However, sodium dicyanocuprate does offer a solubility advantage in DMF solution. The reactivity of either copper(I) cyanide or the dicyanocuprate toward aryl and vinyl halides is distinctly less than the corresponding reactions with diaryl- or dialkylcuprates.[3] A similar low order of reactivity was noted[3b] for the acetylide $(PhC\equiv C)_3CuLi_2$ in which the carbon ligands are electronically similar to cyano functions. Finally, our studies with the delocalized enolate anions derived from malonic esters and from acetophenone have provided no indication that the presence of soluble copper(I) species will accelerate the reactions of these anions with either alkyl or aryl halides. Because of these observations, we are inclined to the belief that the coupling reaction of organocopper(I) compounds with alkyl, vinyl, and aryl halides does not involve preliminary ionization of the carbon–copper(I) bond ($R_2Cu^- \rightleftharpoons RCu + R^-$) since the groups, R, most likely to provide appreciable concentrations of carbanions are those which are least reactive toward halides.

Experimental Section[6]

Starting Materials.—Commercial samples of 1-iodonaphthalene (**1**), 2-chloronaphthalene (**7**), CuCN, and NaCN were used without further purification. Anhydrous LiCN was obtained by reaction of anhydrous HCN with a suspension of LiH; the resulting suspension of LiCN was collected and dried under reduced pressure. Samples of pure *cis*- and *trans*-β-bromostyrene (**3** and **4**) were obtained as described elsewhere.[3b]

Reaction with 1-Iodonaphthalene (1).—To a heated (150–155°) solution of 104 mg (2.10 mmol) of NaCN and 179 mg (2.00 mmol) of CuCN in 10 ml of DMF was added 5.0 ml of a DMF solution containing 1.11 mmol of 1-iodonaphthalene and a known amount of hexamethylbenzene (an internal standard). Aliquots were removed periodically and partitioned between saturated aqueous NaCN and Et_2O. The organic layers were dried, concentrated, and analyzed by glpc. With the column employed,[7] the components were eluted with the following retention times: hexamethylbenzene, 8.0 min; 1-cyanonaphthalene (**4**), 10.3 min; 1-iodonaphthalene (**1**), 15.9 min. The half-life for the reaction was approximately 50 min and after a reaction time of 4 hr, the calculated yield of 1-cyanonaphthalene was 98.5%. A collected[7] sample of the cyanide **4** was identified with an authentic sample by comparison of ir spectra and glpc retention times.

For comparison, a solution containing 179 mg (2.00 mmol) of CuCN, 282 mg (1.11 mmol) of 1-iodonaphthalene, and hexamethylbenzene in 15 ml of DMF was heated to 150–155° for 4 hr. As the reaction progressed a brown precipitate (presumably CuI) separated. The final reaction mixture was worked-up and analyzed[7] as previously described; the calculated yield of 1-cyanonaphthalene (**1**) was 97%. When the same reaction was repeated with a total reaction time of 30 min at 150–155°, the calculated yields were 88% 1-cyanonaphthalene and 12% unchanged 1-iodonaphthalene.

Reaction with *trans*-β-Bromostyrene (2).—A solution of 483 mg (9.85 mmol) of NaCN, 895 mg (9.98 mmol) of CuCN, 891 mg (4.86 mmol) of *trans*-β-bromostyrene, and a known amount of biphenyl (an internal standard) in 10 ml of warm (90°) DMF was heated to reflux. Periodically, aliquots of the reaction solution were removed and partitioned between saturated aqueous NaCN and PhH. The organic layers were dried, concentrated, and analyzed (Table I). With the glpc column employed,[8] the relative retention times of components were as follows: *cis*-β-bromostyrene (**3**), 10.7 min; *trans*-β-bromostyrene (**2**), 11.7 min; biphenyl, 19.1 min; *cis*-cinnamonitrile (**6**), 24.0 min; *trans*-cinnamonitrile (**5**), 34.0 min. A collected[8] sample of the *trans*-nitrile **5**, $n^{27}{}_D$ 1.5995 [lit.[9] bp 150° (30 mm), $n^{20}{}_D$ 1.6031], ir (liquid film), 2220 (conjugated $C\equiv N$), 1625 (conjugated C=C), and 970 cm^{-1} (*trans* CH=CH), was identified with an authentic sample by comparison of ir spectra and glpc retention times. A collected[8] sample of the *cis*-nitrile **6**, $n^{27}{}_D$ 1.5818 [lit.[9] bp 132° (30 mm), $n^{20}{}_D$ 1.5843], had ir absorption (liquid film) at 2220 (conjugated $C\equiv N$), 1615 (conjugated C=C), and 775 cm^{-1} (*cis* CH=CH).

Reaction with *cis*-β-Bromostyrene (3).—A solution prepared from 897 mg (10.0 mmol) of CuCN, 486 mg (9.94 mmol) of NaCN, 912 mg (4.98 mmol) of *cis*-β-bromostyrene, and biphenyl in 10 ml of DMF was heated to 150°. Aliquots were removed periodically and subjected to the previously described work-up and analysis procedures to give the results summarized in Table I.

Reaction with 2-Chloronaphthalene (7).—After a solution prepared from 498 mg (10.1 mmol) of NaCN, 894 mg (9.99 mmol) of CuCN, 812 mg (5.00 mmol) of 2-chloronaphthalene, and hexamethylbenzene (an internal standard) in 10 ml of DMF had been refluxed for 24 hr, the reaction product contained only the unchanged starting material. On the glpc column employed[7] the retention times of relevant compounds were as follows: 2-chloronaphthalene (**7**), 7.5 min; hexamethylbenzene, 9.5 min; 1-cyanonaphthalene (**4**), 12.0 min; and 2-cyanonaphthalene (**8**), 13.5 min.

After a solution of 6.63 g (74.0 mmol) of CuCN and 1.28 g (7.40 mol) of 2-chloronaphthalene in 10.0 ml of HMP had been heated to 230–240° with stirring for 3.0 hr, the crude product amounted to 1.10 g (96%) of crude 2-cyanonaphthalene (**8**), mp 61–64°; no 1-cyanonaphthalene (**4**) was detected in the reaction product.[7] Recrystallization from hexane separated 1.02 g (85%) of 2-cyanonaphthalene as white prisms: mp 65–66° (lit.[10] mp 66°); ir (CCl_4), 2225 cm^{-1} ($C\equiv N$); mass spectrum, molecular ion *m/e* 153, abundant fragments, *m/e* 126, 75, 74, 63, 51, and 50; nmr (CCl_4), δ 8.05 (1 H d, *J* = 0.8 Hz, aryl CH at C-1), 7.3–7.9 (7 H, m, aryl CH).

For comparison, a solution of 1.33 g (14.8 mmol) of CuCN, 738 mg (14.8 mmol) of NaCN, and 661 mg (4.07 mmol) of 2-chloronaphthalene in 10 ml of HMP was heated to 225° for 4 hr during which the reaction mixture turned a very dark color. After the usual isolation and analysis[7] procedures, the calculated yields were 7% 2-cyanonaphthalene (**8**) and 93% starting chloride **7**.

Registry No.—Sodium dicyanocuprate, 21445-44-3; **1**, 90-14-2; **2**, 588-72-7; **3**, 588-73-8; **7**, 91-58-7.

---

[6] All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer, Model 237, grating spectrophotometer. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The nmr spectra were determined at 60 Mc with a Varian Model A-60 nmr spectrometer. The chemical shift values are expressed either in hertz or δ values (parts per million) relative to a tetramethylsilane internal standard. The mass spectra were obtained with a CEC Model 21–130 or a Hitachi (Perkin–Elmer) mass spectrometer. All reactions involving organometallic reagents were conducted under a nitrogen atmosphere. In each case where yields are calculated from gas chromatographic data, the chromatographic apparatus has been calibrated with known mixtures of authentic samples.

[7] A glpc column packed with silicone gum, no. SE-52, suspended on Chromosorb P was employed for this analysis.

[8] A glpc column packed with nitrile silicone gum, no. XE-60, suspended on Chromosorb P was employed for this analysis.

[9] G. B. Kistiakowsky and W. R. Smith, *J. Amer. Chem. Soc.*, **58**, 2428 (1936).

[10] P. Pfeiffer, I. Englehardt, and W. Alfuss, *Ann. Chem.*, **467**, 158 (1928).

A Thermal Isomerization Equilibrium between Conjugated and Unconjugated Unsaturated Keto Esters

PATRIA M. TAYLOR AND GLENN FULLER

Western Regional Research Laboratory, Agricultural Research Service, United States Department of Agriculture, Albany, California 94710

Received January 30, 1969

Instances in which compounds isomerize out of conjugation are quite unusual. In 1958 King[1] observed that, in the absence of oxygen, 12-oxo-*trans*-10-oct-

[1] G. King, *J. Chem. Soc.*, 1485 (1958).

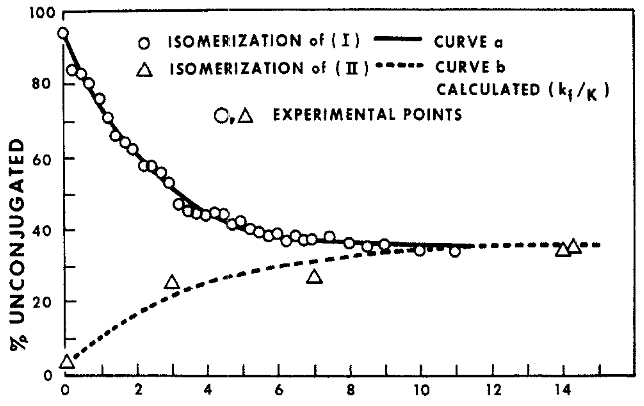
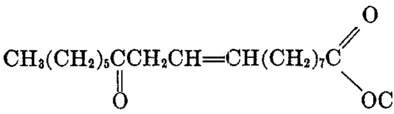
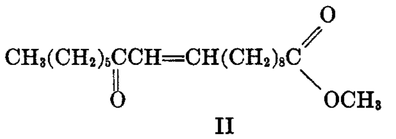


Figure 1.—Kinetic curves for the thermal isomerizations of I and II at 180°.

adecenoic acid (an α,β-unsaturated ketone) isomerized to 12-oxo-*trans*-9-octadecenoic acid (a β,γ-unsaturated ketone), at 78° over a period of 7 days, the equilibrium position favoring the conjugated ketone to an extent of 60–70%. During our studies on thermal isomerizations, we observed a similar α,β-unsaturated ketone isomerizing out of conjugation. Since this suggested that only a small energy difference existed between unconjugated and conjugated forms of these compounds, it was decided to investigate further this phenomenon and verify the structure of the two compounds. For this study, the following compounds were prepared:


$CH_3(CH_2)_5C(=O)CH_2CH{=}CH(CH_2)_7C(=O)OCH_3$

I


$CH_3(CH_2)_5C(=O)CH{=}CH(CH_2)_8C(=O)OCH_3$

II

Compound I, methyl 12-oxo-*cis*-9-octadecenoate, was prepared *via* the chromic acid oxidation of methyl 12-hydroxy-*cis*-9-octadecenoate[2] and further purified *via* silicic acid chromatography[3] for characterization. The infrared spectrum shows absorption at 3020 (CH=CH), 2930 and 2855 (CH_2), 1740 (ester C=O), 1720 (keto C=O), and 730 cm^{-1} [$(CH_2)^{4+}$]. The Raman spectrum verifies the absorbances at 3020, 1740, and 1720 cm^{-1} and also shows absorption at 1653 cm^{-1} (CH=CH). The mass spectral ion pattern of compound I gives a parent mass of 310 and shows that the unconjugated unsaturated ketone is preferentially cleaved on either side of the oxo group (*m/e* 85,113). The nmr spectrum of compound I shows the following: three methyl protons at 0.89 ppm, 18 insulated methylene protons at 1.32 ppm, six shielded methylene protons α to C=C or C=O at *ca.* 2.21 ppm, two methylene protons α to both C=C and C=O at 2.97 and 3.06 ppm, three methoxy protons at 3.6 ppm, and two olefinic protons at 5.46 ppm.

Compound II, methyl 12-oxo-*trans*-10-octadecenoate, was prepared by sulfuric acid catalyzed isomerization of compound I[2] and purified for characterization *via* argentation chromatography.[4] The infrared spectrum of compound II shows absorption at 3020 (CH=CH, slight shoulder), 2930 and 2855 (CH_2), 1740 (ester C=O), 1677 (keto C=O; shifted from 1720 cm^{-1} on conjugation), 1630 (CH=CH; also shifted due to conjugation), 980 (*trans*[5] C=C), and 730 cm^{-1} [$(CH_2)_{4+}$]. The Raman spectrum verifies absorption at 1740, 1677, and 1630 cm^{-1}. Compound II exhibits a maximum absorbance in the ultraviolet at 217 mμ and obeys Beer's law over the concentration range studied (0.48 to 3.56 mg/ml). The extinction coefficient for the conjugated material is 4434. This value is low compared to previously published values on 70% pure material.[1,6] The crude material gives an apparent ϵ of 10,000, but this is probably due to contamination by conjugated dienes and α,β-unsaturated aldehydes. The value for the purified material is consistent with that of other α,β-unsaturated ketones.[7] The mass spectral ion pattern of compound II is more complex than that of I and reflects the stability of the conjugated system, showing less cleavage α to the oxo group (*m/e* 85 and 113) and predominant cleavage between C_9 and C_{10}, at the olefinic carbon β to the oxo group (*m/e* 139). Evidence is seen of a McLafferty rearrangement[8] (*m/e* 240 and 208) and the parent mass appears at 310. Comparison of the nmr spectrum of compound II with that of the unconjugated keto ester I shows that upon conjugation we now have 20 insulated methylene protons at 1.30 ppm (due to the two protons no longer di-α to C=C and C=O) and the two olefinic protons now appear as a singlet at 3.22 ppm; presumably due to the resonance of the conjugated system, the two protons are equivalent and equally shielded.

The thermal isomerizations of I and II were carried out in the absence of solvent, at 180° under a nitrogen atmosphere, the progress of the isomerization being followed by analysis of aliquot samples on glpc. At equilibrium, the mixture was separated by chromatography on silicic acid and silver-saturated ion exchange resin and the resulting compounds were characterized by comparison to I and II. The kinetics of the thermal isomerization of I at 180° are shown in Figure 1, curve a.[9] Let us call the product of this isomerization A. The rate of isomerization of I was completely unaffected by addition of 5% Ionox 330, a hindered-phenol radical trap type inhibitor. The isomerization was first order, with $k_{180°} = 1.38 \times 10^{-4}$ sec^{-1}. By repeating the thermal isomerization at 200° and obtaining $k_{200°} = 4.15 \times 10^{-4}$ sec^{-1}, we could calculate the activation energy, E^*, and thus the entropy change over this temperature range. Thus

$$E_{av}^* = 23.0 \text{ kcal/mol}$$

$$\Delta S_{av} = 48.8 \text{ cal/deg}$$

The equilibrium concentrations of isomers in each case were found to be 36% unconjugated and 64% con-

---

[2] J. Nichols and E. Schipper, *J. Amer. Chem. Soc.*, **80**, 5705 (1958).

[3] E. N. Frankel, C. D. Evans, H. A. Moser, D. G. McConnell, and J. C. Cowan, *J. Amer. Oil Chem. Soc.*, **38**, 130 (1961).

[4] E. A. Emken, C. R. Scholfield, and H. J. Dutton, *ibid.*, **41**, 388 (1964).

[5] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1958, Chapters 3 and 9.

[6] G. W. Ellis, *J. Chem. Soc.*, 9 (1950).

[7] J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, p 12.

[8] F. W. McLafferty, "Mass Spectrometry of Organic Ions," Academic Press, New York, N. Y., 1963, p 430.

[9] k_f was calculated from a plot of log (% unconjugated$_t$ − % unconjugated$_{eq}$) *vs.* time. k_r was calculated from $K_{eq} = k_f/k_r$.

jugated ketones. Compound A was characterized and found to be identical with II by infrared and Raman spectroscopy [1675 (keto C=O), 1630 (CH=CH), and 980 cm^{-1} (*trans* C=C)], uv spectroscopy (ϵ 4,580), nmr, and mass spectrometry. The product of the thermal isomerization of II, which we will refer to as B, shows a mass spectral pattern identical with that of I. The nmr spectrum of B shows peak positions indistinguishable from those of I, but any differences in fine structure that may exist between *cis* and *trans* isomers are obscured by the limitations of resolution of the instrument. The infrared spectrum of B differs from that of I only in its predominantly *trans* configuration, which shifts CH=CH to 1664 cm^{-1},[10] and absorbs at 970 cm^{-1}. These absorptions are confirmed by Raman spectra. Comparison with infrared measurements using methyl-*trans*-9-octadecenoate as standard shows B to contain 74% *trans*-9 I and 26% *cis*-9 I isomers. The overall thermal isomerization may be represented by eq 1.

$$\underset{36\%}{\text{unconjugated I}} \;\underset{k_r}{\overset{k_f}{\rightleftarrows}}\; \underset{64\%}{\text{conjugated II}} \qquad \overset{}{180^\circ/N_2} \qquad (1)$$

No attempt was made to follow the kinetics of k_r, as from the equilibrium constant for eq 1 and the rate constant k_f, one can calculate k_r, which was found to be 0.785×10^{-4} sec^{-1}. Curve b, Figure 1, shows the calculated curve for k_r, and it can be seen that the experimental points verify the shape of the curve.

As no mechanistic study of this isomerization has been attempted, it would be presumptuous to propose a mechanism beyond stating that, from molecular models of the two compounds, several factors suggest a multicenter-type mechanism between the unconjugated and conjugated forms. Some four-center rearrangements reported[11] have the following points in common with the thermal isomerization studies: (1) high temperatures of 180–200° are necessary; (2) they are subject to acid catalysis but it is not required, the acid-catalyzed reaction having a polar mechanism while the uncatalyzed reaction exhibits a four-center type mechanism; (3) α,β conjugation is often associated with multicenter-type mechanisms; and (4) the reactions exhibit a first-order reaction rate, the rate being unaffected by free radical inhibitors.

While the thermal isomerization of unconjugated I to conjugated II is a more efficient preparation of compound II than existing methods, the most significant feature of this isomerization is that, while equilibrium favors the conjugated form, the energy difference between the two forms is so low that the conjugated ketone will reisomerize appreciably to the unconjugated form. Why isomerization occurs out of conjugation in this compound is not understood at the present time, but from characterization of the isomerization products, there is no doubt that the conjugated, α,β-unsaturated ketone II thermally isomerizes to the unconjugated, β,γ form.

Experimental Section

Preparation of Methyl 12-Oxo-*cis*-9-octadecenoate.—The procedure followed is that of Nichols and Schipper,[2] carried out on a 100-g scale. This procedure involves chromic acid oxidation of methyl 12-hydroxy-*cis*-9-octadecenoate (prepared from castor oil). The yield obtained from six different preparations averaged 55%, the purity as determined by glpc being 88–90%. The purity seemed unaffected by the low-temperature crystallizations included in the procedure.

Preparation of Methyl 12-Oxo-*trans*-10-octadecenoate.—This material was prepared from methyl 12-oxo-*cis*-9-octadecenoate *via* sulfuric acid catalysis.[2] The yield obtained was 40%, the purity (glpc) being 65–70%.

Silicic Acid Partition Chromatography.—The silicic acid column was prepared according to Frankel, *et al.*,[3] and was used to further purify I and isomerization product B. The column used was 20 × 400 mm and was packed with 100 g of silicic acid prepared in 20% methanol–benzene and slurried in 1% methanol–benzene. Approximately 300 mg of sample was introduced in 2–3 ml of 1% methanol–benzene and the eluate was collected at the rate of 1.5 ml/min. The column was followed by tlc, the fractions being evaporated to dryness, weighed, and analyzed in acetone solution by glpc. The maximum purity (glpc) obtained was 94% unconjugated and 6% conjugated. This may indicate a slight amount of thermal isomerization under glpc conditions.

Argentation Chromatography.—The method of Emken, *et al.*,[4] was used to purify the conjugated II and isomerization product A. The column used was 20 mm × 180 cm and was packed with 240 g of a very porous large surface area cation-exchange resin which had been previously saturated with silver ions. The sample (300 mg) was introduced in methanol solution and the column was run in methanol with an elution rate of 0.5 to 1.5 ml/min. The maximum purity (glpc) obtained was 94% conjugated ketone.

Thermal Isomerizations.—These isomerizations were run on liquid samples, completely in the absence of any solvent. The amounts of sample varied from 5 g to 3 mg; therefore, the vessels varied from 20-ml three-neck flasks to sealed melting point capillaries. The ratio of surface area of the glass vessel to the volume of solution had no effect on the rate of isomerization or on the products obtained. The isomerizations were always carried out with nitrogen atmosphere at temperatures of 180° or above, using an oil bath controlled by a variac. Both I and II were isomerized in this manner, the products being analyzed *via* glpc, isolated, and characterized.

Chromium Analysis.—Analysis of 10 g of I prepared *via* chromic acid oxidation indicated the presence of 5 ppm of chromium. This trace amount might possibly be acting as a catalyst in the isomerization, although the usual minimum concentrations of catalyst used for double-bond isomerization or conjugation are of the order of 10^4 times this amount at 200° or higher.[12] If the isomerizations were being catalyzed by chromium, then one would not expect the isomerizations to occur on preparative glpc columns, as presuming the chromium compound could survive the 260° injector temperature of the instrument, it would be separated on the column from the high molecular weight aliphatic ketones and be ineffective as a catalyst. As the isomerization is observed to take place in the glpc from periods of time of 0.5 to 12 hr, it is presumed that the chromium does not take part in the isomerization. As all methods of preparation of I involve oxidation *via* chromium[1,2] or aluminum[2,13] compounds, it is doubtful that I or II could be obtained entirely free of traces of these potential catalysts.

Gas–Liquid Partition Chromatography Conditions.—A Varian Aerograph Model 1525[14] equipped with flame ionization detector was used with an injector temperature of 265°, an oven temperature of 225°, and a helium flow of 40 ml/min. Various columns were evaluated for the maximum resolution between unconjugated and conjugated ketones; these included 9% Versamid, 10% GE-XE60, and 10% FFAP. Maximum resolution was obtained with the latter, the analytical column measuring 8 ft × $^1/_8$ in. stainless steel, packed with 10% FFAP on 70/80 Chromosorb W, acid-washed (A-W) DMCS. Samples were introduced in

---

[10] K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p 24.

[11] J. S. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 25.

[12] S. B. Radlove, H. M. Teeter, W. H. Bond, J. C. Cowan, and J. P. Kass, *Ind. Eng. Chem.*, **38**, 997 (1946).

[13] K. Mihara and K. Takaoka, *Nippon Kagaku Zasshi*, **79**, 282 (1958); *Chem. Abstr.*, **54**, 4366*i* (1960).

[14] Reference to a company or product name does not imply approval or recommendation of the product by the U. S. Department of Agriculture to the exclusion of others that may be suitable.

acetone solution, retention times of the unconjugated and conjugated isomers being 10.9 and 15.4 min, respectively. Preparative columns employed were: 7 ft × 0.25 in. aluminum 10% FFAP, 70/80 Chromosorb W; 8 ft × $^3/_8$ in. aluminum, 10% FFAP, 70/80 Chromosorb W; and 20 ft × $^3/_8$ in. aluminum, 20% FFAP on 60/70 Chromosorb W. All samples were injected without dilution by solvent, but on all preparative columns isomerization was noted, presumably due to prolonged times at high temperatures; therefore, preparative chromatography could not be used to further purify the isomers.

Spectroscopic Techniques.—Infrared measurements were carried out on a Perkin-Elmer Model 257 spectrophotometer, using liquids on sodium chloride plates, or solutions of carbon tetrachloride and carbon disulfide. Raman spectra were obtained on a Perkin-Elmer LR-1 spectrophotometer equipped with a 70-mW Ne–He 6328-Å gas laser, using a liquid sample in borosilicate glass capillary cells. Ultraviolet spectra were obtained in cyclohexane solution on a Beckman DK-2 spectrophotometer, using 0.1-mm quartz cells. Nmr measurements were carried out at room temperature on 10% carbon tetrachloride solutions with tetramethylsilane as an internal standard, using a Varian A-60 Model spectrometer. Mass spectrometry was carried out on a Bendix Model 12 time-of-flight mass spectrometer (70 eV).

Registry No.—I (*cis*), 3047-65-2; II (*trans*), 21308-79-2.

Acknowledgment.—The authors wish to express their gratitude to Mrs. S. Kint and Mr. G. Bailey for Raman spectra, Mr. D. Black for mass spectral measurements, and Dr. H. E. De La Mare for nmr spectra and valuable discussions.

Linear Free-Energy Relationship between Alcohol pK_a and Solvolysis Rates of Esters Where Substituent Variation Is in the Alkyl Portion of the Ester

Joseph R. Robinson and Lloyd E. Matheson

School of Pharmacy, University of Wisconsin,
Madison, Wisconsin 53706

Received February 19, 1969

It has previously been shown[1-3] that rates of solvolysis of some acetate esters can be linearly related to the pK_a of the leaving group. The purpose of the present report is to extend this correlation to other ester series, many of which have heretofore not followed a linear free energy relationship, to demonstrate that alcohol pK_a serves as a very effective model for ester solvolysis.

A number of attempts have been made in the past to correlate rates of solvolysis of aliphatic esters with model systems in order to generate linear free energy relationships.[4] The most successful of these, for variation in the acyl portion of aliphatic esters, has been the treatment by Taft.[5] Taft eliminates the variable steric requirement in these reactions by subtracting the rate of acid hydrolysis (mainly sterically controlled) from the rate of alkaline hydrolysis (polar and sterically controlled) to generate polar substituent constant (σ^*). Successful application of σ^*, for a wide variety of reactions, has been made with a Hammett-type expression[6]

$$\log \frac{k}{k_0} = \sigma^*\rho^* \tag{1}$$

In reaction series that follow eq 1, the steric effect can be assumed to be constant or negligible.

For variation in the alkyl portion of aliphatic esters, correlation of hydrolytic rates with σ^* have been unsuccessful.[7] The reason for this failure was shown[7] to be a variable steric requirement in the alkyl portion of the ester; the steric effect was reported to be larger in the alkyl than in the acyl portion of these esters.

Since alcohol dissociation represents the only effective model for aliphatic esters, where substituent variation is in the alcohol portion of the ester, it seems worthwhile to extend this correlation to other series to demonstrate the generality of the procedure.

Table I demonstrates the linear relationship that exists between rates of solvolysis and pK_a of the alcohol for a variety of esters. The symbolism used in Table I has the following meaning: Q is the least-squares fitted slope of a log rate constant *vs.* pK_a plot, S is the standard deviation of points from the line, and R is the correlation coefficient for the line. Every oxygen ester series tested with this model gave excellent correlation, while thiol ester hydrolysis could not be correlated with alcohol pK_a. That thiol ester correlation failed is not surprising considering the difference in size, polarizability, and electron configuration of a mercaptan sulfur and an alcohol oxygen.

It is not at all obvious that alcohol dissociation would serve as a model for ester hydrolysis since it is well known that a considerable steric influence exists in the alkyl portion of aliphatic esters, and steric influence in acid dissociation of alcohols is unexpected. Moreover, Taft,[5d] and Ballinger and Long[8] have reported that the pK_a of alcohols is linearly related to σ^* and one might have supposed, therefore, that correlation of rates of hydrolysis with pK_a would not be feasible, since nonlinearity is observed when rate constants of hydrolysis are plotted against σ^*. However, σ^*, as used by both Taft and by Ballinger and Long, refers to R in RCH_2OH. The interposition of a methylene group between R and OH effectively removes the steric influence. Figure 1 demonstrates the degree of scattering that occurs when σ^* is defined as R in ROH as compared with R in RCH_2OH. It is precisely this steric influence that is paralleled in ester hydrolysis, and for this reason alcohol dissociation is a good model for ester reactions (CPK models of the alcohols show significant shielding of the oxygen for any chain length above ethyl).

It would appear from the above discussion that successful correlation of rates of hydrolysis of aliphatic esters, where substituents are in the alkyl component of the ester, can be made using σ^* if we define σ^* as R in $RCH_2O(C{=}O)R'$. Treatment of the alkaline hydrolysis data for benzoates, in this manner, does show a marked

---

[1] T. C. Bruice, T. H. Fife, J. T. Bruno, and N. E. Brandon, *Biochemistry*, **1**, 7 (1962).

[2] J. F. Kirsch and W. P. Jencks, *J. Amer. Chem. Soc.*, **86**, 837 (1964).

[3] W. P. Jencks and M. Gilchrist, *ibid.*, **90**, 2622 (1968).

[4] J. E. Leffler and E. Grunwald, "Rates and Equilibrium of Organic Reaction," John Wiley & Sons, Inc., New York, N. Y., Chapter 7, 1963.

[5] (a) R. W. Taft, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Chapman and Hall, London, 1956, p 556; (b) R. W. Taft, *J. Amer. Chem. Soc.*, **74**, 3120 (1952); (c) *ibid.*, **74**, 2729 (1952); (d) *ibid.*, **75**, 4231 (1953).

[6] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p 186.

[7] R. W. A. Jones and J. D. R. Thomas, *J. Chem. Soc.*, *B*, 661 (1966).

[8] P. Ballinger and F. A. Long, *J. Amer. Chem. Soc.*, **82**, 795 (1960).