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Facile Decomposition of 9-Substituted 9-Xanthydrols in Basic Media. Dependence of Reaction Behavior on Structure and Metal Ion

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Sterically congested tertiary alcohols may undergo fragmentation to ketones and hydrocarbons (eq 1). Ionic decompositions of alkoxide salts to carbanions and carbonyl compounds in both condensed phase[1] and gas phase[2] have been reported, as have

$$R_3COH \rightarrow R_2C{=}O + RH \qquad (1)$$

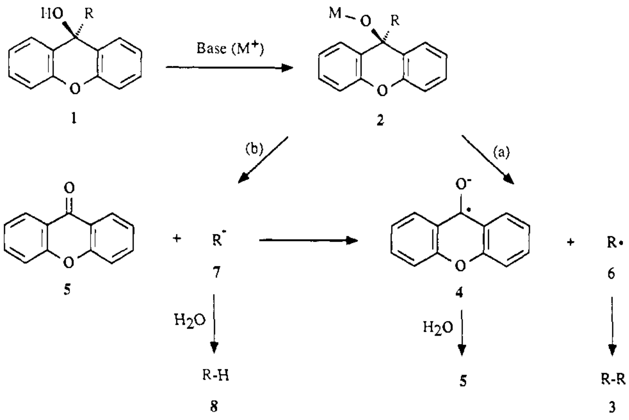
decompositions of alcohols by free-radical pathways.[3] Theoretical and experimental studies of the mechanisms of alkoxide decompositions have considered both heterolytic and homolytic pathways. Here we report the observation of unusual facile fragmentation of the alkoxides of several 9-substituted-9-xanthydrols in THF or C_6D_6 by either ionic or radical processes, depending on the nature of the substituent and the metal.

We synthesized 9-[1-(2,4,6-cycloheptatrienyl)]-9-xanthydrol (**1a**, R = c-C_7H_7), 9-benzyl-9-xanthydrol (**1b**, R = CH_2Ph), and 9-benzhydryl-9-xanthydrol (**1c**, R = $CHPh_2$) by first forming dilithio-9-xanthone by electron transfer to xanthone from lithium metal and 4,4′-di-*tert*-butylbiphenyl (DBB) in THF followed by addition of the appropriate electrophilic organic halide.[4] During the course of those studies we made several curious observations which led us to the investigations reported here. First, although the synthesis of **1a** proceeded in very high yield (>80%) when lithium metal was used, use of sodium led to recovery of the xanthone with no alcohol. Second, treatment of **1a** with KOH and $CHBr_3$ at elevated temperatures in an attempt to form the 9-[1-(2,4,6-cycloheptatrienyl)]-9-xanthyl cation under basic conditions ("deoxidation")[5] resulted in the unexpected formation of xanthone.

To explain these observations, the behavior of **1a–c** under basic conditions was explored. Treatment of either a THF or C_6D_6 solution of **1a** at room temperature with a 4-fold molar excess of KH produced a yellow color which immediately changed first to a deep green and then slowly to deep blue-green. Quenching with H_2O or D_2O after 24 h in both cases produced xanthone (**5**) and ditropyl (**3a**) quantitatively as judged by NMR and GC/MS analyses. No deuterium was incorporated into either product. Treatment of a THF solution of **1a** with KOH gave **5** (>95%), **3a** (>90%), and traces of cycloheptatriene (<1%), troponol (<2%), and tropone (<2%).

Similar treatment of a C_6D_6 solution of **1b** with KH gave a yellow solution of the potassium salt (**2b**) which remained stable for 72 h. Heating to 50 °C for 3 h followed by aqueous quenching produced **5** and toluene. Quenching with D_2O gave $PhCH_2D$. No bibenzyl was observed. Treatment of a THF solution of **1b** with KOH at 50 °C for 3 h yielded **5** and toluene quantitatively. Alcohol **1c** was much more reactive than either **1a** or **1b** when treated with KH in C_6D_6. The original greenish-yellow solution of **2c** steadily decomposed at room temperature. After 70 min it was quenched with H_2O to afford **5** and diphenylmethane. The same results were obtained by using KOH/THF. No 1,1,2,2-tetraphenylethane was observed from **1c**.

Scheme I



The relative decomposition rates of alcohols **1a–c** follow qualitatively the release of steric strain as calculated by molecular mechanics,[6,7] in accordance with previous observations.[1d] The persistence of the dark-colored solution in the decomposition of **1a** but not with **1b** or **1c** suggested the intervention of the radical anion (ketyl) of **5** (**4**) in the pathway to final products. This was confirmed by the observation of the same long-lived ESR signal from both a THF solution prepared from KH and **1a** and a known solution of **4** prepared from **5** and an equivalent of potassium metal.[8] When the known sample of **4** was quenched with water, it produced only **5**.

These observations are best understood by the dichotomy of reaction behavior shown in Scheme I. Alcohol **1a** decomposes primarily by homolytic cleavage through pathway (a) to radical anion **4** and the tropyl radical (**6a**). Ditropyl is then formed by coupling of **6a**, and **5** is formed upon quenching of **4**. Alcohols **1b** and **1c** decompose by way of the normal heterolytic cleavage to ketone **5** and carbanion **7**, i.e., path (b). The novel behavior of **1a** can be understood on the basis of the instability of the tropyl anion[9] contrasted with the relative stability of the tropyl radical.[10,11] Consideration of the heats of formation of the product sets from path (a) vs path (b) as estimated by semiempirical MNDO calculations supports the thermodynamic preference for the homolytic cleavage of **1a**.[12,13] The observation of similar chemical

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(1) (a) Zook, H. D.; March, J.; Smith, D. F. *J. Am. Chem. Soc.* **1959**, *81*, 1617. (b) Cram, D. J. *Fundamentals of Carbanion Chemistry*; Academic Press: New York, 1965; Chapter 4, pp 32 and 33. (c) Arnett, E. M.; Small, L. E.; McIver, R. T., Jr.; Miller, J. S. *J. Org. Chem.* **1978**, *43*, 815. (d) Lomas, J. S.; Dubois, J. E. *J. Org. Chem.* **1984**, *49*, 2067. (e) Partington, S. M.; Watt, C. I. F. *J. Chem. Soc., Perkin Trans. 2* **1988**, 983. (f) Ibrahim, S.; Watt, C. I. F.; Wilson, J. M.; Moore, C. *J. Chem. Soc., Chem. Commun.* **1989**, 161.

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(6) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; ACS Monograph 177; American Chemical Society: Washington, DC, 1982.

(7) Following the method of Lomas and Dubois in which the differences in strain energies between the starting alcohol and the sum of the strain energies of the ketone and hydrocarbon products are compared,[1d] we calculate differences to be 74.4 kcal/mol between the least-reactive **1b** and most-reactive **1c** and 4.6 kcal/mol between **1b** and **1a**.

(8) Details of the ESR experiments will be given in the full paper.

(9) (a) Dauben, H. J., Jr.; Rifi, M. R. *J. Am. Chem. Soc.* **1963**, *85*, 3041. (b) Doering, W. v. E.; Gaspar, P. *J. Am. Chem. Soc.* **1963**, *85*, 3043. (c) Maltz, H.; Kelly, B. A. *J. Chem. Soc., Chem. Commun.* **1971**, 1390. (d) Deganello, G.; Boschi, T.; Toniolo, L. *J. Organomet. Chem.* **1975**, *97*, C46.

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(11) Attempts to trap cycloheptatrienyl anion by conducting the decomposition of **1a** in the presence of an equimolar amount of anthracene failed to give any of the known anthracene–cycloheptatriene adduct in either THF or C_6D_6 solvent. Cf.: Staley, S. W.; Orvedal, A. W. *J. Am. Chem. Soc.* **1974**, *96*, 1618.

(12) Decomposition to give intermediates **4** and **6a** is estimated to be favored over **5** and **7a** by 0.4–19.4 kcal/mol depending on whether restricted or unrestricted Hartree–Fock calculations are performed and whether **7a** is in the triplet or singlet electronic state.[13] Details will be provided in the full paper.

(13) Clark, T. *A Handbook of Computational Chemistry*; Wiley: New York, 1985.

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behavior in both polar THF and nonpolar C_6D_6 solvents lends further support to this interpretation. The fact that the relative rates of decomposition of the three alcohols qualitatively follow the release of steric strain, while the reactions proceed by two fundamentally different mechanisms may simply be fortuitous.

We can also now comment on the question of why alcohol **1a** can be synthesized with lithium metal but not with sodium. Treatment of a THF solution of **1a** with an excess of methyllithium produced the lithium salt **2a** (M = Li). The solution was stable, giving back 85% of **1a** upon aqueous quenching after 24 h. However, when the solution of **2a** was treated with moist 12-crown-4 ether, it behaved as the potassium salt and quickly decomposed to give **5** and **3a** in high yields with no recovery of **1a**. A reasonable interpretation of this behavior is that a more covalent bond between lithium and oxygen compared to sodium or potassium and oxygen permits the lithium salt to persist during the synthesis until quenched during workup, whereas the sodium salt rapidly decomposes to **5** and **3a** by path (a).[14] Such considerations are likely to be important in other syntheses as well.

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[14] Alternatively, the behavior could be discussed in terms of the different reactivity of tight ion pairs.

1,3-Dipole Cascade. A New Method for Azomethine Ylide Formation

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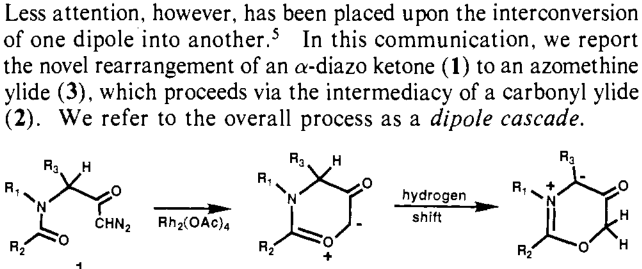
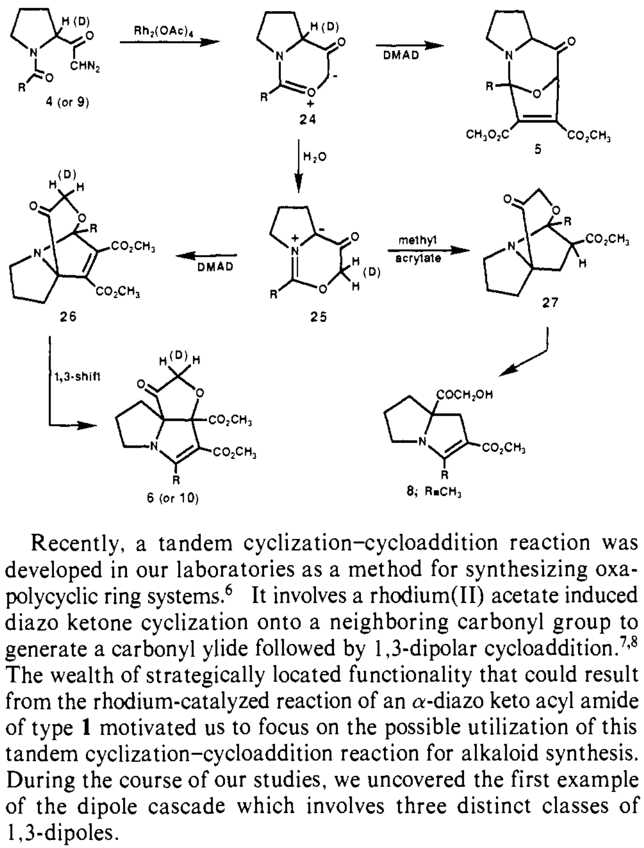
1,3-Dipoles have become extremely valuable intermediates in synthetic organic chemistry.[1] Their best known reaction corresponds to a 1,3-dipolar cycloaddition reaction.[2] The importance of this cycloaddition in organic synthesis derives in large part from its ability to generate five-membered heterocyclic rings containing several contiguous stereogenic centers in one synthetic operation.[3,4] Less attention, however, has been placed upon the interconversion of one dipole into another.[5] In this communication, we report the novel rearrangement of an α-diazo ketone (**1**) to an azomethine ylide (**3**), which proceeds via the intermediacy of a carbonyl ylide (**2**). We refer to the overall process as a *dipole cascade*.

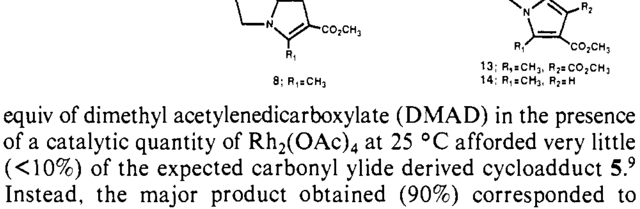


Scheme I



Recently, a tandem cyclization–cycloaddition reaction was developed in our laboratories as a method for synthesizing oxapolycyclic ring systems.[6] It involves a rhodium(II) acetate induced diazo ketone cyclization onto a neighboring carbonyl group to generate a carbonyl ylide followed by 1,3-dipolar cycloaddition.[7,8] The wealth of strategically located functionality that could result from the rhodium-catalyzed reaction of an α-diazo keto acyl amide of type **1** motivated us to focus on the possible utilization of this tandem cyclization–cycloaddition reaction for alkaloid synthesis. During the course of our studies, we uncovered the first example of the dipole cascade which involves three distinct classes of 1,3-dipoles.

Our initial endeavors focused on the behavior of (*S*)-1-acetyl-2-(1-diazoacetyl)pyrrolidine (**4**). Treatment of **4** with 1.5 equiv of dimethyl acetylenedicarboxylate (DMAD) in the presence of a catalytic quantity of $Rh_2(OAc)_4$ at 25 °C afforded very little (<10%) of the expected carbonyl ylide derived cycloadduct **5**.[9] Instead, the major product obtained (90%) corresponded to structure **6**.[9] Unequivocal proof of the proposed structure was obtained by an X-ray single-crystal structure analysis.[10] In a similar manner, dihydropyrrolizines **7** and **8** were isolated in high



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[8] Gillon, A.; Ovadia, D.; Kapon, M.; Bien, S. *Tetrahedron* **1982**, *38*, 1477.

[9] Compound **5** (R = CH_3): NMR ($CDCl_3$, 300 MHz) δ 1.65–1.84 (m, 2 H), 1.70 (s, 3 H), 1.86–1.98 (m, 1 H), 2.14–2.26 (m, 1 H), 2.90–3.04 (m, 2 H), 3.79 (s, 3 H), 3.84 (s, 3 H), 4.09 (td, 1 H, J = 8.1, 1.5 Hz), 4.95 (d, 1 H, J = 1.5 Hz). Compound **6**: δ 1.64–1.76 (m, 1 H), 1.91–2.04 (m, 2 H), 2.30 (s, 3 H), 2.30–2.35 (m, 1 H), 3.27 (ddd, 1 H, J = 11.0, 7.9, 5.5 Hz), 3.45 (dt, 1 H, J = 11.0, 6.8 Hz), 3.71 (s, 3 H), 3.80 (s, 3 H), 4.14 (d, 1 H, J = 17.0 Hz), 4.34 (d, 1 H, J = 17.0 Hz).

[10] Unit cell parameters were determined on a Syntex $P2_1$ automated diffractometer using Mo Kα radiation. Details associated with the X-ray crystal structure are available as Supplementary Material.