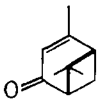
The Acid-Catalyzed and Thermal Reactions of Chrysanthenone

Sir:

In our studies of the photochemistry of verbenone (**1**), we observed an anomalous behavior of **1** on ultraviolet irradiation in acetic acid at slightly elevated temperatures. Thus, irradiation of (−)-verbenone in acetic acid at 25–26° afforded principally (−)-chrysanthenone (**2**) and (+)-2,4,4-trimethylbicyclo[3.1.1]hept-2-en-6-one (**3**) with high retention of optical activity. In contrast, irradiation of **1** at 40–50° for extended periods afforded mixtures of highly racemized **2** and **3** accompanied by varying quantities of two anomalous ketones, (+)-2,6,6-trimethylbicyclo[3.2.0]hept-2-en-7-one (**4**) and (−)-2,4,4-trimethylbicyclo[3.2.0]hept-2-en-7-one (**5**).[1] In this communication we describe the acid-catalyzed and thermal reactions of chrysanthenone which indicate that **4** and **5** are produced from **2** and **3**, respectively, by nonphotolytic ionic processes involving sequential 1,2-alkyl shifts and that chrysanthenone undergoes thermal racemization *via* the ketene **6** at relatively low temperatures.



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Treatment of 500 mg of (−)-chrysanthenone[1,2] (**2**) ($[\alpha]^{25}\mathrm{D}$ −12.2°) with 15 ml of acetic acid at 60° for 77 hr afforded (+)-ketone **4**[3] ($[\alpha]^{25}\mathrm{D}$ +24.2°; ~30% relative retention[4]), isopiperitenone (**7**),[5] and piperitenone (**8**),[6] along with recovered **2** in yields of 31, 3, 5, and 12%, respectively. At 118° consumption of (−)-chrysanthenone ($[\alpha]^{25}\mathrm{D}$ −12.2°) was essentially complete in 60 min and the four ketones **4** ($[\alpha]^{25}\mathrm{D}$ +17.7°; ~22% relative retention[4]), **7**, **8**, and **2** were isolated in 38, 2, 10, and 2% yields, respectively. Catalysis by a stronger Lewis acid allowed rapid isomerization of **2** at room temperature with relatively less racemization. Thus, treatment of 500 mg of (−)-**2** ($[\alpha]^{25}\mathrm{D}$ −26.6°) with a solution of 1.5 ml of boron trifluoride etherate in 15 ml of 1,2-dichloroethane at 26–27° for 30 min afforded (+)-**4** ($[\alpha]^{25}\mathrm{D}$ +174°; 100% relative retention[4]) (26%), **5** (10%), and no recovered **2**. Prolonged treatment (2.5 hr) of (−)-**2** ($[\alpha]^{25}\mathrm{D}$ −12.2°) under the same conditions produced **4** (4%), (+)-**7** ($[\alpha]^{25}\mathrm{D}$ +10.2°)[7] (20%), **8** (6%), thymol (**9**)[8] (1%), and a fourth cyclobutanone, (−)-2,7,7-trimethylbicyclo[3.2.0]hept-2-en-6-one (**10**) (1%): $[\alpha]^{25}\mathrm{D}$ −16.4°; ORD ($CHCl_3$) $[M]_{321}$ −1010°, $[M]_{281}$ +1100°;[9] uv ($CHCl_3$) λ_{max} 301 mμ (ϵ_{max} 35); ir (CCl_4) 5.63 (C=O), 12.30 μ (trisubstituted olefin); nmr ($CDCl_3$) τ 4.60 (m, 1, -C*H*=C<), 6.13 (sextet, 1, $J_1 = J_2 = 8.0 \pm 0.5$, $J_3 = 3.0$ Hz, >C*H*C(=O)–), 7.05 (broadened d, 1, $J = 8.0 \pm 0.5$ Hz, –(–CH=C)C*H*<), 7.3–7.7 (m, 2, >C=CHCH_2–), 8.24 (broad s, 3, –(CH_3)C=C<), 8.71 (s, 3, *exo* –(CH_3)$_2$CC(=O)–, 8.95 (s, 3, *endo* –(CH_3)$_2$)CC(=O)–);[10] mass spectrum (70 eV) *m/e* (relative intensity) 150 (10), 135 (4), 122 (27), 107 (33), 91 (18), 80 (100), 79 (79), 78 (16), 77 (30), 70 (46).[11]

Enhancement of the yields of **7**, **8**, and **9** at the expense of **4** and the appearance of **10** in the latter reaction implicate **4** as an intermediate in the production of these ketones. Disappearance of **2** suggests that the process for conversion of **2** to **4** is essentially irreversible. Evidence for these hypotheses was given by the observation that **4** on treatment with boron trifluoride etherate as above for 2.5 hr did not afford even traces of **2** but did produce **7**, **8**, **9**, and **10** in yields comparable to those obtained from chrysanthenone (**2**).

Extended treatment (24 hr) of **4** with $BF_3 \cdot Et_2O$ in refluxing benzene completely consumed **4** and **10** and produced **8** and **9** in yields of 22 and 5%, respectively. Treatment of isopiperitenone with acetic acid or $BF_3 \cdot Et_2O$ produced only **8** and **9** with no evidence for **4** or **10**; $BF_3 \cdot Et_2O$ treatment of **8** produced only **9** with no evidence for **7**. Treatment of **10** with $BF_3 \cdot Et_2O$ (2.5 hr) produced **4**, **7**, **8**, and **9** in the same relative ratios as observed from **4**. These data suggest that the conversion of **4** to **10** is a reversible process but that the transformations **4** → **7** → **8** → **9** are essentially irreversible under the conditions employed here.

Finally, whereas ketones **7** and **8** were produced in significant quantities from **2**, ketone **4** was stable to refluxing acetic acid. Since the transformation of **2** to **4** is irreversible, the above observation suggests that **7** is produced by a competitive process either from **2** itself or from an intermediate in the transition of **2** to **4**.

In like manner, (+)-2,4,4-trimethylbicyclo[3.1.1]hept-2-en-6-one[1] (**3**), $[\alpha]^{25}\mathrm{D}$ +29.1°, $[M]_{309}$ +2955°, $[M]_{272}$ −3375°,[12] is rearranged to (−)-2,4,4-trimethylbicyclo[3.2.0]hept-2-en-7-one (**5**), $[\alpha]^{25}\mathrm{D}$ −328°, $[M]_{322}$ −17,100°, $[M]_{284}$ +14,700°,[1,12] with $BF_3 \cdot Et_2O$ (0.5 hr; 50% yield of **5**) or refluxing acetic acid (1 hr; 30% yield of **5**).

In order to account for the above observations and

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[1] For a partial description of the photochemical experiments see W. F. Erman, *J. Amer. Chem. Soc.*, **89**, 3828 (1967).

[2] J. J. Hurst and G. H. Whitham, *J. Chem. Soc.*, 2864 (1960).

[3] J. J. Beereboom, *J. Amer. Chem. Soc.*, **85**, 3525 (1963); *J. Org. Chem.*, **30**, 4230 (1965).

[4] The absolute configurations of the enantiomeric chrysanthenones[1,4a] and ketones **4**[4b] have been established. Because the rotation of optically pure **4** has not been established, per cent optical retentions, as recorded here, are relative to the maximum rotation of **4** observed when **2** is rearranged at room temperature with boron trifluoride etherate. Rotations were obtained in chloroform solution. (a) A. Moscowitz, K. Mislow, M. A. W. Glass, and C. Djerassi, *J. Amer. Chem. Soc.*, **84**, 1945 (1962); (b) R. B. Bates, E. P. Blanchard, M. J. Onore, S. K. Paknikar, and C. Steelink, *Chem. Commun.*, 1037 (1967).

[5] G. O. Schenck, O.-A. Neumüller, G. Ohloff, and S. Schroeter, *Ann.*, **687**, 26 (1965).

[6] Ch. Balant, Ch. A. Vodoz, H. Kappeler, and H. Schinz, *Helv. Chim. Acta*, **34**, 722 (1951).

[7] The absolute configuration of (+)-**7** has been established by chemical means.[5]

[8] We thank Dr. D. K. Brain for an authentic specimen of thymol.

[9] The absolute configuration as shown in Chart I for (−)-**10** is implied from the negative Cotton effect. For application of the Cotton effect to ketones containing similarly disposed double bonds see ref 4. We thank Dr. R. S. Treptow for the ORD measurements and interpretation of the curves.

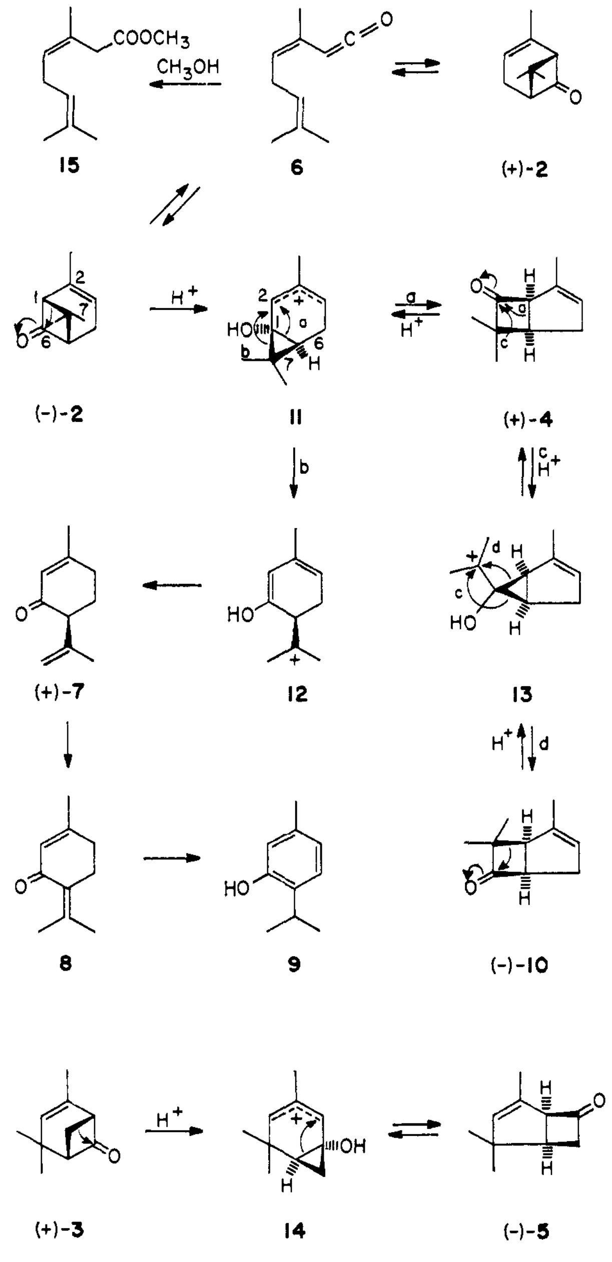
[10] We are indebted to Dr. R. E. Reavill for a second-order analysis of the ABXC system of the nmr spectrum of **10** and for spin-decoupling experiments which allowed proper measurement of coupling constants.

[11] Details of the mass spectrum element map and structure analysis of **10** will be presented in the complete paper. We thank Dr. J. H. Collins and associates for the mass spectral data and their interpretation.

[12] The positive and negative Cotton effects observed for **3** and **5**, respectively, lead to the assigned absolute configurations shown in Chart I (see ref 4a and 9). Assignments of absolute configuration will be discussed in detail in the complete paper.

relative configuration of products, a mechanism for production of products is proposed which involves initial irreversible migration of the 1,7 bond in **2** to produce an intermediate cyclopropanol (**11**). Reversible migration of the 1,6 bond in **11** would afford **4** (path a), the product of kinetic control, while competitive scission of the 1,7 bond would produce **12**, the precursor of **7**, **8**, and **9** (path b). By the same type sequence of 1,2-alkyl shifts **10** would be produced from **4** *via* the intermediate **13** by a reversible process (paths c and d) and **5** from **3** *via* **14** (Chart I).

Chart I



Speculation about the mechanism by which racemized products are formed is obtained from the following observations. When **2** was heated at reflux (81°) under a nitrogen atmosphere in cyclohexane for periods of 16 and 77 hr, the recovered chrysanthenone (75–80% recovery) was 29 and 71% racemized, respectively. Not even trace amounts of the ketone **4** were observed in the reaction mixture. Treatment of **2** with methanol at reflux (65°) for 16 hr produced *seq-cis*-1,7-dimethylocta-3,6-dienoate (**15**)[1] (37% yield) and 43% recovered **2**. The ketone **4** was recovered quantitatively with complete retention of configuration by similar treatment in cyclohexane and methanol. Pyrolysis of **2** ($[\alpha]^{25}\mathrm{D}$ −36.6°) under a nitrogen atmosphere (or in an evacuated sealed tube) at 250° for 20 min afforded **4**, **7**, and **8** in yields of 16, 3, and 18%, respectively. The ketone **4**, though highly racemized, showed significant optical activity ($[\alpha]^{25}\mathrm{D}$ +1.8°).

These observations indicate that **2** undergoes rapid interconversion with **6** even at temperatures as low as 65° at a much faster rate than thermal cyclization of **6** to **4**. Although **4** may be produced directly from **6** at higher temperatures (*i.e.*, 250° or greater), based on the above evidence, it is more probable that loss of retention in the production of **4** from **2** is the consequence of the rapid interconversion of **2** and **6**. Ketone **2** may then be converted to **4** by a slower, yet competitive, ionic process involving sequential 1,2-alkyl shifts.[13] These proposals and other refinements of the mechanism are being considered in further detail and will be reported later.

Acknowledgments. We are grateful to Professor Ernest Wenkert for suggestions concerning the specific mechanisms described here and for making available to us information about his unpublished research on similar acid-catalyzed rearrangements of bicyclo[3.1.1]-heptanones which support our findings here. The excellent technical assistance of Mr. Logan Stone is gratefully acknowledged.

(13) In our complete paper these observations will be used to explain the production of **4** from geranic acid,[3] the racemization of **2** during glpc analysis[4b] and fractional distillation,[1] and the production of products from pyrolysis of **4** at greater than 340°.[3]

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Cyclopropanes by Cycloalkylation of Alkylidenebisdialkylamines

Sir:

We wish to report the first examples of cycloalkylation of alkylidenebisdialkylamines to give cyclopropane derivatives. Whereas cycloalkylation of enamines of cyclic ketones with 1,4-diiodobutane and *o*-xylylene dibromide to give six-membered rings has been reported, no reaction was observed with 1,2-dibromoethane.[1] Enamines of aldehydes were reported to undergo N-alkylation, but not C-alkylation, with 1,2-dibromoethane.[2] In contrast, we have found that reaction of vinylidenebisdimethylamine[3] with 1,2-dibromoethane, mole ratio 2:1, 24 hr at 70°, acetonitrile solvent, afforded, after hydrolysis with dilute sodium hydroxide, 34% of N,N-dimethylcyclopropane-

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(1) G. Opitz and H. Mildenberger, *Ann.*, **650**, 115 (1961).
(2) G. Opitz and H. Mildenberger, *ibid.*, **649**, 26 (1961).
(3) H. Weingarten and W. A. White, *J. Org. Chem.*, **31**, 2874 (1966).