90–92 °C; IR 1716 (s, C=O) cm^{-1}; NMR δ 0.86, 1.13, 1.20 (s, 3 each, Me), 2.46 (s, 3, aromatic Me), 3.40 (s, 3, OMe), 4.16 (dd, 1, J = 14, 6 Hz, H-2), 4.36 (4-line AB, 2, J = 11 Hz, OCH_2), 7.40, 7.80 (d, 2 each, J = 9 Hz, aromatic Hs).

Anal. Calcd for $C_{28}H_{38}O_5S$: C, 69.11; H, 7.87. Found: C, 69.16; H, 7.76.

Ketone 8. A solution of 80 mg of ketone **7** in 10 mL of benzene was added over a 15-min period to a stirring suspension of 48 mg of potassium *tert*-butoxide in 5 mL of benzene under nitrogen at 60 °C and the mixture stirred at this temperature for an additional 30 min. It was poured into ice water and extracted with chloroform. The extract was washed with water, dried, and evaporated. Chromatography of the residue (60 mg) over neutral alumina and elution with 50:1 benzene–ethyl acetate yielded 48 mg of semisolid ketone **8**: IR 1768 (s, C=O) cm^{-1}; NMR δ 0.90, 1.10, 1.26 (s, 3 each, Me), 2.65 (4-line AB, 2, J = 18 Hz, $COCH_2$), 3.43 (s, 3, OMe), 5.48 (m, 1, H-7).

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.32; H, 9.56.

Treatment of 70 mg of the ketone **8** with 2 mL of 2 N sodium deuteroxide in deuterium oxide and 1 mL of dioxane at 70 °C under nitrogen for 27 h, followed by the usual workup, yielded 60 mg of dideuterio **8**, whose ^1H NMR spectrum had lost its two-proton multiplet at 2.65 ppm.[10]

Ketone 9. A mixture of 40 mg of ketone **8** and 200 mg of silica gel in 5 mL of benzene was stirred at room temperature for 6 h and then filtered. Evaporation of the filtrate gave 40 mg of residue, whose crystallization from ether yielded crystalline ketone **9**: mp 86–88 °C; IR 1768 (s, C=O) cm^{-1}; NMR δ 0.83, 0.87, 1.26 (s, 3 each, Me), 2.87 (4-line AB, 2, J = 18 Hz, $COCH_2$), 3.50 (s, 3, OMe), 5.48 (m, 1, H-7).

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.15; H, 9.71.

Deuterium exchange on ketone **9** by the procedure used for the cyclobutanone **8** (vide supra) yielded a dideuterio derivative whose ^1H NMR spectrum showed the loss of the two-proton multiplet at 2.87 ppm.[10]

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(10) P. Ceccherelli, R. Pellicciari, N. F. Golob, R. A. J. Smith, and E. Wenkert, *Gazz. Chim. Ital.*, **103**, 599 (1973).

Ring-Opening Reactions of Electrophilic Cyclopropanes

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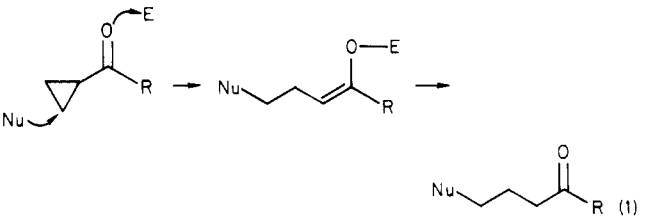
Recent developments in organoheteroatom (e.g., aluminum, silicon, sulfur, and selenium) chemistry have involved reagents in which a hard acid is bound to a soft base. Application of the hard and soft acids and bases principle (HSAB)[1] predicts that the weak hard–soft interaction in the reagent should facilitate reaction pathways involving complementary hard–hard/soft–soft interactions between reagent and substrate. The use of reagents combining nucleophiles with potent oxygenophiles (hard acids) has led to several extremely mild procedures involving the formal addition of a nucleophile to an electron-deficient carbon center. Examples of these reagents include Me_3SiI, Me_2AlSPh, and $MeS–SiMe_3$ in which the silicon and aluminum atoms are hard acids and the iodine and sulfur atoms are soft bases. Transformations such as epoxide ring openings (Me_3SiI,[2] Me_3SiCN[3]), nucleophilic acyl substitutions (Me_2AlSPh,[4] $Me_2AlSePh$[5]), and dealkylation of esters (Me_3SiI,[2] $AlBr_3/PhSH$,[7] $Me_3SiCl/NaI/CH_3CN$[8]), acetals (Me_3SiI[2]), and methyl and benzyl ethers (Me_3SiSR[9]) illustrate successful applications of these reagents. The above reactions suggested the possibility of adding various nucleophiles to cyclopropanes containing an electron-withdrawing substituent under very mild reaction conditions (eq 1). The well-known parallel between



(1)

cyclopropane and olefin chemistry[10] would also suggest a soft β-carbon in a cyclopropyl carbonyl compound in analogy with α,β-unsaturated carbonyl compounds. We have examined nine reagent combinations and three functional group substituents to explore the scope of this homologous Michael[11] addition procedure.

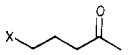
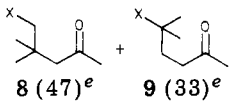
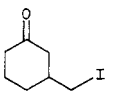
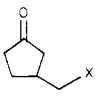
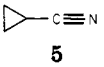
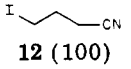
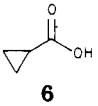
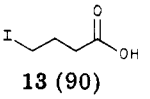
The addition of nucleophiles to cyclopropanes conjugated with electron-withdrawing substituents is well precedented[11] and represents a reactivity umpolung procedure[12] that has been actively investigated in recent years. The ring cleavage of electron-deficient cyclopropanes can be effected under nucleophilic conditions[11] or assisted by the presence of powerful electrophiles. The nucleophilic ring-opening reactions are generally limited to diactivated and highly strained monoactivated cyclopropanes unless very powerful nucleophiles are employed.[13] Lewis and Brønsted acids have been utilized in electrophilicly assisted ring-opening reactions of cyclopropyl ketones but often require vigorous reaction conditions that may result in poor regioselective cleavage.[14] Recent reports describing cleavage of cyclopropyl ketones with trimethylsilyl iodide[15] and acetyl methanesulfonate[16] under mild conditions

(1) T.-L. Ho, "Hard and Soft Acids and Bases Principle in Organic Chemistry", Academic Press, New York, 1977.

(2) For reviews see: A. H. Schmidt, *Aldrichimica Acta*, **14**, 31 (1981); A. H. Schmidt, *Chem.-Ztg.*, **104**, 253 (1980); W. C. Groutas and D. Felker, *Synthesis*, 861 (1980).
(3) W. Lidy and W. Sundermeyer, *Tetrahedron Lett.*, 1449 (1973).
(4) R. P. Hatch and S. M. Weinreb, *J. Org. Chem.*, **42**, 3960 (1977).
(5) A. P. Kozikowski and A. Ames, *J. Org. Chem.*, **43**, 2735 (1978).
(6) D. A. Evans, K. G. Grimm, and L. K. Truesdale, *J. Am. Chem. Soc.*, **97**, 3229 (1975).
(7) M. Node, K. Nishide, M. Sai, and E. Fujita, *Tetrahedron Lett.*, 5211 (1978).
(8) T. Morita, Y. Okamoto, and H. Sakurai, *J. Chem. Soc. Chem. Commun.*, 874 (1978); G. A. Olah, S. C. Narang, B. G. B. Gupta, and R. Malhotra, *J. Org. Chem.*, **44**, 1247 (1979).
(9) S. Hanessian and Y. Guindon, *Tetrahedron Lett.*, 2305 (1980).
(10) A. de Meijere, *Angew. Chem., Int. Ed. Engl.*, **18**, 809 (1979).
(11) S. Danishefsky, *Acc. Chem. Res.*, **12**, 66 (1979).
(12) D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **18** 239 (1979).
(13) A. B. Smith, III, and R. M. Scarborough, Jr., *Tetrahedron Lett.*, 1649 (1978).
(14) (a) E. Giacomini, M. A. Loreto, L. Pellacani, and P. A. Tardella, *J. Org. Chem.*, **45**, 519 (1980); (b) L. Pellacani, P. A. Tardella, and M. A. Loreto, *ibid.*, **41**, 1282 (1976); (c) N. DiBello, L. Pellacani, and P. A. Tardella, *Synthesis*, 227 (1978).
(15) R. D. Miller and D. R. McKean, *J. Org. Chem.*, **46**, 2412 (1981), and references cited therein.
(16) M. Demuth and P. R. Raghavan, *Helv. Chim. Acta*, **62**, 2338 (1979).
(17) U. Joss and H. Schaltegger, *Helv. Chim. Acta*, **52**, 2465 (1969).
(18) H. Hart and R. H. Schlosberg, *J. Am. Chem. Soc.*, **90**, 5189 (1968).
(19) W. E. Truce and L. B. Lindy, *J. Org. Chem.*, **26**, 1463 (1961).

0022-3263/82/1947-3174$01.25/0

Table I. Ring-Opening Reactions of Electrophilic Cyclopropanes

entry	substrate	reagents[a]	rctn conditions, solvent/time, h/temp, °C	X	product(s) (% yield)[b]	ref[c]
1	 1	Me_3SiCl-NaI	CH_3CN/12/25	I[d]	 7 (89)	15
2	1		CH_2Cl_2/30/25	I	7 (85)	
3	1	Me_3SiCl-NaBr	CH_3CN/50/25	Br	7 (94)	17
4	1	Me_3SiCl-LiCl	CH_3CN/26/55	Cl	7 (91)	18
5	1	$AlCl_3$-NaI	CH_3CN/15/25	I	7 (83)	
6	1	$AlCl_3$-Me_3SiSPh	CH_3CN/2[f]/25	PhS	7 (35)[e]	19
7	1	$AlCl_3$-PhSH	CH_3CN/15/55	PhS	7 (43)[e]	
8	1	Me_3SiCl-KCN	CH_3CN/45/55	Cl	7 (62)	
9	1	Me_3SiCl-$ZnCl_2$-KCN	CH_3CN/24/25	Cl	7 (87)	
10	1	Me_3SiCl-$ZnCl_2$-NaSPh	CH_3CN/24/25	Cl	7 (40)	
11	 2	Me_3SiCl-NaI	CH_3CN/12/25	I	 8 (47)[e] 9 (33)[e]	
12	2		CH_2Cl_2/12/25	I	8 (0), 9 (99)	
13	2	Me_3SiCl-NaCl	CH_3CN/24/55	Cl	8 (0), 9 (84)	
14	 3	Me_3SiCl-NaI	CH_3CN/44/25		 10[d] (94)	15, 14a
15	 4	Me_3SiCl-NaI	CH_3CN/44/25	I[d]	 11 (92)	15
16	4	Me_3SiCl-NaBr	CH_3CN/60/25	Br	11 (91)	20
17	4	Me_3SiCl-NaCl	CH_3CN/48/55	Cl[d]	11 (96)	14c
18	 5	Me_3SiCl-NaI	CH_3CN/30/25		 12 (100)	21
19	5	Me_3SiI	CH_2Cl_2/30/25		12 (97)	
20	 6	Me_3SiCl-NaI	CH_3CN/54/25		 13 (90)	22
21	6	HI (4.0 equiv)	CH_3CN/60/25		13 (0)	

[a] Two equivalents of reagent was employed. [b] All yields are based upon crude products which were >95% pure by NMR unless otherwise noted. [c] For previous preparation(s) of these products, see the indicated reference(s). [d] This compound gave spectroscopic data identical with those reported in the literature. [e] Yields were determined by NMR. [f] Days.

prompt us to detail our observations on electrophile-assisted ring-opening reactions of cyclopropyl ketones, acids, and nitriles with nine reagent combinations.

We began our initial investigation with cyclopropyl methyl ketone (1) and examined a variety of electrophile-nucleophile combinations. The use of chlorotrimethylsilane in combination with alkali metal halides afforded excellent yields (entries 1–4, Table I) of the corresponding γ-halo ketones. Longer reaction times or higher temperatures were required for the less nucleophilic bromide and chloride combinations. The combination of chlorotrimethylsilane with potassium cyanide (entries 8 and 9) or sodium thiophenoxide (entry 10) was ineffective in promoting a homo-Michael addition of cyanide or thiophenol to 1. The only product isolated in these experiments was 5-chloro-2-pentanone. Modest yields of 5-(phenylsulfenyl)-2-pentanone, however, could be prepared by reaction of 1 with (phenylthio)trimethylsilane or thiophenol (entries 6 and 7, respectively) in the presence of aluminum chloride. These very modest yields are in marked contrast to the clean and efficient cleavage of 1 with an $AlCl_3$–NaI (entry 5) combination.

We next examined cyclopropyl ketones 2–4 in order to explore the regioselectivity of these ring-opening reactions. Reaction of 2,2-dimethylcyclopropyl methyl ketone (2) with Me_3SiCl–NaI (entry 11) in acetonitrile afforded a nearly equimolar mixture of the two possible structural isomers 8 (X = I) and 9 (X = I). The structures of 8 (X = I) and 9 (X = I) were rigorously established by conversion to 4,4-dimethyl-2-pentanone and 5-methyl-2-hexanone, respectively, by reductive dehalogenation with tri-*n*-butyltin hydride. A concerted S_N2 reaction process would explain the formation of 8 (X = I) while 9 (X = I) would be expected to arise via a reaction pathway having

(20) The enol acetate of 11 (X = Br) has been prepared by cleavage of 4 with acetyl methanesulfonate in the presence of tetramethylammonium bromide. See reference 16.

(21) S. Wolfe and M. G. Jokinen, *Can. J. Chem.*, 57, 1388 (1979).

(22) H. Oelschlaeger, P. Schmersahl, and W. Toporski, *Arch. Pharm.*, 294, 488 (1961); *Chem. Abstr.*, 56, 3343c (1962).

considerable carbenium ion character in the transition state. The use of weaker nucleophiles (e.g., Cl^-, entry 13) or less polar solvents that disfavor solvent-separated ion pairs (entry 12) led to regioselective ring opening favoring the pathway that has considerable carbenium ion character in the transition state. The fused cyclopropyl ketones **3** and **4** also undergo regioselective ring-opening reactions with chlorotrimethylsilane and alkali metal halides (entries 14–17) to afford the corresponding β-(halomethyl)cycloalkanones in excellent yields. Cyclopropyl ketones **2–4** could not, however, be cleanly and efficiently cleaved with $AlCl_3$–PhSH or Me_2AlSPh.[23]

The combination of Me_3SiCl–NaI was also effective in cleaving the less reactive cyclopropyl cyanide (**5**, entry 18) and cyclopropanecarboxylic acid (**6**, entry 20) although it could not be extended to the corresponding alkyl or aryl carboxylic esters. Interestingly, Me_3SiCl–NaI efficiently cleaved cyclopropanecarboxylic acid while 4 equiv of HI were completely ineffective (entry 21).

Finally, it should be noted that the Me_3SiCl–NaI couple appears to be equivalent to the reagent Me_3SiI in effecting cyclopropane ring cleavage (entries 18 and 19). Similarly, the Me_3SiCl–NaI-promoted ring cleavages of cyclopropyl ketones **1**, **3**, and **4** are equivalent in yield and regioselectivity to the Me_3SiI-promoted cleavages recently reported by Miller and McKean.[15] The expense and sensitivity of iodotrimethylsilane to light, moisture, and air makes the chlorotrimethylsilane–sodium iodide combination a very convenient and economical alternative. In addition, the procedure can be readily extended to the preparation of alkyl bromides and chlorides by use of sodium bromide or sodium chloride. Similarly, the thiophenol–aluminum chloride couple appears equivalent to (phenylthio)trimethylsilane in the presence of aluminum chloride (entries 7 and 6).

Our studies have shown that the homologous Michael reaction of conjugated cyclopropanes can, in some instances, be effected under relatively mild conditions when a hard acid is used in combination with a soft base. Nucleophiles such as cyanide, azide, and acetate were ineffective in promoting cyclopropane ring cleavage, and the procedure appears limited to halide and sulfur nucleophiles. It is interesting to note that the 1,2-addition of trimethylsilyl azide[24] and trimethylsilyl cyanide[25] to ketones is well precedented. The Lewis acid mediated conjugate addition of trimethylsilyl cyanide to α,β-unsaturated ketones, however, has only recently been reported.[26] The inability of cyanide and thiophenoxide anions to compete with chloride (entries 8–10) suggests that factors other then the relative softness of the nucleophile may also be involved in these reactions. In summary, the regioselectivity and mildness of these procedures makes them the method of choice for introducing iodide, bromide, or chloride substituents by cleavage of conjugated cyclopropanes.

Experimental Section

Proton NMR spectra were recorded on a Varian EM-360L or JEOL FX-90Q spectrometer. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane as internal standard. Carbon NMR spectra were recorded on a JEOL FX-90Q spectrometer. The δ values are in parts per million downfield from Me_4Si and are referenced with respect to internal $CDCl_3$. Infrared spectra were recorded on either a Perkin-Elmer 710 B or 1310 grating spectrophotometer. Vapor-phase chromatography was done by using a Varian Aerograph Model 90-P or 920 with a 10 ft × $^3/_8$ in. 24.5% Carbowax 20M (absorbed on Chromasorb P) column. The oven was operated at 160 °C, and the helium carrier gas flow rate was 50–100 mL/min. Elemental analyses were determined by Galbraith Laboratories, Inc., Knoxville, TN.

Acetonitrile and dichloromethane were distilled from CaH_2 and stored over 3-Å molecular sieves. Cyclopropyl methyl ketone, cyclopropyl cyanide, and cyclopropanecarboxylic acid were obtained from Aldrich and used without further purification. Cyclopropyl ketones **2**,[27] **3**,[28] and **4**[29] are known compounds and were prepared by an established literature procedure.[30]

Sodium Iodide–Trimethylsilyl Chloride Mediated Cleavage of 2,2-Dimethylcyclopropyl Methyl Ketone (2). Trimethylsilyl chloride (0.527 mL, 4.14 mmol) was added via syringe at room temperature to a solution containing 10 mL of dry acetonitrile, 0.231 g (2.07 mmol) of **2**, and 0.310 g (4.13 mmol) of sodium iodide under nitrogen. A white precipitate formed immediately, and the solution gradually turned a reddish orange and was stirred at room temperature for 14 h. The reaction mixture was poured into 25 mL of 5% Na_2SO_3 saturated with KF and extracted with ether. The organic extracts were washed with water and brine and dried over magnesium sulfate. Removal of solvent in vacuo gave 0.390 g (79% yield) of a red oil containing two regioisomers **8** (X = I) and **9** (X = I) by NMR. Attempted purification by TLC (silica gel, 1000 μm; CH_2Cl_2) afforded as the only isolated product pure 4,4-dimethyl-5-iodo-2-pentanone (**8**, X = I): 0.115 g (23% yield); IR (CCl_4) 2960, 1710, 1360 cm^{-1}; NMR (CCl_4) δ 1.13 (s, 6 H), 2.07 (s, 3 H), 2.45 (s, 2 H), 3.35 (s, 2 H); mass spectrum, *m/e* 181.960 49 ($M^+ - C_3H_6O$) (calcd for C_4H_7I, 181.959 43) for the fragment ion arising from a McLafferty fragmentation.[31]

The presence of the two regioisomers **8** (X = I) and **9** (X = I) was confirmed by reductive dehalogenation of the crude reaction mixture. Tri-*n*-butyltin hydride (0.38 mL, 1.45 mmol) was added via syringe to a red solution containing 0.5 mL of absolute benzene and 0.317 g (1.32 mmol) of the above crude reaction mixture. The solution was stirred at 25 °C for 0.5 h. Preparative gas chromatography of the crude solution afforded two components in a 59:41 ratio. Fraction A gave pure 4,4-dimethyl-2-pentanone: IR (CCl_4) 2970, 1720, 1370, 920 cm^{-1}; NMR (CCl_4) δ 1.00 (s, 9 H), 2.08 (s, 3 H), 2.27 (s, 2 H). Fraction B gave pure 5-methyl-2-hexanone: IR (CCl_4) 2940, 1710, 1350, 1160 cm^{-1}; NMR (CCl_4) δ 0.88 (d, *J* = 6.0 Hz, 6 H), 1.23–1.71 (m, 3 H), 2.12 (s, 3 H), 2.40 (t, *J* = 7.0 Hz, 2 H).

Cyclopropanes **1–6** listed in Table I were efficiently cleaved with trimethylsilyl chloride in combination with NaI, NaBr, or NaCl according to the above general procedure and the specific reaction conditions listed in Table I **7** (X = Br): IR (CCl_4) 2950, 1710, 1360 cm^{-1}; NMR (CCl_4) δ 1.77–2.27 (m, 2 H), 2.10 (s, 3 H), 2.22 (t, *J* = 6.5 Hz, 2 H), 3.38 (t, *J* = 6.0 Hz, 2 H). **7** (X = Cl): IR (CCl_4) 2950, 1710, 1360 cm^{-1}; NMR (CCl_4) δ 1.67–2.17 (m, 2 H), 2.10 (s, 3 H), 2.53 (t, *J* = 6.5 Hz, 2 H), 3.50 (t, *J* = 6.0 Hz, 2 H). **9** (X = Cl): IR (CCl_4) 2970, 2925, 1710, 1390, 1375, 1350, 1155, 1115 cm^{-1}; NMR (CCl_4) δ 1.50 (s, 6 H), 2.07 (s, 3 H), 1.67–2.17 (m, 2 H), 2.33–2.80 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 29.8, 32.3 (2 C), 38.8, 39.5, 69.8, 207.5. Anal. Calcd for $C_7H_{13}ClO$: C, 56.56;

(23) The reaction of cyclopropyl phenyl ketone with trimethylaluminum in the presence of nickel acetylacetonate to afford 1-phenylpentan-1-one has been reported: L. Bagnell, A. Meisters, and T. Mole, *Aust. J. Chem.*, **28**, 821 (1975). Here zerovalent nickel is postulated to be the catalytically active species.

(24) H. Vorbrüggen and K. Krolikiewicz, *Synthesis*, 35 (1979).

(25) D. A. Evans, G. L. Carroll, and L. K. Truesdale, *J. Org. Chem.*, **39**, 914 (1974); D. A. Evans, J. M. Hoffman, and L. K. Truesdale, *J. Am. Chem. Soc.*, **95**, 5822 (1973); K. Deuchert, U. Hertenstein, and S. Hünig, *Synthesis*, 777 (1973).

(26) K. Utimoto, M. Obayashi, Y. Shishiyama, M. Inoue, and H. Nozaki, *Tetrahedron Lett.*, 3389 (1980).

(27) C. Agami, C. Prevost, and J. Aubouet, *Bull. Soc. Chim. Fr.*, 2299 (1967).

(28) H. O. House, A. V. Prabhu, J. M. Wilkins, and L. F. Lee, *J. Org. Chem.*, **41**, 3067 (1976).

(29) J. C. Limasset, P. Amice, and J. M. Conia, *Bull. Soc. Chim. Fr.*, 3981 (1969).

(30) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).

(31) This compound was very unstable toward the usual purification procedures and did not give a satisfactory combustion analysis.

(32) Recent experiments have revealed that cyclopropyl ketone **4** undergoes a nonregioselective ring cleavage when treated with trimethylsilyl chloride and sodium bromide or sodium chloride in acetonitrile at temperatures higher than those indicated in Table I (entries 16–17). In these recent experiments the solutions were heated at reflux.

H, 8.82; Cl, 23.85. Found: C, 56.50; H, 8.71; Cl, 23.94. **9** (X = I): IR (CCl_4) 2980, 2920, 1725, 1370, 1110 cm^{-1}; NMR (CCl_4) δ 1.90 (s, 6 H), 1.47–2.00 (m, 2 H), 2.13 (s, 3 H), 2.43–2.83 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.0, 38.0 (2 C), 43.3 (2 C), 50.4, 207.1. **11** (X = Br): IR (CCl_4) 2970, 1750, 1250, 1160 cm^{-1}; NMR (CCl_4) δ 1.50–2.70 (m, 7 H), 3.43 (d, J = 5.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 28.0, 37.0, 38.4, 38.9, 43.7, 216.9; mass spectrum, m/e 175.983 27, 177.981 40 (calcd for C_6H_9OBr 175.983 67, 177.981 63). **11** (X = Cl): IR (CCl_4) 1755 cm^{-1}; NMR (CCl_4) δ 1.50–2.96 (m, 7 H), 3.68 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 26.9, 38.2, 39.0, 42.5, 48.0, 217.1. **12**: IR (CCl_4) 2950, 2240, 1430 cm^{-1}; NMR (CCl_4) δ 1.80–2.67 (m, 4 H), 3.27 (t, J = 6.0 Hz, 2 H). **13**: IR (CCl_4) 3600–2400 (v br), 1700, 1420, 1210 cm^{-1}; NMR (CCl_4) δ 1.97–2.67 (m, 4 H), 3.23 (t, J = 6.0 Hz, 2 H), 10.90 (s, 1 H).

5-(Phenylsulfenyl)-2-pentanone. Aluminum chloride (2.5 mL, 1.4 M solution of $AlCl_3$ in acetonitrile, 3.5 mmol) was added via syringe to a solution containing 0.195 g (2.31 mmol) of **1** and 10 mL of acetonitrile under nitrogen. Thiophenol (0.48 mL, 4.63 mmol) was added via syringe, and the solution was heated at 55 °C for 15 h, cooled to room temperature, poured into 10% $NaHCO_3$, and extracted with ether. The organic phase was washed with water and brine and dried over magnesium sulfate. Removal of solvent in vacuo gave 0.688 g of a yellow oil. Purification by TLC (silica gel, 1000 μm; CH_2Cl_2) gave pure 5-(phenylsulfenyl)-2-pentanone: 0.1169 g (28% yield);; IR (CCl_4) 3060, 2930, 1718, 1590, 745, 695 cm^{-1}; NMR (CCl_4) δ 1.40–2.07 (m, 2 H), 2.00 (s, 3 H), 2.43 (t, J = 6.5 Hz, 2 H), 2.83 (t, J = 7.0 Hz, 2 H), 6.78–7.20 (m, 5 H).

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Registry No. 1, 765-43-5; 2, 872-75-3; 3, 5771-58-4; 4, 4160-49-0; 5, 5500-21-0; 6, 1759-53-1; 7 (X = I), 3695-29-2; 7 (X = Br), 3884-71-7; 7 (X = Cl), 5891-21-4; 7 (X = SPh), 81358-55-6; 8 (X = I), 82080-21-5; 9 (X = I), 82080-22-6; 9 (X = Cl), 82080-23-7; 10, 72003-75-9; 11 (X = I), 71987-94-5; 11 (X = Br), 82080-24-8; 11 (X = Cl), 66980-41-4; 12, 6727-73-7; 13, 7425-27-6; Me_3SiCl, 75-77-4; NaI, 7681-82-5; NaBr, 7647-15-6; LiCl, 7447-41-8; Me_3SiSPh, 4551-15-9; PhSH, 108-98-5; $ZnCl_2$, 7646-85-7; Me_3SiI, 16029-98-4; NaCl, 7647-14-5; 4,4-dimethyl-2-pentanone, 590-50-1; 5-methyl-2-hexanone, 110-12-3.

General Route for the Facile Transformation of Ortho-Substituted Lithiobithienyls into Amino Derivatives

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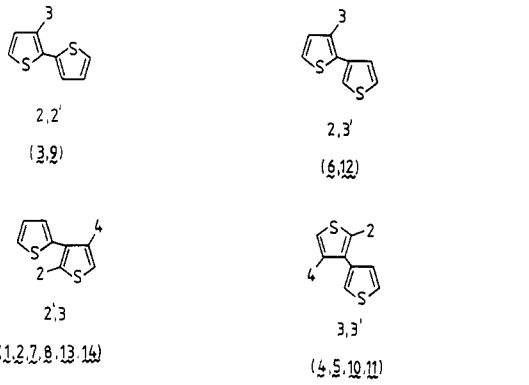
In the thiophene and bithienyl series, metalation and especially halogen–metal exchange with organolithium derivatives followed by the reaction of the thienyllithium derivatives with suitable electrophiles offers a most convenient route to many derivatives.[1,2] However, no convenient direct transformation of organolithium derivatives to amino derivatives is available. Recently, Trost[3] introduced azidomethyl phenyl sulfide as a synthon for NH_2^+. The reaction of Grignard reagents prepared directly or by the reaction of organolithium derivatives with magnesium bromide gave triazenes with azidomethyl phenyl sulfide which upon hydrolysis with strong alkali gave the amino derivatives in good yield. However, according to Trost this route fails with heteroaromatic organometallic reagents.

Chart I



We have for some time been interested in developing mild methods for the preparation of ortho-substituted aminobithienyls in connection with our interest in boron-containing aromatic heterocycles such as borazarobenzodithiophenes.[4] Also other interesting tricyclic systems could be prepared from ortho-substituted aminobithienyls, which like simple aminothiophenes are expected to be rather unstable. 2-Amino-3,3'-bithienyl has previously been obtained as the stannic chloride double salt by reduction of the nitro derivative, and the free amine was considered too unstable to be isolated.[5,6]

In a previous paper we reported a convenient method for the synthesis of azidothiophenes by reaction of the corresponding thienyllithium derivative with *p*-toluenesulfonyl azide followed by fragmentation of the resulting triazene salts.[7] As azidothiophenes can be reduced almost quantitatively to aminothiophenes by hydrogen sulfide[8] or lithium aluminum hydride, we investigated this two-step procedure to ortho-substituted aminobithienyls. The ortho-substituted azido derivatives themselves are interesting intermediates for the synthesis of hitherto unknown dithienopyrroles, which should be available by thermal decomposition.

Of the six possible ortho-substituted bromobithienyls, four have already been described in the literature, and the two hitherto unknown ones, viz., 4'-bromo-2,3'-bithienyl (**1**) and 2'-bromo-2,3'-bithienyl (**2**), were prepared by coupling reactions of (2-thienyl)copper with 3-bromo-4-iodothiophene and 2-bromo-3-iodothiophene, respectively.[9]

(2-Thienyl)copper reacts with 3-bromo-4-iodothiophene, prepared from 3,4-dibromothiophene by halogen–metal exchange and reaction with iodine, in pyridine–TMEDA

(1) Gronowitz, S. in "Organic Sulphur Chemistry, Structure, Mechanism and Synthesis"; Stirling, C. J. M., Ed.; Butterworths: London, 1975; p 203.

(2) (a) Håkansson, R.; Wiklund, E. *Ark. Kemi* **1969**, *31*, 101. (b) Wiklund, E.; Håkansson, R. *Chem. Scr.* **1974**, *6*, 174.
(3) Trost, B. M.; Pearson, W. H. *J. Am. Chem. Soc.* **1981**, *103*, 2483.
(4) Gronowitz, S.; Ander, I. *Chem. Scr.* **1980**, *15*, 23.
(5) Klemm, L. H.; Hsin, W. J. *J. Heterocycl. Chem.* **1975**, *12*, 1183.
(6) (a) Robba, H.; Cugnon de Sevricourt, M. *Bull. Soc. Chim. Fr.* **1976**, 761. (b) Wudl, F.; Zellers, E. T. *J. Am. Chem. Soc.* **1980**, *102*, 4283.
(7) Spagnolo, P.; Zanirato, P. *J. Org. Chem.* **1978**, *43*, 3539.
(8) Gronowitz, S.; Westerlund, C.; Hörnfeldt, A.-B. *Acta Chem. Scand., Ser. B* **1975**, *B29*, 224.
(9) For preparation and synthetic utility of (2-thienyl)copper, see: (a) Nilsson, M.; Ullenius, C. *Acta Chem. Scand.* **1970**, *24*, 2379. (b) Gronowitz, S.; Gjøs, N. *Ibid.* **1971**, *25*, 2596.

0022-3263/82/1947-3177$01.25/0