed by *p*-toluenesulfonic acid or by 2,6-lutidine. All of these results are consistent with a mechanism in which the alkoxy and hydroxy ketones are formed by solvolyses of enol allylic chloride intermediates. A striking preference for reaction with methanol or ethanol, rather than with water, is exhibited during these solvolyses.



From the results in 75% (v/v) H_2O–MeOH the selectivity for reaction of **17** with methanol *vs.* water is *ca.* 27:1. From our perusal of the literature a selectivity of this type in carbonium ion reactions appears to be unprecedented. For example, in the solvolysis of *t*-butyl chloride or *n*-butyl bromide in aqueous methanol the product distribution of the methyl ethers and alcohols corresponds closely to the mole per cents of methanol and water in the solvent.[17] The selectivity for reaction of these enol allylic systems with ethanol appears to be less than with methanol, judging from the 7:1 selectivity shown in the solvolysis of $PhCH_2-COCHClPh$ in 50% (v/v) H_2O–EtOH. Nevertheless, this result appears remarkable inasmuch as both benzhydryl chloride[18] and *t*-butyl chloride[17] show about a 2:1 preference for *water* over ethanol in solvolysis.[19] Furthermore, the competitive reactivities of ethanol, methanol, and water in the solvolysis of triphenylmethyl bromide are 1.0:2.6:3.3.[21]

The effect of sodium phenoxide in methanol is consistent with the result expected from the enol allylic chloride solvolysis mechanism. Sodium phenoxide in methanol is about one-third as effective as a nucleophile as is sodium methoxide toward methyl iodide.[22] The twofold increase in yield of methoxy ketone **11** at the expense of ester **10** on changing from 0.05 *M* NaOMe to 0.05 *M* NaOPh (Table II) must then be due to a decrease in the basicity of the medium; evidently methanol rather than methoxide ion or phenoxide ion is the reactive species. Adopting the view suggested in the previous paper,[3] that ester **10** is derived from the enolate ion and methoxy ketone **11** from the corresponding enol, leads one to expect an increased yield of **11** with decreasing base concentration caused by a shift in the enol–enolate ion equilibrium toward the enol. The disappearance of **10** when excess phenol is present (Table II) is also to be expected. The appearance of phenoxy ketones **14** and **15** in this experiment and particularly in the experiment where 2 *M* sodium phenoxide was used (Table II) suggests that ion pair **17** or the like may be effective in capturing phenoxide ions.

When either chloro ketone **7** or **8** reacted with sodium phenoxide in phenol the phenoxy ketones **14** and **15** were formed in an identical 6:1 ratio. Both **7** and **8** solvolyzed in a methanolic solution 0.05 *M* in base and 0.5 *M* in phenol to give **11** (93%), **14** (1%), and **15** (6%), and in a solution 2 *M* in base and 2 *M* in phenol to give **11** (12%), **14** (6%), and **15** (54%). Thus in the presence of phenoxide ion chloro ketone **8** as well as **7** gave rearranged product. It is noteworthy that in each of these base-catalyzed solvolysis reactions **7** and **8** gave the same product distribution. This

(16) (a) R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 769 (1956); (b) P. B. D. de la Mare, "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1963, Chapter 2: (c) R. A. Sneen and A. M. Rosenberg, *J. Am. Chem. Soc.*, **83**, 895 (1961).

(17) See A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 36–37.

(18) N. T. Fariancci and L. P. Hammett, *J. Am. Chem. Soc.*, **59**, 2542 (1937).

(19) The preference for reaction with alcohols rather than water during solvolysis appears to be characteristic of allylic systems since it has been observed also for the solvolysis of $PhCH{=}CHCHClCH_3$ in aqueous methanol (Ngai Yee, unpublished results). (It is noteworthy that the product from methanolysis of this allylic chloride is $PhCH{=}CHCHOMeCH_3$, which corresponds in structure to that formed from E_1H and E_2H.) In this connection it should be noted that Sneen has observed a high selectivity for capture of the carbonium ion from $CH_2{=}CHCHClCH_3$ by azide ion rather than by water.[20]

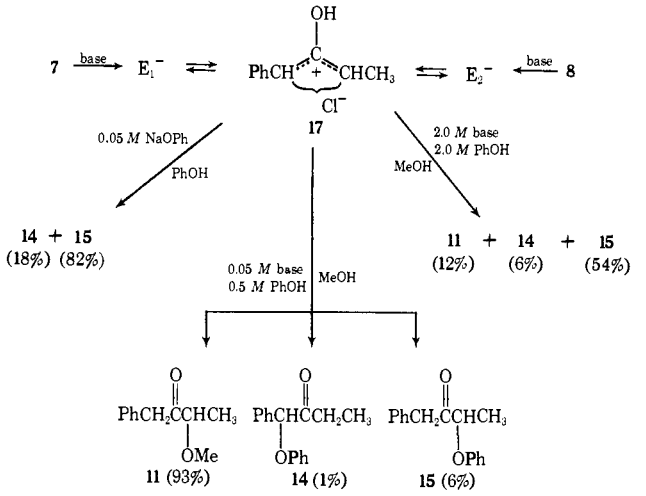
(20) R. A. Sneen and J. W. Larson, *J. Am. Chem. Soc.*, **88**, 2593 (1966); R. A. Sneen, J. V. Carter, and P. S. Kay, *ibid.*, 88, 2594 (1966).

(21) W. Reeve and P. F. Aluotto, *Tetrahedron Lett.*, No. 21, 2557 (1968).

(22) R. G. Pearson, H. Sobel, and J. Songstad, *J. Am. Chem. Soc.*, 90, 319 (1968).

strongly indicates the presence of a common intermediate (**17**) as shown in Scheme III.

Scheme III



Increasing the per cent (by volume) of water in the methanol solvent from 0 to 50% caused an increase in the per cent of α-methoxy ketone from 39 to 64% with a proportional decrease in the per cent of ester. This change in product composition can be explained if it is assumed that the rate of solvolysis of the enol is more sensitive to changes in the ionizing power of the solvent than is that of the enolate ion. This rationale is supported by the sizable Grunwald–Winstein m value for $H_2C{=}CHCHClCH_3$ in aqueous methanol (0.875)[23] as compared to a moderate m value (0.65) in aqueous methanol for the enolate ion of $PhCH_2COCH_2Cl$.[15]

The system $ArCH_2COCH_2Cl$ appears to be relatively unreactive toward base-catalyzed solvolysis, as judged by the results with 2,6-lutidine in methanol and with sodium phenoxide in methanol. This is in contrast to the behavior of the systems **7**, **8**, and **9**. According to the mechanism suggested this is a consequence of the much greater rate of solvolysis of a secondary enol allylic chloride as compared to a primary allylic chloride. It is significant in this respect that α-alkoxy ketone by-products have seldom, if ever, been observed in Favorskii rearrangements of primary α-halo ketones.

Another noteworthy point is the 3–4:1 preference for formation of the methyl ester (**10**), as compared to the corresponding acid, in the reaction of **8** with 75% (v/v) H_2O–MeOH (Table I, footnotes *d* and *e*). This would correspond to a preference of about 30:1 for reaction with methoxide ion rather than hydroxide ion. Differences of this order of magnitude, or larger, are common for the relative reactivity of methoxide and hydroxide ions toward carbonyl groups.[24] The present result can be explained as being due to the relative ease of attack of methoxide and hydroxide on the carbonyl group of a cyclopropanone, which is commonly believed to be the immediate precursor of Favorskii ester products.

Reaction in Aprotic Solvents. With 0.05 M sodium methoxide in methylene chloride the product from **8** was exclusively ester **10**. Because the reaction was carried out under heterogeneous conditions, the actual methoxide concentration was much less than 0.05 M. Absence of α-methoxy ketone formation is consistent with the enol solvolysis mechanism since under these circumstances the concentration of enol should be negligible and its opportunity for solvolysis nil.

Other Possible Mechanisms for Methoxy Ketone Formation. The SN1, SN2, and SN2′ mechanisms for the formation of methoxy ketone **11** from **7** and **8** can be excluded for reasons given earlier and also because it is difficult for these mechanisms to accommodate formation of a single product from two isomeric α-chloro ketones. Reasons for discounting methoxy ketone formation by rearrangement of an allene oxide or epoxy ether intermediate were given above. These rearrangements are also unsatisfactory inasmuch as they predict different products from **7** and **8**. Furthermore, none of these five mechanisms can account for the change in product distribution for **7**, **8**, and **9** with changing methoxide concentration.[3]

It is conceivable that a mobile valence tautomeric equilibrium of the type allene oxide $\rightleftarrows$ dipolar ion $\rightleftarrows$ cyclopropanone is set up.[6b,25] If so, the dipolar ion is the most likely precursor of α-alkoxy ketones. It is difficult to believe, however, that the dipolar ion derived from **7** (or **8**) would show the high degree of discrimination for methanol over water required of the intermediate in this reaction (see above). Furthermore, unless it is assumed that the dipolar ion is formed also under acid catalysis, the constancy of the product distribution recorded in Table I is very difficult to account for by this mechanism. In addition, the enol solvolysis mechanism offers an explanation for (1) the effect of *meta* and *para* substituents on the product distribution in the $ArCH_2COCHClCH_3$ system,[3] (2) the absence of α-methoxy ketone by-products in the Favorskii rearrangement of $ArCH_2COCH_2Cl$, (3) the increase in the quantity of solvolysis products brought about by adding phenol to NaOMe–MeOH solutions, (4) the increase in solvolysis products brought about by adding water to the methanol solvent, (5) the formation of $PhCH_2COCHOMeCH_3$, rather than its isomer, from methanolysis of **7** or **8** (analogy to allylic systems[16c,19]), and (6) the formation of α-phenoxy ketone, rather than ester, as the principal product from a reaction of **7** or **8** with 2 M sodium phenoxide in methanol. It is conceivable that, making the proper assumptions, the dipolar ion mechanism could accommodate these observations, but the enol solvolysis mechanism does so more simply. For these reasons solvolysis of an intermediate enol allylic chloride appears to be the most likely mechanism for production of α-alkoxy ketone by-products under acid or base catalysis in protic solvents.

Application of the Enol Allylic Chloride Mechanism to Other Systems. There are clearly some instances where this mechanism is not applicable, for example, the formation of α-alkoxy ketones from reactions in aprotic solvents. These reactions probably occur by SN2 mechanisms. Also, judging from the behavior of $ArCH_2COCH_2Cl$, solvolysis of primary enol allylic chlorides is too slow to make this mechanism operative. Also, systems such as $Ph_2CBrCOPh$, $Ph_2CBrCOCH_3$, and $Ph_2CBrCOCH_2Ph$ undergo a fairly rapid uncata-

(23) R. H. de Wolfe and W. G. Young, *Chem. Rev.*, **56**, 786 (1956).
(24) W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, 90, 2622 (1968).
(25) Note, however, that 1,3-di-*t*-butylallene oxide rearranges to the corresponding cyclopropanone only with difficulty: R. L. Camp and F. D. Greene, *ibid.*, 90, 7349 (1968).

lyzed methanolysis, apparently by an SN1 mechanism. There are many systems studied previously, however, where the enol allylic halide solvolysis mechanism offers the best explanation for the formation of α-alkoxy by-products. These include (a) the essentially complete conversion of 6-tosyloxyisophorone to 2- and 6-methoxyisophorones at low methoxide concentrations,[2b] (b) formation of 28% of α-methoxycyclohexanone from α-chlorocyclohexanone at low methoxide concentrations,[26] (c) the reaction of 2,6-dibromo-4,4-dipenylcyclohexane with 0.15 *M* NaOMe–MeOH to give 85% 2-methoxy-6-bromo-4,4-diphenylcyclohexanone,[27] (d) formation of a 12-methoxy keto steroid from 3α,20β-dibenzoyloxy-9α-bromo-5β-pregnan-11-one,[5] (e) formation of 30% 12α-methoxy-11-ketoprogesterone by the action of 0.15 *M* NaOMe–MeOH with 9α-bromo-11-ketoprogesterone,[28] (f) conversion of α-chlorocyclohexanone to α-phenoxycyclohexanone by the action of sodium phenoxide in phenol,[7c] (g) formation of high yields of stereoisomeric α-methoxy ketones from the reaction of 9-chloro-*trans*-1-decalone and its *cis* isomer with NaOMe–MeOH,[6a,7a,29] (h) formation of 10% of an α-ethoxy ketone from the reaction of 1 *M* NaOEt–EtOH with 3(a)-bromo-*trans*-2-decalone,[4c] (i) the quantitative conversion of either 2-bromo- or 2-chloro-3,3-diphenylcyclopentanone to the corresponding α-methoxy ketone by the action of 0.1 *M* NaOMe–MeOH,[11] and (j) the quantitative conversion of 1,3-dibromo-1,2-diphenylpropanone to 1-methoxy-1,3-diphenylpropanone by the action of sodium iodide in methanol.[22]

Experimental Section

1-Chloro-1-phenylbutan-2-one (7). Ethyl benzyl ketone (5.75 g, 38.9 mmol) was cooled to 0° and 5.45 g (40.4 mmol) of sulfuryl chloride was added dropwise with stirring over a period of 30 min. After the first 2 drops of sulfuryl chloride were added the temperature was lowered to −20°[30] in a Dry Ice–water–acetone bath, and the mixture was stirred at this temperature for 1 hr after addition was complete. Ether (200 ml) was added and the mixture was extracted with water and sodium bicarbonate. After drying over magnesium sulfate the ether was removed by rotary evaporation and the yellow oil was chromatographed on a 3 × 70 cm silica gel column using 1% ether in hexane as eluent. The first 28 fractions of 250 ml contained no chlorinated product; however, some starting material was recovered from fractions 20 and 21. Fractions 29–34 contained 4.30 g (61%) of only **7**. Fractions 35 contained mainly 1 with some of the isomeric chloride **8**. Following fractions contained a mixture of **7** and **8**, becoming increasingly rich in the latter. Analysis showed λ_{max}^{film} 5.78 μ (C=O); $\delta_{max}^{CCl_4}$ 0.85 (t, 3, CH_3, J = 7.0 Hz), 2.38 (q, 2, CH_2, J = 7.0 Hz), 5.42 (1, CH), 7.22 (5, Ph); $n^{25}D$ 1.5262.

Anal. Calcd for $C_{10}H_{11}ClO$: C, 65.75; H, 6.07. Found: C, 65.60; H, 6.25.

Standard Reaction Procedures for the Solvolysis of 3-Chloro-1-phenylbutan-2-one (8). A. Absence of Methanolysis of 3-Chloro-1-phenylbutan-2-one (8) and 1-Chloro-1-phenylbutan-2-one (7). To 25 ml of absolute methanol at 25° was added 0.5 g of a mixture of two chloro ketones (63% **7** and 37% **8**). The starting materials were quantitatively recovered after 24 hr. Analysis by vpc and nmr showed only a trace (<1%) of methanolysis had occurred. (The results show methoxy ketones do not arise by solvolysis under Favorskii reaction conditions and do not arise without the presence of a catalyst.)

B. In Methanol in the Presence of Lutidine. To a solution of 2,6-lutidine (5 ml) in methanol (15 ml) at room temperature was added 0.50 g (2.74 mmol) of **8**. The mixture was stirred for 12 hr, poured into a separatory funnel containing 400 ml of ether, and extracted three times with 200-ml portions of dilute hydrochloric acid in brine. The organic layer was washed once with brine and dried over magnesium sulfate. After removing the solvent by rotary evaporation below 25° the 0.49 g of oil was analyzed by vpc, nmr, and ir. The product was shown to contain 55% methoxy ketone **11** and 45% unreacted starting material. Recovery was quantitative.

C. In Methanol in the Presence of 0.5 *M* *p*-Toluenesulfonic Acid. To 20 ml of 0.5 *M* *p*-toluenesulfonic acid in methanol was added 0.50 g (2.7 mmol) of **8** and the mixture was stirred for 24 hr at room temperature. Processing as in B gave 0.49 g of oil which was analyzed by vpc peak enhancement, nmr, and ir. The oil was found to contain 56% methoxy ketone **11** and 44% unreacted starting material. Recovery was quantitative.

D. In 50% Aqueous Methanol in the Presence of Lutidine. To a solution containing 5 ml of 2,6-lutidine and 7.5 ml each of methanol and water was added 0.40 g (2.2 mmol) of **8**. After the mixture had been stirred for 12 hr at room temperature it was neutralized with dilute hydrochloric acid (phenolphthalein) and the methanol was removed by rotary evaporation below 25°. Work-up was carried out as described in part B, and 0.39 g of oil was isolated. With analysis by ir, nmr, and vpc peak enhancement the product was identified by methoxy ketone **11** and a trace (<1%) of hydroxy ketone **12**. The yield was quantitative.

E. In 50% Aqueous Methanol in the Presence of 0.5 *M* *p*-Toluenesulfonic Acid. To 25 ml of 50% aqueous methanol (v/v) 0.5 *M* in *p*-toluenesulfonic acid was added 0.40 g (2.2 mmol) of **8**. After stirring for 12 hr at room temperature the mixture was neutralized with dilute sodium hydroxide (phenolphthalein) and the methanol was removed by rotary evaporation below 25°. The reaction was processed as in part B, and 0.39 g of oil was collected. After analysis, by ir, nmr, and vpc peak enhancement, the product was identified as 40% methoxy ketone **11** and no hydroxy ketone **12**. The remainder of the material (60%) was unreacted **8**. The recovery was quantitative.

F. In 75% Aqueous Methanol. A 0.5-g (2.7 mmol) sample of **8** was added to 30 ml of water and 10 ml of methanol and the mixture was stirred for 6 days at room temperature. The methanol was removed by rotary evaporation below 25° and the aqueous solution was extracted twice with 200-ml portions of ether. After the ether extracts were combined and dried over magnesium sulfate, the ether was rotary evaporated below 25°. Analysis by ir and nmr (estimated yields by nmr ±3%) showed 65% unreacted **8**, 25% methoxy ketone **11**, and 10% hydroxy ketone **12**.

G. In 75% Aqueous Methanol in the Presence of 3 *M* *p*-Toluenesulfonic Acid. To a solution containing 30 ml of water, 10 ml of methanol, and 23.1 g of *p*-toluenesulfonic acid was added 0.30 g (1.6 mmol) of **8**. After stirring at room temperature for 4 days the reaction was processed as in part E. The 0.27 g of oil recovered was analyzed by ir, nmr, and vpc peak enhancement and found to be 63% methoxy ketone **11**, 22% hydroxy ketone **12**, and 15% unidentified material.[31]

H. In 75% Aqueous Methanol in the Presence of 1 *M* Lutidine. To a solution of 30 ml of water and 10 ml of methanol 1 *M* in 2,6-lutidine was added 0.50 g (2.7 mmol) of **8**. After stirring for 1 hr at room temperature the reaction was processed as in part D. The 0.48 g of crude product was analyzed by ir, nmr, and vpc peak enhancement and found to be 64% methoxy ketone **11** and 20% hydroxy ketone **12**. Six other products were also present, but none represented greater than a 4% yield and were not characterized.

I. In 75% Aqueous Methanol in the Presence of 0.5 *M* Lutidine and 0.5 *M* Lutidinium *p*-Toluenesulfonate. To a solution of 30 ml of water and 10 ml of methanol 0.5 *M* in *p*-toluenesulfonic acid and 1.0 *M* in 2,6-lutidine was added 0.50 g (2.7 mmol) of **8**. After stirring 3 days at room temperature the reaction was worked up as described in part D. The 0.46 g of crude oil was analyzed by ir, nmr, and vpc peak enhancement and found to contain 64% methoxy ketone **11** and 24% hydroxy ketone **12**. Two other unidentified products were also present.

(26) J. G. Strong, Ph.D. Dissertation, Northwestern University, June 1968.

(27) R. G. Frame, Ph.D. Dissertation, Northwestern University, Aug 1965.

(28) P. A. Diassi and P. M. Palmere, *J. Org. Chem.*, **36**, 5340 (1961).

(29) No obvious explanation for the stereochemistry of these reactions is on hand.

(30) When the sulfuryl chloride was added over a period of 15 min at room temperature to ethyl benzyl ketone a mixture of *ca.* equal amounts of the two isomeric α-chloro ketones was obtained.

(31) The methoxy ketone **11** and hydroxy ketone **12** failed to react further under identical reaction conditions. This demonstrated that the unidentified material was a primary reaction product.

Methanolysis of 1-Chloro-1-phenylbutan-2-one (7) in the Presence of Hydrogen Chloride. Approximately 0.3 g of **7** was dissolved in 50 ml of methanol. Anhydrous hydrogen chloride was passed into the mixture for 5 min while the temperature was maintained at 0°. After standing for 1 hr at room temperature the reaction mixture was poured into a separatory funnel containing 400 ml of ether and extracted three times with a solution of sodium bicarbonate in brine. The ether solution was dried over magnesium sulfate and evaporated to dryness leaving an oil which was analyzed by vpc and nmr. The oil contained 25% isomerized material (**8**) and 50% methoxy ketone **11**. About 25% starting material remained.

In the presence of 0.5 *M* *p*-toluenesulfonic acid 20% of **7** solvolyzed to give methoxy ketone **11** in 15 min at room temperature. The remaining 71% of the material was recovered and found to have undergone no isomerization.

Methanolysis of 1-Chloro-1-phenylbutan-2-one (7) in the Presence of Lutidine. A mixture (0.5 g) consisting of **7** (63%) and **8** (37%) was added to 20 ml of methanol and 5 ml of 2,6-lutidine and the solution was stirred for 18 hr at room temperature. The reaction was processed as in part B of the standard solvolysis procedure. Analysis of the crude oil by vpc and nmr showed the presence of methoxy ketone **11** and the starting materials. It was estimated from the final ratio of the chloro ketones that the methanolysis of **7** to **11** proceeded to the extent of 15–20%.

Solvolysis of 1-Chloro-1,3-diphenylpropan-2-one (9) in 50% Aqueous Methanol in the Presence of Lutidine. The solvolysis of 0.40 g (1.6 mmol) of **9** in a solution of 5 ml of 2,6-lutidine, 7.5 ml of water, and 7.5 ml of methanol proceeded at room temperature for a period of 12 hr. The reaction mixture was processed as in part D of the standard solvolysis reaction procedure. The 0.39 g of product was identified by ir, nmr, and vpc peak enhancement analysis as the methoxy ketone **13** with a trace (less than 1%) of the corresponding hydroxy ketone. The recovery was quantitative.

Solvolysis of 1-Chloro-1,3-diphenylpropan-2-one (9) in 50% Aqueous Methanol in the Presence of 0.5 *M* *p*-Toluenesulfonic Acid. To a mixture of 0.5 *M* *p*-toluenesulfonic acid in 12.5 ml of methanol and 12.5 ml of water was added 0.40 g (1.6 mmol) of **9**. After refluxing on a steam bath for 6 hr the reaction was worked up as described in part E of the standard solvolysis reaction procedure. The 0.39 g of oil recovered was shown by ir, nmr, and vpc peak enhancement analysis to contain essentially all methoxy ketone **13**; a trace of the corresponding hydroxy ketone was detected.

Solvolysis of 1-Chloro-1,3-diphenylpropan-2-one (9) in 50% Aqueous Ethanol in the Presence of 0.5 *M* *p*-Toluenesulfonic Acid. To 12.5 ml of absolute ethanol and 12.5 ml of water which was 0.5 *M* in *p*-toluenesulfonic acid was added 0.40 g (1.6 mmol) of **9**. The mixture was refluxed 2 hr on a steam bath, stirred an additional 20 hr at room temperature, and processed as described in part E of the standard solvolysis reaction procedure. The 0.40 g of crude product (quantitative yield) was identified by ir and nmr (yields estimated by nmr to ±3%) as 30% hydroxy ketone and 70% 1-ethoxy-1,3-diphenylpropan-2-one: λ_{max}^{film} 5.79 μ (C=O), 9.10 (C—O), 13.25, 13.59, and 14.30 (Ph); $\delta_{TMS}^{CDCl_3}$ 1.21 (t, 3, CH_3, J = 7.0 Hz), 3.47 (q, 2, CH_3O, J = 6.5 Hz), 3.58 (1, CH), 4.81 (2, CH_2Ar), 6.9–7.4 (m, 5, Ph), 7.32 (5, Ph).

Solvolysis of 1-Chloro-1,3-diphenylpropan-2-one (9) in 50% Aqueous Ethanol in the Presence of Lutidine. A 0.50-g (2.0 mmol) sample of **9** was added to a mixture of 15 ml of absolute ethanol, 15 ml of water, and 10 ml of 2,6-lutidine. After stirring for 20 hr at room temperature the reaction was processed as in part D. The 0.39 g of crude product was identified by ir and nmr (estimated yields by nmr to ±3%) as 30% hydroxy ketone and 70% ethoxy ketone.

Lack of Methanolysis of 1-Chloro-3-arylpropan-2-ones in the Presence of Lutidine. A 0.5-g sample of 1-chloro-3-(*m*-nitrophenyl)propan-2-one was refluxed in 45 ml of methanol and 5 ml of 2,6-lutidine for 36 hr. The solution was worked up as described in part B of the standard solvolysis reaction procedure and yielded 0.46 g (92%) of an oil. Analysis by nmr, ir, and vpc peak enhancement showed the chloro ketone had undergone no reaction.

A similar methanolysis of 1-chloro-3-(*m*-chloro)propan-2-one also failed to yield any products.

Reaction of 1-Chloro-1-phenylbutan-2-one (7) with 0.05 *M* Sodium Methoxide in Methanol. The reaction of 1.00 g (5.48 mmol) of **7** with 220 ml of 0.05 *M* sodium methoxide was carried out as described in procedure A of the previous paper.[3] Analysis by vpc peak enhancement and ir showed the products to be 70% ester **10** and 30% of methoxy ketone **11**.

If the product had contained 1-methoxy-1-phenylbutan-2-one[32] the following peaks should have appeared in the nmr spectrum: δ 0.85 (t, 3, CH_3, J = 7.5 Hz), 2.43 (q, 2, CH_2, J = 7.5 Hz), 3.25 (3, CH_3O), 4.54 (1, CH), and 7.28 (5, Ph). No signal was observed in the ranges 0.8–1.0, 1.3–3.0, or 3.9–7.0.

Reaction of 1-Chloro-1-phenylbutan-2-one (7). Inverse Addition Procedure. A 0.05 *M* solution of sodium methoxide in methanol (140 ml, 3.4 mmol) was added over a period of 10 hr to 0.50 g (2.7 mmol) of **7** in 50 ml of methanol following the procedure described in part D of the Favorskii reaction conditions.[3] The 0.49 g (98% yield) of oil was chromatographed, and the products were identified by vpc peak enhancement, ir, and nmr as 88% methoxy ketone **11** and 12% ester **10**.[33]

Reaction of 1-Chloro-1-phenylbutan-2-one (7) with Sodium Methoxide in Methanol-O-*d*. The reaction of 0.50 g (2.7 mmol) of **7** with 2.0 *M* sodium methoxide in methanol-O-*d* for 5 min was run following the usual procedure for the Favorskii reaction.[3] The product was identical with ester **10** except that the nmr spectrum showed the integral of the multiplet from δ 2.4 to 3.2 to be 1.20 ± 0.05 instead of 3.0 protons.

Reaction of 8 with 0.05 *M* Base in 50% Aqueous Methanol. A 0.05 *M* base solution was prepared by adding 0.44 g (11 mmol) of sodium hydroxide to 110 ml of water and 110 ml of methanol. The conditions for the reaction of 1.00 g (5.5 mmol) of **8** with the base were the same as those described in part A of the previous paper.[3] The methanol was removed by rotary evaporation and the water was saturated with sodium chloride. The solution was made basic by adding dilute sodium hydroxide and was extracted three times with ether. The remaining aqueous layer was acidified and extracted for carboxylic acid. When the ether fractions were combined, washed, dried, and concentrated the 0.96 g (97% yield) of product was identified by vpc, ir, and nmr as methoxy ketone (**11**), 64%, and ester (**10**), 36%. No hydroxy ketone **12** was detected, and no acid could be isolated.

Reaction of 8 with 0.05 *M* Base in 75% Aqueous Methanol. (See Table I for results at other base concentrations in 75% aqueous methanol.) A 0.05 *M* base solution was prepared by adding 0.22 g (5.5 mmol) of sodium hydroxide to 82 ml of water and 27 ml of methanol. The reaction of 0.50 g (2.7 mmol) of **8** with the base proceeded as above. After the methanol had been removed by rotary evaporation, the water was made basic by adding dilute sodium hydroxide, was saturated with sodium chloride, and was extracted three times with ether. The ether fractions were combined and worked up, and the 0.45 g of product was shown by vpc, ir, and nmr to be 26% ester (**10**), 62% methoxy ketone (**11**), and 12% hydroxy ketone (**12**).

The aqueous solution was acidified and extracted three times with ether. After work-up the 0.04 g of product was analyzed by ir and was shown to be a carboxylic acid, presumably 2-methyl-3-phenylpropionic acid: λ_{max}^{film} 3.42 μ (CO_2H), 5.86 (C=O), 7.90 (C—O), 14.28 (Ph). Nmr analysis was not possible due to the small amount of material. The overall yields for the reaction were methoxy ketone (**11**) 57%, hydroxy ketone (**12**), 11%, methyl ester (**10**), 24%, and acid, 8%.

Reaction of 8 with 0.05 *M* Base in 75% Aqueous Methanol. Inverse Addition Procedure. A 0.05 *M* solution of base in 37 ml of water and 13 ml of methanol was added dropwise with stirring over a period of 6 hr to a solution of 0.50 g (2.7 mmol) of **8** in 75 ml of water and 25 ml of methanol at room temperature. The reaction was processed as described above and gave 0.44 g of oil. The major products were identified by nmr, vpc, and ir analyses as methoxy ketone **11**, 72%, and hydroxy ketone **12**, 20%. Four other minor products were also detected, but none was present in greater than 3% yield.

Reaction of 3-Chloro-1-phenylbutan-2-one (8) with 1 *M* Sodium Phenoxide in Phenol. A 0.50-g (2.7 mmol) sample of **8** was added to 50 ml of 1.0 *M* sodium phenoxide (5 mmol) in phenol and stirred at 50° for 1.5 hr. Water (100 ml) and ether (300 ml) were added, and the ether layer was washed five times with dilute sodium hydroxide to remove all remaining phenol. After the solution was washed with water and dried over magnesium sulfate the ether was rotary evaporated leaving 0.63 g (97%) of oil. A vpc analysis showed two peaks, the first representing 11% of the total product and the second 89%. The major product was identified as 3-

(32) Prepared by refluxing 1-chlorophenylbutan-2-one (7) in methanol for 22 hr, 22% yield.

(33) The relatively slow reaction of 7 apparently allowed the methoxide concentration to increase to the point where some ester was formed.

phenoxy-1-phenylbutan-2-one (**15**): λ_{max}^{film} 5.80 μ (C=O), 6.67 (Ph), 8.09 (Ph—O), 13.26 and 14.45 (Ph); $\delta_{TMS}^{CDCl_3}$ 1.40 (d, 3, CH_3, J = 7.0 Hz), 3.80 (2, CH_2), 4.67 (q, 1, CH, J = 6.65 Hz), 6.7–7.1 (m, 5, OPh), 7.16 (5, Ph); $n^{25}D$ 1.5493; bp 161–165° (0.3 mm).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.12; H, 6.45.

The minor product with the slightly shorter retention time was identified as 1-phenoxy-1-phenylbutan-2-one (**14**): λ_{max}^{film} 5.80 μ (C=O); $\delta_{TMS}^{CDCl_3}$ 0.90 (t, 3, CH_3, J = 7.0 Hz), 2.56 (q, 2, CH_2, J = 7.0 Hz), 5.57 (1, CH), 6.7–7.1 (m, 5, OPh), 7.16 (5, Ph); $n^{25}D$ 1.5540; bp 145–148° (0.3 mm).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.52; H, 6.74.

Reaction of 1-Chloro-1-phenylbutan-2-one (7) with 0.05 *M* Sodium Phenoxide in Phenol. The reaction of 0.50 g (2.7 mmol) of **7** with 110 ml of 0.05 *M* sodium phenoxide (5.5 mmol) in phenol was carried out under the standard Favorskii reaction conditions. The reaction was stirred for 3.5 hr at 50° before work-up. The 0.64 g (97%) of product was shown by nmr, ir, and vpc peak enhancement to be the isomeric phenoxy ketones: **14**, 18% and **15**, 82%.

Reaction of 1-Chloro-1-phenylbutan-2-one (7) with 0.05 *M* Sodium Phenoxide in Phenol, Inverse Addition Procedure. A 0.05 *M* solution of sodium phenoxide in phenol (50 ml) was added dropwise over a period of 4 hr to 0.50 g (2.7 mmol) of **7** in 100 ml of phenol at 50°. The 0.62 g (96%) of product was shown by nmr, ir, and vpc peak enhancement to be the isomeric phenoxy ketones: **14**, 18% and **15**, 82%.

Reaction of 1-Chloro-1-phenylbutan-2-one (7) with 0.05 *M* Base and 0.05 *M* Phenol in Methanol. The reaction of 0.50 g (2.7 mmol) of **7** with 110 ml of 0.05 *M* methanolic base solution (0.52 g of phenol and 0.13 g of sodium, 5.5 mmol each) gave 0.46 g (93%) of crude products which were identified by ir, nmr, and vpc peak enhancement as methyl ester **10** (21%) and methoxy ketone **11** (79%). No phenyl ester of phenoxy ketones were present.[34] Isomer **8** gave an identical result.

Reaction of 1-Chloro-1-phenylbutan-2-one (7) with 0.05 *M* Base and 0.50 *M* Phenol in Methanol. The reaction of 0.50 g (2.7 mmol) of **7** with 110 ml of methanol containing 0.13 g (5.5 g-atom) of sodium and 5.20 g (55 mmol) of phenol gave 0.49 g (94%) of crude products which were identified by ir, nmr, and vpc peak enhancement as methoxy ketone **11** (93%) and isomeric phenoxy ketones **15** (6%) and **14** (1%).[34] Isomer **8** gave an identical result.

Reaction of 1-Chloro-1-phenylbutan-2-one (7) with 2 *M* Sodium Phenoxide in Methanol. The reaction of 0.50 g (2.7 mmol) of **7** with 25 ml of a 2.0 *M* base solution gave 0.56 g (96% yield) of crude product which was identified by ir, nmr, and vpc peak enhancement as the following: methoxy ketone **11** (12%); methyl ester **10** (28%); phenoxy ketones **15** (54%) and **14** (6%).[34] Isomer **8** gave **11** (12%), **10** (25%), **15** (54%), **14** (6%), and phenyl 2-methyl-3-phenylpropionate (3%).

Favorskii Rearrangement of 1-Chloro-3-(*m*-tolyl)propan-2-one (16) with 0.05 *M* Sodium Phenoxide in Methanol. The reaction of 0.32 g (1.8 mmol) of **16**[35] with 70 ml of methanolic solution 0.5 *M* in base (3.5 g-atoms of sodium) and 0.50 *M* in phenol was carried out as described above. The 0.19 g of product (60% yield) was analyzed by nmr, ir, and vpc. Two peaks were present, the first representing 84% and the second 16%. From spectroscopic data the major product was identified as methyl β-(*m*-tolyl)propionate: λ_{max}^{film} 5.79 μ (C=O), 8.67 (CO); $\delta_{TMS}^{CCl_4}$ 2.28 (3, $ArCH_3$), 2.67 (t, 2, CH_2Ar, J = 7.0 Hz), 2.89 (t, 2, CH_2CO, J = 6.5 Hz), 3.57 (3, CH_3O), 6.9–7.3 (m, 4, Ar). The minor product was likewise identified as phenyl β-(*m*-tolyl)propionate: λ_{max}^{film} 5.79 μ (C=O), 8.67 (CO); $\delta_{TMS}^{CCl_4}$ 2.28 (3, $ArCH_3$), 2.68 (t, 2, CH_2Ar, J = 7.0 Hz), 2.97 (t, 2, CH_2CO, J = 6.0 Hz), 6.96 (5, Ph), 6.9–7.3 (m, 4, Ar).

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(34) Under these reaction conditions the phenyl ester was found to be converted to the methyl ester, but the phenoxy ketones are stable.

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Kinetics and Mechanism of *vic*-Diol Dehydration. I. The Origin of Epoxide Intermediates in Certain Pinacolic Rearrangements[1]

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Abstract: The acid-catalyzed pinacolic rearrangements of benzopinacol (tetraphenylethylene glycol), 1,2-di-*p*-tolyl-1,2-diphenylethylene glycol, and tetra-*p*-tolylethylene glycol are characterized by the concurrent formation and accumulation of an intermediate which eventually collapses to form the respective pinacolone products, benzopinacolone (triphenylmethyl phenyl ketone), diphenyl-*p*-tolylmethyl *p*-tolyl ketone, and phenyl di-*p*-tolylmethyl-phenyl ketone, and tri-*p*-tolylmethyl *p*-tolyl ketone. Identification of this intermediate as the epoxide, tetraphenylethylene oxide, 1,2-di-*p*-tolyl-1,2-diphenylethylene oxide, and tetra-*p*-tolylethylene oxide, respectively, was accomplished through spectrokinetic analysis and thin layer chromatography and by observing the kinetic behavior of synthetic material. The origin of the epoxide is due to the proximity of the β-hydroxyl group to the reaction center in the glycol dehydration process. Analysis of titrimetric and spectrophotometric rate measurements performed on the glycols and epoxides established the neighboring group reactivity order as OH $\geq$ *p*-tolyl > phenyl. Due consideration to the energetic requirements for the acid-catalyzed epoxide ring opening leads us to propose a carbonium ion mechanism for these reactions.

For many years the study of pinacolic rearrangements was dominated by a preoccupation with the quantitative evaluation of functional group mobilities. Since this approach proved to be fruitful especially under the able guidance of Bachmann,[4–8] Gomberg,[9]

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