Communications

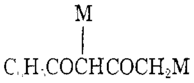
See Editorial, *J. Org. Chem.*, **37**, No. 19, 4A (1972).

Reaction of Dialkali Salts of Benzoylacetone with 2-Chloroquinoline. Evidence for an SRN1 Mechanism in Heteroaromatic Nucleophilic Substitution[1]

Summary: Dialkali metal salts of benzoylacetone have been found to react with 2-chloroquinoline in liquid ammonia to produce 1-phenyl-4-(2-quinolyl)-1,3-butanedione by a radical-chain mechanism.

Sir: In view of recent reports[2-4] concerning the newly discovered SRN1 mechanism for carboaromatic nucleophilic substitution, we wish to describe the present results, which provide strong evidence that a similar mechanism can operate in heteroaromatic substitution.

Recently,[5] we examined the reaction of disodiobenzoylacetone (**1**, M = Na) with 2-chloroquinoline in



$$\overset{\text{M}}{\overset{|}{\text{C}_6\text{H}_5\text{COCHCOCH}_2\text{M}}}$$

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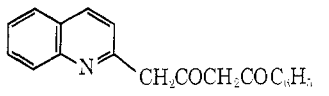

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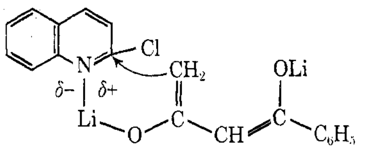
liquid ammonia as a route to β diketone **2** and as a previously unreported type of reaction involving 1,3 dianions such as **1**. However, exposure of 2-chloroquinoline to **1** (M = Na or K) at −33° afforded only modest yields of diketone **2** in spite of the established nucleophilicity of such dianions[6] and the propensity of 2-chloroquinoline toward halogen displacement by carbanionic species.[7] On the assumption that these reactions were proceeding by a classical SNAr2 mechanism,[8] we extended our study to include dilithiobenzoylacetone (**1**, M = Li), in the hope that the more effective coordinating power of lithium would lead to appreciable cationization[8] of the ring nitrogen. It seemed that the desired displacement reaction might then be facilitated by delivery of the terminal carbanion site of **1** to the electrophilic 2 position of the heterocyclic nucleus through a cyclic transition state such as **3**.[8,9] To assess this potential metallic cation effect,



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2-chloroquinoline was allowed to react with 2 mol equiv of dialkali salts **1** (M = K, Na, and Li) in liquid ammonia at −33° for 1 hr under a nitrogen atmosphere to afford ketone **2** in yields of 17, 30, and 71%, respectively.[10] The dramatic increase in the yield of **2** with **1** (M = Li) lent support to the hypothesis presented above.[11] However, on closer examination, it became evident that these reactions were markedly retarded by radical inhibitors. Thus, when 2-chloroquinoline was allowed to react with **1** (M = Li) for 1 hr in the presence of 0.1 equiv of tetraphenylhydrazine (TPH)[2] or *p*-dinitrobenzene (DNB),[12] yields of **2** dropped to 7 or 2%, respectively. Catalytic amounts of oxygen[12] decreased the yield of **2** to <1%. Yields of **2** obtained with **1** (M = Na or K) were also lowered to <1% by DNB.

The inhibitory action of TPH, DNB, and oxygen, coupled with the observation that catalytic amounts of DNB do not destroy **1** (M = K) in the absence of 2-chloroquinoline, indicates that the present reactions occur through a radical-chain mechanism in which inhibition takes place by a chain breaking process. On the basis of this evidence and precedents cited by other investigators,[2-4,13] we propose that the substitutions involving dialkali salts **1** occur *via* the mechanism shown in Scheme I. The enhanced reactivity of **1** (M = Li) may indeed result from coordination of the lithium cation with the ring nitrogen, which

Scheme I[a]

$$2\text{-ClQ} + \text{BAc}^{2-} \longrightarrow 2\text{-ClQ}\cdot^{-} + \text{BAc}\cdot^{-}$$

$$2\text{-ClQ}\cdot^{-} \longrightarrow \text{Q}\cdot + \text{Cl}^{-}$$

$$\text{Q}\cdot + \text{BAc}^{2-} \longrightarrow \text{QBAc}\cdot^{2-}$$

$$\text{QBAc}\cdot^{2-} + 2\text{-ClQ} \longrightarrow \text{QBAc}^{-} + 2\text{-ClQ}\cdot^{-}$$

[a] 2-ClQ = 2-chloroquinoline; BAc^{2-} = benzoylacetone dianion.

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[1] (a) Supported by Grants GM-14340 and NS-10197 from the National Institutes of Health. (b) Abstracted from the Ph.D. dissertation of J. C. Greene, Virginia Polytechnic Institute and State University, Sept 1971. (c) Presented in part at the Southeastern Regional Meeting of the ACS, Nashville, Tenn., Nov 1971.

[2] J. K. Kim and J. F. Bunnett, *J. Amer. Chem. Soc.*, **92**, 7463 (1970).

[3] J. K. Kim and J. F. Bunnett, *ibid.*, **92**, 7464 (1970).

[4] R. A. Rossi and J. F. Bunnett, *ibid.*, **94**, 683 (1972).

[5] J. F. Wolfe and T. P. Murray, *J. Org. Chem.*, **36**, 354 (1971).

[6] For reviews of the chemistry of 1,3 dianions, see T. M. Harris and C. M. Harris, *Org. React.*, **17**, 155 (1969); H. Smith, "Organic Reactions in Liquid Ammonia," Interscience Publishers, New York–London, 1963, pp 55–89.

[7] Y. Mizuno, K. Adachi, and K. Ikeda, *Pharm. Bull.* (*Tokyo*), **2**, 225 (1954).

[8] R. G. Shepherd and J. L. Fiedrick, *Advan. Heterocycl. Chem.*, **4**, Chapter 6 (1965).

[9] W. H. Puterbaugh and R. L. Readshaw [*J. Amer. Chem. Soc.*, **82**, 3635 (1960)] propose a related transition state in the reaction of lithium enolates with α-halo acids.

[10] Details for these and all other experiments described in this paper will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-72-3199. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

[11] This effect is opposite that normally observed in alkylations of dianions such as **1** with primary halides, where dilithio salts are considerably less reactive than their disodio and dipotassio counterparts; see K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 61 (1965).

[12] G. A. Russell and W. C. Danen, *J. Amer. Chem. Soc.*, **90**, 347 (1968).

[13] A. R. Buick, T. J. Kemp, G. T. Neal, and T. J. Stone, *J. Chem. Soc. A*, 666 (1969).

facilitates electron transfer[14] from dianion **1** and initiation of the radical-chain reaction. Apparently such complexation is less pronounced with **1** (M = Na or K).

Studies designed to test the generality of the present radical substitution mechanism with other halogenated heterocycles and carbanions are in progress.

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[14] (a) Quaternization of aromatic azines markedly increases their ease of electrochemical reduction: K. B. Wilberg and T. P. Lewis, *J. Amer. Chem. Soc.*, **92**, 7154 (1970). (b) Although the electron-donor properties of 1,3 dianions have not been extensively investigated, electron transfer does occur with diaryliodonium salts; see K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **29**, 3511 (1964).