1180 *J. Org. Chem.* **1983**, *48*, 1180–1185

$S_{RN}1$ Mechanism in Heteroaromatic Nucleophilic Substitution. Reactions Involving Certain Dihalogenated π-Deficient Nitrogen Heterocycles[1a,b]

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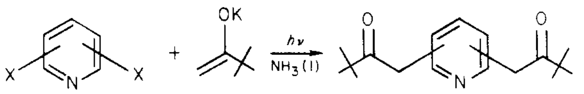
Photostimulated reactions of 2,6-, 2,3-, 3,5-, and 2,5-dihalopyridines (**1a–e**) with pinacolone potassium enolate (**2**) in liquid NH_3 lead to facile replacement of both halogens via a modified $S_{RN}1$ mechanism, which does not involve intermediate formation of monosubstitution products. The potassium salts of phenylacetonitrile (**12a**) and α-ethylphenylacetonitrile (**12b**) react with 2,6-dibromopyridine (**1a**) under similar conditions to afford a mixture of mono- and disubstituted products via a related $S_{RN}1$ process. 4,7-Dichloroquinoline (**16**) undergoes radical-chain displacement of chloride from C_4 with enolate **2**. 2,6-Dichloropyrazine (**18**) and 2,3-dichloropyrazine (**20**) also undergo monosubstitution with **2** and diisopropyl ketone potassium enolate (**22**), but these reactions appear to be mainly addition–elimination (S_NAr) processes. Treatment of 3,6-dichloropyridazine (**27**) with **22** results in addition of **22** to C_4 of the substrate. Photoassisted reaction of 2,4-dichloropyrimidine (**31**) with **12a** leads to exclusive chloride displacement from C_4 via the $S_{RN}1$ mechanism.

In a recent study[2] of heteroaromatic $S_{RN}1$ reactions,[3] we found that 2,6-dibromopyridine (**1a**) and 2,6-dichloropyridine (**1b**) reacted with pinacolone potassium enolate (**2**) under irradiation with near-ultraviolet light in liquid NH_3 to afford disubstitution product **3a** in excellent yield.



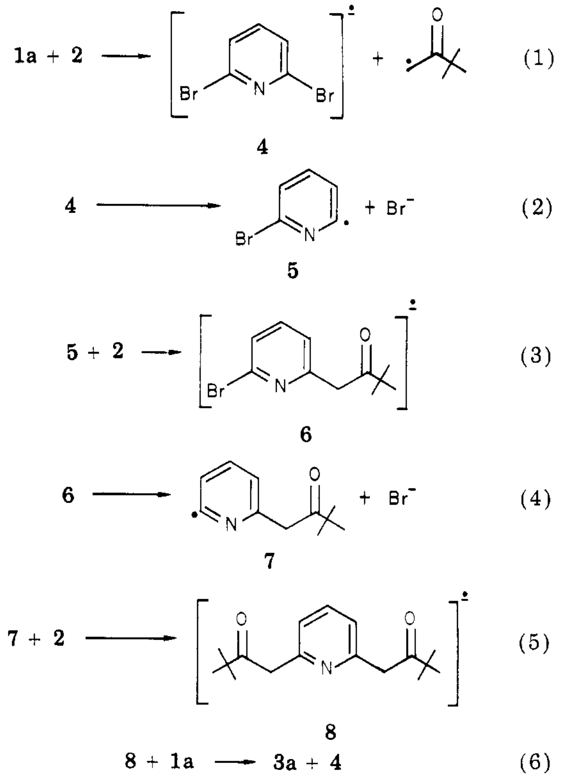
1a, X = Br (2,6)
b, X = Cl (2,6)
c, X = Cl (2,3)
d, X = Cl (3,5)
e, X = Br (2,5)

2

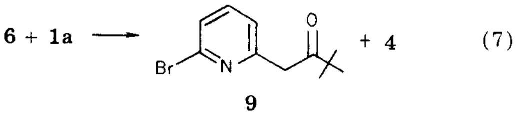
3a (2,6)
b (2,3)
c (3,5)
d (2,5)

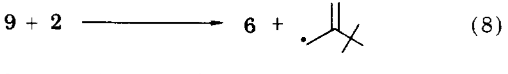
Certain characteristics of these reactions, in particular inhibition by catalytic amounts of the radical scavenger, di-*tert*-butyl nitroxide (DTBN),[4] and the absence of monosubstitution product when the uninhibited reaction was interrupted before substrate **1a** had been consumed, indicated that disubstitution was proceeding via the radical-chain mechanism shown in Scheme I. Equation 1 represents the proposed initiation step, a photoassisted electron transfer from enolate **2** to **1a**.[5] The propagation cycle then begins with step 2, where radical anion **4** fragments to form radical **5** and continues (step 3) by combination of **5** with enolate **2** to form radical anion **6**. The next propagating reaction (step 4) is presumed to involve fragmentation of **6** to form radical **7**, which then combines with **2** to produce radical anion **8** (step 5). Completion of the propagating cycle (step 6) involves electron transfer from **8** to substrate **1a** to form the observed disubstitution product **3a** and radical anion **4**, the latter of which can reenter the proposed scheme at step 2.

Scheme I



An alternative mechanism, which retains the radical-chain character implied by DTBN inhibition, involves the first three steps of Scheme I followed by electron transfer from radical anion **6** to substrate **1a** to form monosubstitution product **9** and radical anion **4** (eq 7). If **9** then accepts an electron from enolate **2** (eq 8), the resulting radical anion, **6**, could proceed through the propagating reactions of eq 4–6.





Thus, the two most likely mechanisms for disubstitution consist of the reactions of Scheme I or the combination of steps 1–3 of Scheme I, followed by reactions 7 and 8, followed by steps 4–6 of Scheme I. These two patterns of

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(1) (a) Supported by Grant CHE-8022538 from the National Science Foundation and Grant NSG 1524 from the National Aeronautics and Space Administration. (b) For the previous paper in this series see: Carver, D. R.; Hubbard, J. S.; Wolfe, J. F. *J. Org. Chem.* **1982**, *47*, 1036. (c) Abstracted in part from the Ph.D. dissertation of D.R.C., Virginia Polytechnic Institute and State University, Aug 1979.

(2) Komin, A. P.; Wolfe, J. F. *J. Org. Chem.* **1977**, *42*, 2481.

(3) For recent reviews of the $S_{RN}1$ reaction in aromatic substitution see: (a) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413. (b) Carver, D. R.; Wolfe, J. F. *Org. Prep. Proc. Int.* **1978**, *10*, 224.

(4) (a) Hoffman, A. K.; Feldman, A. M.; Geblum, E.; Hodgson, W. G. *J. Am. Chem. Soc.* **1964**, *86*, 639. (b) Nelson, S. F.; Bartlett, P. D. *Ibid.* **1966**, *88*, 143.

(5) Hoz, S.; Bunnett, J. F. *J. Am. Chem. Soc.* **1977**, *99*, 4690.

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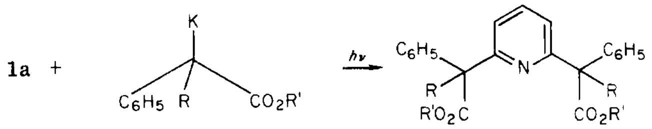
reaction differ from one another with regard to the role of radical anion **6**. In the mechanism outlined in Scheme I, **6** suffers carbon–halogen bond cleavage rather than donating an electron to substrate **1a**. Therefore monosubstitution product **9** (eq 7) *is not* an intermediate. If, however, radical anion **6** were to transfer an electron to **1a** as shown in eq 7, then **9** would be an intermediate in the disubstitution process and might be detected in reactions quenched before all of **1a** had been consumed. The absence of **9** in such reactions led us to propose that the reaction of **1a** with **2** was proceeding via the mechanism represented in Scheme I. However, it is possible that the combined mechanism consisting of steps 1–3, 7, 8, and 4–6 is operating independently, or in concert with the sequence of Scheme I, and that **9** is more reactive than **1a**. This would lead to rapid consumption of **9** and prevent its detection in the interrupted reactions.

In a recent series of papers,[6] Bunnett and co-workers have presented evidence that pathways analogous to those described above occur in photostimulated substitution reactions of dihalobenzenes. The predominant mechanism was found to depend on the nature of the nucleophile as well as the type and relative position of the halogens. In the study described in this paper we have examined the behavior of a series of dihalogenated azines and diazines toward certain carbanion nucleophiles which previously had been shown to participate in $S_{RN}1$ reactions with analogous monohalogenated heterocycles. In order to compare the dihalogenated substrates with their monohalogenated counterparts, liquid NH_3 was employed as the reaction solvent, and photostimulation was provided by lamps emitting maximally at 350 nm.

Results

With Dihalopyridines. Reactions involving 2,3- and 3,5-dichloropyridines (**1c,d**) and 2,5-dibromopyridine (**1e**) are summarized in Table I. Disubstitution products **3b–d** were obtained after 15 min of photostimulation in the presence of excess **2** (expts 1,3, and 5). In a series of experiments not detailed in Table I, **1c–e** were allowed to react with **2** under illumination for 1–5 min. In each instance only the original substrate and the appropriate disubstituted products were produced; monosubstitution products analogous to **9** could not be detected by GC. The presence of 10 mol % of DTBN completely suppressed formation of **3b–d** during 15 min of illumination. Substrate **1c** gave no substitution upon exposure to **2** for 15 min in the dark (expt 2), while **1d** and **1e** gave only traces of diketones **3c** and **3d**, respectively (expts 4 and 6).

Photostimulated reaction of ethyl potassiophenylacetate (**10a**) with **1a** afforded diester **11a** in good yield (expt 7).



10a, R = H; R' = Et
b, R = C_6H_5; R' = Me

11a, R = H; R' = Et
b, R = C_6H_5; R' = Me

The behavior of carbanion **10a** toward **1a** was similar to that observed with enolate **2**. Thus, when the photoinduced reaction was quenched prior to complete consumption of **1a**, diester **11a** and unreacted **1a** were obtained, but monosubstitution product was not found. Substitution did not occur after 1 h in the dark (expt 8), and 10 mol % of DTBN completely inhibited formation of **11a** during 1 h of illumination (expt 9).

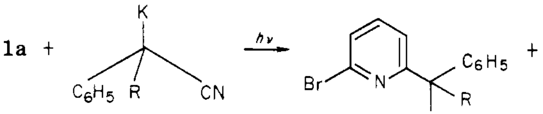
Table I. Reactions of Dihalopyridines with Carbanions

expt	dihalopyridine	carbanion	reaction conditions (time, h)	product	% yield
1	1c, X = Cl	2	*hν* (0.25)	3b	63
2	1c, X = Cl	2	dark (0.25)		*a*
3	1d, X = Cl	2	*hν* (0.25)	3c	43
4	1d, X = Cl	2	dark (0.25)	3c	2
5	1e, X = Br	2	*hν* (0.25)	3d	85
6	1e, X = Br	22	dark (0.25)	3d	3
7	1a, X = Br	10a	*hν* (0.25)	11a	84
8	1a, X = Br	10a	dark (1)		*a*
9	1a, X = Br	10a	*hν*, DTBN (1)		*a*
10	1a, X = Br	10b	*hν* (1)	11b	42
11	1a, X = Br	10b	dark (1)		*a*
12	1a, X = Br	10b	*hν*, DTBN (1)		*a*
13	1a, X = Br	12a	*hν* (0.25)	13a	34
				14a	36
				15a	*b*
14	1a, X = Br	12a	*hν* (0.15)	13a	31
				14a	32
				15a	*b*
15	1a, X = Br	12	dark (0.25)		*a*
16	1a, X = Br	12a	*hν*, DTBN (0.25)		*a*
17	13a	12a	*hν* (1)		*c*
18	1a, X = Br	12b	*hν* (1.5)	13b	17
				14b	25
				15b	52
19	1a, X = Br	12b	dark (1.5)		*a*
20	1a, X = Br	12b	*hν*, DTBN (1.5)		*a*
21	13b	12b	*hν* (1.5)	13b	19
				15b	22

[a] Only starting materials were detected by GC analysis.
[b] Dehalogenated product **15a** was detected by GC and identified by comparison with an authentic sample prepared by $S_{RN}1$ reaction of **12a** with 2-bromopyridine.[20]
[c] Only starting material, **13a**, and dehalogenated product, **15a**, were detected by GC analysis.

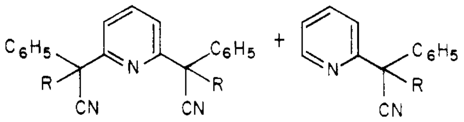
Only diester **11b** was obtained from photoinduced reaction of methyl diphenylacetate carbanion (**10b**) with **1a** (expt 10). Experiments carried out in the dark or with irradiation in the presence of DTBN failed to yield **11b** (expts 11 and 12).

Reactions of potassiophenylacetonitrile (**12a**) with **1a** took a decidely different course from those of **1a** with carbanions **2** and **10a,b**. Photostimulation afforded a mixture of mono- and disubstitution products **13a** and **14a**, respectively, along with dehalogenated product **15a** (expts 13 and 14). The rate of consumption of **1a** was reduced dramatically when the reaction mixture was not illuminated or when DTBN was present (expts 15 and 16). Attempted reaction of monosubstitution product **13a** with carbanion **12a** failed to produce dinitrile **14a** after 1 h of irradiation (expt 17).



12a, R = H
b, R = Et

13a, R = H
b, R = Et



14a, R = H
b, R = Et

15a, R = H
b, R = Et

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[6] (a) Bunnett, J. F.; Creary, X. *J. Org. Chem.* 1974, *39*, 3612. (b) Bunnett, J. F.; Creary, X. *Ibid.* 1974, *39*, 3611. (c) Bunnett, J. F.; Traber, R. P. *Ibid.* 1978, *43*, 1867. (d) Bunnett, J. F.; Shafer, S. J. *Ibid.* 1978, *43*, 1873. (e) Bunnett, J. F.; Shafer, S. J. *Ibid.* 1978, *43*, 1877.

Table II. Reactions of Dihalodiazines with Carbanions

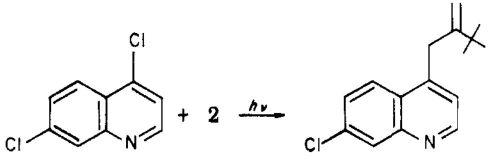
expt	dihalo-diazine	car-banion	reaction conditions (time, h)	prod-uct	% yield
22	18	2	dark (0.25)	19	99
23	18	2	dark, DTBN (0.25)	19	90
24	20	2	dark (0.25)	21	71
25	20	2	dark, DTBN (0.25)	21	70
26	20	22	dark (0.25)	23	20
				24	6
				25	2
				26	5
27	20	22	dark, DTBN (0.25)	23	22
				24	7
28	27	22	hν, dark, or DTBN (0.25)	29	11[a]
				30	48[a]
29	31	12a	hν (0.25)	32	58
30	31	12a	dark or hν and DTBN (0.25)		b

[a] Average yield from three experiments. [b] Only starting materials could be detected by GC analysis.

Photoinduced reaction of potassio-α-ethylphenylacetonitrile (**12b**) afforded a mixture of products similar to that observed with **12a**, except that dehalogenated product **15b** predominated over mono- and disubstituted products **13b** and **14b**, respectively (expt 18). Attempted reactions in the dark or in the presence of DTBN gave only recovered starting materials (expts 19 and 20). Efforts to obtain **14b** by illuminating a mixture of **13b** and carbanion **12b** afforded unreacted **13b** and **15b** but no trace of **14b** (expt 21).

With 4,7-Dichloroquinoline (16). This substrate provided an opportunity to assess the relative reactivity of leaving groups attached to both a π-deficient heterocyclic ring and a benzenoid moiety within the same molecular framework. Such an arrangement of potential reaction centers has not been examined previously in $S_{RN}1$ studies. On the basis of earlier competitive experiments[2,7] involving 2-chloroquinoline, 2-bromopyridine, and iodobenzene, it was anticipated that reaction of **16** with enolate **2** might occur with selective replacement of chloride from C_4.

Exposure of **16** to excess **2** under illumination for 30 min produced a monoketone (70%) with elemental composition consistent with structure **17**, while a similar experiment conducted without light led to return of **16** in 89% yield. Although the simple ^1H NMR and ^{13}C NMR spectra of the substitution product were consistent with structure **17**, they did not provide sufficient evidence to rule out completely substitution at C_7. That displacement of chloride from C_4 had indeed occurred was established unequivocally by the following ^1H decoupling experiments: A small (0.5 Hz) coupling was observed between the methylene protons of the ketonic side chain (δ 4.32) and a ring proton (δ 7.25), assumed to be the C_3 proton of **17**.[8] Irradiation of the signal at δ 4.32 removed this coupling and caused sharpening and enhancement (ca. 40%) of the signal at δ 7.25.

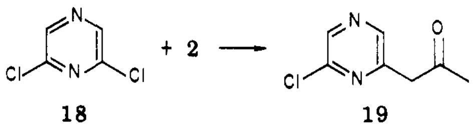


16 **17**

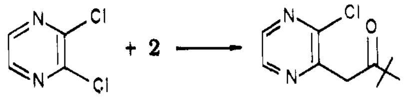
Assignment of the signal at δ 7.25 to the C_3 proton was confirmed by a decoupling experiment in which it was shown to be coupled to the C_2 proton (δ 8.90).[8]

With Dihalodiazines. Reactions of 2,6- and 2,3-dichloropyrazines (**18** and **20**), 3,6-dichloropyridazine (**27**), and 2,4-dichloropyrimidine (**31**) are summarized in Table II.

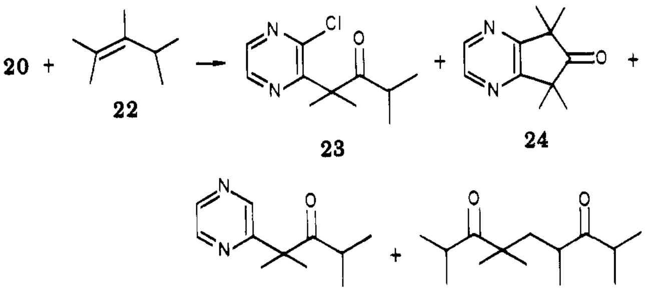
Treatment of **18** with excess enolate **2** in the dark afforded an essentially quantitative yield of monosubstitution product **19** (expt 22). Addition of 15 mol % of DTBN did not significantly reduce the yield of **19** (expt 23). Similar results were obtained with 2,3-dichloropyrazine (**20**), which afforded monoketone **21** with enolate **2** in both dark and dark-inhibited reactions (expts 24 and 25). When diisopropyl ketone enolate **22** was employed as the nucleophile with substrate **20** in the dark, a considerable amount of intractable material was obtained, along with products **23**–**26** (expt 26). Photostimulation did not improve the poor material balance or change the product distribution; however, **25** and **26** were not observed in the presence of DTBN (expt 27).



18 **19**

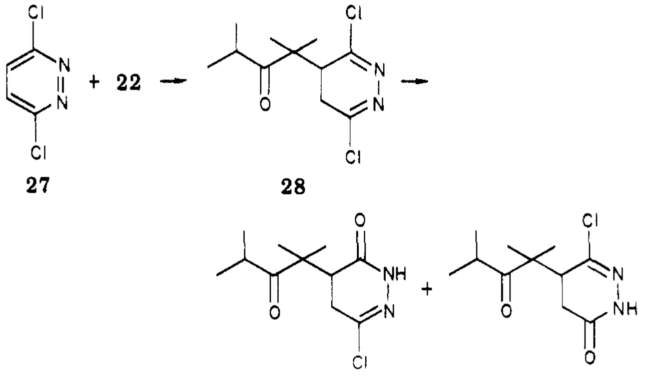


20 **21**



23 **24** **25** **26**

Reactions of 3,6-dichloropyridazine (**27**) with enolate **22** under photostimulation, dark, or inhibited conditions produced good yields of the highly labile addition product **28**, which underwent hydrolysis in the presence of wet silica gel to give dihydropyridazinones **29** and **30** (expt 28).



29 **30**

2,4-Dichloropyrimidine (**31**) reacted smoothly with carbanion **12a** under photostimulation to give exclusively the 4-substituted product **32** (expt 29). Starting materials were recovered when the reaction mixture was illuminated

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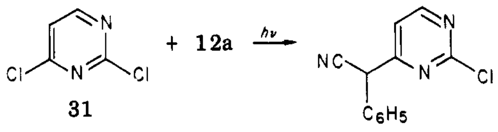
[7] Hay, J. V.; Wolfe, J. F. *J. Am. Chem. Soc.* **1975**, *97*, 3702.

[8] Batterham, T. J. "NMR Spectra of Simple Heterocycles"; Taylor, E. C.; Weissberger, A., Eds.; Wiley: New York, 1973; pp 306–308.



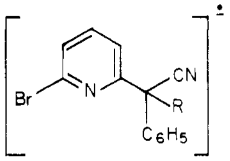
31 **32**

in the presence of DTBN or when the reactants were mixed in the dark (expt 30). The position of substitution was established by ^{1}H NMR decoupling. Thus, a small (0.5 Hz) coupling was observed between the side-chain methine proton (δ 5.33) and the C_5 proton of the pyrimidine ring (δ 7.44).[9] Irradiation of the signal at δ 5.33 removed this coupling and led to sharpening and enhancement of the signal at δ 7.44.

Discussion

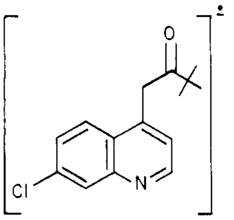
The rate of carbon–halogen bond cleavage in π-deficient heteroaromatic radical anions[10] has been shown to depend on (1) the free electron density at the carbon bearing the halogen,[11] (2) the strength of such bonds,[12] and (3) the redox potential of the substrate–radical anion couple.[12] For example, the rate of carbon–halogen bond fragmentation in radical anions generated electrochemically from isomeric halogen derivatives of a given heteroaromatic system can be correlated with the free electron density at the appropriate carbon in the radical anion of the nonhalogenated parent. Positions of highest electron density undergo loss of halide ion most rapidly. The relative stability of radical anions similarly derived from halogenated heteroaromatics also correlates nicely with the polarographic half-wave reduction potential ($E_{1/2}$) of the unsubstituted π system.[12,13] Thus, the more negative the $E_{1/2}$ value for a particular parent molecule, the more rapidly radical anions produced from its halogenated derivatives undergo carbon–halogen bond cleavage. On the basis of these considerations, the tendency for dihalopyridines **1a–e** to undergo exclusive disubstitution with ketone and ester enolates appears to be mainly attributable to the relatively negative reduction potentials for **1a–e** and consequently for radical anion intermediates such as **6**. Thus, **6** and its isomeric analogues suffer carbon–halogen bond fission (Scheme I, step 4) more rapidly than they transfer an electron to the original substrate (eq 7). If one uses the pyridine,[10,14] 2-picoline,[10,14] and 3-picoline[10,15] radical anions as approximate models for the monohalogenated radical anions presumed to be involved in these reactions, the respective free electron densities in these species indicate that **1a** and **1b** would be most likely to undergo disubstitution, that **1e** would be most prone to monosubstitution, and that **1c** and **1d** might undergo both mono- and disubstitution. However, the fact that **1a–e** all undergo disubstitution indicates that this consideration is of little importance in the dihalopyridine series.

The appearance of both mono- and disubstitution products in reactions of nitrile-stabilized carbanions **12a,b** with **1a** and the discovery that monosubstitution products **13a,b** are not converted to disubstitution products **14a,b** under conditions of the original reaction provide a compelling indication that radical anions **33a,b** are the precursors of **13a,b** as well as **14a,b**. It is not clear at present if this results from a lower free electron density at C_6 of **33a,b** than in radical annion **6**, from a less negative reduction potential for **33a,b** than for **6**, or some combination of these factors. The source of dehalogenated products **15a,b** is assumed to be the radicals produced by carbon–bromine bond cleavage in radical anions **33a,b**. Additional details as to whether the reductive process occurs via electron transfer followed by protonation or through hydrogen atom transfer[16] are not available at this time.



33a, R = H
b, R = Et

4,7-Dichloroquinoline (**16**) exhibits exclusive monosubstitution via the $S_{RN}1$ process, thereby indicating that radical anion **34** donates an electron to **16** faster than chloride is expelled. This can be viewed as arising from low free electron density at C_7 of **34**[10,14,17] and a less negative reduction potential[13] for **34** than for radical anions such as **6**.



34

The monosubstitution and cyclizations observed for dichloropyrazines **18** and **20** with ketone enolates **2** and **22** appear to result almost exclusively from ionic (S_NAr)[18] displacement of chloride, as evidenced by the fact that DTBN had essentially no influence on the success of these reactions. These results are in contrast with the smooth $S_{RN}1$ reactions that occur when 2-chloropyrazine is exposed to enolate **2**, even in the dark.[19] Apparently the presence of two halogens on the pyrazine nucleus increases the susceptibility of **18** and **20** to formation of the σ complexes required for S_NAr reactions to the extent that this mode of substitution overshadows the $S_{RN}1$ process. Formation of traces of dehalogenated product **25** and dimer **26**[16] in photostimulated reactions is suggestive of some small amount of radical-chain substitution. The absence of these products in reactions carried out with DTBN also supports a minor role for this mode of reaction.

The tendency for 3,6-dichloropyridazine (**27**) to undergo mainly ionic addition with enolate **22** to form **28** is consistent with earlier observations that 3-chloro-6-meth-

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(9) See ref 8, pp 97–113.

(10) For an excellent discussion of heteroaromatic radial anions see: Hanson P. *Adv. Heterocycl. Chem.* **1979**, *25*, 206–209.

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(12) (a) Alwair, K.; Grimshaw, J. *J. Chem. Soc.*, **1973**, 1811. (b) Grimshaw, J.; Trocha-Grimshaw, J. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1383. (c) For a discussion of this phenomenon as it applies to $S_{RN}1$ reactions see: Saveant, J. M. *Acc. Chem. Res.* **1980**, *13*, 323 and references cited therein.

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oxypyridazine reacted with **22** to give a mixture of addition and $S_{RN}1$ products.[19] The facility with which addition of **22** to **27** occurs may result from the relative positions of the two halogens and the ring nitrogens in the substrate. These four atoms are ideally situated to provide both resonance and inductive stabilization of the σ complex required for production of **28**.

The selective monosubstitution and $S_{RN}1$ character which accompanies reactions of 2,4-dichloropyrimidine (**31**) with carbanion **12a** is consistent with the less negative $E_{1/2}$ value of pyrimidine vs. pyridine[13] and the low free electron density at C_2 vs C_4 of the pyrimidine radical anion.[10,13]

Experimental Section

General Methods. All reactions were conducted under an inert atmosphere (N_2 or Ar). Photostimulated reactions were performed by using a Rayonet RPR-240 reactor equipped with four 12.5-W bulbs which had maximum emission at 350 nm; exceptions to this irradiation procedure are noted. Solvents were redistilled before use; ethereal solvents were distilled from $LiAlH_4$. Quenching and processing of reactions were performed under atmospheric conditions unless otherwise noted.

Gas chromatographic (GC) analyses and separations were carried out by using a Varian 90-P or 1200 instrument. The columns employed were 6 ft × 0.25 in. and contained 2% Carbowax on Chromosorb supports. Temperatures of 153–235 °C were used; benzoate and phthalate esters were employed as internal standards. For compounds **13–15** GC analyses were conducted by using 5% OV-275–Chromosorb, XF1150 columns. Short-column chromatography with hexane–ethyl acetate mixtures as indicated were used for large-scale separations and isolations; silica gel with mesh size >230 was used. Preparative TLC (PTLC) was carried out by using plates made with EM Merck PF254 Type 60 silica gel.

Infrared (IR) spectra were recorded on Perkin-Elmer 621 and Beckman Acculab 1 spectrophotometers. ^1H NMR spectra were recorded on a Varian EM-390 instrument or a JEOL F 90Q with tetramethylsilane as an internal standard. Melting points were observed on a Thomas-Hoover oil bath apparatus and are uncorrected. Mass spectra were obtained on a Varian 1210 GC mass spectrometer by using electron-impact (70 eV) ionization. Elemental analysis were performed by VPI and SU Analytical Services or by Galbraith Laboratories (Knoxville, TN).

Reactions were generally carried out by one of the following procedures. Exceptions are noted for individual reactions.

Procedure A. Photostimulated Reactions. Unless otherwise indicated, potassium amide (11.25 mmol in 150–175 mL of liquid NH_3) was generated in a cylindrical Dewar flask (unsilvered) according to earlier descriptions.[1b,19] An anhydrous ethereal solution of the ketone, ester, or nitrile (11.25 mmol) was added slowly (1.5 min) via syringe. After 5 min, the lamps were turned on. The aromatic substrate (3.0 mmol) was added as an ethereal solution. After an appropriate irradiation period, the ammonical solution was poured into a 1-L beaker containing 3.5–4 g of solid NH_4Cl. The reaction vessel was washed with ether (2 × 100 mL), and the ethereal washings were added to the ammonia solution. The ammonia was allowed to evaporate; the evaporation was sometimes accelerated by gentle warming on a hot plate. The ether was decanted, and the ammonium salts were washed with ether (2 × 100 mL). The combined ethereal solutions were dried ($MgSO_4$) and filtered. The solvent was removed under reduced pressure to afford crude products.

Procedure B. Dark Reactions. In most experiments, potassium amide (11.5 mmol in 200 mL of liquid NH_3) was generated under nitrogen in a 250-mL three-necked flask coupled with a dry ice condenser. The ketone, ester, or nitrile was added as an ethereal solution via syringe. The flask was wrapped with several layers of dark cloth, and the room lights were extinguished. An ethereal solution of the aromatic substrate was then added via syringe. After an appropriate reaction period, the reaction was quenched and worked up as described in procedure A.

Inhibited reactions were accomplished by adding di-*tert*-butyl nitroxide (DTBN) to the enolate anions before addition of the aromatic substrates.

Reaction of 2,3-Dichloropyridine (1c) with Pinacolone Enolate 2. Procedure A, employing 23.0 mmol of enolate **2**, gave a red oil. Chromatography on a PTLC plate (30:70 ether–hexane) gave a 63% yield of 2,3-bis(3,3-dimethyl-2-oxobutyl)pyridine (**3b**) as a yellow oil.

Procedure B returned starting material.

Reactions of 3,5-Dichloropyridine (1d) with Enolate 2. Procedure A (23.0 mmol oe enolate) gave a yellow oil. GC analysis indicated an 80% yield of 3,5-bis(3,3-dimethyl-2-oxobutyl)pyridine (**3c**). Chromatography on a short column gave a 46% yield of **3c** as pale yellow needles, mp 103–105 °C. Repetition of the above procedures with 10 mol % of DTBN as inhibitor reduced the formation of **3c** to <15% (GC analysis).

Reactions of 2,5-Dibromopyridine (1e) with Enolate 2. Procedure A gave a red oil; GC analysis indicated that this material was >85% 2,5-bis(3,3-dimethyl-2-oxobutyl)pyridine (**3d**). Chromatography on a PTLC plate (30:70 ether–hexane) gave **3d** as yellow needles from heptane; mp 87.5–88.5 °C.

Procedure B returned mostly starting material; GC analysis indicated <3% of **3d**.

Reactions of 2,6-Dibromopyridine (1a) with Ethyl Potassiophenylacetate (10a). Procedure A, using 40 mmol of ethyl phenylacetate and 10 mmol of **1a**, afforded a clear oil after 1 h of irradiation. Vacuum distillation removed 3.02 g of ethyl phenylacetate. The residual viscous oil solidified on standing. The solid was pulverized, washed thoroughly with hexane, filtered, and dried to yield 3.40 g (84%) of 2,6-bis(α-carbethoxybenzyl)pyridine (**11a**, mp 81–86 °C) as a mixture of diastereomers. One recrystallization from chloroform–hexane afforded an analytical sample as colorless crystals which softened at 90 °C and then melted at 93–96 °C. Addition of DTBN (10 mol %) completely inhibited the reaction, and a dark experiment gave only starting material (GC and ^1H NMR). GC analyses of **11a** were carried out on a Porapak Q column.

Reactions of 1a with Methyl Potassiodiphenylacetate (10b). Procedure A, employing 25 mmol of **10b** and 12 mmol of **1a**, afforded a solid, which was recrystallized from hexane–ethyl acetate to afford 42% of 2,6-bis(α-phenyl-α-carbomethoxybenzyl)pyridine (**11b**), mp 164–165 °C.

Neither procedure B nor illuminated experiments in the presence of DTBN gave detectable amounts of **11b**.

Reactions of 1a with Potassiophenylacetonitrile (12a). Procedure A, using 75 mmol of **12a** and 10 mmol of **1a**, produced an oil. Excess phenylacetonitrile was removed by vacuum distillation, and the remaining oil was chromatographed on a silica gel column with hexane–ethyl acetate (4:1). Following elution of a small amount of residual phenylacetonitrile, a pale yellow band was eluted and concentrated to give 0.93 g (34%) of 2-bromo-6-(α-cyanobenzyl)pyridine (**13a**), mp 90–92 °C. An analytical sample was prepared by recrystallization from ether–hexane as colorless crystals, mp 91–92 °C. A second yellow band was then eluted and concentrated to a viscous orange oil which crystallized when triturated with ether to give 1.10 g (36%) of 2,6-bis(α-cyanobenzyl)pyridine (**14a**) as a mixture of diastereomers, mp 105–110 °C. Recrystallization from ether-hexane afforded an analytical sample as white crystals, mp 106–110 °C.

Procedure B and DTBN-inhibited experiments returned the starting nitrile and **1a** almost quantitatively. GC analyses were done on an XF 1150 column.

Reaction of 1a with Potassioethylphenylacetonitrile (12b). From procedure A, with 4 mmol of anion **12b** and 2 mmol of **1a** followed by the usual workup, was obtained an oil. This crude product mixture was subjected to GC analysis on either 5% OV-275 or OV-17 on Chromosorb W columns. The three reaction products **13b**, **14b**, and **15b** were identified by comparison of their retention times with authentic samples prepared by ethylation of **13a** and **14a** and by $S_{RN}1$ reaction of 2-bromopyridine with anion **12a**.[20] Samples of each were compound were collected by preparative GC and exhibited the following analytical properties. **13b** (oil): GC/MS, m/e (relative intensity) 300/302 (M^+, 53/50), 287/285 (96/100), 274/272 (74/86), 273/271 (43/32), 192 (93). **14b** (oil): GC/MS m/e (relative intensity) 365 (M^+, 20), 350 (71),

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[20] Moon, M. P. Ph.D. Dissertation, Virginia Polytechnic Institute and State University, Dec 1978.

337 (100), 208 (80). **15b** (oil): *m/e* (relative intensity) GC/MS 222 (M$^+$, 44), 207 (100), 194 (32), 193 934), 192 (37), 165 (5).

Reaction of 4,7-Dichloroquinoline (16) with Enolate 2. Procedure A (30-min irradiation) gave a yellow solid. Chromatography on TLC silica gel (short column, hexane–ethyl acetate eluant) produced **17** as a white solid, mp 108–110 °C (from hexane).

Reaction of 2,6-Dichloropyrazine (18) with Enolate 2. Procedure B gave a yellow oil. GC analysis indicated >99% of 2-(3,3-dimethyl-2-oxobutyl)-6-chloropyrazine (**19**). Procedure B, using 15 mol % of DTBN, gave a 90% yield of **19**, which was isolated as a light yellow oil by chromatography on a PTLC plate (40:60 CH$_2$Cl$_2$–hexane).

Reaction of 2,3-Dichloropyrazine (20) with Enolate 2. Procedure B gave a red oil which was largely 2-(3,3-dimethyl-2-oxobutyl)-3-chloropyrazine (**21**). GC analysis indicated a 71% yield. An analytical sample was isolated as a light yellow oil by preparative GC. No disubstitution product could be isolated. Repeating procedure B with 15 mol % DTBN gave a 70% yield (GC) of **21**.

Reaction of 2,3-Dichloropyrazine (20) with Diisopropyl Ketone Enolate 22. Procedure B (employing 23.0 mmol of **22**) gave a red tar containing (GC analysis) 2% of 2-(1,1,3-trimethyl-2-oxobutyl)pyrazine (**25**), 20% of 2-chloro-3-(1,1,3-trimethyl-2-oxobutyl)pyrazine (**23**) as an oil, pyrazino[2,3-c]-2,2,5,5-tetramethylcyclopentanone (**24**, mp 78 °C); and 5% of 2,4,4,6,8-pentamethyl-3,7-dioxononane (**26**). Repetition of procedure B with 10 mol % of DTBN present gave the following results (analysis by GC): **21**, 23%; **24**, 7%.

Reactions of 3,6-Dichloropyridazine (27) with Enolate 22. Procedures A, B, and A with 10 mol % of DTBN as inhibitor all gave the same results; a yellow oil was obtained in each case. Careful dilution of the oil with hexane and cooling below 30 °C gave an unstable white solid which could not be fully characterized but appeared to be **28**: mp 50 °C dec; ^{1}H NMR δ 3.0 (m, 4 H, CH$_2$, and CH), 1.20 (m, 12 H, CH$_3$). Allowing an ethereal solution of this crude product to stir with wet silica gel for 24 h gave a mixture of products isolated by PTLC (60:40 ether–hexane). These compounds were identified as 4-(1,3-dimethyl-2-oxobutyl)-6-chloro-4,5-dihydropyridazin-3-one (**29**, mp 133 °C) and 5-(1,3-dimethyl-2-oxobutyl)-6-chloro-4,5-dihydropyridazin-3-one (**30**), mp 131–133 °C.

Reactions of 2,4-Dichloropyrimidine (31) with 12a. Procedure A gave a yellow oil. Chromatography on 50 g of silica gel afforded 2-chloro-4-(α-cyanobenzyl)pyridine (**32**) as a clear oil which crystallized over a period of several days to give a white solid: 58% yield; mp 64–66 °C MS, *m/e* (relative intensity) 231 (M$^+$, 46), 229 (M$^+$, 100), 228 (97), 204 (14), 203 (18), 202 (38), 194 (30), 193 (21), 167 (17), 166 (15), 141 (17), 140 (27), 116 (32), 113 (17). Procedure B or procedure A with 10 mol % of DTBN returned starting materials.

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Registry No. **1a**, 626-05-1; **1c**, 2402-77-9; **1d**, 2457-47-8; **1e**, 624-28-2; **2**, 55440-76-1; **3b**, 84960-21-4; **3c**, 84960-22-5; **3d**, 84960-23-6; **10a**, 82545-62-8; **10b**, 84960-24-7; **11a**, 84960-25-8; **11b**, 84960-26-9; **12a**, 75782-32-0; **12b**, 84960-27-0; **13a**, 84960-28-1; **13b**, 84960-29-2; **14a** (isomer 1), 84960-30-5; **14a** (isomer 2), 84960-31-6; **14b** (isomer 1), 84960-32-7; **14b** (isomer 2), 84960-33-8; **15b**, 19395-42-7; **16**, 86-98-6; **17**, 84960-34-9; **18**, 4774-14-5; **19**, 84960-35-0; **20**, 4858-85-9; **21**, 84960-36-1; **22**, 84960-37-2; **23**, 84986-92-5; **24**, 84960-38-3; **25**, 75782-31-9; **26**, 65738-41-2; **27**, 141-30-0; **28**, 84960-39-4; **29**, 84960-40-7; **30**, 84960-41-8; **31**, 3934-20-1; **32**, 84960-42-9.

Supplementary Material Available: ^{1}H NMR, IR, and analytical data for all new compounds (3 pages). Ordering information is given on any current masthead page.

Carbanion Photochemistry. 7. The $S_{RN}1$ vs. S_{ET} Photoarylation of Triphenylmethyl Anion[1]

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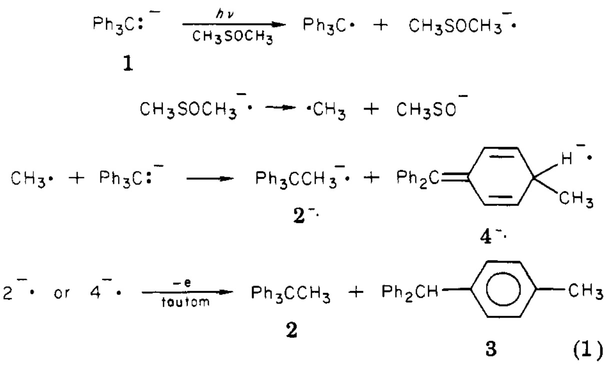
Irradiation of (triphenylmethyl)lithium in tetrahydrofuran containing bromobenzene, iodobenzene, or diphenyl sulfoxide produced three major products: tetraphenylmethane (TPM), biphenylyldiphenylmethane (BDM), and 2-(triphenylmethyl)tetrahydrofuran (TTF). The product composition was a function of anion and acceptor concentration and reflected the competition among solvent, triphenylmethyl anion, and triphenylmethyl radical. Product composition studies thus provide detailed information about the key steps in the mechanism.

Carbon–carbon bond-forming reactions that proceed via a preliminary electron-transfer step are now recognized as being an extremely important class of reactions, both synthetically and mechanistically. We have been particularly interested in that subset of these reactions which proceed through the intervention of a photochemically excited resonance-stabilized carbanion. Irradiation of triphenylmethyl ("trityl") anion (**1**) in dimethyl sulfoxide leads to efficient formation of two primary products, 1,1,1-triphenylethane (**2**) and *p*-tolyldiphenylmethane (**3**), through a mechanism involving initial electron transfer (see Scheme I).[2] Although this mechanism involves steps that are also involved in the radical chain mechanism known as the $S_{RN}1$ mechanism,[3] it differs in three important respects. First, no chain mechanism is observed. Second,

Scheme I



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[1] For our previous paper, see: Tolbert, L. M.; Siddiqui, S. *J. Am. Chem. Soc.* **1982**, *104*, 4273.

[2] Tolbert, L. M. *J. Am. Chem. Soc.* **1980**, *102*, 6808.