or air[3] as catalysts has been reported. It is of interest to note that these investigators did not report the formation of any dicarbonyl compound, although it is known that alcohols are readily oxidized to the carbonyl group. Traynelis and Hergenrother,[4] for instance, have reported the oxidation of a large number of benzyl alcohols using DMSO with a stream of air passing through the reaction medium.

Believing that α-hydroxy ketones should readily oxidize to the diketone with DMSO, we proceeded to investigate this reaction. Several methods for the oxidation of alcohols with DMSO have been reported.[5,6] In our investigation, the method of Albright and Goldman[5] using DMSO in the presence of acetic anhydride was used. We now report the smooth oxidation of several acyloins to the diketone in good yield.

It is believed the oxidation proceeds through an intermediate **1** formed by the reaction of the sulfoxide with the acetic anhydride[5,7] (Scheme I). This species can then be attacked by the OH of the acyloin to give rise to the alkoxysulfonium salt **2**, which subsequently loses a proton to give the dicarbonyl compound **3**.

SCHEME I

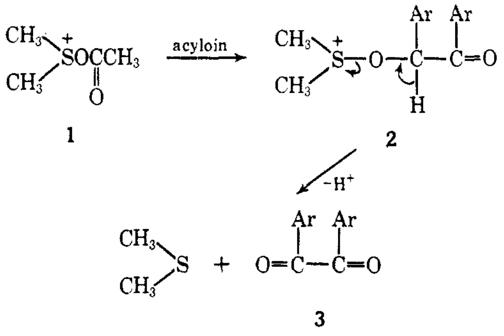

Table I gives the melting points and percentage yields of the products obtained in the oxidation. The yields of the dicarbonyl compounds obtained in the oxidation of benzoin and anisoin were good, indicating that little or no cleavage of the α-hydroxy ketone took place. The comparative low yield in the furoin to furil oxidation may be due to cleavage or to formation of degradation products. The nature of these is currently under investigation. Infrared studies of the diketone obtained in each case showed the absence of the OH and confirmed the structure of the product. The results of an elemental analysis[8] of each diketone agreed with the theoretical calculations. The diketone was further confirmed by the preparation of a 2,4-dinitrophenylhydrazone (2,4-DNPH) derivative as indicated in Table I.

TABLE I

RESULTS OF OXIDATION WITH DMSO

| Compd oxidized | Product | Yield, % | Mp (lit.), °C | Mp (lit.) of 2,4-DNPH derivative, °C |
|---|---|---|---|---|
| Benzoin | Benzil | 77 | 93.5–94.5 (95) | 187–189 (189, 185) |
| Anisoin | Anisil | 88 | 131–133 (133) | 188[a] (unknown) |
| Furoin | Furil | 31 | 162–164 (165) | 212.5–213 (215) |

[a] The substance obtained upon reaction of anisil with the 2,4-DNPH reagent was submitted to infrared analysis and to a molecular weight determination with a mass spectrometer (CEC-21-103C, direct probe). Both analyses confirmed the suspicion that the derivative obtained was actually the mono-2,4-dinitrophenylhydrazone of anisil.

Preliminary investigations with two aliphatic acyloins, namely, 3-hydroxy-2-butanone and 2-hydroxycyclohexanone, indicate that DMSO–acetic anhydride solution does oxidize aliphatic acyloins to the diketone. However, using the same procedure as that used for the aromatic acyloins only low yields were obtained. Present investigations are concerned with modifying this procedure.

## Experimental Section

**Oxidation of α-Hydroxy Ketone.**—The α-hydroxy ketone (0.01 mole) was placed in a flask containing 20 ml of acetic anhydride and 30 ml of DMSO. After stirring at room temperature for approximately 16 hr, the contents of the reaction flask were poured into 250–300 ml of ice water. The aqueous solution was extracted with three 50-ml portions of ether, benzene, or $CHCl_3$. The extract was washed with three 50-ml portions of 5% $NaHCO_3$ solution and four 50-ml portions of water, then dried with anhydrous $Na_2SO_4$ and decolorized with Norit. Following filtration, the organic solvent was removed using a rotatory evaporator, leaving the crystalline diketone. One recrystallization usually gave a relatively pure product. For melting points, yields, and melting points of the 2,4-dinitrophenylphyrazones prepared, see Table I.

**Registry No.**—Dimethyl sulfoxide, 67-68-5; benzil, 134-81-6; anisil, 1226-42-2; anisil 2,4-DNPH derivative, 13449-03-1; furil, 492-94-4.

**Acknowledgments.**—M. V. D. gratefully acknowledges a 1966 Research Initiation Summer Faculty Fellowship from the University of Colorado Council on Research and Creative Work.

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[3] T. Tsuji, *Tetrahedron Letters*, 2413 (1966).

[4] V. J. Traynelis and W. L. Hergenrother, *J. Am. Chem. Soc.*, **86**, 298 (1964).

[5] J. D. Albright and L. Goldman, *ibid.*, **87**, 4214 (1965).

[6] K. E. Pfitzner and J. G. Moffatt, *ibid.*, **85**, 3027 (1963).

[7] J. D. Albright and L. Goldman, *ibid.*, **89**, 2416 (1967).

[8] Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

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# Aromatic Cyclodehydration of 2-Benzylphenyl and 2-(1-Naphthylmethyl)phenyl Benzo[*b*]thienyl Ketones[1]

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The currently accepted mechanism for Bradsher's aromatic cyclodehydration reaction[3] was postulated in 1949 (see Chart I).[4] The reaction involves reversible protonation of the carbonyl oxygen atom to form a

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[3] C. K. Bradsher, *J. Am. Chem. Soc.*, **62**, 486 (1940).

[4] C. K. Bradsher and F. A. Vingiello, *ibid.*, **71**, 1434 (1949).

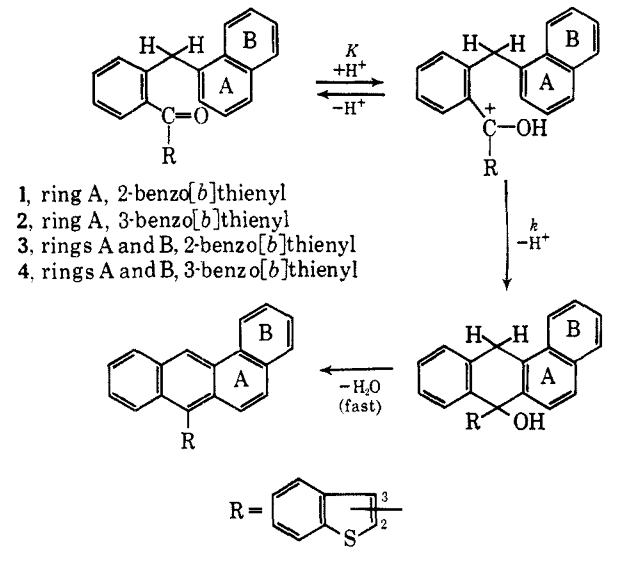
TABLE I

RATE CONSTANTS FOR THE HYDROBROMIC ACID CATALYZED CYCLIZATION OF BENZO[*b*]THIENYL KETONES IN ACETIC ACID[a]

| Ketone | Product | Temp, °C | $k \times 10^6$,[b] sec$^{-1}$ | Relative[c] rate |
|---|---|---|---|---|
| 2-Benzylphenyl 2-benzo[*b*]thienyl ketone (**1**) | 9-(2-Benzo[*b*]thienyl)anthracene | 97.1 | 7.90 | |
| | | 87.5 | 3.36 | 4 |
| | | 77.8 | 1.70 | |
| 2-Benzylphenyl 3-benzo[*b*]thienyl ketone (**2**) | 9-(3-Benzo[*b*]thienyl)anthracene | 97.1 | 1.95 | |
| | | 87.5 | 0.87 | 1 |
| | | 77.8 | 0.75 | |
| 2-(1-Naphthylmethyl)phenyl 2-benzo[*b*]thienyl ketone (**3**) | 7-(2-Benzo[*b*]thienyl)benz[*a*]anthracene | 97.1 | 294.0 (46.8)[d] | |
| | | 87.5 | 170.0 (18.6)[d] | 151 |
| | | 77.8 | 92.7 (6.4)[d] | |
| 2-(1-Naphthylmethyl)phenyl 3-benzo[*b*]thienyl ketone (**4**) | 7-(3-Benzo[*b*]thienyl)benz[*a*]anthracene | 97.1 | 69.5 (12.2)[d] | |
| | | 87.5 | 41.7 (5.8)[d] | 36 |
| | | 77.8 | 23.6 (3.2)[d] | |

[a] 1.0 *M* hydrobromic acid; anhydrous medium. [b] Average of three to four determinations. [c] Compared at 97.1°. [d] 1.0 *M* hydrobromic acid–5.0 *M* water.

CHART I



carbonium ion which then undergoes electrophilic substitution on an aromatic nucleus to form a dihydro alcohol. The alcohol readily dehydrates under reaction conditions, forming the completely aromatic product. As illustrated, the reaction rate is controlled by the protonation equilibrium ($K$) and the electrophilic substitution ($k$) reactions ($k_{\text{obsd}} = Kk$).[5]

Kinetic studies are complicated by the weak protonating ability of the acid medium. A comparison of the ultraviolet spectra of ketones **1** and **2** dissolved in 95% ethanol, glacial acetic acid, and a 1.0 *M* anhydrous hydrobromic acid–acetic acid mixture demonstrated no shifts in absorption peaks. Significant protonation by the acid medium should have altered absorption patterns.[6]

This problem becomes manifest when one considers the effects of substituents on reaction rates. The two mechanistic steps which control the reaction rate are possibly of comparable magnitudes and have opposing electrical requirements. Electron-releasing substituents bonded to the carbonyl group would enhance the degree of protonation; however, at the same time the positive character and reactivity of the carbonium ion would be decreased. The measured result should reflect a cancellation of electronic effects. This observation has been noted in some cases,[4] and it has been suggested that steric considerations might be important and should not be ignored.[7,8]

The purpose of this investigation was to study the rates at which various ketones undergo aromatic cyclodehydration in order to evaluate the relative significance of electronic and steric effects. The ketones selected for this study, **1**–**4**, were prepared as previously reported.[9]

The kinetic data presented in Table I reveal a pseudo-first-order rate law with respect to ketones and clearly demonstrate: (1) a fourfold variation in rate with respect to the linkage of the benzo[*b*]thiophene moiety to the carbonyl group (compare ketones **1** and **3** with **2** and **4**, respectively), (2) a large enhancement in the reaction rate proceeding from cyclization into a phenyl ring (ketones **1** and **2**) to ring closure into a naphthyl system (ketones **3** and **4**), and (3) a retarding of the reaction rate by addition of water to the acid medium.

The noted decrease in the reaction rate accompanying the addition of water to the acid medium was as expected. Water reduces the acidity of the medium, concomitantly reversing the protonation equilibrium.[10] Likewise, considering the mechanism proposed in Chart I, one would expect faster cyclization into a naphthalene ring than into a benzene ring. The different substituents would have little or no electronic effect on the protonation equilibrium[11] and only the attack of the carbonium ion on the aromatic system need be considered. It is generally known that naphthalene is more susceptible to electrophilic substitution than benzene. The fact that cyclization occurs approximately 36 times

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(5) F. A. Vingiello, J. G. van Oot, and H. H. Hannabass, *J. Am. Chem. Soc.*, **74**, 4546 (1952).

(6) R. Stewart and K. Yates, *ibid.*, **80**, 6355 (1958).

(7) E. Berliner, *ibid.*, **66**, 533 (1944).

(8) F. A. Vingiello and J. R. Thornton, *J. Org. Chem.*, **31**, 659 (1966).

(9) F. A. Vingiello and P. D. Henson, *ibid.*, **31**, 1357 (1966).

(10) L. K. Brice and R. D. Katstra, *J. Am. Chem. Soc.*, **82**, 2669 (1960).

(11) This point is substantiated by a comparison of the carbonyl stretching frequencies of the two pairs of ketones. The 2-benzo[*b*]thienyl ketones, **1** and **3**, absorb at 1656 and 1657 cm$^{-1}$ and the 3-benzo[*b*]thienyl ketones, **2** and **4**, absorb at 1650 and 1647 cm$^{-1}$, illustrating no significant difference between phenyl and naphthyl substitution.

faster into a naphthalene ring demonstrates that the higher electron density overcomes the statistical advantage of a phenyl ring.

Explanation of rate variations concomitant with changes in the position of benzo[*b*]thiophene substitution is not so simple. Since the benzo[*b*]thiophene moiety is bonded to the carbonyl group, variations in positions of linkage affect both the equilibrium and electrophilic substitution steps. The fourfold difference in the rates of the 2- and 3-benzo[*b*]thienyl ketones suggest either a difference in the electrical susceptibility of the two rate-controlling steps or, more probably, steric control of the reaction.[8]

The latter is substantiated by an examination of the activation parameters for the reactions (see Table II). It is readily apparent from a consideration of Table II that the cyclodehydration reactions involve rather large negative entropies of activation. A comparison of Tables I and II reveals that the 2-benzo[*b*]thienyl ketones, **1** and **3**, which cyclize faster than their corresponding 3 isomers, **2** and **4**, also have higher activation energies. If one evaluates the relative reaction rates of the 2-benzo[*b*]thienyl ketones *vs.* the 3-benzo[*b*]thienyl derivatives in terms of the isokinetic relationship,[12] it is apparent that the differences are due to entropy ($\Delta S^*$) effects. Molecular models reflect increased steric requirements for ring closure of the 3-benzo[*b*]thienyl ketones, and a plot of $\Delta H^*$ *vs.* $\Delta S^*$ for the reactions gives a straight line with a slope of 333°*K* or 60°C. Certainly a greater number of reactions must be studied to give credence to the accuracy of the isokinetic temperature, in part due to the vagaries of this thermodynamic method.[13] However, cyclodehydration reactions of the type studied are generally performed well above 60°, either in boiling acetic acid (118°) or at higher temperatures in sealed tubes.

TABLE II

ACTIVATION PARAMETERS FOR CYCLODEHYDRATION REACTIONS

| Ketone | $E_a$,[a] kcal/mole | $\Delta H^*$,[b] kcal/mole | $\Delta S^*$,[b] eu |
|---|---|---|---|
| 2-Benzylphenyl 2-benzo[*b*]thienyl ketone (**1**) | 20.6 | 19.9 | −28.8 |
| 2-Benzylphenyl 3-benzo[*b*]thienyl ketone (**2**) | 16.0 | 15.3 | −44.3 |
| 2-(1-Naphthylmethyl)phenyl 2-benzo[*b*]thienyl ketone (**3**) | 16.7 | 16.0 | −31.8 |
| 2-(1-Naphthylmethyl)phenyl 2-benzo[*b*]thienyl ketone (**3**) | 26.1[c] | 25.4[c] | −10.2[c] |
| 2-(1-Naphthylmethyl)phenyl 3-benzo[*b*]thienyl ketone (**4**) | 14.4 | 13.7 | −45.6 |
| 2-(1-Naphthylmethyl)phenyl 3-benzo[*b*]thienyl ketone (**4**) | 17.6[c] | 16.9[c] | −36.1[c] |

[a] Determined graphically from log *k* *vs.* 1/*T*. [b] Calculated from absolute rate equation at 87.5°. [c] 5.0 *M* water in acid medium.

This idea of the differences in the reaction rates of 2- *vs.* 3-benzo[*b*]thienyl ketones being due to entropy factors is further substantiated by examination of previous rate data for cyclodehydration reactions.[4,5,7] Only those ketones which would have marked differences in their stereochemical requirements have significantly different reaction rates. This consideration applies only to those ketones which vary in the nature of the group bonded to the carbonyl, *i.e.*, R group, and not for those which differ with regard to the aromatic system undergoing alkylation.

It has been pointed out by Bunnett[14] that variation of rates within a reaction series may be due to changes in either or both enthalpy and entropy of activation. He describes four categories: mainly due to $\Delta H^*$ with $\Delta S^*$ virtually constant, mainly due to $\Delta S^*$ with $\Delta H^*$ virtually constant, due to random changes in both $\Delta H^*$ and $\Delta S^*$, and due to a parallel variation in $\Delta H^*$ and $\Delta S^*$, *i.e.* a plot of $\Delta H^*$ *vs.* $\Delta S^*$ is linear. Ketones which vary in the nature of the R group appear to fit the last category.

However, if one alters the reaction medium or the ring system into which cyclization occurs, electronic factors become increasingly important. As illustrated in Tables I and II, cyclization into a naphthalene ring has a lower energy of activation and faster rate than does ring closure into a phenyl ring. This is in accord with the greater electrophilic susceptibility of naphthalene. Also, one notes comparatively small entropy differences for the reactions, which suggests that these reactions might fit into the first enthalpy–entropy category listed above. By similar analogy, addition of water to the acid medium increases the energy of activation by reversing the protonation equilibrium and slows the reaction rate. The fact that a rather large increase in entropy of activation is exhibited when water is added to the anhydrous acid medium suggests that ion-pair formation in the low dielectric acid contributes to the over-all entropy requirements for the reactions.[15]

## Experimental Section

**Materials.**—The four ketones and their respective cyclodehydration products were synthesized according to procedures previously described[9] and were analytically pure. Redistilled reagent grade acids were used and the reaction media were 1.0 *M* hydrobromic acid in anhydrous and aqueous (5.0 *M* water) acetic acid. The former solution was prepared by the addition of a calculated volume of acetic anhydride to 47.6% hydrobromic acid followed by dilution with acetic acid to the desired volume. The latter solution was prepared by dilution of the hydrobromic acid with acetic acid.

Reaction vessels were made by sealing one end of a 15-in. piece of Pyrex tubing (i.d. 10 mm, o.d. 12 mm). Reaction mixture samples (10 cc) were pipetted into the vessels which were then sealed, leaving about 5 cc of air space remaining in the sealed vessel.

**Determination of Rate Constants.**—The technique involved a spectrophotometric determination of the product of a reaction, which in this investigation was either an anthracene or a benz[*a*]anthracene. Absorbances were measured using a Beckman Model DU spectrophotometer and the analyses were made at 380 and 390 mμ wavelengths which minimized interference from ketone and solvent decomposition. Rate constants and thermodynamic data were determined graphically.

**Registry No.**—**1**, 7530-55-4; **2**, 5705-65-7; **3**, 5691-34-9; **4**, 6248-56-2.

**Acknowledgment.**—The authors wish to thank Terry St. Clair, Richard Giglio, and Donald Wiseley for performing some of the kinetic analyses.

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(12) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, p 325.

(13) J. E. Leffler, *J. Org. Chem.*, **31**, 533 (1966).

(14) J. F. Bunnett in "Techniques of Organic Chemistry," Vol. VIII, Part I, 2nd ed, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1961, pp 177–205.

(15) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., Inc., New York, N. Y., 1959, p 102.