Journal of the Chinese Chemical Society, **1994**, *41*, 803-811

Formation of Pyrrole Derivatives from Heteroatom-Substituted Acetonitriles

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Aminomalononitrile reacted with conjugated carbonyl compounds to give 3*H*-pyrrolines. Treatment of 2-chloro-2-phenylthioacetonitrile with alkenes in the presence of potassium t-butoxide afforded 1-phenylthiocyclopropanecarbonitriles, which reacted with nucleophiles in 1,2-, 1,4- or 1,6-addition modes. The 1,2-adducts (cyclopropylimines) rearranged *in situ* to give substituted pyrroles.

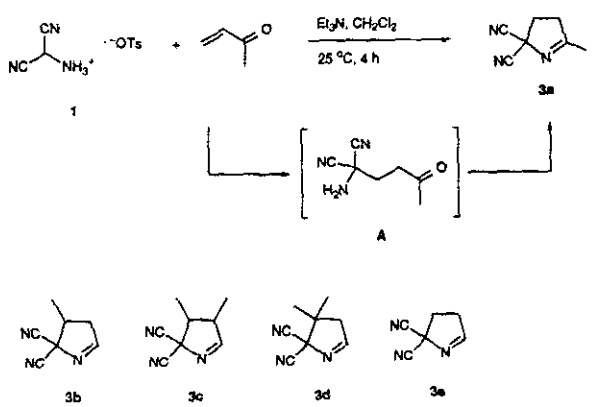
INTRODUCTION

The chemistry of the cyano group has been reviewed.[1] Heteroatom-substituted acetonitriles such as cyanohydrins, aminonitriles, halonitriles and thioacetonitriles are versatile reagents in synthetic chemistry.[2] For example, their α-carbanions can function as acyl nucleophiles in alkylation, acylation, carbonyl addition and Michael reaction. We describe here the reactions of two heteroatom-substituted acetonitriles, aminomalononitrile *p*-toluenesulfonate **1** and 2-chloro-2-phenylsulfenylacetonitrile **2**, that lead to formation of pyrrole derivatives.

RESULTS AND DISCUSSION

Freeman and coworkers reported that reaction of **1** and benzaldehyde in MeOH produces 4-amino-4-methoxy-1-phenyl-2-aza-1,3-butadiene-3-carbonitrile.[3] We found that **1** reacted with conjugated carbonyl compounds in a different manner. When **1** was stirred with methyl vinyl ketone in the presence of triethylamine (Scheme I), 5,5-dicyano-2-methyl-3*H*-pyrroline was obtained in 81% yield. The reactions of **1** and α,β-unsaturated aldehydes also afforded the corresponding 3*H*-pyrrolines **3b-e**, although in smaller yields. 3*H*-Pyrrolines are useful building blocks for synthesis of alkaloids.[4] Formation of pyrrolines is presumably initiated by 1,4-addition of the anion of **1** to conjugated carbonyl compounds, giving intermediate **A**, followed by intramolecular condensation of the amine and carbonyl groups.

Scheme I



Substitution of chloroacetonitrile with benzenethiol gave 2-phenylthioacetonitrile, which was subject to chlorination with sulfuryl chloride to afford 2-chloro-2-phenylthioacetonitrile (**2**).[5] When **2** was treated with potassium t-butoxide in the presence of various alkenes,[6] cyclopropanation products **4a-j** were obtained (Table 1). The reaction with ethyl vinyl ether (entries 1-7) was studied in detail using varied bases (Et_3N, PhLi, LDA or KOH) with or without cosolvent HMPA. The cyclopropane **4a** obtained in most cases had the phenylthio and ethoxy groups on the same face (*cis*-configuration). In ^{1}H NMR spectra, the H-2 signal of *cis*-**4a** appeared at a lower field (δ 3.94) than that of *trans*-isomer (δ 3.69) due to the deshielding effect of the cyano group.[7] When *cis*-**4a** was treated with t-BuOK/t-BuOH at 25 °C, a mixture of *cis*- and *trans*-isomers was obtained in equal amounts after 24 h. However, no epimerization of *trans*-**4a** occurred under the similar conditions, presumably because H-2 of *trans*-isomer was blocked by the phenylthio group on the same face.

Cyclopropanation with 2-methyl-1,3-butadiene (entry 11) occurred exclusively at the more substituted double bond to give **4e**, whereas reaction with 1,3-pentadiene (entry 12) gave predominantly the cyclopropanation products **4f** from reaction at the terminal double bond. Yields of the cyclopropanation products were small, as the reaction was generally accompanied by side-product bis(phenylthio)acetonitrile and by recovery of starting material **2**. In cyclopropanation with methyl acrylate (entry 13), 1,4-adduct **5** was also obtained in a small proportion.

Dedicated to Professor Sung-Mao Wang (王松茂) on the occasion of his seventieth birthday.

Table 1. Cyclopropanation of 2-Chloro-2-phenylthioacetonitrile **2** with Alkenes

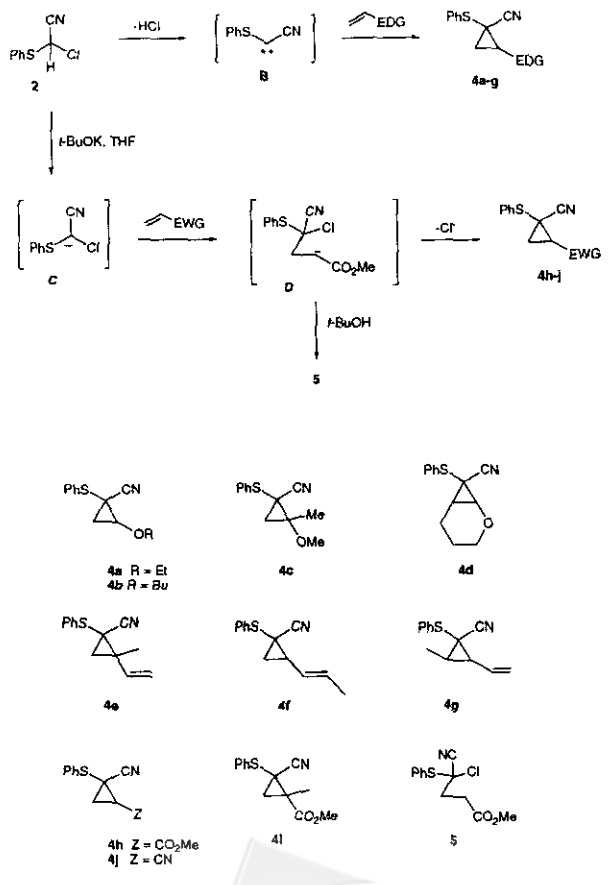
Entry	Alkene	Reaction conditions	Products (yield/%)
1	ethyl vinyl ether	*t*-BuOK, THF, 25 °C, 24 h	**4a** (30, *cis*)
2	ethyl vinyl ether	*t*-BuOK, THF/HMPA, 25 °C, 21 h	**4a** (21, *cis*)
3	ethyl vinyl ether	PhLi, PhH/Et_2O, 25 °C, 72 h	**4a** (32, *cis/trans* = 2.6)
4	ethyl vinyl ether	PhLi, PhH/Et_2O/HMPA, 25 °C, 21 h	**4a** (25, *trans*)
5	ethyl vinyl ether	Et_3N, THF, 25 °C, 48 h	**4a** (12, *cis/trans* = 1)
6	ethyl vinyl ether	LDA, THF, -78 °C to 25 °C, 16 h	**4a** (6, *cis*)
7	ethyl vinyl ether	KOH, H_2O, ultrasound, 4 °C, 5 h	-
8	butyl vinyl ether	*t*-BuOK, THF, 25 °C, 24 h	**4b** (29, *cis*)
9	2-methoxypropene	*t*-BuOK, THF, 25 °C, 24 h	**4c** (26, *cis/trans* = 1)
10	3,4-2*H*-pyran	*t*-BuOK, THF, 25 °C, 24 h	**4d** (16, *exo/endo* = 1)
11	2-methyl-1,3-butadiene	*t*-BuOK, THF, 25 °C, 24 h	**4e** (30, *cis/trans* = 1)
12	1,3-pentadiene	*t*-BuOK, THF, 25 °C, 24 h	**4f** (24, *trans/cis* = 2) + **4g** (6)
13	methyl acrylate	*t*-BuOK, THF, 25 °C, 24 h	**4h** (18, *cis*) + **5** (2)
14	methyl methacrylate	*t*-BuOK, THF, 25 °C, 24 h	**4i** (16, *cis/trans* = 1)
15	acrylonitrile	*t*-BuOK, THF, 25 °C, 24 h	**4j** (6, *cis/trans* = 1)

The cyclopropanation products generally existed as mixtures of *cis*- and *trans*-isomers except **4b** or **4h** having only the *cis*-configuration. The stereochemistry was tentatively assigned by analysis of ^{1}H NMR spectra as for **4a**. For example, the H-2 signal of *cis*-**4b** appeared at δ 3.93 near the value δ 3.94 of the corresponding signal in *cis*-**4a**. The C-3 methyl group in *cis*-**4c** occurred at a lower field δ 1.74 than that in *trans*-**4c** (δ 1.64). The two H-3 signals in *cis*-**4c** had similar values (δ 1.67 and 1.60). The two H-3 signals of *trans*-**4c** occurred, however, at δ 1.96 and 1.28 as one proton was concurrently deshielded by the cyano and methoxy groups, whereas the other was shielded by the methyl and phenylthio groups. The H-1 signal in *exo*-**4d** displayed at δ 4.01, whereas the H-1 signal in *endo*-**4d** appeared at a lower field δ 4.28 because of the deshielding effect of the cyano group.

According to the above results, 2-chloro-2-phenylthioacetonitrile might eliminate HCl to give phenylthioacetonitrile carbene intermediate **B**,[8] which reacted with the electron-rich alkenes to afford cyclopropanation products **4a-g** (Scheme II). The cyclopropanations with electron-deficient alkenes giving **4h-j**, however, likely proceeded with addition and elimination via intermediates **C** and **D**.[9] Isolation of 1,4-addition product **5** supports this mechanism. In the presence of base, 2-chloro-2-phenylthioacetonitrile might also eliminate PhSH, which counterattacked **2** to give bis(phenylthio)acetonitrile.

Functionalized cyclopropanes have attacted chemists' interests for both synthetic and theoretical aspects.[10] We investigated the nucleophilic reactions of 2-phenylthiocyclopropanecarbonitriles **4a-c** and **4g** (Table 2), and found 1,2-, 1,4- and 1,6-additions occurred in appropriate cases.[11]

Scheme II



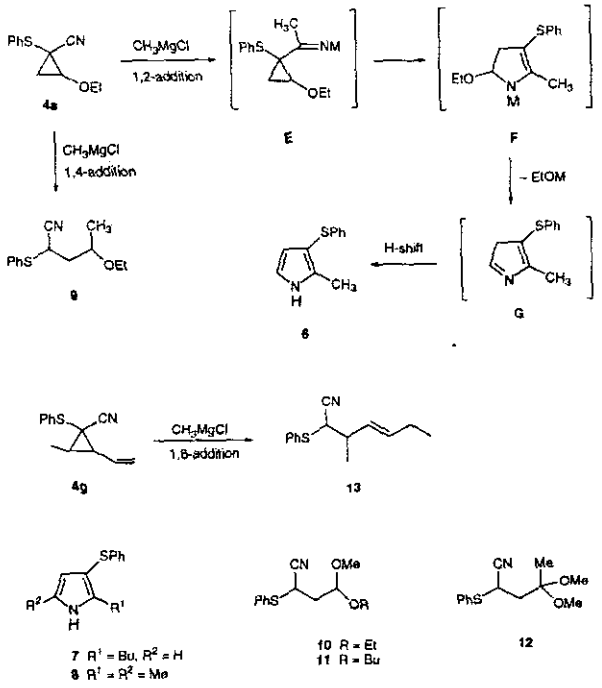
Grignard reagent CH_3MgCl attacked **4a** exclusively at the cyano group (1,2-addition) at -78 °C to give cyclopropylimine anion **E**, which rearranged to pyrroline **F** and led to pyrrole **6** in 60% yield (Scheme III). When the reaction was carried out at 25 °C, **6** and 1,4-addition product **9** were ob-

Table 2. Nucleophilic Reactions of Cyclopropanecarbonitriles **4a-c** and **4g**

Reactant	Reaction conditions	Products (yield/%)
4a	CH_3MgCl, Et_2O, -78 °C (10 min) to 25 °C over 2 h	**6** (60)
4a	CH_3MgCl, Et_2O, 25 °C, 40 min	**6** (30) + **9** (22)
4a	BuLi, THF, 25 °C, 24 h	**7** (35)
4a	$NaBH_4$, MeOH, 25 °C, 48 h	**10** (70)
4b	CH_3MgCl, Et_2O, -78 °C (10 min) to 25 °C over 2 h	**6** (46)
4b	BuLi, THF, 25 °C, 24 h	**7** (28)
4b	$NaBH_4$, MeOH, 25 °C, 48 h	**11** (72)
4c	CH_3MgCl, Et_2O, -78 °C (10 min) to 25 °C over 2 h	**8** (57)
4c	$NaBH_4$, MeOH, 25 °C, 48 h	**12** (76)
4g	CH_3MgCl, Et_2O, -78 °C (10 min) to 25 °C over 2 h	**13** (58)

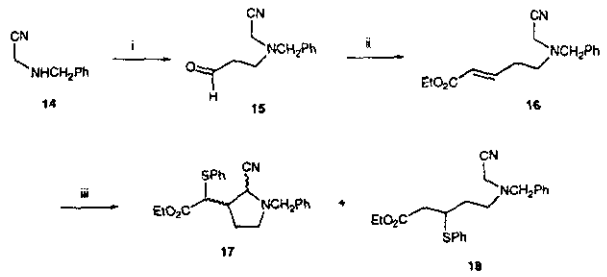
tained in 30% and 22% yields, respectively. The reaction of **4a** with butyllithium gave exclusively pyrrole **7**, either at -78 °C or 25 °C. Treatment of **4a** with $NaBH_4$ in MeOH resulted in 1,4-addition of MeOH, giving acetal **10** instead of a reduction product. In these 1,4-addition reactions, the nucleophile invariably attacked the cyclopropane ring at the carbon having an alkoxy substituent. Compounds **4b** and **4c** behaved similarly in nucleophilic reactions with CH_3MgCl, BuLi or $NaBH_4$/MeOH. Vinylcyclopropanecarbonitrile **4g** reacted with CH_3MgCl, however, exclusively in the 1,6-addition mode to give **13** in 58% yield. Compounds **10** and **11** can be considered as derivatives of 1,3-propanedial with one site protected as acetal and the other activated as thioacetonitrile umpolung.

Scheme III



We found also that a pyrrolidine **17** was obtained by intramolecular Michael reaetion of aminonitrile **16**. Aminonitrile **16** containing the moiety α,β-unsaturated ester was prepared from a Wittig-Horner reaction of the corresponding aldehyde (Scheme IV). On treatment of **16** with a base LDA, the formed aminonitlile α-anion underwent intramolecular Michael addition and the intermediate was trapped with an electrophile diphenyldisulfide to give pyrrolidine **17** in 44% yield. We previously reported preparation of 2-(*N*-methylanilino)-2-phenylthioacetonitrile by the reaction of the α-anion of 2-(*N*-methylanilino)acetonitrile with PhSSPh.[12] In the case of **16**, the intramolecular Michael reaction appeared more rapid than sulfenylation with PhSSPh. A side-product **18** was obtained, presumably derived from counterattack of the released benzenethiolate ion on **16**.

Scheme IV



Reagents and conditions. (i) CH_2=CHCHO, Et_3N, CH_2Cl_2, 25 °C, 4h; 95%. (ii) $EtO_2CCH_2PO(OEt)_2$, KOH, THF, 25 °C, 1.3 h; 69%. (iii) LDA, PhSSPh, THF, -78 °C, 1 h; **17** (44%), **18** (11%).

EXPERIMENTAL SECTION

Infrared spectra were measured on a Perkin-Elmer 983G infrared spectrophotometer. ^{1}H NMR spectra were recorded at 200 or 300 MHz (Bruker AC-200 or AM-300WB spectrometer); tetramethylsilane was used as internal stand-

ard. ^{13}C NMR spectra were recorded at 50 or 75 MHz. Mass spectra were recorded (Finnigan TSQ46c spectrometer) at an ionizing energy 70 eV or 20 eV. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-HX 110 spectrometer. HPLC was preformed on a chromatograph (Hitachi L-6200) with a μ-Porasil column (7 mm, 25 cm × 0.78 cm) with a rate 5 mL/min of flow of eluent.

Aminomalononitrile *p*-tolenensulfonate **1** was purchased (Aldrich, U.S.A.). 2-Chlorophenylthioacetonitrile **2** was prepared by chlorination of 2-phenylthioacetonitrile with SO_2Cl_2.[5]

5,5-Dicyano-2-methyl-3*H*-pyrroline 3a

To a suspension of aminomalononitrile *p*-toluenesulfonate (380 mg, 1.5 mmol) in CH_2Cl_2 (5 mL) was added Et_3N (0.45 mL, 3 mmol). The salt dissolved, methyl vinyl ketone (0.08 mL, 1 mmol) was added, and the clear solution was stirred at 25 °C for 4 h. The reaction mixture was washed with water and brine. The organic phase was dried (Na_2SO_4), filtered, concentrated and chromatographed on a silica-gel column with eluent EtOAc/hexane (20:80) to give **3a** (107 mg, 81%). Oil; IR (neat) 2251, 1628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.96 (2 H, t, J = 7.7 Hz), 2.75 (2 H, t, J = 7.7 Hz), 2.23 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 186.3 (s), 114.2 (s), 62.7 (s), 39.7 (t), 36.1 (t), 19.5 (q); MS *m/z* (rel intensity) 133 (M^+, 27), 105 (100); HRMS calcd for $C_7H_7N_3$ (M^+) 133.0640, found *m/z* 133.0632.

5,5-Dicyano-4-methyl-3*H*-pyrroline 3b

Condensation of aminomalononitrile *p*-toluenesulfonate with crotonaldehyde by a procedure similar to that for **3a** gave the corresponding pyrroline **3b** in 30% yield. Oil; IR (neat) 2249, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.01 (1 H, s), 3.14 (1 H, dd, J = 12.1, 4.5 Hz), 3.01 (1 H, m), 2.63 (1 H, dd, J = 12.1, 4.7 Hz), 1.42 (3 H, d, J = 4.8 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 176.7 (s), 114.0 (s), 113.3 (s), 53.4 (s), 44.8 (t), 42.3 (d), 15.8 (q); MS *m/z* (rel intensity) 134 (M^++1, 31), 105 (26), 91 (69), 54 (100); HRMS calcd for $C_7H_7N_3$ (M^+) 133.0640, found *m/z* 133.0672.

5,5-Dicyano-3,4-dimethyl-3*H*-pyrroline 3c

Condensation of aminomalononitrile *p*-toluenesulfonate with tiglic aldehyde by a procedure similar to that for **3a** gave the corresponding pyrroline *cis*-**3c** in 7% yield. Oil; IR (neat) 2241, 1689, 1609 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.92 (1 H, s), 3.26 (1 H, dq, J = 7.8, 7.5 Hz, H-3), 2.99 (1 H, dq, J = 7.8, 7.3 Hz, H-4), 1.34 (3 H, d, J = 7.3 Hz), 1.19 (3 H, d, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 180.8 (d), 114.1 (s), 112.3 (s), 53.1 (s), 47.9 (d), 45.2 (d), 11.9 (q), 11.7 (q); MS *m/z* (rel intensity) 146 (M^+-1, 8), 132 (50), 68 (100); HRMS calcd for $C_8H_9N_3$ (M^+) 147.0796, found *m/z* 147.0793.

5,5-Dicyano-4,4-dimethyl-3*H*-pyrroline 3d

Condensation of aminomalononitrile *p*-toluenesulfonate with 3-methyl-2-butenal by a procedure similar to that for **3a** gave the corresponding pyrroline **3d** in 8% yield. Oil; IR (neat) 2231, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.01 (1 H, s), 2.79 (2 H, s), 1.43 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 176.7 (d), 116.1 (s), 112.0 (s), 59.1 (s), 51.1 (t), 47.5 (s), 24.6 (q); MS *m/z* (rel intensity) 146 (M^+-1, 29), 132 (79), 68 (100); HRMS calcd for $C_8H_9N_3$ (M^+) 147.0796, found *m/z* 147.0832.

5,5-Dicyano-3*H*-pyrroline 3e

Condensation of aminomalononitrile *p*-toluenesulfonate with acrolein by a procedure similar to that for **3a** gave the corresponding pyrroline **3e** in 32% yield. Oil; IR (neat) 2217 (CN), 1616 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.02 (1 H, s, H-2), 3.05 (2 H, t, J = 8.0 Hz, H-3), 2.70 (2 H, t, J = 8.0 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 176.2 (d, C-2), 113.9 (s, CN), 63.1 (s, C-5), 38.1 (t, C-3), 34.6 (t, C-4); MS *m/z* (rel intensity) 119 (M^+, 31), 91 (100); HRMS calcd for $C_6H_5N_3$ (M^+) 119.0483, found *m/z* 119.0477.

Exemplary Procedure for Cyclopropanation of 2-Chloro-2-phenylthioacetonitrile with Alkenes

To a solution of t-BuOK (340 mg, 3 mmol) in THF (7 mL) was added sequentially ethyl vinyl ether (3 mL, 30 mmol) and 2-chloro-2-phenylthioacetonitrile (550 mg, 3 mmol). The dark brown solution was stirred for 24 h at 25 °C. Water was added, the reaction mixture was concentrated and extracted several times with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), filtered, concentrated and chromatographed on a silica-gel column by elution with EtOAc/hexane (2:98) to give the cyclopropanation product *cis*-**4a** (197 mg, 30%). The results of reactions with other alkenes are listed in Table 1.

2-Ethoxy-1-phenylthiocyclopropanecarbonitrile 4a

Cis-isomer: Oil, TLC (EtOAc/hexane, 5:95) R_f = 0.14; IR (neat) 2336 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.59-7.3 (5 H, m), 3.94 (1 H, dd, J = 7.0, 5.6 Hz, H-2), 3.62 (2 H, q, J = 7.0 Hz), 1.86 (1 H, dd, J = 7.2, 7.0 Hz, H-3), 1.50 (1 H, dd, J = 7.2, 5.6 Hz, H-3), 1.26 (3 H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 133.1 (s), 130.9 (d, 2 C), 129.2 (d, 2 C), 127.9 (d), 120.9 (s, CN), 68.1 (t, -OCH_2-), 65.3 (d, C-2), 24.9 (t, C-3), 18.8 (s, C-1), 14.7 (q); MS *m/z* (rel intensity) 219 (M^+, 48), 190 (39), 162 (100), 135 (95), 110 (45), 91 (21), 82 (21). *Trans*-isomer: Oil, TLC (EtOAc/hexane, 5:95) R_f = 0.23; IR (neat) 2336 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57-7.26 (5 H, m), 3.69 (1 H, dd, J = 6.9, 4.7 Hz), 3.56 (2 H, q, J = 7.0 Hz), 1.89 (1 H, dd, J = 6.9, 4.7 Hz), 1.55 (1 H, t, J = 6.9 Hz), 1.26 (3 H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 132.5 (s), 131.9 (d), 129.4 (d), 128.7 (d), 119.6 (s), 67.5 (t), 66.8 (d), 25.7 (t), 19.9 (s), 14.8 (q); MS *m/z* (rel intensity) 219 (M^+, 44), 190 (44), 162 (100), 135 (95), 110 (45), 91 (23), 82 (20); HRMS

calcd for $C_{12}H_{13}NOS$ (M^+) 219.0718, found *m/z* 219.0706.

2-Butoxy-1-phenylthiocyclopropanecarbonitrile 4b

Cis-isomer: Oil, TLC (EtOAc/hexane, 5:95) R_f = 0.24; IR (neat) 2221 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57-7.29 (5 H, m), 3.93 (1 H, dd, *J* = 7.1, 5.6 Hz), 3.65-3.45 (2 H, m), 1.85 (1 H, dd, *J* = 7.2, 7.1 Hz), 1.68-1.59 (2 H, m), 1.53 (1 H, dd, *J* = 7.2, 5.6 Hz), 1.46-1.32 (2 H, m), 0.92 (3 H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 133.1 (s), 130.7 (d), 129.1 (d), 127.8 (d), 72.3 (t), 65.4 (d), 31.2 (t), 24.9 (t), 18.9 (t), 18.7 (s), 13.6 (q); MS *m/z* (rel intensity) 247 (M^+, 25), 191 (84), 162 (100); HRMS calcd for $C_{14}H_{17}NOS$ (M^+) 247.1031, found *m/z* 247.1033.

2-Methyl-2-methoxy-1-phenylthiocyclopropanecarbonitrile 4c

Trans-isomer: Oil, HPLC (EtOAc/hexane, 7:93) t_R = 14.1 min; IR (neat) 2226 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55-7.31 (5 H, m), 3.43 (3 H, s), 1.96 (1 H, d, *J* = 6.6 Hz), 1.64 (3 H, s), 1.28 (1 H, d, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 133.0 (s), 130.5 (d), 129.4 (d), 128.1 (d), 70.3 (s), 54.8 (q), 31.1 (t), 24.2 (s), 15.4 (q); MS *m/z* (rel intensity) 219 (M^+, 38), 43 (100); HRMS calcd for $C_{12}H_{13}ONS$ (M^+) 219.0718, found *m/z* 219.0725. *Cis*-isomer: Oil, HPLC (EtOAc/hexane, 7:93) t_R = 16.5 min; IR (neat) 2225 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55-7.32 (5 H, m), 3.41 (3 H, s), 1.74 (3 H, s), 1.67 (1 H, d, *J* = 6.7 Hz), 1.60 (1 H, d, *J* = 6.7 Hz); ^{13}C NMR ($CDCl_3$) δ 133.3 (s), 130.8 (d), 129.3 (d), 127.9 (d), 120.2 (s), 69.2 (s), 55.6 (q), 31.4 (t), 25.0 (s), 18.4 (q); MS *m/z* (rel intensity) 219 (M^+, 26), 43 (100); HRMS calcd for $C_{12}H_{13}ONS$ (M^+) 219.0718, found *m/z* 219.0711.

7-Phenylthio-2-oxobicyclo[4.1.0]heptane-7-carbonitrile 4d

Exo-isomer: Oil, HPLC (EtOAc/hexane, 10:90) t_R = 15.9 min; IR (neat) 2226 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.44-7.26 (5 H, m), 4.01 (1 H, d, *J* = 6.9 Hz), 3.81 (1 H, m), 3.39 (1 H, m), 2.16 (2 H, m), 1.96 (1 H, m), 1.84 (1 H, m), 1.51 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 133.0 (s), 129.3 (d), 127.5 (d), 118.3 (s), 64.7 (C-1, and C-3), 29.1 (d), 22.8 (s), 20.7 (t), 16.9 (t); MS *m/z* (rel intensity) 231 (M^+, 67), 84 (100). *Endo*-isomer: HPLC (EtOAc/hexane, 10:90) t_R = 20.4 min; IR (neat) 2226 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54-7.25 (5 H, m), 4.28 (1 H, d, *J* = 7.1 Hz), 3.90 (1 H, m), 3.45 (1 H, m), 2.12 (2 H, m), 2.02 (1 H, m), 1.94 (1 H, m), 1.49 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 132.3 (s), 129.5 (d), 129.2 (d), 127.4 (d), 120.8 (s), 65.0 (d), 61.1 (t), 26.3 (d), 22.7 (s), 21.7 (t), 15.9 (t); MS *m/z* (rel intensity) 231 (M^+, 67), 84 (100); HRMS calcd for $C_{13}H_{13}NOS$ (M^+) 231.0718, found *m/z* 231.0724.

2-Ethenyl-2-methyl-1-phenylthiocyclopropanecarbonitrile 4e

Trans-isomer: Oil, TLC (EtOAc/hexane, 5:95) R_f = 0.43; IR (neat) 2225 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42-7.24 (5 H, m), 5.87 (1 H, dd, *J* = 17.9, 10.9 Hz), 5.36 (1 H, br d, *J* = 17.9 Hz), 5.28 (1 H, br d, *J* = 10.9 Hz), 1.85 (1 H, d, *J* = 5.9 Hz), 1.50 (3 H, s), 1.38 (1 H, d, *J* = 5.9 Hz); ^{13}C NMR ($CDCl_3$) δ 138.3 (d), 130.9 (s), 129.1 (d), 128.8 (d), 127.2 (d), 120.0 (s), 117.0 (t), 34.8 (s), 29.1 (t), 24.4 (s), 16.8 (q); MS *m/z* (rel intensity) 215 (M^+, 22), 110 (100). *Cis*-isomer: Oil, TLC (EtOAc/hexane, 5:95) R_f = 0.43; IR (neat) 2225 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43-7.25 (5 H, m), 5.92 (1 H, dd, *J* = 17.3, 10.5 Hz), 5.30 (1 H, br d, *J* = 17.3 Hz), 5.22 (1 H, br d, *J* = 10.5 Hz), 1.71 (1 H, d, *J* = 5.8 Hz), 1.60 (3 H, s), 1.54 (1 H, d, *J* = 5.8 Hz); ^{13}C NMR ($CDCl_3$) δ 136.8 (d), 133.1 (s), 129.5 (d), 129.3 (d), 127.5 (d), 119.9 (s), 117.7 (t), 33.9 (s), 29.9 (t), 24.9 (s), 20.2 (q); MS *m/z* (rel intensity) 215 (M^+, 32), 110 (100); HRMS calcd for $C_{13}H_{13}NS$ (M^+) 215.0769, found *m/z* 215.0762.

1-Phenylthio-2(*E*)-propenylcyclopropanecarbonitrile 4f

A mixture of *cis*- and *trans*-isomers (1:2): TLC (EtOAc/hexane, 5:95) R_f = 0.27; HPLC (EtOAc/hexane, 5:95) t_R = 9.6 min; IR (neat) 2223 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50-7.23 (5 H, m, PhH), 5.83-5.69 (1 H, m), 5.38-5.24 (1 H, m), 2.70 (d, *J* = 13.0 Hz, H-2)/2.50 (d, *J* = 13.0 Hz), 2.00 (dd, *J* = 13.8, 8.3 Hz, H-3)/1.90 (dd, *J* = 13.8, 8.7 Hz), 1.74 (d, *J* = 10.4 Hz, CH_3)/1.70 (d, *J* = 9.8 Hz), 1.30 (1 H, dd, *J* = 11.6, 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 132.9/132.8 (s), 131.8/130.6 (d), 130.2, 129.1, 127.7/130.1, 129.1, 127.7, 124.8/124.4 (d), 121.5 (s, CN), 32.2/27.5 (d, C-2), 24.3/23.4 (t, C-3), 18.8 (s, C-1), 18.0/13.6 (q); MS *m/z* (rel intensity) 215 (M^+, 25), 110 (100); HRMS calcd for $C_{13}H_{13}NS$ (M^+) 215.0769, found *m/z* 215.0772.

2-Ethenyl-3-methyl-1-phenylthiocyclopropanecarbonitrile 4g

Compound **4g** existed as a single isomer: Oil, HPLC (EtOAc/hexane, 5:95) t_R = 8.4 min; IR (neat) 2224 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.72-7.67 (2 H, m), 7.50-7.42 (3 H, m), 5.72 (1 H, dd, *J* = 17.1, 10.1 Hz), 5.32 (1 H, d, *J* = 17.1 Hz), 5.23 (1 H, d, *J* = 10.1 Hz), 2.20 (1 H, d, *J* = 7.5 Hz), 1.66 (1 H, m), 1.42 (3 H, d, *J* = 6.1 Hz); ^{13}C NMR ($CDCl_3$) δ 132.5 (d), 132.9 (s), 129.6 (d), 129.3 (d), 127.5 (d), 119.8 (t), 119.6 (s), 40.2 (d), 30.1 (d), 25.1 (s), 15.3 (q); MS *m/z* (rel intensity) 214 (M^+-1, 35), 109 (100); HRMS calcd for $C_{13}H_{13}NS$ (M^+) 215.0769, found *m/z* 215.0770.

Methyl 2-cyano-2-phenylthiocyclopropanecarboxylate 4h

Oil, TLC (EtOAc/hexane, 10:90) R_f = 0.19; IR (neat) 2236, 1727 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57-7.38 (5 H, m), 3.78 (3 H, s), 2.48 (1 H, dd, *J* = 8.5, 7.0 Hz), 2.17 (1 H, dd, *J* = 7.0, 5.5 Hz), 1.76 (1 H, dd, *J* = 8.5, 5.5 Hz); ^{13}C NMR ($CDCl_3$) δ 167.7 (s, C=O), 131.8, 131.4, 129.6, 129.0, 117.6 (s, CN), 52.8 (q, OCH_3), 31.8 (d, C-1), 23.3 (t, C-3), 21.5 (s, C-2); MS *m/z* (rel intensity) 233 (M^+, 53), 173 (100); HRMS

calcd for $C_{12}H_{11}NO_2S$ (M^+) 233.0510, found *m/z* 233.0491.

Methyl 2-cyano-1-methyl-2-phenylthiocyclopropanecarboxylate 4i

Cis-isomer: Oil, TLC (EtOAc/hexane, 10:90) R_f = 0.23; IR (neat) 2229, 1734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.49-7.33 (5 H, m), 3.70 (3 H, s), 2.08 (1 H, d, J = 6.0 Hz), 1.68 (3 H, s), 1.62 (1 H, d, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 168.7 (C=O), 131.8, 131.2, 129.3, 128.4, 118.5 (s, CN), 52.7 (q, OCH_3), 36.4 (s), 27.6 (t), 24.9 (s), 18.8 (q); MS *m/z* (rel intensity) 247 (M^+, 100), 232 (35), 188 (83). *Trans*-isomer: Oil, TLC (EtOAc/hexane, 10:90) R_f = 0.23; IR (neat) 2230, 1727 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50-7.34 (5 H, m), 3.82 (3 H, s), 2.46 (1 H, d, J = 6.0 Hz), 1.64 (3 H, s), 1.35 (1 H, d, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 170.0 (s, C=O), 131.8 (s), 130.2 (d), 129.5 (d), 128.2 (d), 118.5 (s), 53.1 (q), 35.9 (s), 27.7 (t), 25.5 (s), 15.8 (q); MS *m/z* (rel intensity) 247 (M^+, 100), 232 (37), 188 (80); HRMS calcd for $C_{13}H_{13}NO_2S$ (M^+) 247.0667, found *m/z* 247.0660.

1-Phenylthiocyclopropane-1,2-dicarbonitrile 4j

A mixture of *cis*- and *trans*-isomers (1:1): TLC (EtOAc/hexane, 10:90) R_f = 0.4; IR (neat) 2247 (CN); ^1H NMR ($CDCl_3$) δ 7.75-7.43 (5 H, m), 2.52 (dd, J = 9.5, 7.1 Hz, H-2, *cis*)/2.29 (dd, J = 9.1, 6.9 Hz, *trans*), 2.15 (dd, J = 7.1, 5.9 Hz, H-3)/2.10 (dd, J = 9.1, 6.3 Hz), 1.99 (dd, J = 9.5, 5.9 Hz, H-3)/1.82 (dd, J = 6.9, 6.3 Hz); ^{13}C NMR ($CDCl_3$) δ 133.9/132.4, 130.1, 130.0/129.9, 129.8, 116.8/115.4 (CN), 23.8 (C-3), 22.3/22.1 (C-1), 16.8/16.7 (C-2); MS *m/z* (rel intensity) 200 (M^+, 96), 173 (100); HRMS calcd for $C_{11}H_8N_2S$ (M^+) 200.0408, found *m/z* 200.0437.

Methyl 4-chloro-4-cyano-4-phenylthiobutanoate 5

Oil, TLC (EtOAc/hexane, 10:90) R_f = 0.3; IR (neat) 2234 (CN), 1708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84-7.44 (5 H, m), 3.74 (3 H, s), 2.89-2.65 (4 H, m); ^{13}C NMR ($CDCl_3$) δ 171.4 (s, C=O), 137.2 (d), 131.5 (d), 129.5 (d), 127.6 (s), 115.8 (s, CN), 65.7 (s, C-4), 52.2 (q, OCH_3), 37.8 (t, C-3), 30.3 (t, C-2); MS *m/z* (rel intensity) 269 (M^+, 54), 234 (26), 202 (57), 174 (100), 160 (73), 128 (25), 109 (85), 65 (31); HRMS calcd for $C_{12}H_{12}{}^{35}ClNO_2S$ (M^+) 269.0277, found *m/z* 269.0280.

Exemplary Procedure for the Reactions of Cyclopropanecarbonitriles 4a-c and 4g with Nucleophiles

To a cold (-78 °C) solution of **4c** (100 mg, 0.46 mmol) in Et_2O (5 mL) was added dropwise a solution of CH_3MgCl (2.8 mmol, 1 mL of 2.8 M solution in ether). The reaction mixture was stirred at -78 °C for 10 min, warmed to 25 °C over 2 h, and quenched by addition of a saturated NH_4Cl aqueous solution. The mixture was concentrated and extracted several times with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), filtered, concentrated and chromatographed on a silica gel column by elution with EtOAc/hexane (2:98) to give pyrrole **8** (52 mg, 57%). The results of reactions of the cyclopropanecarbonitriles with other nucleophiles are listed in Table 2.

2-Methyl-3-phenylthiopyrrole 6

Oil, TLC (EtOAc/hexane, 10:90) R_f = 0.22; IR (neat) 3407 (NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.20 (1 H, br s, NH), 7.24-7.00 (5 H, m), 6.72 (1 H, d, J = 5.6 Hz, H-5), 6.25 (1 H, d, J = 5.6 Hz, H-4), 2.27 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 140.6 (s, C-3), 129.6 (s, C-2), 129.3 (s), 128.6 (d), 125.3 (d), 124.3 (d), 116.6 (d, C-5), 114.8 (d, C-4), 11.3 (q); MS *m/z* (rel intensity) 189 (M^+, 100), 174 (20), 162 (12), 147 (19), 112 (21), 80 (11); HRMS calcd for $C_{11}H_{11}NS$ (M^+) 189.0612, found *m/z* 189.0587.

2-Butyl-3-phenylthiopyrrole 7

Oil, TLC (EtOAc/hexane, 5:95) R_f = 0.2; IR (neat) 3402 (NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.19 (1 H, br s, NH), 7.21-7.03 (5 H, m), 6.75 (1 H, t, J = 1.9 Hz), 6.26 (1 H, t, J = 1.9 Hz), 2.68 (2 H, t, J = 5.0 Hz), 1.53 (2 H, m), 1.28 (2 H, m), 0.86 (3 H, t, J = 4.8 Hz); ^{13}C NMR ($CDCl_3$) δ 140.9 (s), 137.9 (s), 131.9 (s), 128.5 (d), 125.3 (d), 124.2 (d), 116.7 (d), 114.9 (d), 31.9 (t), 25.6 (t), 22.3 (t), 13.8 (q); MS *m/z* (rel intensity) 231 (M^+, 81), 188 (100); HRMS calcd for $C_{14}H_{17}NS$ (M^+) 231.1082, found *m/z* 231.1074.

2,5-Dimethyl-3-phenylthiopyrrole 8

Oil, TLC (EtOAc/hexane, 10:90) R_f = 0.24; IR (neat) 3381 (NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (1 H, br s, NH), 7.19-7.03 (5 H, m), 5.89 (1 H, s), 2.34 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 140.8 (s), 131.0 (s), 128.6 (d, 2 C), 126.5 (s), 125.3 (d, 2 C), 124.2 (d), 120.3 (s), 111.8 (s), 13.0 (q), 11.3 (q); MS *m/z* (rel intensity) 203 (M^+, 100); HRMS calcd for $C_{12}H_{13}NS$ (M^+) 203.0769, found *m/z* 203.0771.

4-Ethoxy-2-phenylthiopentanenitrile 9

Isomer a: Oil, TLC (EtOAc/hexane, 10:90) R_f = 0.42; IR (neat) 2233 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65-7.58 (2 H, m), 7.43-7.37 (3 H, m), 4.02 (1 H, dd, J = 11.2, 4.9 Hz, H-2), 3.66 (2 H, m), 3.38 (1 H, m), 1.95 (2 H, m, H-3), 1.89 (3 H, t, J = 6.9 Hz), 1.88 (3 H, d, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 134.6 (3 C), 129.4 (3 C), 119.2 (CN), 72.2 (d), 64.2 (t), 40.3 (t), 33.7 (d), 19.3 (q), 15.4 (q); MS *m/z* (rel intensity) 235 (M^+, 19), 189 (100); HRMS calcd for $C_{13}H_{17}NOS$ (M^+) 235.1031, found *m/z* 235.1056. Isomer b: Oil, TLC (EtOAc/hexane, 10:90) R_f = 0.33; IR (neat) 2234 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63-7.58 (2 H, m), 7.43-7.36 (3 H, m), 3.98 (1 H, dd, J = 9.6, 5.0 Hz), 3.77 (1 H, m), 3.66 (1 H, m), 3.38 (1 H, m), 2.04 (1 H, m), 1.82 (1 H, m), 1.19 (3 H, t, J = 6.9 Hz), 1.18 (3 H, d, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 134.6, 129.4, 119.8 (CN), 70.7 (d), 64.1 (t), 39.2 (t), 33.6

(d), 19.2 (q), 15.5 (q); MS *m/z* (rel intensity) 235 (M^+, 21), 189 (100); HRMS calcd for $C_{13}H_{17}NOS$ (M^+) 235.1031, found *m/z* 235.1032.

4-Ethoxy-4-methoxy-2-phenylthiobutanenitrile 10

Oil, HPLC (EtOAc/hexane, 7:93) t_R = 15 min; IR (neat) 2235 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64-7.53 (2 H, m), 7.43-7.34 (3 H, m), 4.68 (1 H, t, *J* = 5.8 Hz, H-4), 3.83 (1 H, t, *J* = 7.7 Hz, H-2), 3.61 (2 H, q, *J* = 7.1 Hz), 3.35 (3 H, s, OCH_3), 2.09 (2 H, dd, *J* = 7.7, 5.8 Hz, H-3), 1.22 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 134.7, 129.6, 129.4 (d), 130.2 (s), 118.9 (s, CN), 100.6 (d, C-4), 62.7 (t), 53.6 (q), 36.0 (t, C-3), 32.7 (d, C-2), 15.2 (q); MS *m/z* (rel intensity) 251 (M^+, 11), 219 (35), 205 (53), 190 (15), 174 (38), 162 (29), 148 (38), 135 (29), 121 (37), 109 (33), 89 (52), 61 (100); HRMS calcd for $C_{13}H_{17}NO_2S$ (M^+) 251.0980, found *m/z* 251.0987.

4-Butoxy-4-methoxy-2-phenylthiobutanenitrile 11

Oil, HPLC (EtOAc/hexane, 7:93) t_R = 8.4 min; IR (neat) 2236 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64-7.60 (2 H, m), 7.44-7.37 (3 H, m), 4.68 (1 H, t, *J* = 5.8 Hz), 3.83 (1 H, t, *J* = 7.7 Hz), 3.62 (1 H, m), 3.45 (1 H, m), 3.35 (3 H, s), 2.10 (2 H, t, *J* = 6.7 Hz), 1.57 (2 H, m), 1.52 (2 H, m), 0.92 (3 H, t, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 134.7, 129.6, 129.4, 118.9 (s), 100.8 (d), 67.0 (t), 53.6 (q), 36.0 (t), 32.7 (d), 31.7 (t), 19.3 (t), 13.8 (q); MS *m/z* (rel intensity) 279 (M^+, 7), 61 (100); HRMS calcd for $C_{15}H_{21}NO_2S$ (M^+) 279.1293, found *m/z* 279.1308.

4,4-Dimethoxy-2-phenylthiopentanenitrile 12

Oil, HPLC (EtOAc/hexane, 7:93); t_R = 13.5 min; IR (neat) 2235 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.66-7.61 (2 H, m), 7.44-7.34 (3 H, m), 3.80 (1 H, t, *J* = 7.7 Hz), 3.18 (3 H, s), 3.17 (3 H, s), 2.16 (2 H, d, *J* = 7.7 Hz), 1.40 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 134.7, 129.6, 129.4, 130.6 (s), 119.6 (s), 99.9 (s), 48.5 (q), 48.4 (q), 39.8 (t), 32.1 (d), 21.4 (q); MS *m/z* (rel intensity) 251 (M^+, 6), 89 (100); HRMS calcd for $C_{13}H_{17}NO_2S$ (M^+) 251.0980, found *m/z* 251.0965.

3-Methyl-2-phenylthio-4(*E*)-heptenenitrile 13

Isomer a: Oil, HPLC (EtOAc/hexane, 7:93) t_R = 9.6 min; IR (neat) 2230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60-7.57 (2 H, m), 7.40-7.36 (3 H, m), 5.36 (1 H, dt, *J* = 16.4, 5.9 Hz, H-5), 5.41 (1 H, dd, *J* = 16.4, 7.7 Hz, H-4), 3.68 (1 H, d, *J* = 5.9 Hz, H-2), 2.64 (1 H, m), 2.06 (2 H, m), 1.28 (3 H, d, *J* = 6.9 Hz), 1.00 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 135.2 (d), 133.8 (d), 131.9 (s), 129.4 (d), 129.2 (d), 128.9 (d), 118.3 (s), 44.4 (d), 39.3 (t), 25.4 (d), 17.5 (q), 13.5 (q); MS *m/z* (rel intensity) 231 (M^+, 15), 149 (100). Isomer b: Oil, HPLC (EtOAc/hexane, 7:93) t_R = 10.8 min; IR (neat) 2230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60-7.57 (2 H, m), 7.40-7.35 (3 H, m), 3.68 (1 H, dt, *J* = 16.4, 6.0 Hz), 5.44 (1 H, dd, *J* = 16.4, 8.2 Hz), 3.61 (1 H, d, *J* = 6.0 Hz), 2.62 (1 H, m), 2.08 (2 H, m), 1.27 (3 H, d, *J* = 6.7 Hz), 1.01 (3 H, t, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 135.8 (d), 133.8 (d), 131.9 (s), 129.4 (d), 129.1 (d), 127.9 (d), 118.5 (s), 44.5 (d), 39.6 (t), 25.4 (d), 18.9 (q), 13.5 (q); MS *m/z* (rel intensity) 231 (M^+, 15), 149 (100); HRMS calcd for $C_{14}H_{17}NS$ (M^+) 231.1082, found *m/z* 231.1077.

(*N*-Benzyl-3-Oxopropylamino)acetonitrile 15 and Ethyl 5-(*N*-Cyanomethylbenzylamino)-2(*E*)-pentenoate 16

Benzylaminoacetonitrile **(14)** was prepared by substitution of chloroacetonitrile with benzylamine in the presence of Et_3N. A solution of benzylaminoacetonitrile (1.46 g, 10 mmol), acrolein (0.67 g, 12 mmol) and Et_3N (1.5 mL, 10 mmol) in CH_2Cl_2 (15 mL) was stirred at 25 °C for 4 h to give a crude product **15** (1.91 g, 95%). The product, partially decomposing on silica gel, was used for the subsequent Wittig-Horner reaction without furthur purification. To a solution of **15** (1.91 g) and triethyl phosphonoacetate (2.25 g, 10 mmol) in THF (30 mL) was added a suspension of KOH (1 g, 20 mmol) in THF (30 mL). The reaction mixture was stirred for 75 min, filtered, concentrated and chromatographed on a silica-gel column by elution with EtOAc/hexane (10:90) to give *E*-**16** (1.79 g, 69%). **15**: Oil, TLC (EtOAc/hexane, 20:80) R_f = 0.22; ^1H NMR ($CDCl_3$) δ 9.70 (1 H, t, *J* = 2.0 Hz, CHO), 7.33-7.26 (5 H, m), 3.66 (2 H, s), 3.43 (2 H, s), 2.99 (2 H, t, *J* = 6.5 Hz), 2.61 (2 H, dt, *J* = 6.5, 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 200.6 (d, CHO), 136.4 (s), 128.7 (d), 128.4 (d), 127.7 (d), 114.4 (s, CN), 57.9 (t), 47.0 (t), 41.2 (t), 41.0 (t). **16**: Oil, TLC (EtOAc/hexane, 20:80) R_f = 0.15; IR (neat) 2230 (CN), 1710 (C=O), 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33-7.24 (5 H, m), 6.92 (1 H, dt, *J* = 15.7, 6.9 Hz), 5.88 (1 H, d, *J* = 15.7 Hz), 4.17 (2 H, q, *J* = 7.1 Hz), 3.65 (2 H, s), 3.48 (2 H, s), 2.75 (2 H, t, *J* = 6.9 Hz), 2.44 (2 H, m), 1.29 (3 H, t, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 165.7 (s, C=O), 145.4 (d, C-3), 136.6 (s), 128.7 (d), 128.4 (d), 127.6 (d), 122.7 (d), 114.1 (s), 59.9 (t), 57.9 (t), 52.2 (t), 40.9 (t), 29.8 (t), 14.1 (q); MS *m/z* (rel intensity) 272 (M^+, 1), 246 (50), 159 (54), 91 (100); HRMS calcd for $C_{16}H_{20}N_2O_2$ (M^+) 272.1525, found *m/z* 272.1517.

Ethyl 2-(1-Benzyl-2-cyanopyrrolid-3-yl)-2-phenylthioacetate 17 and Ethyl 5-(*N*-Cyanomethylbenzylamino)-3-phenylthiopentanote 18

Under a nitrogen atmosphere, BuLi (5 mmol, 3.75 mL of 1.6 M solution in hexane) was added dropwise to a cold (-78 °C) solution of diisopropylamine (0.75 mL, 5 mmol) in THF (10 mL). After 30 min, a solution of **16** (1.36 g, 5 mmol) in THF (3 mL) was added dropwise. The mixture was stirred for 20 min at -78 °C, and a solution of diphenyldisulfide (1.44 g, 6 mmol) in THF (4 mL) was added dropwise. The reaction mixture was stirred at -78 °C

for 1 h and warmed to 25 °C for 10 h. The mixture was quenched by addition of saturated NH_4Cl aqueous solution, concentrated, and extracted several times with EtOAc. The organic phase was dried (Na_2SO_4), filtered, concentrated and chromatographed on a silica-gel column by elution with EtOAc/hexane (5:95) to give **17** (0.84 g, 44%) and **18** (0.21 g, 11%). The four isomers of **17** (1:1:1:1) were further separated by HPLC with elution of EtOAc/hexane (10:90). Isomer a: Oil, HPLC (EtOAc/hexane, 10:90) t_R = 10.8 min; IR (neat) 2223 (CN), 1716 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50-7.26 (10 H, m), 4.12 (2 H, q, J = 7.1 Hz), 3.91 (1 H, d, J = 6.7 Hz, H-2′), 3.81 (1 H, d, J = 14.0 Hz), 3.66 (1 H, d, J = 14.0 Hz), 3.05 (1 H, m), 2.81 (1 H, m, H-3′), 2.61 (1 H, m), 2.35 (1 H, m), 1.92 (1 H, m), 1.18 (3 H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 170.6 (s, CO), 137.1 (s), 134.2 (d), 129.2 (s), 129.1 (d), 128.7 (d), 128.6 (d), 128.5 (d), 127.6 (d), 115.0 (s, CN), 61.5 (t), 57.7 (d), 56.6 (t), 52.7 (d), 50.4 (t), 42.0 (d), 27.6 (t), 13.9 (q); MS *m/z* (rel intensity) 380 (M^+, 42), 289 (27), 271 (26), 197 (30), 179 (37), 110 (41), 91 (100). Isomer b: Oil, HPLC (EtOAc/hexane, 10:90) t_R = 12 min; IR (neat) 2224, 1717 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.48-7.26 (10 H, m), 4.10 (2 H, t, J = 7.2 Hz), 3.88 (1 H, d, J = 13.1 Hz), 3.64 (1 H, d, J = 13.1 Hz), 3.61 (1 H, d, J = 9.9 Hz), 3.56 (1 H, d, J = 2.2 Hz), 2.97 (1 H, m), 2.83 (1 H, m), 2.60 (1 H, m), 2.14 (2 H, m), 1.15 (3 H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 170.8 (s), 137.2 (s), 133.8 (d), 131.9 (s), 129.2 (d), 128.6 (d), 128.5 (d), 127.6 (d), 116.7 (s), 61.5 (t), 57.0 (d), 56.0 (t), 55.2 (d), 50.9 (t), 44.7 (d), 27.3 (t), 14.0 (q); MS *m/z* (rel intensity) 380 (M^+, 73), 91 (100). Isomer c: Oil, HPLC (EtOAc/hexane, 10:90) t_R = 14.4 min; IR (neat) 2222, 1727 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41-7.26 (10 H, m), 4.15 (3 H, m), 3.86 (1 H, d, J = 13.1 Hz), 3.78 (1 H, d, J = 13.1 Hz), 3.58 (1 H, d, J = 11.0 Hz), 3.03 (1 H, m), 2.86 (1 H, m), 2.60 (1 H, m), 2.21 (1 H, m), 1.59 (1 H, m), 1.21 (3 H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 170.6 (s), 137.2 (s), 133.6 (d), 131.9 (s), 129.1 (d), 128.6 (d), 128.5 (d), 127.5 (d), 116.7 (s), 61.4 (t), 56.2 (d), 55.7 (t), 55.2 (d), 51.0 (t), 44.8 (d), 28.1 (t), 14.0 (q); MS *m/z* (rel intensity) 380 (M^+, 55), 91 (100). Isomer d: HPLC (EtOAc/hexane, 10:90) t_R = 16.8 min; IR (neat) 2222, 1727 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54-7.25 (10 H, m), 4.10 (3 H, m), 3.84 (1 H, d, J = 12.7 Hz), 3.75 (1 H, d, J = 12.7 Hz), 3.11 (1 H, m), 2.87 (1 H, m), 2.62 (1 H, m), 2.16 (1 H, m), 1.61 (1 H, m), 1.33 (3 H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 170.6 (s), 137.2 (s), 133.9 (d), 131.8 (s), 129.0 (d), 128.7 (d), 128.6 (d), 128.5 (d), 127.6 (d), 115.1 (s), 61.3 (t), 57.7 (d), 56.3 (t), 53.1 (d), 50.5 (t), 42.4 (d), 27.5 (t), 13.9 (q). MS *m/z* (rel intensity) 380 (M^+, 65), 91 (100); HRMS calcd for $C_{22}H_{24}N_2O_2S$ (M^+) 380.1558, found *m/z* 380.1556. **18**: Oil, HPLC (EtOAc/hexane, 10:90) t_R = 19 min; IR (neat) 2223, 1727 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.48-7.26 (10 H, m), 4.13 (2 H, q, J = 7.2 Hz), 3.70 (1 H, d, J = 13.4 Hz), 3.60 (1 H, d, J = 13.4 Hz), 3.48 (1 H, d, J = 17.5 Hz), 3.31 (1 H, d, J = 17.5 Hz), 2.95-2.46 (5 H, m), 1.90 (1 H, m), 1.71 (1 H, m), 1.25 (3 H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 171.4 (s), 137.0 (s), 133.5 (s), 133.1 (d), 129.0 (d), 128.6 (d), 128.5 (d), 127.8 (d), 127.6 (d), 114.7 (s), 60.7 (t), 58.2 (t), 51.1 (t), 42.4 (d), 40.9 (t), 40.6 (t), 31.9 (t), 14.2 (q); MS *m/z* (rel intensity) 383 (M^+, 59), 356 (48), 342 (85), 291 (77), 223 (37), 159 (90), 135 (40), 91 (100); HRMS calcd for $C_{22}H_{26}N_2O_2S$ (M^+) 382.1715, found *m/z* 382.1723.

ACKNOWLEDGMENT

We thank the National Science Council (NSC 83-0208-M-002-041) of Republic of China for financial support, and Professor T.-K. Yang (National Chung-Hsing University) for helpful discussion at the early stage of this research work.

Received April 8, 1994.

Key Words

Aminomalononitrile; 2-Chloro-2-phenylthioacetonitrile; 1-Phenylthiocyclopropanecarbonitrile; 3*H*-Pyrroline; Pyrrole.

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