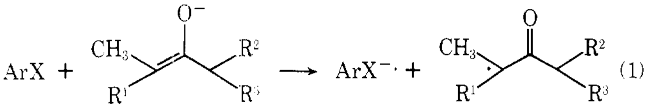
Communications

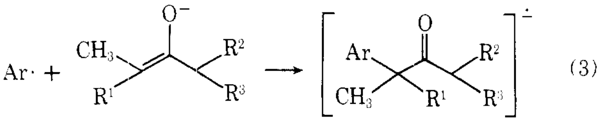
Evidence for Intermolecular Hydrogen Atom Transfer in Photostimulated $S_{RN}1$ Reactions Involving Ketone Enolates

Summary: Photostimulated $S_{RN}1$ reaction of potassio-2,4-dimethyl-3-pentanone with iodobenzene is accompanied by a competing reaction in which 2,4,4,6,8-pentamethylnonane-3,7-dione is formed by a mechanism originating with β-hydrogen abstraction from the enolate by phenyl radical.

Sir: Photostimulated reactions of ketone enolates with carboaromatic and heteroaromatic halides have been shown to afford products resulting from introduction of an aryl or heteroaryl residue at the α carbon of the ketone.[1–4] Considerable evidence[1–5] has been gathered to show that these nucleophilic substitutions occur via a radical chain mechanism designated as $S_{RN}1$[6] and generalized in eq 1–4. Initiation (eq 1) is probably provided by electron transfer from the enolate to the aromatic substrate, perhaps through formation of a charge-transfer complex.[6] Subsequent propagating steps involve fragmentation of the aryl radical anion to form an aryl radical and halide ion (eq 2), combination of the aryl radical with the enolate (eq 3), and then electron transfer from the resulting radical anion to another substrate molecule (eq 4).


(1)

$$ArX^{-}\cdot \longrightarrow Ar\cdot + X^{-} \qquad (2)$$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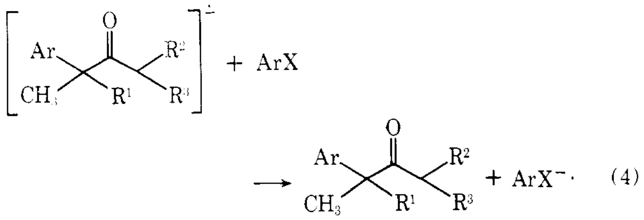
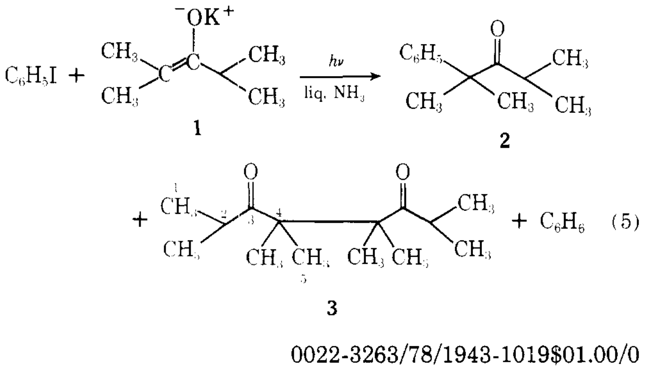
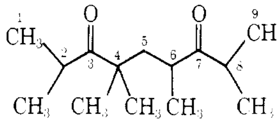

(4)

Although such reactions have been found to be rather general, the potassio salts of acetophenone and propiophenone react poorly with halobenzenes, while reactions of tertiary enolates are accompanied by a competing ketone dimerization.[1] For example, under illumination potassio-2,4-dimethyl-3-pentanone (1) reacts sluggishly with iodobenzene to form phenylated ketone 2 (32%) accompanied by benzene (20%) and 20% of a dimeric product which has been assigned structure 3[1,3] (eq 5). In contrast to this, 1 reacts with 2-bromopyridine[2] and 2-chloroquinoline[3] to give the expected α-heteroaryl ketones unaccompanied by significant amounts of dimer.

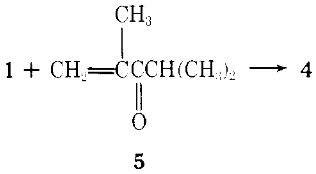

1
2
3
(5)

When we repeated the reaction of 1 with iodobenzene as described previously,[1] we found that ketone 2 and benzene were formed in essentially the yields reported.[7] However, the dimeric product isolated (preparative GLC) from this reaction, as well as from the reaction of 1 with 2-bromopyridine, *is not* 3. Instead, the ^{1}H NMR and ^{13}C NMR spectra[8] require assignment of structure 4[9] to this compound. Thus, the ^{1}H NMR spectrum contains an ABX pattern of δ_A 1.42, δ_B 2.15, and δ_X 2.56, with J_{AB} = 14, J_{AX} = 3, and J_{BX} = 7 Hz. This pattern is inconsistent with structure 3, but in accord with 4, since the diastereotopic protons at C-5 of the latter compound would be expected to give rise to an ABX spin system through coupling with the methine hydrogen at C-6. Besides the ABX pattern, two septets arising from the methine protons at C-2 and C-8 are distinguishable at δ 2.67 (J = 6 Hz) and 3.07 (J = 7 Hz), as well as a methyl multiplet (21 H) at δ 1.10.


4

The proton-decoupled ^{13}C NMR spectrum of 4 contains two carbonyl resonances at 217.4 and 219.3 ppm, along with 12 peaks attributable to saturated carbon atoms.[10] The ^{1}H NMR spectrum of an authentic sample of 3, prepared from 2,4-dibromo-2,4-dimethyl-3-pentanone by means of zinc–copper couple[11] or by the action of acetyl peroxide on 2,4-dimethyl-3-pentanone,[1] consists of a doublet at δ 1.04 (J = 7 Hz), a singlet at δ 1.24, and a septet at δ 3.14 (J = 7 Hz) in a ratio of 12:12:2. The ^{13}C NMR spectrum of 3 is characterized by resonances for one carbonyl carbon at 219.4 ppm and four saturated carbons at 20.1, 22.3, 35.6, and 53.3 ppm for C-1, C-5, C-2, and C-4, respectively. The IR spectrum of 3, which contained a carbonyl band at 1700 cm^{-1}, is nearly identical with that of 4.

Assignment of structure 4 is substantiated by our obtaining the same substance, with identical spectra, from Michael addition of 1 to 5 (eq 6). From 5[13] (20 mmol) and 1 (21 mmol) in 100 mL of liquid ammonia, allowed to react 60 min in the dark, 4 was isolated in 65% yield.



$$1 + CH_2{=}\overset{\overset{\displaystyle CH_3}{|}}{C}\underset{\underset{\displaystyle O}{\|}}{C}CH(CH_3)_2 \longrightarrow 4 \qquad (6)$$

5

Interpretation of the formation of 4 is suggested by a recent report of Semmelhack and Bargar.[12] They showed by a series of deuterium labeling experiments that aryl radicals produced during intramolecular photo-$S_{RN}1$ reactions can abstract a hydrogen atom from the β position of the side-chain enolate to effect reductive dehalogenation of the aromatic ring with

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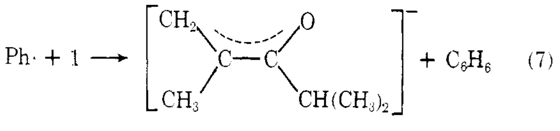
concomitant generation of an α,β-unsaturated ketone function in the side chain. Similarly, ester enolates containing β hydrogens effect reduction of aryl halides by intermolecular hydrogen atom transfer.[12]

Accordingly, we postulate that phenyl radical, besides adding to **1** (eq 3), abstracts a β hydrogen as shown in eq 7. Thereby formed are benzene and **6**, which is the radical anion of **5**.



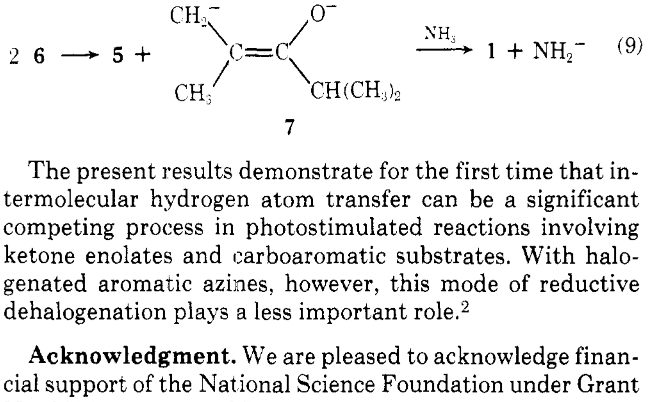
6

Being the radical anion of an α,β-unsaturated ketone, **6** is probably too stable to transfer an electron rapidly to iodobenzene, as in eq 8. Were that to happen a propagation cycle

$$\mathbf{6} + \mathrm{PhI} \not\rightarrow \mathbf{5} + [\mathrm{PhI}]^{-\cdot} \qquad (8)$$

comprising steps 2, 7, and 8 would coexist with the normal $S_{RN}1$ cycle of steps 2, 3, and 4, and no interpretation of the sluggishness of the overall reaction of PhI with **1** would be offered. (The very low $S_{RN}1$ reactivity of acetophenone enolate ions with aryl and heteroaryl halides is probably of similar origin, the radical anion $[ArCH_2COPh]^{-\cdot}$ being unable to transfer an electron rapidly enough to ArX, as in step 4, to maintain the propagation cycle.)

The sluggishness of the overall reaction of PhI with **1** suggests that termination steps accompany or follow the formation of benzene and **4**. We suggest that disproportionation of **6**, as in eq 9, is the termination step. Dianion **7** is rapidly protonated to form **1**, as shown, and **1** adds to **5** to form **4** (eq 6).



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The present results demonstrate for the first time that intermolecular hydrogen atom transfer can be a significant competing process in photostimulated reactions involving ketone enolates and carboaromatic substrates. With halogenated aromatic azines, however, this mode of reductive dehalogenation plays a less important role.[2]

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References and Notes

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(6) J. K. Kim and J. F. Bunnett, *J. Am. Chem. Soc.*, **92**, 7463 (1970).
(7) We observed that negligible reaction occurred in the dark (2% in 3 h).
(8) NMR spectra were obtained at 100 MHz for ^{1}H NMR and at 25.15 MHz for ^{13}C NMR from $CDCl_3$ solutions using Me_4Si as an internal standard.
(9) This compound [bp 80–83 °C (0.6 Torr); IR (neat) 1705 cm^{-1} (C=O)] gave a satisfactory combustion analysis.
(10) The saturated carbon absorbances and their tentative assignments are as follows: δ 18.7 and 18.9 (C-2 and/or C-8 CH_3), 19.9 (C-6 CH_3), 20.1 and 20.3 (C-2 and/or C-8 CH_3), 23.7 and 25.3 (C-4 CH_3), 34.1 (C-5), 39.8 (C-6), 41.2 and 41.4 (C-2 and C-8), and 41.3 ppm (C-4).
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(13) Enone **5** was prepared from 2-bromo-2,4-dimethylpentan-3-one according to the procedure of A. Bienvenue and B. Duchatellier, *Tetrahedron*, **28**, 833 (1972).

James F. Wolfe,* Marcus P. Moon, Mark C. Sleevi
Department of Chemistry, Virginia Polytechnic
Institute and State University
Blacksburg, Virginia 24061

Joseph F. Bunnett, Raymond R. Bard
University of California
Santa Cruz, California 95064

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Reactions in Dry Media. Ferric Chloride Adsorbed on Silica Gel. A Multipurpose, Easily Controllable Reagent[1]

Summary: $FeCl_3$ adsorbed on a chromatographic type silica gel was found to be effective for rapid, high yield and selective dehydration of alcohols, as well as for pinacol and acyloin type rearrangements. The same reagent containing ca. 2% water epimerizes tertiary alcohols and converts epoxides into diols.

Sir: One of the advantages of reactions on solid adsorbents is their use as support for selective reagents which are inefficient or inactive in solution.[1,2] We report on the use of such a reagent, consisting of ferric chloride adsorbed on chromatographic grade silica gel for rapid, high yield, selective dehydration and epimerization of alcohols, epoxide openings, and rearrangements involving carbonium or oxonium ion intermediates.[3]

When silica gel (Merck Kiesegel 60, particle size 0.063–0.200 mm, 70–230 mesh) is mixed with ~10% its weight of hydrated ferric chloride ($FeCl_3 \cdot 6H_2O$) dissolved in a polar volatile solvent (such as methanol, acetone, ether, etc.), followed by evaporation at ~50–60 °C under high vacuum (0.1 Torr) for ~3 h, a dry yellowish-brown powder is obtained.[4,5] This powder is an effective reagent for dehydration of allylic, tertiary, and sterically strained secondary alcohols, as exemplified in Table I.

The dehydrations are performed either by dissolving the substrate in a volatile solvent, mixing it with ~100 times its weight of reagent, and evaporating to dryness under high vacuum or when the substrate is volatile, by mixing it directly with the reagent. After being left for a short time at room temperature, the products are eluted from the silica gel with an organic solvent. The dehydrations are very fast, generally taking place immediately on contact of the substrate with the adsorbed reagent, and resulting in high yields of pure products.

Addition of ~2% water by weight to the dry $FeCl_3$–SiO_2 reagent results in a bright yellow powder (wet $FeCl_3$–SiO_2 reagent) which is still capable of dehydrating allylic alcohols, and to a lesser extent, tertiary alcohols. However, high water concentration (>10%) may completely deactivate this reagent.

We have observed that the wet $FeCl_3$–SiO_2 reagent in some cases efficiently epimerizes tertiary carbinols. Thus both *cis*- and *trans*-1,4-dimethylcyclohexanols were converted quantitatively to an equilibrium mixture of the two epimers, consisting of 56% of the trans epimer.[6] When these cyclohexanols were labeled with ^{18}O, the ensuing mixture of epimers was devoid of the label. On the other hand, by using wet $FeCl_3$–SiO_2 reagent prepared by adding $H_2{}^{18}O$ to the dry $FeCl_3$–SiO_2

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