

Figure 2. Nucleophilic solvation estimated by R as a function of the reactivity. (Data from Table II.)

smaller in this olefin series than in α -methylstyrenes (transition state 1) although the two series have similar reactivities. On the other hand, R for 1-pentene, where the transition-state charge is delocalized in the bridging bromine atom 3, is smaller than that of the α -methylstyrene of similar reactivity (Table III).¹⁰

The ρ values in the solvents of Table II are given in Table IV. There is a rough trend toward an inverse relationship between the reactivity and the ρ value in each olefin series. However this relationship is in no way linear as expected for a strictly unimolecular dissociation.¹¹ This is particularly striking for α -methylstyrene, the olefin the most sensitive to nucleophilic solvation: ρ in methanol is close to ρ in aqueous ethanol but quite different from ρ in acetic acid although the reactivity varies steadily. It appears that nucleophilic solvation causes a leveling of the ρ values for bromination in alcoholic solvents; a similar effect has been pointed out in solvolysis.¹²

It is clear that there is nucleophilic solvation in the rate-determining step of bromination. This solvent effect is minor as compared to its previously recognized effects, polarity and electrophilic assistance to the departure of the leaving bromide ion.⁸ The stabilization provided by nucleophilic solvation depends on several factors: (i) the reactivity (the more reactive the olefin, the less important the stabilization; this can be due to a Hammond effect); (ii) the charge delocalization (a bridged transition state is less solvated than a carbocationic transition state and substituents able to delocalize the charge by resonance diminish strongly the magnitude of the solvent stabilization); (iii) crowding of the double bond also decreases its magnitude.¹ Intervention of nucleophilic solvation has an incidence on the LFER parameters of bromination: the p or m values for the nucleophilically assisted process are smaller than those expected for a unimolecular dissociation. More work is in progress to obtain quantitative data on this last effect.

Experimental Section

Materials. The substituted 1,1-diphenylethylenes and α -methylstyrenes are synthesized and purified as already described.^{4,5}

(10) In this comparison, it is assumed that there is no charge delocalization in the ring substituted by a strongly electron-attracting group such as trifluoromethyl.

(11) The ρ values are selectivity indices; there should exist an inverse linear relationship between ρ and $\log k$ if the mechanism does not change with the solvent: A. Pross, *Adv. Phys. Org. Chem.*, **14**, 69 (1977); B. Giese, *Ang. Chem., Int. Ed. Engl.* **16**, 125 (1977).

(12) D. J. McLennan and P. L. Martin, *J. Chem. Soc., Perkin Trans. 2*, 1091 (1982); S. G. Shafer and J. M. Harris, *J. Org. Chem.*, **46**, 2164 (1981); T. W. Bentley and C. T. Bowen, *J. Chem. Soc., Perkin Trans. 2*, 557 (1978).

Origin and treatment of solvents and salts are given in the preceding note.¹

Kinetic Measurements and k Determinations. The kinetic procedures used for aryleolefin bromination are those described in the preceding note.¹

Registry No. p -CF₃C₆H₄C(Ph)=CH₂, 345-88-0; Ph₂C=CH₂, 530-48-3; p -MeOC₆H₄C(Ph)=CH₂, 4333-75-9; m -CF₃C₆H₄C(Ph)=CH₂, 368-79-6; PhC(CH₃)=CH₂, 98-83-9; p -MeOC₆H₄C(CH₃)=CH₂, 1712-69-2.

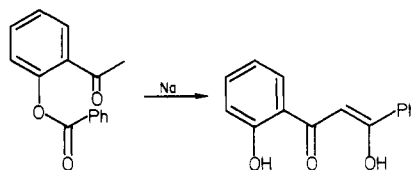
Aliphatic Acyl Transfer in the Baker-Venkataraman Reaction

George A. Kraus,* Brian S. Fulton, and Soon Hyung Woo

Department of Chemistry, Iowa State University, Ames, Iowa 50011

Received March 6, 1984

Base-mediated acylation reactions represent an important connective tool for organic chemists. Both the acetoacetic ester condensation¹ and the Claisen reaction² have been extensively used to produce β -keto esters and β -diketones, respectively. Harris and co-workers have elegantly demonstrated the effectiveness of the Claisen reaction through several syntheses of polyketide-derived natural products.³ Both reactions, however, have some limitations. For example, significant problems are often encountered when esters bearing acidic hydrogen atoms are employed in the Claisen reaction. The reactions often proceed in low yield due to competing side reactions. When methods for the kinetic generation of enolate anions in aprotic media were developed,^{4,5} the acylation of enolates with anhydrides or acid chlorides provided a useful route to β -dicarbonyl compounds.⁶ The major side reaction, O-acylation, could be minimized either by inverse addition⁷ or by the use of acyl cyanides⁸ or acylimidazoles⁹ instead of acid chlorides. For certain systems intramolecular acylation is possible. In the example shown in eq. 1 the Baker-Venkataraman



reaction¹⁰ is used to generate a β -diketone. This intramolecular acyl transfer reaction has become a major re-

(1) Hauser, C. R.; Hudson, B. E., Jr. *Org. React. (N.Y.)* **1942**, **1**, 266.
(2) Hauser, C. R.; Swamer, F. W.; Adams, J. T. *Org. React. (N.Y.)* **1954**, **8**, 59.

(3) Sandifer, R. M.; Bhattacharya, A. K.; Harris, T. M. *J. Org. Chem.* **1981**, **46**, 2260 and references therein.

(4) Creger, P. L. *J. Am. Chem. Soc.* **1967**, **89**, 2500.

(5) Ketones: Stork, G.; Kraus, G. A.; Garcia, G. A. *J. Org. Chem.* **1974**, **39**, 3459. Acid dianions: Pfeffer, P. E.; Silbert, L. S.; Chirinko, J. M. *Ibid.* **1972**, **37**, 451. Ester anions: Rathke, M. W.; Deitch, J. *Tetrahedron Lett.* **1971**, 2953. Hydrazones: Enders, D.; Weuster, D. *Ibid.* **1978**, 2853.

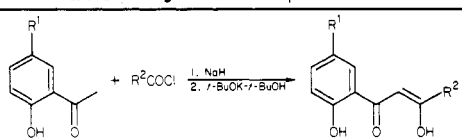
(6) House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; Chapter 11.

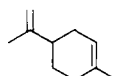
(7) Beck, A. K.; Hoekstra, M. S.; Seebach, D. *Tetrahedron Lett.* **1977**, 1187.

(8) Howard, A. S.; Meerholz, C. A.; Michael, J. P. *Tetrahedron Lett.* **1979**, 1339.

(9) Denniff, P.; Whiting, D. A. *Chem. Commun.* **1966**, 712.

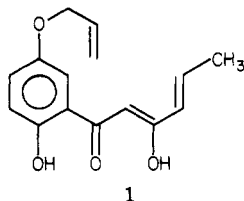
(10) Hauser, C. R.; Swamer, F. W.; Adams, J. T. *Org. React. (N.Y.)* **1954**, **8**, 168-172.

Table I. Synthesis of β -Diketones


entry	R ¹	R ²	conds ^a	yield %	compd
1	H	CH ₃ CH=CH	A	54	4
2	OCH ₂ CH=CH ₂	CH ₃ CH=CH	A	55	1
3	OCH ₂ CH=CH ₂	CH ₃ (CH=CH) ₂	A	57	5
4	OCH ₂ CH=CH ₂	CH ₃ (CH=CH) ₂	B	31	
5	OCH ₂ CH=CH ₂	CH ₃ (CH=CH) ₂	C	63	
6	H	CH ₃	A	28	6 ^c
7	H	C ₆ H ₁₁	A	52	7
8	H	CH ₂ =CH	A	6	
9	H	PhCH=CH	A	61	8
10	H	Ph	A	64	9 ^d
11	OCH ₂ CH=CH ₂	5-Brfuryl	A	50	10
12	OCH ₂ CH=CH ₂		A	68	11

^a A, one-pot reaction; B, one-pot reaction, *i*-Pr₂NLi added in second step instead of *t*-BuOK-*t*-BuOH; C, one-pot reaction, DMF used instead of THF. ^b TLC analysis indicated that the aryl ester had been formed. However, no recognizable products were obtained after the addition of the *t*-BuOK-*t*-BuOH. ^c Identical with known compound prepared from 2 and ethyl acetate. ^d Identical with known compound.¹⁴

action in flavone chemistry.¹¹ Interestingly, the use of this reaction appears to have been confined to the transfer of aromatic or heteroaromatic acyl groups.¹² Additionally, the vigorous reaction conditions often employed would not be compatible with sensitive functionality. In this paper we report the results of a study to determine the scope and limitations of this reaction when aliphatic acyl groups are transferred. The impetus for this study was provided by the low yields encountered when β -diketones such as 1 were synthesized by way of intermolecular routes.



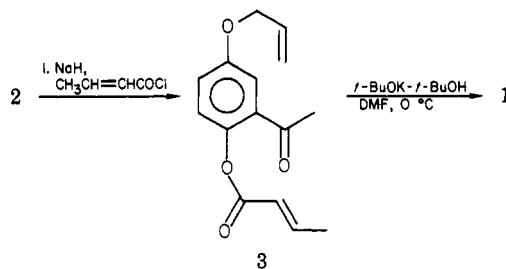
The condensation of 5-(allyloxy)-2-hydroxyacetophenone (2) with ethyl crotonate under a variety of conditions failed to afford 1. The reaction of the dianion of 2 (2.1 equiv of *i*-Pr₂NLi, 0 °C or -78 °C) with crotonoyl chloride furnished variable yields of 1. However, generation of keto ester 3 followed by reaction with the potassium *tert*-butoxide-*tert*-butyl alcohol complex¹³ provided a 45% yield of 1. A distinctive feature of the proton NMR spectrum of 1 is a sharp singlet around δ 6.1 for the vinylic hydrogen at C-2. While the two-step process involving the isolation of 3 was convenient, both reactions could, in principle, be conducted

(11) Thakar, K. A.; Muley, P. R. *Ind. J. Chem. B* 1975, 14, 226.

(12) For isolated examples with aliphatic acyl groups, see: Ullal, V. V.; Shah, R. C.; Wheeler, T. S. *J. Chem. Soc.* 1940, 1499. Virkar, V. V.; Wheeler, T. S. *Ibid.* 1939, 1679.

(13) Pearson, D. E.; Buehler, C. A. *Chem. Rev.* 1974, 74, 45. The complex is mentioned on p 46.

(14) Wheeler, T. S. "Organic Synthesis"; Wiley: New York, 1963; Collect. Vol. IV, p 478. Their mp was 120 °C.



in the same reaction vessel. This proved to be the case. The yield for the one-pot procedure was 55%. Table I depicts the results obtained from several experiments. Entries 3 and 4 demonstrate that the potassium enolate is significantly superior to the lithium enolate in the acyl transfer step. Entry 6 illustrates a limitation of this reaction. When the ester group has α -protons that are comparable in acidity to the ketone, a mixture of products is obtained. In this case, the major products were derived from the ester enolate. Competitive deprotonation notwithstanding, this modification will become a useful alternative to existing intermolecular pathways. In view of the variable yields obtained in the traditional Baker-Venkataraman reaction, the conditions developed here should furnish higher yields and permit its extension to more elaborate and sensitive flavones.

Experimental Section

Unless otherwise noted, materials were obtained from commercial suppliers and were used without purification. Diethyl ether and THF were distilled from LiAlH₄ prior to usage. Dichloromethane was distilled from P₂O₅. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were determined on a Beckman IR-4250 spectrometer. Nuclear magnetic resonance spectra were determined on a Varian EM-360 60-MHz instrument. Carbon-13 NMR spectra were determined on a JOEL FX-90Q Fourier transform instrument. Both proton and carbon chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. High-resolution mass spectra were recorded on an AEI MS-902 high-resolution mass spectrometer. Analyses were performed by Galbraith Laboratories.

General Conditions for the Acyl Transfer Reaction. To a suspension of 1 equiv of sodium hydride (hexanes washed) in dry tetrahydrofuran (0.5 M) was added by syringe a solution of the requisite *o*-hydroxyacetophenone (1 equiv) in THF. The reaction mixture was allowed to warm to ambient temperature for 30 min and then cooled to 0 °C. After the addition of the acid chloride (1 equiv) at 0 °C, the resulting yellow solution was stirred for 1 h at 0 °C. The *tert*-butoxide/*tert*-butyl alcohol complex (2 equiv) was then added rapidly as a solid. The deep red solution was stirred at 0 °C for 1 h. Two equivalents of glacial acetic acid were then added followed by water. After ether extraction, the organic layer was dried and concentrated in vacuo. Column chromatography on silica gel with various mixtures of hexane and methylene chloride provided pure products.

3-Hydroxy-1-(2-hydroxyphenyl)hexa-2,4-dien-1-one (4): NMR (CDCl₃) δ 1.90 (d, *J* = 7 Hz, 3 H), 5.64–7.7 (m, 6 H), 6.03 (s, 1 H), 12.07 (s, 1 H), 14.50 (s, 1 H); IR (Nujol) 1630, 1560, 770 cm⁻¹. Anal. Calcd for C₁₂H₁₂O₃; C, 70.58; H, 5.92. Found: C, 70.84; H, 5.79.

3-Hydroxy-1-[5-(allyloxy)-2-hydroxyphenyl]hexa-2,4-dien-1-one (1): NMR (CDCl₃) δ 1.92 (d, *J* = 7 Hz, 3 H), 5.2–7.7 (m, 8 H), 4.57 (d, *J* = 4 Hz, 2 H), 6.05 (s, 1 H); IR (Nujol) 1640, 1570, 790 cm⁻¹.

3-Hydroxy-1-[5-(allyloxy)-2-hydroxyphenyl]octa-2,4,6-trien-1-one (5): NMR (CDCl₃) δ 1.88 (d, *J* = 5 Hz, 3 H), 4.48 (d, *J* = 5 Hz, 2 H), 5.12–6.4 (m, 6 H), 6.07 (s, 1 H), 6.80–7.32 (m, 3 H), 11.72 (s, 1 H), 14.7 (br s, 1 H); IR (CCl₄) 1635, 1555, 770, 750 cm⁻¹. Anal. Calcd for C₁₇H₁₈O₄; C, 71.31; H, 6.34. Found: C, 71.52; H, 6.48.

3-Hydroxy-1-(2-hydroxyphenyl)oct-2-en-1-one (7): NMR (CDCl₃) δ 0.62–1.95 (m, 9 H), 2.10–2.72 (m, 2 H), 6.13 (s, 1 H),

6.68–7.78 (m, 4 H), 12.07 (s, 1 H), 15.12 (s, 1 H). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 72.02; H, 8.17.

3-Hydroxy-1-(2-hydroxyphenyl)-5-phenylpenta-2,4-dien-1-one (8): NMR ($CDCl_3$) δ 6.30 (s, 1 H), 6.42–7.80 (m, 11 H), 12.40 (s, 1 H), 15.02 (br s, 1 H). Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found: C, 76.48; H, 5.37.

3-Hydroxy-1-[5-(allyloxy)-2-hydroxyphenyl]-3-(5-bromo-2-furyl)prop-2-en-1-one (10): NMR ($CDCl_3$) δ 4.56 (d, $J = 4$ Hz, 2 H), 5.15–6.40 (m, 3 H), 6.50 (d, $J = 3$ Hz, 1 H), 7.08–7.46 (m, 5 H), 10.50 (s, 1 H), 14.10 (br s, 1 H).

3-[4-(2-Propenyl)cyclohexenyl]-3-hydroxy-1-[5-(allyloxy)-2-hydroxyphenyl]prop-2-en-1-one (11): NMR ($CDCl_3$) δ 1.78 (br s, 3 H), 1.92–2.60 (m, 7 H), 4.50 (d, $J = 5$ Hz, 2 H), 4.75 (br s, 2 H), 5.12–6.15 (m, 3 H), 6.21 (s, 1 H), 6.80–7.35 (m, 4 H), 11.80 (s, 1 H), 15.40 (s, 1 H). Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.07; H, 7.17.

Acknowledgment. We thank the Alfred P. Sloan Foundation for partial support of this work.

Registry No. 1, 90554-75-9; 2, 40815-75-6; 3, 90554-76-0; 4, 90554-77-1; 5, 90554-78-2; 6, 90541-51-8; 7, 90554-79-3; 8, 39103-35-0; 9, 39103-33-8; 10, 90554-80-6; 11, 90554-81-7; HO-C₆H₄-o-Ac, 118-93-4; CH₃(CH=CH)₂COCl, 90554-82-8; CH₃COCl, 75-36-5; *n*-C₅H₁₁COCl, 142-61-0; CH₂=CHCOCl, 814-68-6; PhCH=CHCOCl, 102-92-1; PhCOCl, 98-88-4; BrC=CHCH=C(COCl)O, 26726-16-9; CH₂=C(CH₃)CHCH₂CH=C(COCl)C-H₂CH₂, 90554-83-9; CH₃CH=CHCOCl, 10487-71-5.

Hard Acid and Soft Nucleophile Systems. 9¹ Cleavage of Activated Carbon–Carbon Double Bonds with a Hard Lewis Acid and Ethanethiol

Kaoru Fuji,* Takeo Kawabata, Manabu Node, and
Eiichi Fujita

Institute for Chemical Research, Kyoto University,
Kyoto 611, Japan

Received February 8, 1984

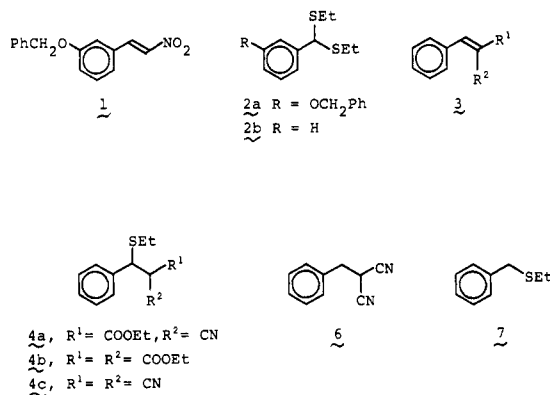
The principle of hard and soft acids and bases (HSAB)² has played an important role in understanding the chemoselectivity of reactions^{3,4} and in the development of new reactions. Recently we have reported cleavage reactions of a variety of carbon–oxygen bonds of ethers⁵ and esters⁶ using combinations of a hard acid and a soft nucleophile. Coordination of a hard acid with the oxygen atom, which is a hard base, activates the carbon–oxygen bond followed by attack of a soft nucleophile on the carbon atom, which is regarded as a soft acid, to accomplish a carbon–oxygen bond cleavage. As both the pulling factor and the pushing factor are indispensable in this type of reactions, the transition state is situated between S_N1 and S_N2 dis-

placement at the carbon atom in the mechanistic spectrum.

Almost all covalent bonds have more or less hard–soft dissymmetry as well as charge dissymmetry. Thus, carbon–heteroatom bonds as well as carbon–oxygen bonds are cleaved with an appropriate combination of a hard acid and a soft nucleophile.⁷ This account describes the cleavage of carbon–carbon double bonds bearing activating group(s) with a hard Lewis acid and ethanethiol.⁸

Results and Discussion

A combination of boron trifluoride etherate and ethanethiol has proved to be effective for deblocking the benzyl protecting group of alcohols and phenols.⁹ However, attempted deblocking of 1 with this reagent resulted in the formation of an unexpected product 2a in 48% yield,¹⁰ by



cleavage of the carbon–carbon double bond. A similar reaction occurred to afford 2b in 88% yield when a styrene derivative 3a was treated with boron trifluoride etherate and ethanethiol at room temperature for 8 days (Table I, entry 1). In order to find a more effective catalyst for the cleavage, we examined other Lewis acids. Except for lanthanide chlorides (entries 6–8), the harder a Lewis acid is, the greater activity it possesses. The order of the activity of metal halides (entries 2–5) corresponds to that of their reported hardness.¹¹ Rare earth chlorides are hard Lewis acids¹¹ and have been reported to be effective catalysts for acetalization of aldehydes.¹² However, no double-bond cleavage occurred with rare earth chlorides, but the reaction ceased at the Michael addition stage, giving 4a in some cases (entries 6 and 7). This might be attributed to their weak Lewis acidities.¹³ It appears that the double-bond cleavage requires a hard acid that also has strong Lewis acidity. Aluminum chloride and bromide are satisfactory Lewis acids in this respect.

The double bond in styrene derivatives 3b–h was cleaved under similar reaction conditions to afford 2b in fair to good yields. Attempted reaction of nitroolefins 3b and 3c with aluminum chloride resulted in the formation of an unidentifiable mixture of products. Ethyl cinnamate did not give 2b with aluminum chloride or bromide in ethanethiol and dichloromethane at room temperature after 2.5 h but furnished ethyl 3-(ethylthio)-3-phenylpropionate¹⁴

(1) For part 8 in this series, see: Node, M.; Kawabata, T.; Ohta, K.; Watanabe, K.; Fujimoto, M.; Fujita, E.; Fuji, K. *J. Org. Chem.*, in press.

(2) Pearson, R. G. *J. Am. Chem. Soc.* 1963, 85, 3533.

(3) For a review, see: (a) Pearson, R. G. "Hard and Soft Acids and Bases"; Dowden, Hutchinson, & Ross Inc.; Stroudsburg, 1973. (b) Ho, T.-L. "Hard and Soft Acids and Bases Principle in Organic Chemistry"; Academic Press: New York, 1977.

(4) For a recent example, see: Semmelhack, M. F.; Tamura, R. *J. Am. Chem. Soc.* 1983, 105, 4099.

(5) (a) Node, M.; Hori, H.; Fujita, E. *J. Chem. Soc., Perkin Trans. 1* 1976, 2237. (b) Node, M.; Nishide, K.; Fuji, K.; Fujita, E. *J. Org. Chem.* 1980, 45, 4275. (c) Node, M.; Ohta, K.; Kajimoto, T.; Nishide, K.; Fujita, E.; Fuji, K. *Chem. Pharm. Bull.* 1983, 31, 4178.

(6) (a) Node, M.; Nishide, K.; Sai, M.; Fuji, K.; Fujita, E. *J. Org. Chem.* 1981, 46, 5163. (b) Node, M.; Nishide, K.; Ochiai, M.; Fuji, K.; Fujita, E. *Ibid.* 1981, 46, 5163.

(7) Node, M.; Kawabata, T.; Ohta, K.; Watanabe, K.; Fuji, K.; Fujita, E. *Chem. Pharm. Bull.* 1983, 31, 749.

(8) For a preliminary report, see: Fuji, K.; Kawabata, T.; Node, M.; Fujita, E. *Tetrahedron Lett.* 1981, 22, 875.

(9) Fuji, K.; Ichikawa, K.; Node, M.; Fujita, E. *J. Org. Chem.* 1979, 44, 1661.

(10) Fuji, K.; Kawabata, T.; Fujita, E. *Chem. Pharm. Bull.* 1980, 28, 3662.

(11) Klopman, G. *J. Am. Chem. Soc.* 1968, 90, 223.

(12) Luche, J.-L.; Gemol, A. L. *J. Chem. Soc., Chem. Commun.* 1978, 976.

(13) Gemol, A. L.; Luche, J.-L. *J. Org. Chem.* 1979, 44, 4187.