washed with 3 × 50 mL of saturated $NaHCO_3$ and 50 mL of water, dried over $MgSO_4$, and concentrated in the rotary evaporator to give a brown oil, 784 mg. Chromatography of this oil over 30 g of silica gel with petroleum ether removed the resolving agent and produced two fractions of an oil whose IR and NMR spectra exactly match those obtained earlier in this laboratory[2] for (*R*)-(+)-α-phenylneopentyl chloride, $[\alpha]^{24}_D$ +104.5° (0.0440 g/mL, THF) on fraction 1 (0.440 g, 86.4%): NMR ($CDCl_3$) δ 1.0 (9 H, s, 4.7 (1 H, s), 7.4 (5 H, m).

Run 2. **10** (1.553 g, 3.616 mmol) produced 531 mg (80%) of (+)-**2**, $[\alpha]^{26}_D$ +102°. Bulb-to-bulb short-path distillation at 0.04 torr with warm water heating at 52–55 °C and dry ice/acetone chilling at −50 °C gave an analytical sample whose specific rotation was unchanged, $[\alpha]^{24}_D$ 101° (0.2335 g/15.5 mL, THF). Anal. Calcd for $C_{11}H_{15}Cl$: C, 72.32; H, 8.28; Cl, 19.41. Found: C, 71.41, 71.40; H, 8.18, 8.17; Cl, 18.72, 18.86. Gas chromatographic analysis of this sample (8ft, 3% OV 101) in a H-P 5880 A instrument showed two trace impurities in addition to (+)-**2**. The ^1H NMR integrated correctly and redistillation failed to remove the impurities. The $[\alpha]^{26}_D$ of +113° (68.9 mg/20 mL acetone) suggests that rotations in acetone are greater than in THF.

Acknowledgment. We gratefully acknowledge the support of the City University's Faculty Research Award Program through PSC-CUNY research awards (662017 to H.H., 6-64209 to H.E.Z.). We thank Professor V. Gold of King's College, London for his kind hospitality and help during a Fellowship Leave (to H.H.). We are grateful to Brendan Lee (Brooklyn College) for help in the synthesis and to Jane Elliot (King's College, London) for assistance in obtaining the NMR spectra. D.A.B. thanks the City University of New York for a Graduate Professional Opportunities Program fellowship.

Registry No. (±)-**1**, 57377-60-3; (+)-(*R*)-**1**, 23439-91-0; (*S*)-**1** (lithium alkoxide), 100702-90-7; (*S*)-**1** (chloro carbonate), 100837-35-2; (+)-(*S*)-**2**, 100895-65-6; (*R*)-**2**, 82323-56-6; **3**, 118-92-3; **4**, 525-76-8; (±)-**5**, 100702-92-9; (±)-**6**, 100702-93-0; (±)-**7**, 100702-94-1; (±)-**8**, 100702-95-2; (*R*)-**10**, 100702-97-4; Bu_3P, 998-40-3; CCl_4, 56-23-5; (*R*)-$(C_6H_5)_2CHCH(C_6H_5)C(CH_3)_3$, 100702-91-8; $(C_6H_5)_2CHLi$, 881-42-5; *t*-BuCl, 507-20-0.

Reactions of 2-Halothiazoles with Ketone Enolates and Nitrile Carbanions[1a]

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Photostimulated reactions of 2-chlorothiazole (**1a**), 2-chloro-4-methylthiazole (**1b**), and 2-chloro-5-methylthiazole (**1c**) with pinacolone potassium enolate (**2a**) in liquid NH_3 lead to formation of mono- and bis-2-thiazolyl ketones **3a–c** and **4a–c** via the $S_{RN}1$ mechanism. A similar reaction with 2-bromothiazole (**1d**) gave **3a** but no **4a**. Reaction of **1a** with **2a** in the dark, or with the potassium enolate of diisopropyl ketone (**2b**) under near-UV irradiation or in the dark, does not result in chloride displacement. Instead, carbinols **5a–b**, derived from initial ionization of H_5 of **1a** followed by aldol-type condensation of the resulting carbanion (**11**) with neutral ketone, are produced in good yields. Carbanion **11** can also be produced in synthetically useful concentrations by metalation of **1a** with KNH_2, *n*-BuLi, and LDA, with the latter base being most effective. Carbanions derived from acetonitrile, propionitrile, and phenylacetonitrile react smoothly with **1a** in liquid NH_3 to give the corresponding monosubstitution products resulting from chloride displacement. However, these reactions appear to proceed by an addition–elimination (S_NAr) mechanism rather than an $S_{RN}1$ process.

In a continuing study[2] of heteroaromatic nucleophilic substitution reactions which take place via a radical chain ($S_{RN}1$)[3] process, we have begun to investigate the suitability of halogenated π-excessive heterocycles as substrates in such reactions. Although the participation of various classes of π-deficient heterocycles in $S_{RN}1$ reactions has now been demonstrated,[2] the only π-excessive substrates studied thus far are the 2- and 3-halothiophenes.[4] We now wish to describe the results of an investigation in which 2-halothiazoles **1a–d** were employed as π-excessive substrates in reactions with ketone enolate and nitrile carbanion nucleophiles.

Results

Reactions with Ketone Enolates. Photostimulated reaction of 2-chlorothiazole (**1a**) with 4 equiv of the potassium enolate of pinacolone (**2a**), generated by means of KNH_2 in liquid NH_3, afforded a 53% yield of monosubstitution product **3a** along with 25% of disubstitution product **4a** (exp 1, Table I). 2-Bromothiazole (**1d**) reacted similarly to give a 44% yield of **3a**, but no **4a** was found to be present by TLC or ^1H NMR analysis (expt 2).

When denied the catalytic effect of near-UV illumination, reactions of **1a** with enolate **2a** and with the potassium enolate of diisopropyl ketone (**2b**) took a decidedly different course. Thus, exposure of **1a** to excess **2a** in the dark gave carbinol **5a** in 70% isolated yield (expt 3). Addition of 10 mol % of the radical scavenger, di-*tert*-butyl nitroxide (DTBN)[5] to an illuminated reaction of **1a** with

(1) (a) Supported by NSF Grant No. CHE 80-22538. (b) Abstracted in part from the Ph.D. dissertation of Dillender, S. C., Jr., Virginia Polytechnic Institute and State University, December 1983.

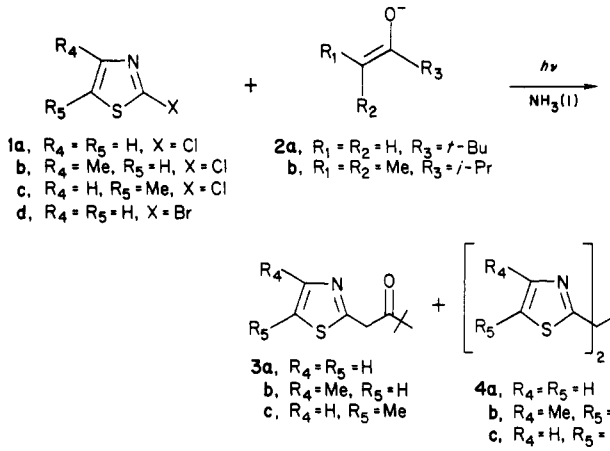
(2) See: Moon, M. P.; Komin, A. P.; Morris, G. F.; Wolfe, J. F. *J. Org. Chem.* **1983**, *48*, 2392 and references cited therein.

(3) (a) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413. (b) Wolfe, J. F.; Carver, D. R. *Org. Prep. Proced. Int.* **1978**, *10*, 224. (c) Rossi, R. A.; deRossi, R. H. "Aromatic Substitution by the $S_{RN}1$ Mechanism", ACS Monograph 178; American Chemical Society: Washington, DC, 1983.

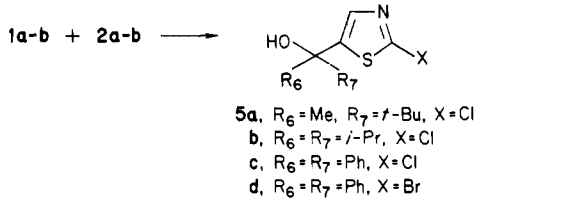
(4) Bunnett, J. F.; Gloor, B. F. *Heterocycles* **1976**, *5*, 377.

(5) (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.

0022-3263/86/1951-1184$01.50/0



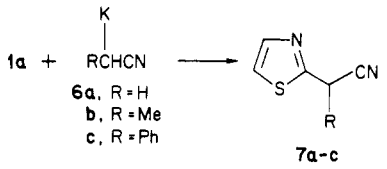
2a produced carbinol **5a** (27%) and recovered **1a** (62%), but no detectable amounts of ketones **3a** or **4a** (expt 4).



Exposure of substrate **1d** to **2a** in the dark afforded only unreacted **1d**. Treatment of **1a** with **2b** under illumination gave carbinol **5b** in 77% yield (expt 5); none of the expected ketone resulting from chloride displacement could be detected. A similar reaction carried out in the dark also afforded **5b** in 83% yield (expt 6). When enolate **2b** was prepared using LDA in THF at −78 °C and allowed to react with **1a** in the dark, an essentially quantitative yield of **5b** was obtained (expt 7).

The photoassisted reaction of 2-chloro-4-methylthiazole (**1b**) with **2a** gave 2-thiazolyl ketones **3b** and **4b** (expt 8). Similarly, 2-chloro-5-methylthiazole (**1c**) reacted with **2a** to afford ketones **3c** and **4c** (expt 9). However, in contrast to the results obtained in the dark reaction with substrate **1a**, exposure of **1b** and **1c** to excess **2a** in the dark gave only recovered starting materials, and no carbinol product corresponding to **5a** could be detected from the ^{1}H NMR spectrum of the crude reaction mixture (expt 10–11).

Reactions with Nitrile Carbanions. Reactions of potassioacetonitrile (**6a**), potassiopropionitrile (**6b**), and potassiophenylacetonitrile (**6c**) with **1a** in liquid NH_3 either under photostimulation, in the dark, or with 10 mol % of *p*-dinitrobenzene (DNB) or DTBN gave good yields of the corresponding 2-substituted products **7a–c** (expt 12–20). As can be seen from Table I, product yields in



the irradiation reactions are consistently lower, suggesting that the nitrile products may be susceptible to light induced degradation. The high yields obtained with **6a** after only a 5-min reaction period (expt 14 and 16) illustrate the high reactivity of **1a** toward these nitrile carbanions.

Discussion

Formation of ketones **3a–c** in the photoassisted reactions of **1a–c** with pinacolone enolate (**2a**) and the suppression of the reaction of **1a** with **2a** by 10 mol % of DTBN provide good evidence that chloride displacement takes place via the radical-chain ($S_{RN}1$) mechanism illustrated for **1a** in Scheme I. It also seems likely that disubstitution products **4a–c** arise by a similar mechanistic pathway involving the enolates derived from the corresponding monosubstitution products, **3a–c**.

In light of the established acidity[6] of the C_5 proton of **1a**, the formation of carbinols **5a–b** may be accounted for as outlined in Scheme II. Initially, the C_5 proton of **1a** is abstracted by the ketone enolate **2a–b** to form carbanion **11** and the neutral ketone, which then condense to give alkoxide **12**. Acidification of the reaction mixture affords carbinols **5a–b**. The use of excess enolate[7] and the es-

Table I. Reactions of 2-Halothiazoles with Ketone Enolates and Nitrile Carbanions in Liquid NH_3

expt	substrate	nucleophile	conditions[a,b]	products	yield, %
1	**1a**	**2a**	*hν*	**3a**	53
				4a	25
2	**1d**	**2a**	*hν*[c]	**3a**	44
3	**1a**	**2a**	dark	**5a**	70
4	**1a**	**2a**	*hν*, inhibited[d]	**5a**	27[e]
5	**1a**	**2b**	*hν*	**5b**	77
6	**1a**	**2b**	dark	**5b**	83
7	**1a**	**2b**[f]	dark[g]	**5b**	100
8	**1b**	**2a**	*hν*	**3b**	64
				4b	10
9	**1c**	**2a**	*hν*	**3c**	67
				4c	7
10	**1b**	**2a**	dark		*h*
11	**1c**	**2a**	dark		*h*
12	**1a**	**6a**	*hν*	**7a**	79
13	**1a**	**6a**	dark	**7a**	96
14	**1a**	**6a**	dark[i]	**7a**	85
15	**1a**	**6a**	dark, inhibited[d]	**7a**	96
16	**1a**	**6a**	dark,[i] inhibited[j]	**7a**	98
17	**1a**	**6b**	*hν*	**7b**	62
18	**1a**	**6b**	dark	**7b**	83
19	**1a**	**6c**	*hν*	**7c**	48
20	**1a**	**6c**	dark	**7c**	56

[a] Reaction time 1 h. [b] Ratio of enolate to substrate of 4:1. [c] Reaction time 15 min. [d] 10 mol % of DTBN was used as inhibitor. [e] None of the substitution products **3a** and **4a** were detected by ^{1}H NMR; 62% of **1a** was recovered. [f] Generated from LDA in THF at −78 °C. [g] Reaction time 1.5 h. [h] Only starting materials were detected by ^{1}H NMR. [i] Reaction time 5 min. [j] 10 mol % of DNB was used as inhibitor.

Table II. Reactions of Metalated 2-Halothiazoles with Electrophiles

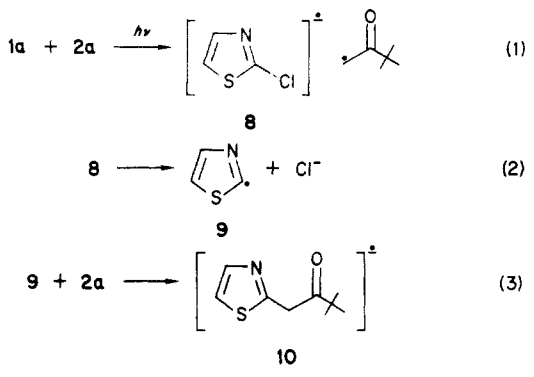
expt	base (equiv)	solvent	halothiazole	electrophile	product	yield, %
21	KNH_2 (4)	NH_3	**1a**	Ph_2CO	**5c**	66
22	LDA (2)	THF	**1a**	Ph_2CO	**5c**	100
23	*n*-BuLi (1)	THF	**1a**	Ph_2CO	**5c**	45[a]
24	LDA (2)	THF	**1d**	Ph_2CO	**5d**	35
25	*n*-BuLi (1)	THF	**1a**	$CH_3COC(CH_3)_3$	**5a**	33
26	LDA (2)	THF	**1a**	CH_3I	**1c**	52
27	LDA (2)	THF	**1a**	D_2O	**1a**-d_1	*b*

[a] Along with 55% of recovered Ph_2CO. [b] Reaction gave 70% incorporation of deuterium at C_5.

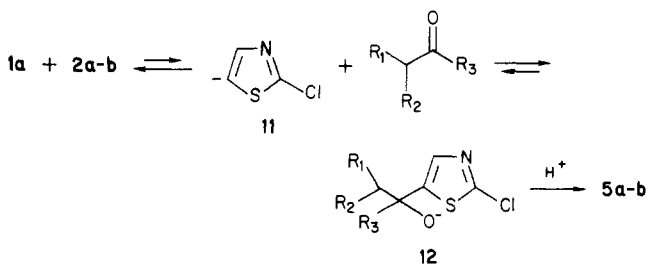
(6) The kinetic acidity of the C_5 proton of thiazoles has been well documented. (a) For examples of C_5 metalation of **1a** by means of *n*-BuLi, see: Noyce, D. S.; Fike, S. A. *J. Org. Chem.* **1973**, *38*, 3316. (b) For examples of H-D exchange studies, see: Olofson, R. A.; Landesberg, J. M.; Houk, K. N.; Michelman, J. S. *J. Am. Chem. Soc.* **1966**, *88*, 4265. Coburn, R. A.; Landesberg, J. M.; Kemp, D. S.; Olofson, R. A. *Tetrahedron* **1970**, *26*, 685, and ref 13. (c) For correlation of kinetic acidities from ^{13}C–^{1}H one bond coupling constants see: Pedersen, E. B. *J. Chem. Soc., Perkin Trans. 2* **1977**, 473.

(7) When the reaction of **1a** with 1 equiv of **2b** was attempted, **1a** was quantitatively recovered.

Scheme I



Scheme II



sentially irreversible formation of **12** presumably overcome the unfavorable equilibrium associated with generation of **11**.

Evidence that **11** is a viable intermediate in the formation of the observed condensation products was obtained by the series of trapping experiments summarized in Table II. Thus, when **1a** was treated with 4 equiv of KNH_2 in liquid NH_3 followed by quenching of the reaction mixture with benzophenone, carbinol **5c** was produced in 66% yield (expt 21). Similar experiments employing LDA and *n*-BuLi[6a,8] to generate **11** afforded **5c** in yields of 100 and 45%, respectively (expt 22 and 23).[9] These reactions clearly demonstrate the superiority of LDA over *n*-BuLi as a metalating agent for **1a**.[10] Metalation at C_5 of **1d** was also accomplished by means of LDA as shown by reaction with benzophenone to give carbinol **5d** in 35% yield (expt 24). Reaction of pinacolone with **11**, produced by reaction of **1a** with *n*-BuLi, yielded 33% of carbinol **5a** (expt 25). That substitution indeed occurs at C_5 was substantiated by conversion of **1a** to 2-chloro-5-methylthiazole (**1c**) via reaction with LDA followed by methyl iodide (expt 26).

Further evidence for the intermediacy of carbanion **11** was obtained by analysis of the ^1H NMR spectra of a mixture of **1a** and LDA in THF-d_8 at −60 °C. Thus, the two doublets for H_5 (δ 7.38) and H_4 (δ 7.48) of **1a** are replaced by a sharp singlet at δ 7.36 for the uncoupled H_4 proton of **11**. Quenching with D_2O gave 70% incorporation of deuterium at C_5 by ^1H NMR and mass spectral analysis (expt 27), while addition of water resulted in regeneration of the spectrum of **1a**. Monitoring of the ^1H NMR spectrum from −60 °C to −10 °C showed that **11** begins to decompose at ca. −20 °C.

The tendency of diisopropyl ketone enolate (**2b**) to give only carbinol **5b**, even in photostimulated reactions with **1a**, may result from the fact that this enolate is a less effective initiator of the $S_{RN}1$ process than pinacolone enolate.[11] Consequently, the reactions of Scheme II compete successfully with the radical-chain mechanism of Scheme I.

The failure of 4- and 5-methyl-2-chlorothiazoles (**1b–c**) to yield carbinol products with enolate **2a** undoubtedly results from the low acidity of the ring protons of these compounds[9a] relative to **1a**. The acidity order $H_5 > H_4$ is well established for thiazole and 2-substituted thiazoles.[6] The acidity of H_4 of **1c** is further diminished by the +I effect of the 5-methyl group to the point where metalation at C_4 does not occur with either LDA or *n*-BuLi at −78 °C.[12] Apparently in the case of **1b**, the +I effect of the 4-methyl group reduces the acidity of H_5 to the extent that ionization does not occur in the presence of **2a**. Furthermore, the reduction in acidity is so pronounced that LDA, which readily converts **1a** to carbanion **11**, fails to ionize H_5 in **1b** as evidenced by the fact that treatment of **1b** with LDA followed by quenching with either benzophenone, methyl iodide, or D_2O gave only recovered **1b**. A similar argument based on inductive effects may be invoked to account for the difference in reactivities of **1a** and its 2-bromo analogue, **1d** in dark reactions with enolate **2a**. The lack of reactivity of **1d** when treated with excess **2a** suggests that H_5 of **1d** is not sufficiently acidic to be ionized by **2a** and that a stronger base, e.g. LDA, is required for metalation (expt 24). The decreased acidity of the C_5 proton of **1d** may be rationalized in terms of the weaker −I effect of −Br vs. −Cl.[13]

On the basis of the observation that nitrile carbanions **6a–c** react rapidly with **1a** in the dark or in the presence of radical scavengers DTBN and DNB, the clear implication is that these reactions do not proceed via a radical-chain process, but rather occur by an ionic S_NAr mechanism. This addition–elimination scheme has been found to be applicable to a large number of nucleophilic substitution reactions, involving 2-halothiazoles.[14]

In conclusion, it should be noted that the results of the present study can serve as the basis for useful synthetic manipulations in the thiazole series. For example, the facile metalation at C_5 of **1a** with LDA provides entry to 5-substituted 2-chlorothiazoles. Subsequent nucleophilic displacement of chloride via $S_{RN}1$ or S_NAr reactions can then afford 2,5-disubstituted thiazoles from a single, readily available precursor, **1a**.

Experimental Section

General. Photostimulated reactions were conducted in a Rayonet RPR-240 photochemical reactor equipped with four 12.5-W lamps emitting maximally at 350 nm. Commercial anhydrous liquid NH_3 (Matheson) was used directly from the tank. Tetrahydrofuran (THF) was distilled from potassium under dry nitrogen. Chromatographic solvents were distilled before use. All other solvents were used without further purification. 2-Chlorothiazole (**1a**) and 2-bromothiazole (**1d**) were prepared according to the procedure of Ganapathi and Vankataraman.[15]

(8) (a) Knaus, G.; Meyers, A. I. *J. Org. Chem.* **1974**, *39*, 1192. (b) Crousier, J.; Metzger, J. *Bull. Soc. Chim. Fr.* **1967**, *11*, 4134.

(9) It is interesting to contrast the metalation reactions of 2-chlorothiazole (**1a**) and 2-bromothiazole (**1d**) with *n*-BuLi. With **1a**, metalation results from proton abstraction at C_5, whereas **1d** has been shown to undergo metal–halogen exchange at C_2, see: Kurkjy, R. P.; Brown, E. V. *J. Am. Chem. Soc.* **1952**, *74*, 6260.

(10) Incomplete metalation at C_5 of **1a** with *n*-BuLi has been observed previously;[6a] however, there appear to be no previous reports of metalation of **1a** with LDA.

(11) Carver, D. R.; Komin, A. P.; Hubbard, J. S.; Wolfe, J. F. *J. Org. Chem.* **1981**, *46*, 294.

(12) Trapping experiments using benzophenone and methyl iodide gave only unreacted **1c**.

(13) Forlani, L.; Magagni, M.; Todesco, P. E. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1145.

(14) (a) Bosco, M.; Forlani, L.; Liturri, V.; Riccio, P.; Todesco, P. E. *J. Chem. Soc. B* **1971**, 1373. (b) Mizuno, Y.; Adachi, K.; Ikeda, K. *Pharm. Bull.* **1954**, *2*, 225.

(15) Ganapathi, K.; Vankataraman, A. *Proc. Indian Acad. Sci., Sect. A* **1945**, *22A*, 343.

2-Chloro-4-methylthiazole (**1b**)[16] and 2-chloro-5-methylthiazole (**1c**)[17] were prepared as described in the literature. All reactants were purified by distillation or recrystallization. Routine ^1H NMR spectra were recorded on a Varian EM-390 spectrometer using tetramethylsilane (Me_4Si) as the internal standard. The low-temperature ^1H NMR studies were performed on a Jeol PS-100 spectrometer equipped with a variable-temperature probe. Infrared spectra were determined on a Perkin-Elmer 710B or a Beckman IR-20A-X spectrometer. Mass spectra were obtained on a Varian MAT-112 mass spectrometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Melting points were determined by use of a Thomas-Hoover melting point apparatus and are uncorrected. Analytical thin-layer chromatography (TLC) was conducted on Eastman 13181 silica gel sheets with fluorescent indicator. Flash chromatography[18] was performed with Merck silica gel (230–400 mesh) under compressed air by use of an 80:20 hexane–ethyl acetate mixture as the eluent. Kugelrohr distillations were conducted with an Aldrich Kugelrohr distillation apparatus at 50–70 °C (0.1 mm).

Procedure A. Photostimulated Reactions Using KNH_2 in Liquid NH_3. Approximately 200 mL of anhydrous ammonia was introduced directly into a cylindrical Dewar flask (unsilvered) equipped with a two-armed adapter, a dry ice condenser, and a metal stirring bar under an atmosphere of nitrogen. A solution of potassium amide (17.0 mmol) was then prepared by the addition of potassium metal according to the procedure of Hauser.[19] An anhydrous ethereal solution of the appropriate ketone (17.0 mmol) was added dropwise via syringe and the reaction solution was stirred for ca. 20 min to allow for anion formation. The lights of the photochemical reactor were turned on and 4.2 mmol of the halthiazole in 10 mL of anhydrous ether was added dropwise via syringe. After irradiation for an appropriate time the reaction mixture was quenched by pouring the liquid NH_3 solution directly onto solid ammonium chloride (3.5 g) in a 2-L beaker. The reaction vessel was then rinsed with ether (2 × 100 mL) and the ethereal washings were added to the NH_3 solution. Evaporation of the NH_3 was facilitated by warming on a hot plate. The remaining ethereal solution was filtered and the solid residue was washed with ether (2 × 100 mL). The combined ethereal solutions were dried ($MgSO_4$) and filtered. Evaporation of the ether using a rotary evaporator yielded the crude products.

Procedure B. Dark Reactions Using KNH_2 in Liquid NH_3. These reactions were conducted in the same manner as described in Procedure A except that the photoreactor was carefully wrapped with several layers of black cloth and the surrounding lights were extinguished prior to addition of the halothiazole.

In inhibited reactions, either di-*tert*-butyl nitroxide (DTBN) or *p*-dinitrobenzene (DNB) was added to the enolate solution before addition of the halothiazole.

Procedure C. Reactions Involving the Use of LDA in THF. Into a 250-mL three-neck round-bottomed flask equipped with a thermometer, rubber septa, and a Teflon stirring bar was added 50 mL of THF and 3.5 mL (18.0 mmol) of *N,N*-diisopropylamine via syringe under an atmosphere of nitrogen. The flask was then immersed in a dry ice–acetone bath, and the solution was cooled to −78 °C. To the stirred solution was added dropwise via syringe 17.0 mmol of *n*-BuLi over a period of 5–10 min. After the addition was complete, the reaction mixture was stirred at −78 °C for ca. 30 min to assure formation of lithium diisopropylamide (LDA). At this point, either 17.0 mmol of the appropriate ketone or 8.4 mmol of the halothiazole was added dropwise via syringe. The mixture was then stirred for 20 min to assure anion formation. Light was then excluded as described in procedure B and a solution of either 4.2 mmol of the 2-halothiazole or 17.0 mmol of benzophenone or methyl iodide in THF solution was added dropwise via syringe. The reaction mixture was stirred at −78 °C for 2 h and then quenched by pouring the solution directly over a slurry of ice and 100 mL of 2 M hydrochloric acid solution. The acidified solution was extracted with either ether or methylene chloride (4 × 50 mL) and the combined extracts were dried ($MgSO_4$) and concentrated on a rotary evaporator to yield the crude products.

Procedure D. Metalation Reactions with *n*-BuLi in THF. A solution of the halothiazole (1.67 mmol) in 20 mL of THF was added via syringe under nitrogen to a 100-mL three-neck round-bottomed flask equipped with a thermometer, rubber septa, and a Teflon stirring bar. The flask was then cooled in a dry ice–acetone bath to −78 °C and 1.1 mL of a 1.55 M solution of *n*-BuLi (1.70 mmol) in hexane was added slowly via syringe. The resulting solution was stirred for 5 min and a solution of 1.67 mmol of the appropriate electrophile in 10 mL of THF was added. The mixture was stirred for 1 h at −78 °C and then quenched by pouring onto a slurry of ice and 2 M HCl. The acidified solution was extracted with methylene chloride (2 × 50 mL), and the extracts were combined, dried (Na_2SO_4), and concentrated on a rotary evaporator to give the crude products.

Reactions of Pinacolone Enolate (2a) with 1a. (A) Irradiated: Procedure A was followed to give a dark green liquid. Flash chromatographic separation of the crude reaction mixture yielded 0.41 g (53%) of 1-(2-thiazolyl)-3,3-dimethyl-2-butanone (**3a**) and 0.14 g (25%) of 1,1-bis(2-thiazolyl)-3,3-dimethyl-2-butanone (**4a**) as colorless liquids. **3a**: IR (neat) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.28 (s, 9 H, *t*-Bu), 4.27 (s, 2 H, CH_2), 7.28 (d, 1 H, H_5), 7.73 (d, 1 H, H_4); MS, *m/e* (relative intensity) 183 (M^+, 85), 126 (46), 99 (28), 85 (31), 71 (100). Anal. Calcd for $C_9H_{13}NOS$: C, 59.02; H, 7.10; N, 7.66; S, 17.49. Found: C, 58.91; H, 7.20; N, 7.72; S, 17.31. **4a**: IR (neat) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.12 (s, 9 H, *t*-Bu), 6.52 (s, 1 H, CH), 7.24 (d, 1 H, H_5), 7.70 (d, 1 H, H_4); MS, *m/e* (relative intensity) 266 (M^+, 24), 209 (55), 182 (52), 57 (100). Anal. Calcd for $C_{12}H_{14}N_2OS_2$: C, 54.14; H, 5.26; N, 10.52. Found: C, 54.31; H, 5.47; N, 10.75.

(B) Dark. Procedure B gave a yellow liquid which consisted of one component by TLC analysis. Kugelrohr distillation yielded 0.64 g (70%) of 2-(2-chlorothiazol-5-yl)-3,3-dimethyl-2-hydroxybutane (**5a**) as a colorless liquid: IR (neat) 3580 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 1.00 (s, 9 H, *t*-Bu), 1.54 (s, 3 H, CH_3), 2.33 (s, 1 H, OH), 7.24 (s, 1 H, H_4). Anal. Calcd for $C_9H_{14}ClNOS$: C, 49.32; H, 6.39; N, 6.39; S, 14.61. Found: C, 49.65; H, 6.69; N, 6.67; S, 14.49.

(C) Irradiated and Inhibited. This reaction was carried out under conditions identical with those described in procedure A except that 10 mol % of DTBN was added prior to the addition of **1a**. The orange oil thus obtained showed two major product components by TLC, and these were separated by column chromatography to give 0.25 g (27%) of **5a** and 0.31 g (62%) of recovered **1a**.

Photostimulated Reaction of Pinacolone Enolate (2a) with 1d. Procedure A using 10 mmol of **2a** and 2.5 mmol of **1d** gave, after column chromatography, 0.29 g (44%) of **3a**. None of the disubstitution product, **4a**, could be detected by TLC or ^1H NMR analysis.

When this reaction was attempted in the dark according to procedure B, only unreacted **1d** was obtained.

Photostimulated Reaction of Pinacolone Enolate (2a) with 1b. Procedure A employing 8.0 mmol of **2a** and 2.0 mmol of **1b** yielded a green liquid. The crude product mixture was separated by column chromatography to afford 0.24 g (64%) of 1-(4-methylthiazol-2-yl)-3,3-dimethyl-2-butanone (**3b**) and 0.03 g (10%) of 1,1-bis(4-methylthiazol-2-yl)-3,3-dimethyl-2-butanone (**4b**) as pale yellow oils. **3b**: ^1H NMR ($CDCl_3$) δ 1.25 (s, 9 H, *t*-Bu), 2.41 (s, 3 H, CH_3), 4.22 (s, 2 H, CH_2), 6.82 (s, 1 H, H_5); MS, *m/e* (relative intensity) 197 (M^+, 8), 140 (20), 113 (19), 85 (25), 57 (100). **4b**: ^1H NMR ($CDCl_3$) δ 1.25 (s, 9 H, *t*-Bu), 2.42 (s, 6 H, CH_3), 6.39 (s, 1 H, CH), 6.80 (s, 2 H, H_5); MS, *m/e* (relative intensity) 294 (M^+, 26), 210 (100), 138 (17), 85 (35), 57 (67).

In a similar reaction carried out in the dark only unreacted **1b** was recovered.

Photostimulated Reaction of Pinacolone Enolate (2a) with 1c. Procedure A was followed and the product mixture obtained from 8.0 mmol of **2a** and 2.0 mmol of **1c** was chromatographed to give 0.26 g (66%) of 1-(5-methylthiazol-2-yl)-3,3-dimethyl-2-butanone (**3c**) and 0.02 g (7%) of 1,1-bis(5-methylthiazol-2-yl)-3,3-dimethyl-2-butanone (**4c**) as nearly colorless oils. **3c**: ^1H NMR ($CDCl_3$) δ 1.25 (s, 9 H, *t*-Bu), 2.40 (s, 3 H, CH_3), 4.15 (s, 2 H, CH_2), 7.31 (s, 1 H, H_4); MS, *m/e* (relative intensity) 197 (M^+, 12), 140 (30), 113 (44), 85 (24), 57 (100). **4c**: ^1H NMR ($CDCl_3$) δ 1.25 (s, 9 H, *t*-Bu), 2.40 (s, 6 H, CH_3), 6.30 (s, 1 H, CH), 7.35 (s, 2 H, H_4); MS, *m/e* (relative intensity) 294 (M^+, 12), 210 (66), 85 (16), 72 (20), 57 (100).

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An attepted dark reaction of **1c** and **2a** returned only starting materials.

Reaction of Diisopropyl Ketone Enolate (2b) with 1a. (A) Irradiated. Procedure A yielded a homogeneous dark yellow liquid by TLC. Kugelrohr distillation afforded a white, crystalline solid that was recrystallized from hexane–ethyl acetate to give 0.75 g (77%) of 3-(2-chlorothiazol-5-yl)-2,4-dimethyl-3-hydroxypentane (**5b**), mp 99–100 °C: IR ($CHCl_3$) 3580 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 0.90 (m, 12 H, CH_3), 1.88 (br s, 1 H, OH), 2.10 (m, 2 H, CH), 7.20 (s, 1 H, H_4); MS, *m/e* (relative intensity) 235 (2), 233 (M^+, 4), 192 (33), 190 (90), 150 (36), 148 (100). Anal. Calcd for $C_{10}H_{16}ClNOS$: C, 51.50; H, 6.87; N, 6.00; S, 13.73. Found: C, 51.30; H, 6.89; N, 5.84; S, 13.90.

(B) Dark. Procedure B gave 0.84 g (83%) of **5b**, and procedure C afforded an essentially quantitative yield of **5b** (homogeneous reaction mixture weighed 0.98 g). Samples of **5b** obtained in the dark reactions were identical (^1H NMR, TLC comparison) with **5b** from the illuminated reaction.

Treatment of **1a** according to procedure C with only 1 equiv of **2b** from 4.2 mmol of LDA resulted in quantitative recovery of **1a**.

Reaction of Potassioacetonitrile (6a) with 1a. (A) Irradiated. Procedure A was followed to give a homogeneous (TLC) dark green liquid, Kugelrohr distillation of which yielded 0.41 g (79%) of 2-cyanomethylthiazole (**7a**) as a colorless liquid: IR (neat) 2230 cm^{-1} (C≡N); ^1H NMR ($CDCl_3$) δ 4.22 (s, 2 H, CH_2), 7.30 (d, 1 H, H_5), 7.69 (d, 1 H, H_4); MS, *m/e* (relative intensity) 124 (M^+, 83), 97 (9), 59 (8), 58 (100), 57 (13). Anal. Calcd for $C_5H_4N_2S$: C, 48.39; H, 3.23; N, 22.58; S, 25.81. Found: C, 47.79; H, 3.20; N, 22.15; S, 25.08.

(B) Dark. Procedure B gave a dark yellow liquid, which following Kugelrohr distillation yielded 0.50 g (96%) of **7a**. From procedure B, with 10 mmol of **6a** and 2.5 mmol of **1a**, there was obtained after a 5 min reaction period 0.26 g (85%) of **7a**.

(C) Dark and Inhibited. Procedure B was followed except that 10 mol % of DTBN was added to the reaction flask before addition of **1a**. This procedure yielded 0.50 g (96%) of **7a**. Procedure B, employing 10 mmol of **6a**, 2.5 mmol of **1a**, and 10 mol % of DNB afforded 0.30 g (98%) of **7a** after 5 min.

Reaction of Potassiopropionitrile (6b) with 1a. (A) Irradiated. When procedure A was followed, a dark yellow liquid containing two components (TLC) was obtained. Separation of this mixture by flash chromatography yielded crude 2-(α-cyanoethyl)thiazole (**7b**). After Kugelrohr distillation, 0.36 g (62%) of **7b** was obtained as a clear yellow liquid: IR (neat) 2220 cm^{-1} (C≡N); ^1H NMR ($CDCl_3$) δ 1.91 (d, 3 H, CH_3), 4.40 (q, 1 H, CH), 7.29 (d, 1 H, H_5), 7.70 (d, 1 H, H_4); MS, *m/e* (relative intensity) 138 (M^+, 88), 137 (70), 111 (82), 58 (100), 57 (21). Anal. Calcd for $C_6H_6N_2S$: C, 52.17; H, 4.35; N, 20.29. Found: C, 52.26; H, 4.67; N, 20.08.

(B) Dark. Procedure B afforded a dark yellow liquid which was subjected to Kugelrohr distillation to yield 0.48 g (83%) of **7b**.

Reaction of Potassiophenylacetonitrile (6c) with 1a. (A) Irradiated. Procedure A produced a dark brown liquid which was shown by TLC analysis to consist of three components. Flash chromatography yielded unreacted phenylacetonitrile, 0.48 g of crude 2-(α-cyanobenzyl)thiazole (**7c**), and 0.32 g of an intractable tar. Kugelrohr distillation of crude **7c** gave 0.40 g (48%) of **7c** as a colorless liquid: IR (neat) 2350 cm^{-1} (C≡N); ^1H NMR ($CDCl_3$) δ 5.58 (s, 1 H, CH), 7.30 (m, 6 H, a, H_5), 7.68 (d, 1 H, H_4). Anal. Calcd for $C_{11}H_8N_2S$: C, 66.00; H, 4.00; N, 14.00. Found: C, 65.70; H, 4.21; N, 13.73.

(B) Dark. Procedure B gave a dark red liquid. Flash chromatographic separation afforded 0.04 g of phenylacetonitrile, 0.47 g (56%) of **7c**, and 0.04 g of a black tar.

2-Chloro-5-(diphenylhydroxymethyl)thiazole (5c). (A) Via Metalation of 1a with KNH_2. Into a cylindrical Dewar flask wrapped with several layers of black cloth and containing a slurry of KNH_2[19] (17 mmol) in 200 mL of liquid NH_3 was added a solution of 0.50 g (4.2 mmol) of **1a** in 10 mL of anhydrous ether. After stirring for 20 min, a solution of 0.76 g (4.2 mmol) of benzophenone in 10 mL of ether was added and the resulting mixture was stirred for 1 h. Following the workup as described in procedure A, a bronze oil was obtained. Purification by flash chromatography and Kugelrohr distillation gave 0.83 g (66%) of **5c** as a colorless oil: IR (neat) 3540 cm^{-1} (OH) ^1H NMR ($CDCl_3$) δ 3.52 (s, 1 H, OH), 7.00 (s, 1 H, H_4), 7.29 (m, 10 H, a); MS, *m/e* (relative intensity) 303 (7), 30 (M^+, 15), 226 (19), 224 (49), 198 (36), 198 (100), 148 (21), 146 (56). Anal. Calcd for $C_{16}H_{12}ClNOS$: C, 63.79; H, 3.99; N, 4.65; S, 10.63. Found: C, 63.50; H, 4.23; N, 4.38; S, 10.36.

(B) Via Metalation of 1a with LDA. Procedure C was followed except that 4.2 mmol each of **1a**, LDA, and benzophenone was used. The bronze oil thus obtained was purified by flash chromatography to afford an essentially quantitative yield of **5c**.

Similar attempted reactions of **1b** and **1c** employing 2 equiv of LDA, led to recovery of starting materials and no carbinol product could be detected by ^1H NMR.

(C) Via Metalation of 1a with *n*-BuLi. Procedure D gave a mixture containing 0.23 g (45%) of **5c** and 0.17 g (55%) of recovered benzophenone as islated by flash chromatography.

When subjected to the same reaction conditions, **1c** failed to give any carbinol product, and was quantitatively recovered.

2-Bromo-5-(diphenylhydroxymethyl)thiazole (5d). From procedure C, with 0.16 g (1.0 mmol) of **1d** and 2.0 mmol of LDA, the crude product was obtained as a dark oil, which was chromatographed to give 0.12 g (35%) of **5d** as a yellow oil: ^1H NMR ($CDCl_3$) δ 3.46 (s, 1 H, OH), 6.87 (s, 1 H, H_4), 7.32 (m, 10 H, a); MS, *m/e* (relative intensity) 347 [$(M+2)^+$, 1.9], 345 (M^+, 1.6), 267 (49), 190 (33), 105 (100), 77 (90).

2-(2-Chlorothiazol-5-yl)-3,3-dimethyl-2-hydroxybutane (5a) via Metalation of 1a with *n*-BuLi. Procedure D gave 0.12 g (33%) of **5a** as a yellow oil after chromatography. This compound was identical with **5a** obtained in the dark reaction of **1a** with enolate **2a**.

2-Chloro-5-methylthiazole (1c) via Metalation of 1a with LDA. This reaction was conducted in the same manner as procedure C using 0.50 g (4.2 mmol) of **1a** and 17 mmol each of LDA and methyl iodide to yield 0.30 g (52%) of **1c**[17] as a colorless liquid.

Under similar conditions, **1b** and **1c** failed to undergo methylation. When the methylation reaction was attempted with *n*-BuLi using procedure D, no methylation product was obtained with **1c**.

5-Deuterio-2-chlorothiazole. Procedure C, using 0.50 g (4.2 mmol) of **1a**, 17 mmol of LDA, and 34 mmol of D_2O gave **1a** with ca. 70% deuterium incorporation at C_5 by ^1H NMR and MS analysis: ^1H NMR ($CDCl_3$) δ 7.52 (s, 1 H, H_4), 7.20 (d, 0.3 H, H_5); MS, *m/e* (relative intensity) 122 (24), 121 (11), 120 (M+1, 65) 119 (M^+, 22), 59 (100), 58 (46), 57 (10).

Attempted deuteration of **1b** under the same conditions failed. ^1H NMR and MS analysis of **1b** isolated from this reaction showed no incorporation of deuterium at C_5.