Solvent Effects in Heteroaromatic $S_{RN}1$ Reactions[1a]

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Several solvents other than liquid ammonia were tested as possible media for heteroaromatic $S_{RN}1$ reactions. Using the reaction of potassioacetone with 2-chloroquinoline as a model system, it has been demonstrated that tetrahydrofuran and dimethylformamide permit the $S_{RN}1$ reaction to proceed satisfactorily under photostimulation with Pyrex-filtered light. A significant amount of thermally induced $S_{RN}1$ reaction occurred in each of these solvents. Results obtained in 1,2-dimethoxyethane, dimethyl sulfoxide, ether, and benzene were less satisfactory. In tetrahydrofuran, photostimulated reaction of potassio-2,4-dimethyl-3-pentanone with 2-chloroquinoline proceeded smoothly, potassioacetone reacted slower with 2-bromopyridine than with 2-chloroquinoline, and attempted reaction of potassioacetone with iodobenzene gave only a trace of phenylacetone. Potassioacetophenone and lithioacetone both failed to show appreciable reactivity toward 2-chloroquinoline upon irradiation in tetrahydrofuran.

Aromatic nucleophilic substitutions via the $S_{RN}1$ mechanism were discovered by Kim and Bunnett in 1970.[2] This new type of reaction enabled the substitution of appropriate nucleofuges[3] or leaving groups on unactivated carboaromatic systems with suitable nucleophiles. These reactions are believed to proceed by the chain mechanism shown in Scheme I, in which Ar–X represents an aromatic substrate with nucleofugal group X and N^- is an appropriate nucleophile. Initiation (eq 1) involves an electron transfer to the substrate. The radical anion thus formed expels the nucleofuge (eq 2) and the resulting aryl radical combines with the nucleophile to form a product radical anion (eq 3). The propagating cycle is completed by transfer of an electron from the product radical anion to another substrate molecule (eq 4). Initiation has been shown to be effected by near-UV light,[4] by dissolved alkali metals,[5] and by electrochemical means.[6,7]

Scheme I

$$\mathrm{Ar{-}X} + e \rightarrow [\mathrm{Ar{-}X}]^{-\cdot} \qquad (1)$$

$$[\mathrm{Ar{-}X}]^{-\cdot} \rightarrow \mathrm{Ar}\cdot + \mathrm{X}^- \qquad (2)$$

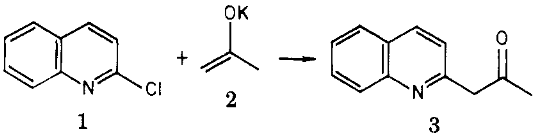
$$\mathrm{Ar}\cdot + \mathrm{N}^- \rightarrow [\mathrm{Ar{-}N}]^{-\cdot} \qquad (3)$$

$$[\mathrm{Ar{-}N}]^{-\cdot} + \mathrm{Ar{-}X} \rightarrow \mathrm{Ar{-}N} + [\mathrm{Ar{-}X}]^{-\cdot} \qquad (4)$$

It is apparent from recent reviews[8,9] that liquid ammonia has been the solvent of choice for a majority of aromatic $S_{RN}1$ reactions. No systematic study of other solvents was available until 1976 when Bunnett and co-workers[10] published the results of an investigation dealing with solvent effects in the $S_{RN}1$ reaction of potassium diethyl phosphite and several other nucleophiles with halobenzenes and phenyltrialkylammonium salts. Satisfactory results were obtained employing acetonitrile, *tert*-butyl alcohol, dimethyl sulfoxide (Me_2SO), *N*,*N*-dimethylformamide (DMF), 1,2-dimethoxyethane (DME), and *N*,*N*-dimethylacetamide, while tetramethylenesulfone, *N*-methyl-2-pyrrolidone, hexamethylphosphoramide, *tert*-butylamine, and water were less suitable. Reaction rates and product yields in the solvents investigated were generally lower than those observed in liquid ammonia. Recently, Me_2SO has been employed as solvent for $S_{RN}1$ reactions of phenyl halides with the potassium enolate of pinacolone,[11] potassium diphenylphosphide,[12] and dimsyl anion.[13] Reactions of aryl halides with phenoxide ion apparently occur by the $S_{RN}1$ mechanism in aqueous *tert*-butyl alcohol;[14] phenoxide salts are unreactive in liquid ammonia.[15]

The discovery that halogenated heteroaromatic azines react with ketone enolates via a photoinduced $S_{RN}1$ mechanism in liquid ammonia[16-19] prompted us to undertake an investigation of solvent effects in heteroaromatic $S_{RN}1$ reactions. The only previous reports of such reactions in solvents other than liquid ammonia have involved thermally induced substitution on 4-bromoisoquinoline with thiophenoxide ion in methanol,[20] reactions of potassium superoxide with halogenated quinolines and isoquinolines in Me_2SO,[21] and reactions of 5-halogeno-2*H*,3*H*-benzo[*b*]thiophene-2,3-diones with several nucleophiles in Me_2SO.[22]

In the present study, the reaction of 2-chloroquinoline (**1**) with potassioacetone (**2**) to form 2-acetonylquinoline (**3**) was chosen as the initial model system for testing a series of representative solvents. This reaction (eq 5) proceeds cleanly via the $S_{RN}1$ mechanism upon photostimulation in liquid ammonia.[18] We were particularly interested in determining if THF, DME, and DMF would support these reactions, for if they did, it might be possible to extend the synthetic scope of $S_{RN}1$ reactions to include carbanion salts which are too basic or insoluble for use in liquid ammonia.



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[1] (a) This research was supported by the National Science Foundation, Grant No. CHE 74-20520. (b) Taken from the Ph.D dissertation of M. P. Moon, Virginia Polytechnic Institute and State University, Dec 1978.

[2] J. K. Kim and J. F. Bunnett, *J. Am. Chem. Soc.*, **92**, 7463, 7464 (1970).

[3] J. Mathieu, A. Allais, and J. Vallas, *Angew. Chem.*, **72**, 71 (1960).

[4] R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, **38**, 1407 (1973).

[5] R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, **38**, 3020 (1973).

[6] W. J. M. van Tilburg, C. J. Smit, and J. J. Scheele, *Tetrahedron Lett.*, 2113 (1977).

[7] J. Pinson and J. M. Saveant, *J. Am. Chem. Soc.*, **100**, 1506 (1978).

[8] J. F. Bunnett, *Acc. Chem. Res.*, **11**, 413 (1978).

[9] J. F. Wolfe and D. R. Carver, *Org. Prep. Proc. Int.*, **10**, 224 (1978).

[10] J. F. Bunnett, R. G. Scamehorn, and R. P. Traber, *J. Org. Chem.*, **41**, 3677 (1976).

[11] R. G. Scamehorn and J. F. Bunnett, J. *Org. Chem.*, **42**, 1449 (1977).

[12] J. R. Bunnett and J. E. Swartz, *J. Org. Chem.*, **44**, 340 (1979).

[13] S. Rajan and K. Muralimohan, *Tetrahedron Lett.*, 483 (1978).

[14] S. Rajan and P. Sridaran, *Tetrahedron Lett.*, 2177 (1977).

[15] J. F. Bunnett and J. E. Sundberg, *J. Org. Chem.*, **41**, 1702 (1976).

[16] J. F. Wolfe, J. C. Green, and T. Hudlicky, *J. Org. Chem.*, **37**, 3199 (1972).

[17] J. V. Hay, T. Hudlicky, and J. F. Wolfe, *J. Am. Chem. Soc.*, **97**, 374 (1975).

[18] J. V. Hay and J. F. Wolfe, *J. Am. Chem. Soc.*, **97**, 3702 (1975).

[19] A. P. Komin and J. F. Wolfe, *J. Org. Chem.*, **42**, 2481 (1977).

[20] J. A. Zoltewicz and T. M. Oestreich, *J. Am. Chem. Soc.*, **95**, 6863 (1973).

[21] T. Yamaguchi and H. C. van der Plas, *Recl. Trav. Chim. Pays-Bas*, **96**, 89 (1977).

[22] F. Ciminale, G. Bruno, L. Testafarri, M. Tiecco, and G. Martelli, *J. Org. Chem.*, **43**, 4509 (1978).

Table I. Reactions of 1 with 2 in Several Solvents

expt. no.	solvent	time, h	conditions[a]	% composit[b]	
				1	3
1[c]	NH_3	1.0	UV	0	90
2[c]	NH_3	1.0	UV, DNB	91	2
3[c]	NH_3	1.0	Dk	86	1
4	THF	1.0	UV	13	82
5	THF	0.25	UV	38	52
6	THF	1.0	UV-vis	28	53
7	THF	1.0	Dk	61	28
8	THF	1.0	UV, DTBN	75	17
9	THF	1.0	UV, DNB	78	14
10	THF	1.0	UV-vis, DTBN	90	8
11	THF	1.0	UV-vis, DNB	88	3
12	THF	1.0	Dk, DTBN	86	2
13	THF	1.0	Dk, DNB	77	2
14	DME	1.0	UV-vis	59	28
15	DME	1.0	Dk	78	9
16	DME	1.0	UV-vis, DTBN	90	2
17	DME	1.0	UV-vis, DNB	85	2
18	DME	1.0	Dk, DTBN	87	2
19	DME	1.0	Dk, DNB	84	2
20	ether	2.0	UV	89	9
21	DMF	1.0	UV-vis	3	74
22	DMF	0.25	UV-vis	27	52
23	DMF	0.25	Dk	44	36
24	DMF	0.25	UV-vis, DTBN	62	13
25	DMF	0.25	UV-vis, DNB	61	15
26	DMF	0.25	Dk, DTBN	74	8
27	DMF	0.25	Dk, DTBN	92	4
28	benzene	1.0	UV-vis	89	4

[a] UV and UV-vis represent irradiations at 300-350 nm and 350-750 nm, respectively. Dk represents a dark reaction. DTBN is di-*tert*-butyl nitroxide and DNB is *p*-dinitrobenzene). [b] These percentages were determined by GC analysis using the internal standard method.[26] With the exceptions of experiments 20 and 28, the values reported are averages of at least two experiments. [c] Data taken from ref 18.

Results and Discussion

Enolate **1** and related potassium salts were generated from the appropriate ketone by means of potassium hydride.[23] Reactions were conducted without illumination (dark), with illumination from three ordinary 15-W fluorescent bulbs emitting at 350–750 nm (UV-vis), and with illumination from four 12.5-W bulbs emitting maximally at 350 nm (UV). The radical chain character of the reactions was tested using the inhibitors *p*-dinitrobenzene (DNB)[24] and/or di-*tert*-butyl nitroxide (DTBN).[25] Table I[26] contains the results obtained for the reaction of eq 5 in several solvents. The first three entries are data obtained earlier for this system in liquid ammonia.[18] All percentages given are yields determined by gas chromatography.

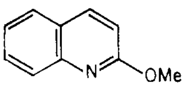
Experiments 4–13 are reactions conducted in THF. Irradiation at 350 nm for 1 h in this solvent afforded **3** in yields similar to those obtained in liquid ammonia (compare experiments 1 and 4). Shorter periods of UV irradiation (experiment 5) lead to reduced yields of **3**. Photostimulation with ordinary fluorescent light was less effective than irradiation employing the narrower band near-UV source (compare experiments 6 and 4). That the photostimulated reactions in THF were proceeding mainly by the $S_{RN}1$ mechanism was evidenced by the dramatic reduction in yields of **3** observed in the presence of 5 mol % of DTBN and DNB (experiments 8–11). Although the reaction of **1** with **2** proceeds very slowly in liquid ammonia when denied illumination (experiment 3), a similar dark reaction in THF afforded **3** in 28% yield (experiment 7). This appears to be largely a thermally induced[11,12] radical chain substitution rather than an ionic displacement since DTBN and DNB inhibit the formation of **3** in the dark (experiments 12 and 13).

Table II. Reactions of 1 with 2 in Me_2SO

expt. no.	time, min	conditions[a]	base	% composit[b]	
				1	3
29	5	UV-vis	KH	24	37
30	5	UV-vis	*t*-BuOK	83	8
31	15	UV-vis	KH		32[c]
32	15	UV-vis	*t*-BuOK	60	18
33	60	UV-vis	*t*-BuOK	15	37
34	5	UV-vis, DTBN	KH	45	11
35	5	UV-vis, DTBN	*t*-BuOK	94	
36	5	Dk	KH		69
37	60	Dk	*t*-BuOK	30	40

[a] UV-vis represents irradiation at 350-750 nm. DTBN is di-*tert*-butyl nitroxide. Dk represents a dark reaction. [b] Percentages were determined by GC analysis using the internal standard method.[26] [c] Isolated yield.

Results obtained in DME (experiments 14–19) followed the same trends as those in THF; however, the rate of reaction in the former solvent was only about one-half that observed in THF. Photostimulated reactions in DME were accompanied by formation of small amounts (<5%) of substitution products **4** and **5**. The $S_{RN}1$ character of the photostimulated reactions in DME was supported by the reduced yields of **3** obtained upon inhibition (experiments 16 and 17).



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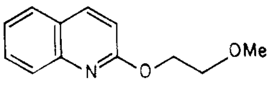

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Of the solvents listed in Table I, DMF allowed the $S_{RN}1$ reaction of eq 5 to proceed the fastest (experiments 21 and 22). There was also a significant dark reaction in this solvent (experiment 23). Inhibition (experiments 24–27) demonstrated that both dark and irradiated reactions take place by the $S_{RN}1$ mechanism. Material balances were consistent among themselves, but lower than those found in the other solvents of Table I, presumably because of the difficulty associated with removing unreacted **1** and product **3** from aqueous DMF prior to analysis. When DNB was used as inhibitor the reaction mixtures took on an intense color. This raised some question as to whether the inhibitory action of DNB was actually due to radical anion interception or merely caused by absorption of near-UV light necessary for photostimulation. Comparison of the inhibitory efficiencies of DNB and DTBN, which generates no color upon admixture with the reactants, showed them to be nearly equal (experiments 24 and 25). Thus, inhibition by DNB must arise mainly from radical anion oxidation.

Included in Table I are reactions employing ether (experiment 20) and benzene (experiment 28), neither of which showed promise as a viable reaction medium.

Data for a series of reactions using Me_2SO as solvent are given in Table II. These experiments were characterized by poor material balances and erratic results. Five exper-

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[23] C. A. Brown, *J. Org. Chem.*, **39**, 1324, 3913 (1974).

[24] R. C. Kerber, G. W. Urry, and N. Kornblum, *J. Am. Chem. Soc.*, **86**, 3904 (1964).

[25] (a) A. K. Hoffmann, A. M. Feldmann, E. Gelblum, and W. G Hodgson, *J. Am. Chem. Soc.*, **86**, 639 (1964). (b) S. F. Nelson and P. D. Bartlett, *J. Am. Chem. Soc.*, **88**, 143 (1966).

[26] H. M. McNair and E. J. Bonelli, "Basic Gas Chromatography", Varian Aerograph, Walnut Creek, CA, 1968, Chapter VII.

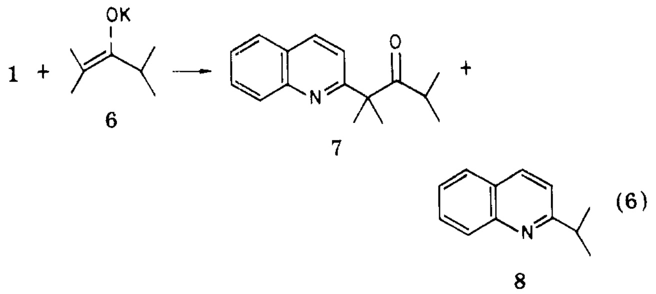
Table III.[a] Reactions of 1 with 6 in THF

expt. no.	time, h	condition[b]	% composition[c] 1	7	8
38	1.0	UV-vis	2	65 (94)	25
39	1.0	UV, DTBN	37	44	9
40	0.5	UV-vis	3	78	10
41	0.25	UV-vis	4	85 (98)	7
42	0.25	UV-vis, DTBN	83	15	
43	0.25	Dk	39	40	
44	0.25	Dk, DTBN	78	17	

[a] The molar ratio of 1 to 6 used in these experiments was 1:2. [b] UV-vis represents irradiation at 350–750 nm. DTBN is di-*tert*-butyl nitroxide. Dk represents a dark reaction. [c] Percentages were determined by GC analysis using the internal standard method.[26] Numbers in parentheses represent yields in liquid ammonia.[18]

iments (experiments 30, 32, 33, 35, and 37) were conducted using potassium *tert*-butoxide instead of potassium hydride to generate enolate **2**. Even though this base–solvent system has been employed with good success in previous $S_{RN}1$ reactions,[11,12] it was unsatisfactory in this study.

Other Reaction Systems in THF. On the basis of the results in Table I, THF was used as solvent for testing several other reactions known to occur by the $S_{RN}1$ mechanism in liquid ammonia. To this end, reactions of **1** with potassio-2,4-dimethyl-3-pentanone (**6**) were studied and the results are given in Table III. Photostimulation at 350–750 nm for 1 h resulted in nearly complete consumption of **1** with formation of the expected ketone **7** accompanied by 2-isopropylquinoline (**8**) (experiment 38). When reaction times were reduced to 0.5 and 0.25 h, yields of **7** increased at the expense of **8** (experiments 40 and 41), implying that **8** is derived from **7**. Formation of **8** can be rationalized in terms of the reaction of **7** with excess enolate **6** as shown in eq 7. Cleavage of **7** is facilitated by the absence of ionizable hydrogens adjacent to the heterocyclic moiety. In contrast to this, ketone **3** does not undergo appreciable cleavage because excess **2** can abstract an acidic methylene hydrogen from **3** to form a stable enolate ion, which in turn is resistant to carbonyl addition.



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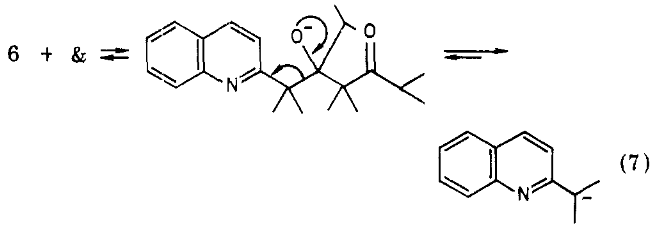

(7)

Photostimulated and dark reactions of enolate **6** with **1** proceed more rapidly than analogous reactions of enolate **2** with **1** (compare experiments 6 and 7 with experiments 41 and 43). Inhibition of both dark and illuminated reactions by DTBN was observed (experiments 42 and 44), but it was less pronounced than in reactions of **2** with **1** (experiments 10 and 12). Dimerization of **6** to form 2,4,4,6,8-pentamethylnonane-3,7-dione, a major competing process when **6** is treated with iodobenzene in liquid ammonia,[27] was not observed.

Finally, four other combinations of enolates and substrates which had been previously tried in liquid ammonia were also tested in THF. Data from these experiments appear in Table IV along with results from the closest corresponding reaction in liquid ammonia. 2-Bromopyridine proved to be significantly less reactive than **1** toward enolate **2** in THF (experiment 45 and 46). For example, UV-stimulated reaction of **1** with **2** affords 82% of 2-acetonylquinoline (**3**) after 1 h (experiment 4), while reaction of 2-bromopyridine with **2** yields only 33% of 2-acetonylpyridine in the same time (experiment 45). Under essentially identical conditions of irradiation, reaction of **2** with 2-bromopyridine is essentially quantitative within 15 min in liquid ammonia.[18]

Iodobenzene yielded only a trace of phenylacetone after 2 h of irradiation with **2** in THF (experiment 47). The corresponding reaction in liquid ammonia yields 67% of phenylacetone after 3 h.[4]

Potassioacetophenone, a poor nucleophile toward **1** in liquid ammonia,[18] failed to show evidence of reaction with **1** in THF (experiment 48).

Lithioacetone, prepared from acetone by means of lithium diisopropylamide, failed to react with **1** after 2 h of 350-nm irradiation at −78 °C (experiment 50). A similar reaction conducted for 10 h at ambient temperature using 350–750-nm light afforded mainly (60%) *N*,*N*-diisopropyl-2-aminoquinoline (experiment 49).

Conclusions

The relative rates of photoinduced consumption of substrate **1** by potassium enolate **2** at ambient temperature increase with respect to solvent as follows: benzene $\simeq$ ether $\ll$ DME $<$ THF $<$ DMF $<$ Me_2SO. This order of reactivity parallels the increasing order of dielectric constants of the respective solvents.[28] However, for preparative purposes the more polar solvents DMF, and especially Me_2SO, appear to offer no advantages over THF, in which substitution proceeds at very respectable rates with a minimum of side reactions. We currently are unable to provide a rationale for the erratic nature of results obtained with Me_2SO.

The sluggish reaction of **2** with 2-bromopyridine and the lack of reactivity of **2** toward iodobenzene in THF argue for use of liquid ammonia for these and other reactions involving similar nucleophiles and substrates. Based on the present results and earlier work by Bunnett and coworkers,[10] DMF would seem to be a reasonably good solvent for less reactive heteroaromatics, while Me_2SO may be suitable for carboaromatic substrates if one chooses not to use liquid ammonia.

The lack of $S_{RN}1$ reactivity of iodobenzene with **2** in THF could conceivably result from several factors. For example, solvation effects have been shown to exert a strong influence on formation and reactivity of radical anions.[29] Perhaps THF is more effective in solvating and thus facilitating formation of the radical anions derived from **1** than the corresponding intermediates arising from iodobenzene. Alternatively, phenyl radicals, which have been shown to be more efficient than quinolyl radicals in

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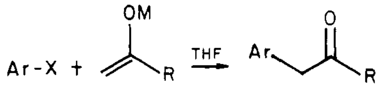
(27) J. F. Wolfe, M. P. Moon, M. C. Sleevi, J. F. Bunnett, and R. R. Bard, *J. Org. Chem.*, **43**, 1019 (1978).

(28) J. A. Riddick and W. B. Bunger, "Techniques of Chemistry", Vol. II, Wiley, New York, 1970.

(29) J. Smid, in "Ions and Ion Pairs in Organic Reactions", M. Szwarc, Ed, Wiley-Interscience, New York, 1972, Chapter 3.

Table IV. Reactions of Enolates with Various Substrates in THF



expt. no.	Ar-X	R	M	time, h	conditions[a]	% composition[b] Ar-X	% composition[b] product
45	2-bromopyridine	CH_3	K	1.0	UV	66	33 (100)[c]
46	2-bromopyridine	CH_3	K	3.0	UV	36	64 (100)[c]
47	iodobenzene	CH_3	K	2.0	UV	~quant.	tr (67)[d]
48	2-chloroquinoline	C_6H_5	K	2.5	UV-vis	quant.	O (14)[e]
49	2-chloroquinoline	CH_3	Li	10	UV-vis	17 (18)	14 (48)[f,g]
50	2-chloroquinoline	CH_3	Li	2	UV[h]	quant.	

[a] UV represents irradiation of 300–350 nm. UV-vis represents irradiation at 350–750 nm. [b] Percentages given were determined by GC analysis using the internal standard method.[26] [c] Yield obtained with UV irradiation for 0.25 h in liquid ammonia.[19] [d] Yield obtained with UV irradiation for 3 h in liquid ammonia.[4] [e] Yield obtained with UV irradiation for 3 h in liquid ammonia.[18] [f] Yield obtained with UV irradiation for 1 h in liquid ammonia.[17] [g] *N,N*-diisopropyl-2-aminoquinoline was the major (60%) product observed. [h] Reaction temperature of −78 °C.

abstracting hydrogen atoms from enolate **6** in liquid ammonia,[27] may show a similar preference for α hydrogens of THF. This would provide termination of the radical-chain sequence shown in Scheme I by providing a nonproductive alternative to the combination of phenyl radicals with enolate **2** (eq 3). A recent report[12] that the reaction of lithium diphenylphosphide with aryl halides apparently occurs via the $S_{RN}1$ mechanism in THF, and that best yields are obtained when the halide is added to excess of the phosphide salt, argues for hydrogen atom abstraction as a major source of difficulty with phenyl radicals in THF. However, the present reactions were conducted by addition of iodobenzene to excess **2**, and still the reaction failed. It is possible that diphenylphosphide ion is a sufficiently more powerful nucleophile than enolate **2**, thus allowing combination of phenyl radicals with the former to compete effectively with hydrogen atom transfer from THF.

The poor reactivity of lithioacetone with **1** in THF (experiments 49 and 50) provides another example of the generally low reactivity of lithio ketones toward heteroaromatic halides.[18,19] This cation effect, which may result from unfavorable ion-pairing and aggregation, is currently under investigation in our laboratories.

Experimental Section

General. All reactions were conducted under an atmosphere of nitrogen at ambient temperature (25–35 °C) unless noted otherwise. The 350–750-nm (UV-vis) photostimulated reactions were performed using a standard Pyrex round-bottomed flask in an apparatus consisting of a 20 × 25 × 51 cm aluminum enclosure containing three 15-W commercial fluorescent bulbs.[1b] The 350-nm (UV) photostimulated reactions were conducted using a water-cooled Pyrex reaction vessel[1b] in a Rayonet RPR-240 photochemical reactor[30] equipped with four 12.5-W bulbs emitting maximally at 350 nm. Dark reactions were conducted in a darkened laboratory using standard Pyrex glassware wrapped with aluminum foil or a black shroud.

Gas chromatographic (GC) analyses and separations were accomplished on Varian Associates 90-P or 1200 instruments using columns of 2.5, 7.5, or 10% Carbowax 20M on Chromosorb G-HP or Chromosorb W-HP and operating between 150 and 225 °C. GC yields were determined by the internal standard method. Quinoline, 4-methylquinoline, diallyl phthalate, and dibutyl phthalate were employed as internal standards. ^1H NMR spectra were determined on a JEOL JMN-PS-100 spectrometer at 100 MHz using tetramethylsilane as reference. Infrared spectra were produced on a Beckman IR-20A-X spectrophotometer. Microanalyses were determined in this Department by Constance D. Anderson, Jorge I Bedia, Elizabeth K. Cassity, T. E. Glass, or Roger W. Stringham on a Perkin-Elmer 240 elemental analyzer. Melting points were observed on a Thomas-Hoover apparatus and are uncorrected.

Tetrahydrofuran (THF) was refluxed over lithium aluminum hydride several hours prior to distillation. 1,2-Dimethoxyethane (DME) was refluxed over sodium hydride and fractionated several times through a column packed with glass helices. Calcium hydride was used to dry dimethylformamide (DMF) and to initially dry dimethyl sulfoxide (Me_2SO) before their distillation at reduced pressure. M_2SO was further purified by treatment with sodium amide and distillation under vacuum. All purified solvents were stored in bottles under an argon atmosphere and over molecular sieves. Commercial potassium *tert*-butoxide was sublimed prior to use. 2-Bromopyridine was distilled from barium oxide and 2-chloroquinoline (**1**) was fractionated at reduced pressure. Potassium hydride (KH) and all other chemicals were used without further purification.

The following experiments are representative and serve as examples for conducting any of the reactions described in the foregoing sections of the paper.

Photostimulated Reaction of 2-Chloroquinoline (1) with Potassioacetone (2) in THF at 350 nm. A 24% dispersion of KH in mineral oil (6.35 g, 37.5 mmol) was washed with hexane in a water-cooled Pyrex reaction vessel.[1b] After the solid had settled, the hexane was drafted off and the flask was flushed with argon. THF (125 mL) was added and the vessel kept under a positive pressure of nitrogen. Acetone (2.8 mL, 37.5 mmol) was slowly introduced and washed down the walls of the flask with additional THF. Immediate evolution of hydrogen was observed. The vessel was lowered into the Rayonet reactor and irradiation was begun. 2-Chloroquinoline (**1**) (1.64 g, 10 mmol) dissolved in THF was then added. After 1 h, the reaction was quenched with 10 mL of water and 4-methylquinoline (0.202 g, 1.91 mmol) was added as an internal standard for GC analysis. The aqueous layer was extracted with ether, and these extracts were combined with the THF layer. The organic solution was dried with $MgSO_4$, filtered, concentrated under aspirator vacuum, and analyzed by gas chromatography. Results appears in Table I, experiment 4. 2-Acetonylquinoline (**3**) was identified by comparison with an authentic sample.[17,31]

Inhibited Photostimulated Reaction of 1 with 2 in THF at 350–750 nm. A suspension of 6.35 g (37.5 mmol) of hexane-washed KH in 125 mL of THF was prepared in a 250-mL round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and an inlet and an outlet for nitrogen. Acetone (3 mL, 37.5 mmol) was added slowly. Vigorous hydrogen evolution was observed and measured (1.1 L) with a gas buret. The pale-yellow anion solution was transferred to the illuminated reactor operating with commercial 15-W lamps.[1b] Addition of a THF solution of **1** (1.64 g, 10 mmol) and DNB (0.084 g, 0.5 mmol) followed. After 1 h, the dark solution was quenched with water and 4-methylquinoline (0.332 g, 2.3 mmol) was added as internal standard for GC analysis. The aqueous layer was separated and extracted with

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(30) Manufactured by the Southern New England Ultra Violet Co., Middletown, CT.

(31) M. T. Wiess and C. R. Hauser, *J. Am. Chem. Soc.*, 71, 2023 (1949).

ether. The ethereal extracts and the THF layer were combined, dried with $MgSO_4$, filtered, concentrated under aspirator vacuum, and, finally, analyzed by GC. Results appear in Table I, experiment 13.

Photostimulated Reaction of 1 with 2 in DME at 350–750 nm. A 24% dispersion of KH in mineral oil (3.13 g, 18.75 mmol) was weighed into a 125-mL flask equipped with a Teflon-coated magnetic stirring bar and an inlet and an outlet for nitrogen. The mixture was washed with hexane and, after the solid had settled, the hexane was removed and replaced with 70 mL of DME. While stirring the solution, acetone (1.5 mL, 18.75 mmol) was slowly added as vigorous hydrogen evolution was observed. Illumination was begun and 0.82 g (5 mmol) of **1** dissolved in DME was added. The intensely orange solution was quenched with a small amount of water after 1 h. The aqueous layer was extracted with ether. The ethereal extracts and the DME layer were combined, dried with $MgSO_4$, filtered, and concentrated under aspirator vacuum. Preparative GC of the mixture afforded unreacted **1**, 2-acetonylquinoline (**3**), and a trace of quinaldine, which apparently arose from cleavage of **3**. 2-Methoxyquinoline (**4**) was isolated as a colorless oil: IR (neat) ν 1020, 1110 cm^{-1} (C–O); ^{1}H NMR ($CDCl_3$) δ 4.04 (s, 3 H, OCH_3), 6.78–7.88 (m, 6 H, aromatic). 1-Methoxy-2-quinolyloxyethane (**5**) was isolated as a pale-yellow oil: IR (neat) ν 1045, 1110 cm^{-1} (C–O); ^{1}H NMR ($CDCl_3$) δ 3.45 (s, 3 H, CH_3), 3.80 (m, 2 H, CH_2), 4.64 (m, 2 H, CH_2), 6.88–7.96 (m, 6 H, aromatic).

Inhibited Dark Reaction of 1 with 2 in DMF. A 24% dispersion of KH in mineral oil (3.13 g, 18.75 mmol) was weighed into a 125-mL flask equipped with a Teflon-coated magnetic stirring bar and an inlet and an outlet for nitrogen. The mixture was washed with hexane, and while the solid was settling, the solution was cooled in an ice bath to ca. 0 °C. The hexane was replaced with 65 mL of DMF. The cloudy solution was stirred until it became clear and acetone (1.5 mL, 18.75 mmol) was added slowly. The solution was allowed to return to room temperature and the flask was wrapped in aluminum foil. After extinguishing the room lights and closing the shades, a solution of **1** (0.82 g, 5 mmol) and DTBN (0.04 g, 0.28 mmol) in DMF was added to the flask. The mixture was quenched after 15 min with a little water, and 4-methylquinoline (0.148 g, 1.03 mmol) was added as internal standard. The solution was diluted with about 300 mL of water and extracted several times with ether. The ethereal extracts were combined, dried with $MgSO_4$, filtered, concentrated under aspirator vacuum, and analyzed by GC. Results appear in Table I, experiment 24.

Dark Reaction of 1 with 2 in Me_2SO. Freshly sublimed potassium *tert*-butoxide (2.1 g, 18.75 mmol) was quickly weighed into a 125-mL round-bottomed flask equipped with a teflon-coated stirring bar and an inlet and an outlet for nitrogen. The flask was flushed with argon and 65 mL of Me_2SO was transferred through a cannula to the reaction flask. After 15 min, acetone (1.5 mL, 18.75 mmol) was added to the stirred solution. The flask was wrapped in aluminum foil and also draped with a black shroud. The room lights were extinguished and a solution of **1** (0.82 g, 5 mmol) in Me_2SO was added. After 1 h, water was added to quench the reaction and 4-methylquinoline (0.113 g, 0.79 mmol) was added as a GC standard. The mixture was diluted with 300 mL of water and extracted with ether several times. The ethereal extracts were combined, dried with $MgSO_4$, filtered, concentrated under aspirator vacuum, and analyzed by GC. Results appear in Table II, experiment 37.

Photostimulated Reaction of 1 with 2 in Me_2SO at 350–750 nm. To 3.13 g (18.75 mmol) of hexane-washed KH in 70 mL of Me_2SO was added 1.5 mL (20 mmol) of acetone. Illumination was begun and 0.82 g (5 mmol) of **1** was added. After 15 min, 10 mL of water was added to quench the reaction. Approximately 300 mL of water was added to further dilute the mixture, which was then extracted several times with ether. The combined extracts were dried with $MgSO_4$, filtered, and concentrated to give a crude orange solid. Recystallization from aqueous ethanol yielded 0.29 g (32%) of **3**, mp 75–75.5 °C (lit.[31] mp 76–77 °C); see Table II, experiment 31. The IR and ^{1}H NMR spectra of this material were identical with those of an authentic sample of **3**.[17,31]

Photostimulated Reaction of 1 with Potassio-2,4-dimethyl-3-pentanone (6) in THF at 350–750 nm. To a suspension of KH (10 mmol) in 50 mL of THF was added 1.14 g (10 mmol) of 2,4-dimethyl-3-pentanone. After 30 min, formation of **6** was assumed to be complete. Illumination was begun and 0.82 g (5 mmol) of **1** was added. The resulting maroon solution was irradiated for 1 h and quenched with 5 mL of water. Diethyl phthalate (0.26 g, 0.93 mmol) was added as the GC standard. The reaction mixture was processed in the usual fashion and analyzed by GC. Results appear in Table III, experiment 40.

Preparative GC of a similar reaction mixture afforded 2-isopropylquinoline (**8**) as a colorless oil: ^{1}H NMR (CCl_4) δ 1.42 (d, 6 H, CH_3), 3.26 (sept, 1 H, isopropyl CH), 7.2–8.1 (m, 6 H, aromatic).

Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.50; H, 7.73.

Chromatography of the reaction mixture on silica gel eluting with ethyl acetate afforded 2-(2-quinolyl)-2,4-dimethyl-3-pentanone (**7**) as white needles, mp 93–94 °C [lit.[18] bp 131–132 °C (1.3 mm)]. Spectral properties of **7** were identical with those of an authentic sample.[18]

Photostimulated Reaction of 2-Bromopyridine with 1 in THF at 350 nm. A solution of 37.5 mmol of **1** was prepared in 125 mL of THF as described above. Irradiation was begun and 1.58 g (10 mmol) of 2-bromopyridine was added. After 3 h of irradiation the reaction solution was quenched with 10 mL of water. Quinoline (0.235 g, 1.82 mmol) was added as internal standard and the reaction was processed in the usual fashion. Results appear in Table IV, experiment 46.

Photostimulated Reaction of 1 with Lithioacetone in THF at 350 nm. To 4.05 g (40 mmol) of diisopropylamine dissolved in 100 mL of THF contained in a 125-mL round-bottomed flask cooled in a dry ice–2-propanol bath was added 40 mmol of *n*-butyllithium in hexane. The resulting solution was stirred for 15 min, acetone (2.32 g, 40 mmol) was added, and stirring was continued for 15 min. The solution was then transferred to the photolysis reaction vessel equipped with a cold finger filled with dry ice–2-propanol. 2-Chloroquinoline (**1**) (1.64 g, 10 mmol) was added and irradiation was conducted at ca. −70 °C for 2 h. The reaction mixture was quenched with water, diallyl phthalate (0.23 g, 1.1 mmol) was added as internal GC standard, and workup was conducted in the usual manner. Results are given in Table IV, experiment 50. See Table IV, experiment 49, for results of a related reaction conducted with illumination at 350–750 nm for 10 h.

Registry No. **1**, 612-62-4; **2**, 35648-48-7; **3**, 1531-30-2; **4**, 6931-16-4; **6**, 51689-86-2; **7**, 56564-67-1; **8**, 17507-24-3; acetone, 67-64-1; Me_2SO, 67-68-5; 2,4-dimethyl-3-pentanone, 565-80-0; 2-bromopyridine, 109-04-6; lithioacetone, 67863-40-5; iodobenzene, 591-50-4; potassioacetophenone, 15480-89-4; 2-acetonylpyridine, 6302-02-9; 2-(2-quinolyl)acetophenone, 1531-38-0; *N*,*N*-diisopropyl-2-aminoquinoline, 71370-73-5.