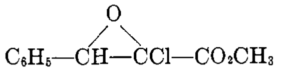
Molecular Rearrangements. III. The Nature of the Darzens Condensation Product from Benzaldehyde and Methyl Dichloroacetate[1]

RICHARD N. McDONALD AND PETER A. SCHWAB[2]

Department of Chemistry, Kansas State University, Manhattan, Kansas

Received February 4, 1964

It has been recently reported[3] that the Darzens condensation of methyl dichloroacetate and benzaldehyde with a suspension of sodium methoxide in dry ether yields the α-chloro epoxide, methyl 2-chloro-2,3-epoxy-3-phenylpropanoate (I). These authors reported that their product was stable to concentrated sulfuric acid at 150° for 5 hr., but was decomposed by base to a dehydrochlorinated polymer. The former observation made us quite skeptical of the assignment of structure from our past experiences with the acid-sensitive nature of α-chloro epoxides.

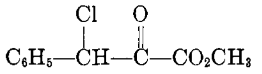


I

Our interests in the rearrangement and chemistry of α-chloro epoxides[1] prompted us to repeat this Darzens condensation. We have found that a yellow liquid is the only isolable product of the reaction and is obtained in 64% yield. Its chemical and physical properties agree with those reported[3] except for an absorption band at 945 cm.$^{-1}$ which the Russian authors attributed to an epoxide ring vibration. Since benzoic acid has a strong band at 945 cm.$^{-1}$, we believe that this absorption band is due to the acid as a contaminant. We found that the crude product contained this band after only a few aqueous base washings, but after several more base washings and careful fractional distillation, the absorption band was absent from the spectrum.

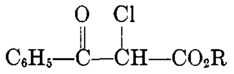
The infrared absorption spectrum of the yellow liquid product exhibited a single, sharp carbonyl peak at 1724 cm.$^{-1}$. This single carbonyl absorption may have led the Russian investigators to the assumption that only one carbonyl group was present. This need not be the case since pyruvic acid and its esters also exhibit a single, sharp carbonyl absorption.[4]

The nuclear magnetic resonance spectrum of this product was most convincing that the structural assignment was incorrect. An epoxide ring proton with an α-phenyl substituent is expected at approximately τ 6.0. This is observed for the proton of *trans*-2,3-diphenyl-2,3-epoxypropionitrile (τ 5.98), of *trans*-stilbene oxide (τ 6.32), and in styrene oxide (τ 6.17).[5] We, however, observed the proton absorption in the Darzens condensation product at τ 3.85. Since this low τ-value is indicative of a highly deshielded proton and since we have already observed the instability of α-chloro epoxides and their rearrangement to α-chloro ketones, this allows two isomeric α-chloro keto esters for consideration as possible structures for this product. They are methyl chlorophenylpyruvate (II) and methyl α-chlorobenzoylacetate (III, R = CH_3). The single carbonyl in the infrared spectrum is highly suggestive of II rather than III.



$C_6H_5\text{—}\overset{\text{Cl}}{\text{C}}\text{H—}\overset{\text{O}}{\text{C}}\text{—}CO_2CH_3$

II



$C_6H_5\text{—}\overset{\text{O}}{\text{C}}\text{—}\overset{\text{Cl}}{\text{C}}\text{H—}CO_2R$

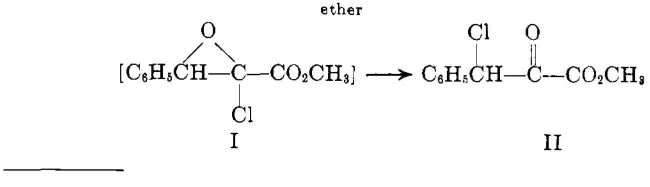
III

We, therefore, carried out independent syntheses of both II and III (R = Et). Methyl chlorophenylpyruvate (II) was prepared by chlorination of methyl phenylpyruvate with lithium chloride and copper(II) chloride in dimethylformamide[6] giving only a 21% yield of the α-chloro ketone (II), whereas sulfuryl chloride chlorination gave a 54% yield of methyl chlorophenylpyruvate (II). Its chemical, physical, and spectral properties were identical with those of the Darzens condensation product.

Treatment of ethyl benzoylacetate with lithium chloride and copper(II) chloride in dimethylformamide gave no reaction; however, treatment with sulfuryl chloride gave a 91% yield of ethyl α-chlorobenzoylacetate (III, R = Et). The nuclear magnetic resonance absorption frequency of the single proton of this compound occurred as a singlet at τ 4.41.

Attempts to prepare the intermediate α-chloro epoxide I by peroxidations of methyl *trans*-α-chlorocinnamate (IV) were carried out. However, treatment of IV with either perbenzoic acid, trifluoroperacetic acid using disodium hydrogen phosphate as base, basic 30% hydrogen peroxide in acetonitrile,[7] or 97% *t*-butyl hydroperoxide using Triton B as base[8] gave no evidence of reaction and only starting material was obtained.

Allowing for the normal mechanism of the Darzens condensation applying to this case with the intermediacy of the α-chloro epoxide I, this then establishes another example of predominant chlorine migration in an epoxide–carbonyl rearrangement and permits the following reaction scheme to be written. It is also of interest to note that none of the alternative product of hydrogen migration, III or its methyl ether, could be isolated from the Darzens condensation. This then infers that chlorine migration is greatly favored, if not exclusively favored, in the rearrangement.



---

[1] For paper II in this series, see R. N. McDonald and P. A. Schwab, *J. Am. Chem. Soc.*, **85**, 4004 (1963).

[2] This paper comprises a portion of the dissertation submitted by P. A. Schwab to the Graduate School of Kansas State University, Dec., 1963, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[3] V. F. Martynov and M. I. Titov, *Zh. Obschch. Khim.*, **32**, 319 (1962); *Chem. Abstr.*, **57**, 12,373*c* (1962).

[4] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1960, p. 141.

[5] N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962, Spectrum No. 193.

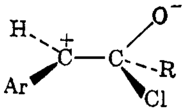
[6] E. M. Kosower, W. J. Cole, G. S. Wu, D. E. Cardy, and G. Meisters, *J. Org. Chem.*, **28**, 630 (1963).

[7] D. H. Rosenblatt and G. H. Broome, *ibid.*, **28**, 1290 (1963).

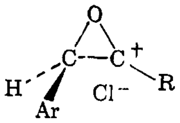
[8] G. B. Payne and P. H. Williams, *ibid.*, **26**, 651 (1961).

This result is of interest in two respects: (1) that chlorine migration accompanies the epoxide–carbonyl rearrangement under basic (or neutral) conditions in the relatively nonpolar solvent, ether, and (2) its mechanistic implications.

Our previous results[1] of chlorine migration in the epoxide–carbonyl rearrangement at the time appeared to be reasonably accommodated by a mechanism involving either a slow ring-opening step to a dipolar structure V (R = Ar′) followed by a fast intramolecular transfer of chlorine, or formation of an ion pair VI (R = Ar′) which collapses intramolecularly to yield the observed α-chloro ketone products. However, in the present case R is equal to carbomethoxy. This would make the ion pair VI less likely, assuming that a single mechanism is operative independent of the nature of Ar and R. Involvement of V, or a modification of it, would also be in line with other ring-opening reactions of epoxides, *e.g.*, bimolecular attack by some nucleophiles,[9] where bond breaking has progressed further than bond making in the transition state of the rate-determining step.



V



VI

Studies are presently under way which are expected to decide more fully these mechanistic questions.

Experimental[10]

The Reaction of Benzaldehyde and Methyl Dichloroacetate with Sodium Methoxide.—In a 250-ml. three-necked round-bottom flask equipped with a reflux condenser fitted with a drying tube, a mechanical stirrer, and a solid addition apparatus, was placed 30 g. (0.2 mole) of methyl dichloroacetate, 22 g. (0.2 mole) of benzaldehyde, and 100 ml. of anhydrous ether. While stirring at 0°, 15 g. (0.25 mole) of powdered sodium methoxide was added in small amounts. After complete addition, the yellow heterogeneous reaction mixture was allowed to warm up to room temperature and then refluxed for 1.5 hr. After completion of the reaction, water was added to dissolve all the insoluble salts. The ether layer was separated, washed several times with water, and dried over anhydrous magnesium sulfate. After the removal of solvent under reduced pressure, a thick yellow oil remained. This was fractionally distilled collecting 21 g. (64%) of a yellow liquid boiling at 135–137° (6 mm.), $n^{20}\text{D}$ 1.5302. This yellow liquid was redistilled through a spinning band column, collecting the fraction boiling at 84–86° (0.03 mm.) [lit.[3] b.p. 135° (6 mm.), $n^{20}\text{D}$ 1.5260, 66% yield].

Anal. Calcd. for $C_{10}H_9O_3Cl$: C, 56.49; H, 4.27; Cl, 16.67. Found: C, 56.60; H, 4.35; Cl, 16.58.

The spectral properties of this compound consist of the following: infrared spectrum, 3.3 and 3.4 (vw), 5.8 (s), 6.7 (vw), 6.9 and 7.0 (w), 7.7 (m), 7.9 and 8.0 (m), 9.0 (shoulder), 9.9 (s), 11.5 (m), 13.4 (shoulder), and 14.2 (s) μ; n.m.r. spectrum, τ 2.67 (5), 3.85 (1), 6.30 (3).

Methyl Phenylpyruvate.—In a 250-ml. round-bottom flask fitted with a reflux condenser and a drying tube were placed 26 g. (0.146 mole) of phenylpyruvic acid,[11] 25 ml. of methanol, 60 ml. of ethylene chloride, and 1 g. of *p*-toluenesulfonic acid. This was then refluxed for 15 hr., cooled, washed with a 10% sodium carbonate solution and water, and dried over anhydrous magnesium sulfate. Removal of solvent under reduced pressure gave 25 g. of a yellow oil which was recrystallized from Skellysolve B giving 12 g. (43%) of pure methyl phenylpyruvate, m.p. 71–73° (lit.[12] m.p. 75°).

Methyl Chlorophenylpyruvate. A. Using Sulfuryl Chloride.—In a 100-ml. three-necked round-bottom flask fitted with a reflux condenser with a drying tube, an addition funnel, and a magnetic stirrer is placed 14 g. (0.08 mole) of methyl phenylpyruvate in 50 ml. of carbon tetrachloride. While stirring at 45–50°, 11 g. (0.082 mole) of sulfuryl chloride was added dropwise. After addition the reaction mixture was allowed to react for 2.5 hr. This was then washed three times with water and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure leaving a yellow oil. Fractional distillation afforded 9 g. (54%) of methyl chlorophenylpyruvate boiling at 83–84.5° (0.03 mm.), $n^{20}\text{D}$ 1.5361. The infrared and n.m.r. spectra of this compound were identical to the compound obtained by the Darzens condensation reaction.

B. **Using the Method of Kosower.**[6]—In a 100-ml. three-necked flask fitted with a mechanical stirrer, thermometer, and reflux condenser were placed 18.7 g. (0.11 mole) of copper(II) chloride dihydrate, 2.3 g. (0.054 mole) of lithium chloride, and 30 ml. of dimethylformamide. After heating to 80° while stirring, 8 g. (0.045 mole) of methyl phenylpyruvate was added and this mixture was stirred at 80–90° for 1.5 hr. The dark reaction mixture was diluted with 30 g. of ice followed by sufficient dimethylformamide to dissolve the small amount of precipitated copper(I) chloride. The clear green reaction mixture was extracted with four 50-ml. portions of ether. The ether layers were combined, washed with 100 ml. of water, and dried over anhydrous magnesium sulfate. Removal of solvent under reduced pressure gave 5 g. of a light orange oil. Fractional distillation gave 2 g. (21% yield) of the desired product, b.p. 84–85° (0.07 mm.), $n^{20}\text{D}$ 1.5282).

Ethyl α-Chlorobenzoylacetate.—This reaction was carried out in the same manner as part A in the synthesis of methyl chlorophenylpyruvate, using the following reactants: 14 g. (0.073 mole) of ethyl benzoylacetate in 50 ml. of carbon tetrachloride and 11 g. (0.082 mole) of sulfuryl chloride. Distillation afforded a clear colorless liquid boiling at 106–108° (0.03 mm.), $n^{20}\text{D}$ 1.5318 [lit.[13] b.p. 175–177° (10 mm.), $n^{20}\text{D}$ 1.532]. Fifteen grams (91%) of pure ethyl α-chlorobenzoylacetate was obtained.

The spectral properties of this compound were as follows: infrared spectrum, 3.6 (vw), 3.9 (m), 5.7 (s), 6.0 (s), 6.3 and 6.4 (m), 6.7 (vw), 6.8 (w), 6.9 (m), 7.2 (w), 7.3 (m), 7.6 (m), 7.7 (s), 7.9 (s), 8.3 (m), 8.5 (s), 8.6 (m), 8.8 (w), 9.0 (vw), 9.1 (w), 9.3 (vw), 9.8 (m), 10.0 (m), 10.5 (w), 11.4 (w), 12.1 (m), 12.8 (w), 13.0 (w), 13.6 (w), and 14.5 (s) μ; n.m.r. spectrum, τ 1.92–2.14 and 2.40–2.62 (multiplets, 5), 4.41 (1), 5.79 (quartet, 2), and 8.83 (triplet, 3).

2,3-*trans*-Diphenyl-2,3-epoxypropionitrile.—This epoxide was prepared according to Payne and Williams,[8] m.p. 70–71°, 74% yield (lit.[8] m.p. 70–70.5°, 76% yield).

***trans*-Stilbene Oxide.**—This epoxide was prepared according to Reif and House[14]; m.p. 68–69°, 82% yield (lit.[14] m.p. 68–69°, 70–75% yield).

Acknowledgment.—The authors wish to express their appreciation to the Research Corporation for a Frederick–Gardner–Cottrell grant-in-aid support to this research. Financial assistance from the National Science Foundation for the purchase of the Varian A-60 n.m.r. spectrometer is also gratefully acknowledged.

---

(9) See J. K. Addy and R. E. Parker, *J. Chem. Soc.*, 915 (1963), and previous papers in their series, and references cited therein.

(10) All melting points were taken on a Kofler hot stage and are corrected. Boiling points are uncorrected. Infrared absorption spectra were determined on a Perkin-Elmer Model 137 double beam recording spectrophotometer. N.m.r. spectra were determined on a Varian A-60 recording spectrophotometer using carbon tetrachloride as solvent (unless otherwise stated) with tetramethylsilane as the internal standard and are singlets unless otherwise noted. Other numbers in parenthesis are the relative integrated areas. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

(11) R. M. Herbst and D. Shemin, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 519.

(12) R. Hemmerle, *Compt. rend.*, **162**, 758 (1916).

(13) E. L. Hirst, A. K. Macbeth, and D. Traill, *Proc. Roy. Irish Acad.*, **37*B***, 47 (1925); *Chem. Abstr.*, **19**, 2931 (1925).

(14) D. J. Reif and H. O. House, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p. 860.