Enol Allyl Chlorides as Precursors to α-Alkoxy Ketones

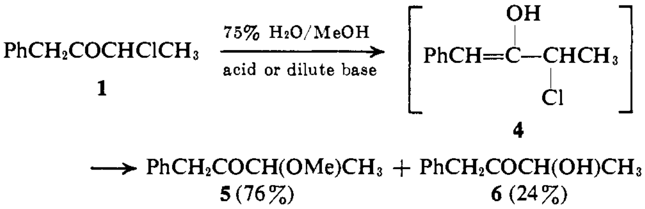
Sir:

α-Alkoxy ketones are common by-products in the Favorskii rearrangement. With certain α-halo ketones they can be made to become the predominant or even the exclusive product.[1] Mechanisms that have been considered to account for their formation include: SN2,[2] SN2′,[3] rearrangement of an epoxy ether,[2,4] cleavage of an alkylidene oxide,[4] and reaction of a dipolar ion[1,5] or cyclopropanone[1,5a] intermediate with the (alcohol) solvent. The SN2 mechanism has been discounted for valid reasons in a number of systems.[1,4] The results of a recent labeling experiment in which α-phenoxycyclohexanone-1,2,6-^{14}C was formed from α-chlorocyclohexanone-1,2-^{14}C by the action of sodium phenoxide in phenol ruled out SN2 and SN2′ pathways.[6,7] It was concluded that the α-phenoxy ketone in this instance was formed by way of either a dipolar ion or cyclopropanone intermediate.[6] It is the purpose of this paper to present evidence to show that still another mechanism, namely, solvolysis of an enol allylic chloride, is responsible for the formation of α-alkoxy ketones from the chloro ketones $\mathrm{PhCH_2COCHClCH_3}$ (**1**), $\mathrm{PhCHClCOCH_2CH_3}$ (**2**), and $\mathrm{PhCH_2COCHClPh}$ (**3**), and to suggest that this mechanism may be responsible for α-alkoxy ketone formation in at least some of the systems previously studied.

In the preceding paper evidence was presented to show that the conversion of **1** to the methoxy ketone $\mathrm{PhCH_2COCH(OMe)CH_3}$ (**5**) in dilute methanolic sodium methoxide occurred by methanolysis of the enol allylic chloride $\mathrm{PhCH{=}C(OH)CHClCH_3}$ (**4**). Additional evidence is now presented to support this view not only for **1** but also for the isomeric chloro ketone **2**, and for the analogous chloro ketone **3**. Evidence is also presented to show that certain allylic carbonium ions have a strong preference for reaction with methanol rather than water in aqueous methanol.

Chloro ketones **1**, **2**, and **3** are relatively inert to methanolysis in the absence of acidic or basic catalysts. The acid-catalyzed reactions of **1**, **2**, and **3** to form α-methoxy ketones are almost certain to proceed by methanolysis of the enol allylic chlorides. 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 **1** 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 have been applied to **1**, **2**, and **3**.

In 50% v/v $\mathrm{H_2O}$–MeOH (*ca.* 70 mole % $\mathrm{H_2O}$) acid-catalyzed (3 or 6 M *p*-toluenesulfonic acid) solvolysis of **1** gave methoxy ketone **5** and no more than a trace of $\mathrm{PhCH_2COCH(OH)CH_3}$ (**6**). Even in 75% v/v $\mathrm{H_2O}$–MeOH (*ca.* 90 mole % water) more **5** (*ca.* 76%) than **6** (*ca.* 24%) was obtained.[8] An essentially identical product distribution (*i.e.*, 76% **5** and 24% **6**) was obtained with **1** in 75% v/v $\mathrm{H_2O}$–MeOH 1 M in 2,6-lutidine or in 75% v/v $\mathrm{H_2O}$–MeOH 0.02 M in base (NaOH–NaOMe). The same product distribution was also obtained when 1.1 equiv of a 0.05 M solution of base was added to a solution of **1** over a 6-hr period in this system.



$$\underset{\mathbf{1}}{\mathrm{PhCH_2COCHClCH_3}} \xrightarrow[\text{acid or dilute base}]{75\%\ \mathrm{H_2O/MeOH}} \underset{\mathbf{4}}{\left[\mathrm{PhCH{=}\overset{\overset{\displaystyle OH}{|}}{C}{-}\underset{\underset{\displaystyle Cl}{|}}{C}HCH_3}\right]} \longrightarrow \underset{\mathbf{5}\,(76\%)}{\mathrm{PhCH_2COCH(OMe)CH_3}} + \underset{\mathbf{6}\,(24\%)}{\mathrm{PhCH_2COCH(OH)CH_3}}$$

Reaction of **3** with 50% v/v $\mathrm{H_2O}$–MeOH in acidic medium gave a result similar to that with **1**; *i.e.*, the product was $\mathrm{PhCH_2COCH(OMe)Ph}$ (**7**) and little or no hydroxy ketone was formed. An identical result was obtained using 2,6-lutidine as the catalyst. The reaction of **3** with 0.05 M base (NaOH–NaOMe) in this solvent gave a mixture of **7** and $\mathrm{PhCH_2CHPhCO_2Me}$ (relative yields 78 and 22%) with only a trace of hydroxy ketone.

Another test of the mechanism was made possible by the observation that the acid-catalyzed methanolysis of **2** gave **5**, the product of a rearrangement, and none of the "normal product," $\mathrm{PhCH(OMe)COCH_2CH_3}$ (**8**). This is not entirely unexpected since the presumed intermediate is $\mathrm{PhCHClC(OH){=}CHCH_3}$ and solvolyses of allylic chlorides often give rearranged products.[9] Reaction of **2** with 0.05 M sodium methoxide also gave **5** to the apparent exclusion of **8** (30% of **5** and 70% of Favorskii ester, **9**, were obtained).

Reaction of either **1** or **2** with 2 equiv of 0.05 M sodium phenoxide in methanol gave **5** (*ca.* 77%) and $\mathrm{PhCH_2CH(CH_3)CO_2Me}$ (**9**, *ca.* 23%). This result shows that with a [MeOH]/[NaOPh] ratio of *ca.* 900/1 the carbonium ion reacts preferentially with methanol. According to the mechanism proposed,[10] **5** is formed by solvolysis of the enol $\mathrm{PhCH{=}C(OH)CHClCH_3}$ (**4**), and **9** is formed by attack of base on the product of solvolysis of the corresponding enolate ion with which the enol is in equilibrium.

$$\left.\begin{array}{l}\underset{\mathbf{1}}{\mathrm{PhCH_2COCHClCH_3}}\\ \underset{\mathbf{2}}{\mathrm{PhCHClCOCH_2CH_3}}\end{array}\right\rangle \xrightarrow[\text{MeOH}]{0.05\ M\ \text{NaOPh}} \underset{\mathbf{5}\ (ca.\ 77\%)}{\mathrm{PhCH_2COCH(OMe)CH_3}} + \underset{\mathbf{9}\ (ca.\ 23\%)}{\mathrm{PhCH_2CH(CH_3)CO_2Me}}$$

The mechanism predicts that an increase in the acidity of the medium should increase the concentration of the enol (**4**) and result in a larger yield of products derived

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(1) A. W. Fort, *J. Am. Chem. Soc.*, **84**, 2620, 2625 (1962).

(2) (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. Troéfou¨l, *Compt. Rend.*, 240, 1115 (1955); (c) E. J. Smissman, T. J. Lemke, and O. Kristiansen, *J. Am. Chem. Soc.*, **88**, 334 (1966).

(3) J. S. G. Cox, *J. Chem. Soc.*, 4508 (1960); P. A. Diassi and R. M. Palmere, *J. Org. Chem.*, **26**, 5240 (1961).

(4) H. O. House and H. W. Thompson, *ibid.*, **28**, 164 (1963); H. O. House and G. A. Frank, *ibid.*, **30**, 2948 (1965).

(5) (a) N. J. Turro and W. B. Hammond, *J. Am. Chem. Soc.*, **87**, 3258 (1965); (b) R. C. Cookson, M. J. Nye, and G. Subrahmanyam, *J. Chem. Soc.*, *C*, 473 (1967).

(6) W. B. Smith and C. Gonzalez, *Tetrahedron Letters*, 5751 (1966).

(7) Rearrangement of an epoxy ether or cleavage of an alkylidene oxide are also excluded as possibilities by these results.

(8) This surprising preference for reaction of the carbonium ion with methanol rather than with water appears to be characteristic of an allyl carbonium ion of the type $[\mathrm{PhCH{\overset{\dots}{-}}CH{\overset{\dots}{-}}CHR}]^+$ since solvolysis of $\mathrm{PhCH{=}CHCHClCH_3}$ has been found to give over 75% of $\mathrm{PhCH{=}CHCH(OMe)CH_3}$ in 75% v/v $\mathrm{H_2O}$–MeOH (E. L. Yee, unpublished results).

(9) See, *e.g.*, R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 794 (1956).

(10) F. G. Bordwell, M. W. Carlson, and A. C. Knipe, *J. Am. Chem. Soc.*, **91**, 3949 (1969).

therefrom. In agreement with this it was found that the reaction of **1** in methanol with 0.05 *M* NaOPh in the presence of an increased concentration of phenol (0.5 *M*) gave **5** (93%), $PhCH_2COCH(OPh)CH_3$ (6%), and $PhCH(OPh)COCH_2CH_3$ (1%) to the exclusion of ester **9**.

The enol solvolysis mechanism is probably responsible for the formation of α-alkoxy ketone by-products from Favorskii rearrangements carried out with *dilute* sodium alkoxides and alcohols in a number of other systems.[1,2c,3,6,11] This side reaction is avoided in aprotic media and at high alkoxide concentrations in protic media. This is no doubt at least part of the reason that better yields of Favorskii rearrangement products are obtained at high alkoxide than at low alkoxide concentrations.[12]

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[11] J. G. Strong, Ph.D. Dissertation, Northwestern University, 1968, found that the yield of α-methoxy ketone increased markedly at the expense of Favorskii ester when low methoxide concentrations were used with α-chlorocyclohexanone and a number of its derivatives. R. G. Scamehorn, Ph.D. Dissertation, Northwestern University, 1968, found that 2-chloro- or 2-bromo-3,3-diphenylcyclopentanone reacted with 0.1 *M* NaOMe in MeOH at 0° to give an essentially quantitative yield of α-methoxy ketone.

[12] G. Stork and I. J. Borowitz, *J. Am. Chem. Soc.*, **82**, 4307 (1960).

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Tetraphenylthieno[3,4-*c*]thiophene. A Stable Nonclassical Thiophene

Sir:

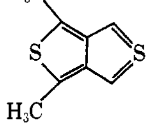
We have reported previously evidence for the transient existence of 1,3-dimethylthieno[3,4-*c*]thiophene (**1**), a derivative of a 10π-electron aromatic system for which the only uncharged resonance contributors are structures containing tetravalent sulfur.[1] We now report the synthesis of tetraphenylthieno[3,4-*c*]thiophene (**2**), an isolable and remarkably stable derivative of this same unusual aromatic system.

The reaction of tetrabenzoylethane[2] (**3**) with phosphorus pentasulfide in refluxing xylene afforded, in 46% yield, 1,3-dihydro-1,3,4,6-tetraphenylthieno[3,4-*c*]thiophene (**4**), mp 195–196°. The nmr spectrum of **4** showed two benzylic protons as a singlet at δ 5.74 and the four phenyls as a 20-proton multiplet in the range of δ 6.9–7.3. The mass spectrum of **4** showed the molecular ion as the base peak at 446, the only other significant higher mass peak appearing at 369 ($M - C_6H_5^+$, 20%).[3]

Periodate oxidation[4] of **4** gave in 96% yield the corresponding sulfoxide **5**, mp 234–235° dec, molecular weight 462 by mass spectrometry. The infrared spectrum of **5** showed a band at 9.6 μ characteristic of sulfoxides, while its nmr spectrum showed two protons α to the sulfoxide group at δ 5.37 and a 20-proton aromatic multiplet at δ 7–7.5.

Dehydration of sulfoxide **5** with refluxing in acetic anhydride[5] (N_2, 4 hr) afforded in 87% yield tetraphenylthieno[3,4-*c*]thiophene (**2**), mp 245–248°, as glistening purple needles, $\lambda_{max}^{C_2H_4Cl_2}$ 255 mμ (ε 17,000), 296 (20,000), and 553 (13,000). The nmr spectrum of **2** consists of a single sharp band at δ 7.12 suggesting that the phenyl groups lie considerably out of the plane of the thienothiophene system.[6] The mass spectrum indicates a very stable molecule showing a base peak for the molecular ion at 444, the next strongest peak above mass 130 being the M^{2+} peak (11%) at 222.

The thienothiophene **2** could also be obtained in a single operation (3% yield) by the direct reaction of tetrabenzoylethylene[7] (**6**) with phosphorus pentasulfide



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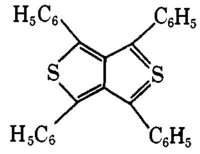
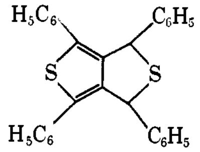


2

$(C_6H_5CO)_2CHCH(COC_6H_5)_2$

3



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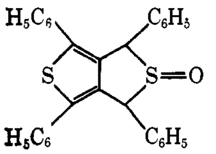
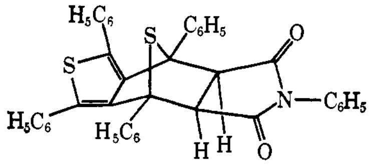


5

$(C_6H_5CO)_2C{=}C(COC_6H_5)_2$

6



exo
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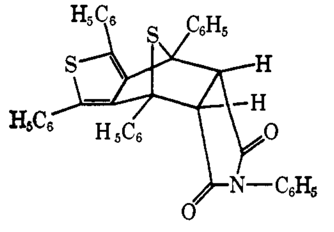

endo
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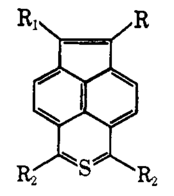

9, $R_1 = Br; R_2 = C_6H_5$

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[1] M. P. Cava and N. M. Pollack, *J. Am. Chem. Soc.*, **89**, 3639 (1967).

[2] R. D. Abell, *J. Chem. Soc. Transactions*, **101**, 997 (1912).

[3] Nmr spectra were determined in $CDCl_3$. All melting points are uncorrected. Satisfactory analyses were obtained for all new compounds. Mass spectra were recorded on an Atlas CH4 spectrometer.

[4] N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, 27, 282 (1962).

[5] M. P. Cava and N. M. Pollack, *J. Am. Chem. Soc.*, **88**, 4112 (1966).

[6] An analogous system occurs in 1,8-diphenylnaphthalene; see H. O. House, R. W. Magin, and H. W. Thompson, *J. Org. Chem.*, **28**, 2403 (1963).

[7] A. Andres, Dissertation, Strassburg, 1911.