Journal of Sulfur Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713926081

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S. Forgber[a]; D. Cleve[a]; W. -D. Rudorf[a]
[a] Institute of Organic Chemistry, Martin Luther University Halle-Wittenberg, Halle, Germany

To cite this Article Forgber, S. , Cleve, D. and Rudorf, W. -D.(2005) 'Reaction of CH-acidic compounds with thiacumulenes and alkylation with dihaloalkanes', Journal of Sulfur Chemistry, 26: 6, 499 — 507
To link to this Article: DOI: 10.1080/00268970500470266
URL: http://dx.doi.org/10.1080/00268970500470266

Journal of Sulfur Chemistry
Vol. 26, No. 6, December 2005, 499–507

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RESEARCH ARTICLE

Reaction of CH-acidic compounds with thiacumulenes and alkylation with dihaloalkanes

S. FORGBER, D. CLEVE and W.-D. RUDORF*

Institute of Organic Chemistry, Martin Luther University Halle-Wittenberg, Kurt-Mothes-Str. 2, 06099 Halle, Germany

(Received 29 September 2005; in final form 13 November 2005)

Dithiocarboxylation of CH-acidic compounds **1** and stepwise alkylation of primarily formed dithiolates **2** yielded ketene dithioacetals **5a,b** or methylenebis(dithiocarbonates) **12a–c**. Reaction of **5a**,**b** with nucleophiles afforded thiophene **7** and dithioacetals **8**, **9a**,**b**, **11**, respectively. 1,3-Thiazetidines **14a**,**c**,**e** and thiazolidines **14b**,**d**,**f** were prepared by thiocarbamoylation of **1b**,**c**,**e** and subsequent alkylation with dihaloalkanes.

Keywords: E/Z-isomers; Acrylonitriles; Acrylates; Methylenebis(dithiocarbonates); 1,3-Thiazetidines; Thiazolidines

1. Introduction

The chemistry of push-pull alkenes continues to attract the remarkable attention due to their utilisation as building blocks for four-, five- and six-membered rings [1, 2]. Previously we prepared the first unsymmetrical S,S′-dialkyl N-(arenesulfonyl)carbondithioimidates [3]. As a part of our research programme, dithiocarboxylation and thiocarbamoylation of CH-acidic compounds and subsequent alkylation especially with dihaloalkanes have also been investigated [4, 5]. Reactions with dihalomethanes have not been properly studied yet and are of significant interest from both a synthetic and spectroscopic point of view. Push-pull alkenes with a halomethylthio group are of great strategic value in molecular construction and occupy a central role in the syntheses of heterocyclic compounds. The structural peculiarities of donor-acceptor substituted alkenes are associated with E/Z isomerism about $C_\alpha = C_\beta$ and low barriers to internal rotation about the ethylenic bond [6].

2. Results and discussion

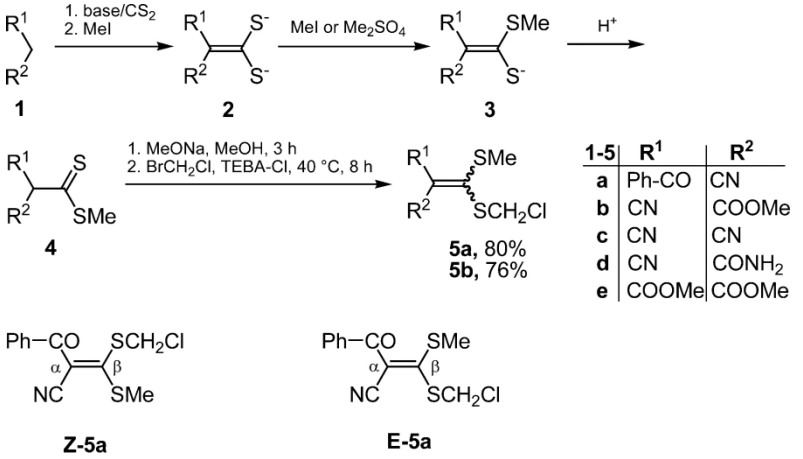
The reaction of benzoylacetonitrile (**1a**) with carbon disulfide in the presence of sodium hydride in dimethyl sulfoxide and successive methylation yields dithiocarboxylic ester **4a** [4].

*Corresponding author. Email: wolf-dieter.rudorf@chemie.uni-halle.de

Journal of Sulfur Chemistry
ISSN 1741-5993 print/ISSN 1741-6000 online © 2005 Taylor & Francis
http://www.tandf.co.uk/journals
DOI: 10.1080/00268970500470266

Chloromethylation with bromochloromethane succeeds under mild conditions using phase-transfer catalysis and gives the 2-benzoyl-3-chloromethylthio-3-methylthio-acrylonitrile (**5a**).

In the ^{1}H NMR spectrum two sets of signals can be observed for the SMe and SCH_2 groups. The signals at δSMe = 2.50 ppm and δSCH_2 = 5.14 ppm belong to the Z-isomer and the signals at δSMe = 2.82 ppm and δSCH_2 = 4.99 ppm to the E-isomer. The singlets of the SMe and of the SCH_2 groups of the Z- and E-isomers have an intensity ratio of Z: E = 1:1.3. Using Eu(fod)$_3$ as shift reagent the statement mentioned above is proved. There are different paramagnetic shift values of E- and Z-groups. For the Z-isomer the relative shifts are $\Delta\delta$SMe = 0.15 ppm and $\Delta\delta SCH_2$ = 0.19 ppm and for the E-isomer $\Delta\delta$SMe = 0.21 ppm and $\Delta\delta SCH_2$ = 0.14 ppm.



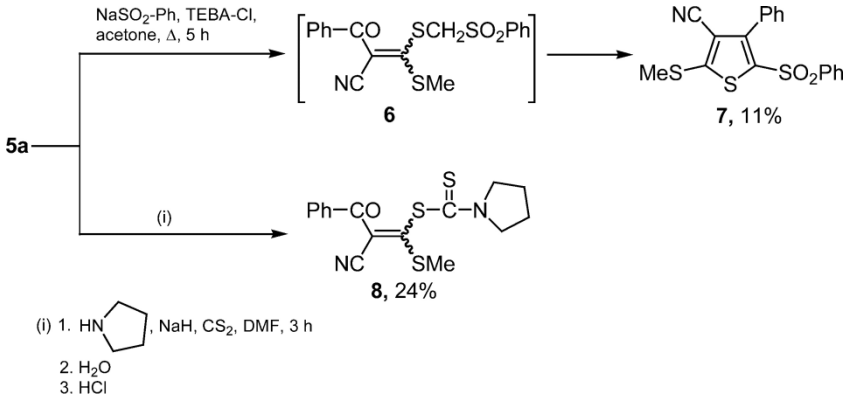
SCHEME 1

Two sets of signals also are evident in the ^{13}C NMR spectrum. By polarisation of the double bond in push-pull alkenes the signal of the C_α-atom is shifted to a higher field ($\delta_{C(\alpha)}$ = 112.4 and 112.8 ppm) whereas the C_β-atom signal is shifted to a lower field ($\delta_{C(\beta)}$ = 168.7 and 170.8 ppm).

The constituents of the product mixture could also be separated by GC-MS. For the E- and Z-isomers mass spectra were obtained supporting the structure of the ketene S,S-acetals **5a**. The mass spectrum of one isomer shows a molecular peak but in the spectrum of the other one the fragment [M-·Cl]$^+$ is the peak of the highest m/z. Assignment of the spectra to E- or Z-isomers was not possible.

Using aroyl-cyano-ketene-S,S-acetals and appropriate dinucleophiles numerous types of heterocycles could be synthesized [4, 5, 7–9]. The introduction of a halomethylthio group leads to additional syntheses. Sodium benzenesulfinate is a suitable nucleophile to react with the chloromethyl group of 2-benzoyl-3-chloromethylthio-3-methylthio-acrylonitrile (**5a**). Subsequent intramolecular cyclisation forms the thiophene **7**. An isolation of the open-chain compound **6** failed.

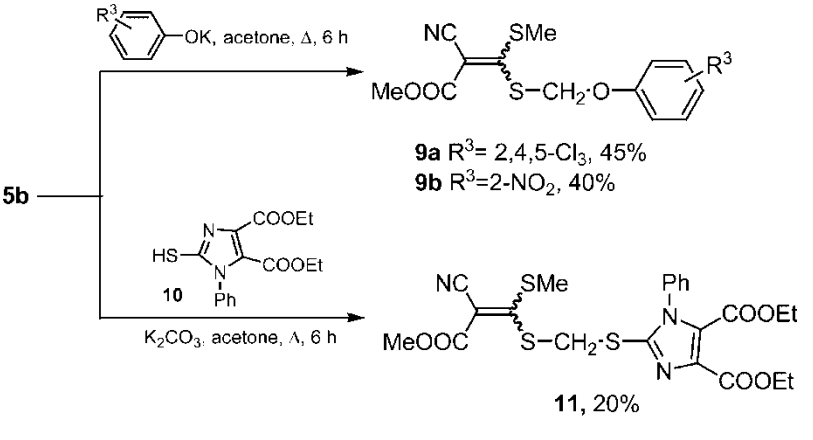
Reacting with sodium pyrrolidinedithiocarboxylate an attack on C_β-atom of the double bond is observed. Elimination of chloromethanethiolate gives 2-benzoyl-3-methylthio-3-(pyrrolidin-1-yl-thiocarbonylthio)-acrylonitrile **8**. In the ^{1}H NMR spectrum only one set of signals was observed. The protons of the methylthio group appear as singlet at δ = 2.58 ppm whereas multiplets at δ = 1.78 and δ = 3.03 ppm are characteristic of the pyrrolidine ring.

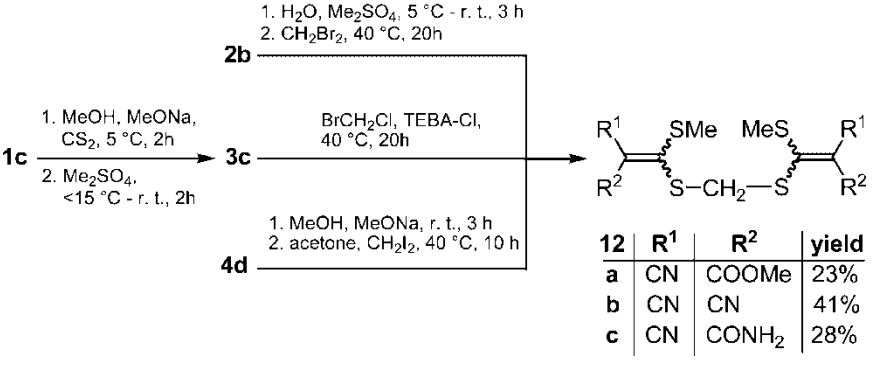


SCHEME 2

The readily accessible methyl dithiocarboxylate **4b** [10, 11] reacts with bromochloromethane to form methyl 3-chloromethylthio-2-cyano-3-methylthioacrylate (**5b**) which can react with phenolates to give **9a**,**b** and with thiolate **10** to give methyl imidazolylthiomethylthio-acrylate **11**.

In the ^{1}H NMR spectrum of **5b** two sets of the proton signals are observed, indicating existing E/Z-isomers (ratio 1:1). For the trichlorophenoxy-methylthio compound **9a** and the





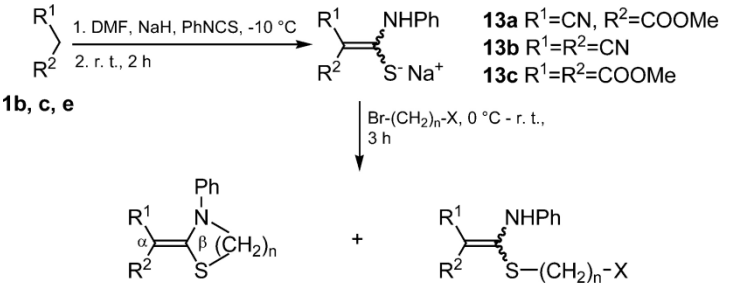
12	R^1	R^2	yield
a	CN	COOMe	23%
b	CN	CN	41%
c	CN	$CONH_2$	28%

SCHEME 3

methyl acrylate **11** an isomer ratio of about 1:2 can be estimated from the two sets of the SMe proton signals whereas for **9b** the ratio is 1:8.

Dithiocarboxylation of methyl cyanoacetate (**1b**), malononitrile (**1c**) or cyanoacetamide (**1d**) and subsequent stepwise alkylation of the primarily formed dithiolates **2** with dimethylsulfate and a dihalomethane remarkably lead to the exclusive formation of methylenebis(dithiocarbonates) **12a–c**.

Thiocarbamoylation of malonic acid derivatives (**1b**,**c**,**e**) with phenyl isothiocyanate gives sodium salts **13a–c** that were not isolated. Alkylation with bromochloromethane and dibromomethane, respectively, yields 1,3-thiazetidines **14a**,**c**,**e**. On the other hand, using 1,2-dibromoethane affords thiazolidines **14b**,**d**,**f**. Only in the alkylation of **13a** with bromochloromethane cyclisation was not observed. S-alkylation leads to methyl 3-anilino-3-chloromethylthio-2-cyanoacrylate **15** in low yield.



14	R^1	R^2	n	yield
a	CN	COOMe	1	47%
b	CN	COOMe	2	19%
c	CN	CN	1	42%
d	CN	CN	2	90%
e	COOMe	COOMe	1	18%
f	COOMe	COOMe	2	61%

SCHEME 4

3. Conclusions

Compounds **5**, **8**, **9** and **11–15** are push-pull alkenes bearing electron-donating substituents on one end of a C=C double bond and electron-withdrawing substituents on the other end. With increased π-electron delocalisation, the central C=C double bond becomes evermore polarized and its π-bond order is reduced. Rotational barriers of such compounds are significantly lowered. In summary, due to the E/Z isomerism about C_α=C_β, two sets of signals were observed for some of the resonances of **5a** and **b**, **9a** and **b**, **11**, **12a** and **c** and **15** in both the ^{1}H and ^{13}C NMR spectra. For compounds **8**, **14a** and **b**, and **15**, only one set of ^{1}H signals was observed due to the one isomer as the energy difference between the two possible isomers is too large and only the more stable isomer is present.

4. Experimental

Melting points were determined with a Boetius micro heating stage (Carl Zeiss Jena) and are uncorrected. Elemental analyses were performed with a CHNS-932 LECO analyzer. Column

chromatography was carried out using silica gel 60 (0.063–0.200 mm, Merck). Analytical thin-layer chromatography was performed on Merck silica gel plates (60 F-254). IR spectra were recorded on a Zeiss-Spectrometer SPECORD IR or a Perkin-Elmer FT-IR Spectrometer SPECTRUM 1000. Mass spectra (EI) were taken on an AMD 402 spectrometer (Intectra GmbH) and (CI) on a Finnigan MAT 90 (Finnigan, Bremen). ^{1}H and ^{13}C NMR spectra were run on Bruker spectrometers WP 200 and AC 80; $CDCl_3$ was used as solvent, unless otherwise stated, with TMS as internal standard. GC-MS analyses were performed on a Hewlett Packard 5890 gas chromatograph coupled to a mass spectrometric detector. The capillary column used was a HP-Ultra 2 (methylphenylsilicone, 12.5 m × 0.25 mm id).

4.1 *2-Benzoyl-3-chloromethylthio-3-methylthioacrylonitrile (5a)*

A mixture of **4a** (3.53 g, 15 mmol) [4] and NaOMe (0.81 g, 15 mmol) in dry MeOH (20 ml) was stirred at r. t. for 3 h. The solvent was then evaporated under reduced pressure, and the resulting residue was stirred with bromochloromethane (50 ml) and benzyltriethylammonium chloride (0.5 g, 2.2 mmol) at 40 °C for 8 h. The solid was filtered off and the solvent of the filtrate removed. The resultant oil was purified by column chromatography with petrol ether-diethyl ether (1:1) as the eluent to give **5a** (3.41 g, 80%); mp 52–55 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ2.50 (s, 3H, SMe); 2.82 (s, 3H, SMe); 4.99 (s, 2H, SCH_2); 5.14 (s, 2H, SCH_2); 7.44–7.60 (m, 6H, arom.); 7.87–7.93 (m, 4H, arom.). ^{1}H NMR [200 MHz, 10^{-2} molar solution in 0.7 ml $CDCl_3$, 25 mg Eu(fod)$_3$]: δ 2.65 (s, 3H, SMe); 3.03 (s, 3H, SMe); 5.13 (s, 2H, SCH_2); 5.33 (s, 2H, SCH_2). ^{13}C NMR (20 MHz, $CDCl_3$): δ 19.9 (SMe); 20.7 (SMe); 47.3 (SCH_2); 48.5 (SCH_2); 112.4 (C_α); 112.8 (C_α); 116.3 (CN); 128.8; 129.4; 134.0; 135.6; 168.7 (C_β); 170.8 (C_β); 186.8 (CO). Elemental analysis calculated for $C_{12}H_{10}ClNOS_2$ (283.80): C 50.79, H 3.55, Cl 12.49, N 4.94, S 22.60; found C 50.61, H 3.51, Cl 12.35, N 4.85, S 22.53%. GC-MS (CI; methane), $t_R = 11.52$; $m/z = 250$ ([M-·Cl+2·H]$^{+\cdot}$, 100), 204 (13), 202 ([M-·SCH_2Cl]$^+$, 4), 172 (11), 158 (6), 105 ($C_6H_5CO^+$, 37), 99 ($C_7H_7^+$, 91). $t_R = 13.60$; $m/z = 284$ ([M+·H]$^{+\cdot}$, 51), 250 (39), 248 ([M-·Cl]$^+$, 32), 234 ([M-·CH_2Cl]$^{+\cdot}$, 20), 204 (37), 202 ([M-·SCH_2Cl]$^{+\cdot}$, 22), 172 (18), 105 ($C_6H_5CO^+$, 81), 99 ($C_7H_7^+$, 100).

4.2 *Methyl 3-chloromethylthio-2-cyano-3-methylthioacrylate (5b)*

The procedure was the same as described above using **4b** [10] (2.84 g, 15 mmol). Yield: 2.71 g (76%); mp 52–54 °C. ^{1}H NMR (80 MHz, $CDCl_3$): δ 2.60 (s, 3H, SMe); 2.75 (s, 3H, SMe); 3.79 (s, 3H, COOMe); 3.81 (s, 3H, COOMe); 5.04 (s, 4H, 2 SCH_2). Elemental analysis calculated for $C_7H_8ClNO_2S_2$ (237.73): C 35.37, H 3.39, N 5.89; found C 35.48, H 3.33, N 5.85%. MS: $m/z = 237$ (M$^{+\cdot}$, 83), 222 (21), 188 (94), 141 (81), 97 (100). IR (KBr): ν (cm^{-1}) = 2190 (CN), 1685 (COOMe).

4.3 *2-Methylthio-4-phenyl-5-phenylsulfonyl-3-thiophenecarbonitrile (7)*

A stirred solution of **5a** (3.55 g, 12.5 mmol), sodium benzenesulfinate (2.05 g, 12.5 mmol) and benzyltriethylammonium chloride (0.75 g, 3.3 mmol) in dry acetone (50 ml) was heated under reflux for 5 h. The precipitate was filtered off. After evaporation of the acetone, the resultant oily residue was purified by column chromatography with methylene chloride to provide 0.51 g (11%) of **7**, mp 117–121 °C (methanol). ^{1}H NMR (80 MHz, $CDCl_3$): δ 2.73 (s, 3H, SMe); 7.10–7.56 (m, 10H, arom.). ^{13}C NMR (50 MHz, $CDCl_3$): δ 18.5 (SMe); 111.6 (CN); 112.6; 127.6; 128.3; 128.8; 129.7; 129.8; 133.6; 137.1; 140.1; 148.0; 158.3. Elemental analysis calculated for $C_{18}H_{13}NO_2S_3$ (371.50): C 58.20, H 3.53, N 3.77, S 25.89; found C 58.17, H 3.48, N 3.77, S 26.03%. MS: $m/z = 371$ (M$^{+\cdot}$, 17), 219 (9), 187 (100), 158 (38),

141 (100), 106 (31), 91 (9), 77 (18). IR (KBr): ν (cm^{-1}) = 2220 (CN), 1580, 1520, 1480, 1445, 1400, 1350, 1320, 1145, 1090.

4.4 *2-Benzoyl-3-methylthio-3-(pyrrolidin-1-yl-thiocarbonylthio)acrylonitrile (8)*

Sodium hydride (72 mg, 3 mmol) and carbon disulfide (0.23 g, 3 mmol) were added to a stirred solution of pyrrolidine (0.21 g, 3 mmol) in dry dimethylformamide (15 ml). After 20 min **5a** (0.85 g, 3 mmol) was added portionwise and stirring was continued for 3 h. Then the solution was poured into ice-water (80 ml), extracted with chloroform (2 × 50 ml) and water layer acidified with diluted hydrochloric acid. The resulting solid was collected by filtration and crystallized from methanol to give 0.25 g (24%) or pure **8**, mp 130–133 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.78 (m, 4H, $NCH_2C\underline{H}_2C\underline{H}_2$); 2.58 (s, 3H, SMe); 3.03 (m, 4H, H_2CNCH_2); 7.33–7.36 (m, 3H, arom.); 7.62 (d, 2H, arom.). Elemental analysis calculated for $C_{16}H_{16}N_2OS_3$ (348.51): C 55.14, H 4.63, N 8.04, S 27.60; found C 55.35, H 4.72, N 8.23, S 27.41%. MS (CI; methane; 120 eV): m/z = 235 (52), 188 (35), 111 (31), 105 ($C_6H_5CO^+$, 100), 77 (30), 70 (16).

4.5 *Methyl 2-cyano-3-methylthio-3-(phenoxy-methylthio)acrylates (9a,b)*

A mixture of methyl 3-(chloromethylthio)-2-cyano-3-methylthioacrylate (**5b**; 4.75 g, 0.02 mol) and potassium 2,4,5-trichlorophenolate (4.71 g, 0.02 mol) in dry acetone (50 ml) was heated under reflux for 6 h. The solid was filtered off and the solvent of the filtrate removed. The resultant oily residue was purified by column chromatography on silica gel with $CHCl_3$ as eluent to give 3.59 g (45%) of **9a**. In a similar way, **9b** was prepared in 40% yield.

4.5.1 Methyl 2-cyano-3-methylthio-3-(2,4,5-trichlorophenoxy-methylthio)acrylate (9a). Mp 117–119 °C. ^{1}H NMR (100 MHz, $CDCl_3$): δ 2.50 (s, 3H, SMe); 2.70 (s, 3H, SMe); 3.79 (s, 3H, COOMe); 3.82 (s, 3H, COOMe); 5.63 (s, 4H, 2O-CH_2-S); 7.04 (s, 2H, arom.); 7.41 (s, 2H, arom.). Elemental analysis calculated for $C_{13}H_{10}Cl_3NO_3S_2$ (398.72): C 39.16, H 2.53, N 3.51; found C 39.33, H 2.60, N 3.54%. MS (EI, 70 eV): m/z = 209 ([$C_6H_2Cl_3$-O-CH_2]$^+$, 21), 195 ([$C_6H_2Cl_3$-O]$^+$, 99), 174 ([$C_6H_2Cl_2$-O-CH_2]$^+$, 37), 125 ([C_6H_2Cl-O]$^+$, 24), 97 {[(NC)(MeOOC)C]$^+$, 100}. IR (KBr): ν (cm^{-1}) = 2205 (CN), 1710 (COOMe).

4.5.2 Methyl 2-cyano-3-methylthio-3-(2-nitrophenoxy-methylthio)acrylate (9b). Mp 83.5–84 °C. ^{1}H NMR (100 MHz, $CDCl_3$): δ 2.50 (s, 3H, SMe); 2.68 (s, 3H, SMe); 3.74 (s, 3H, COOMe); 3.79 (s, 3H, COOMe); 5.67 (s, 2H, O-CH_2-S); 5.70 (s, 2H, O-CH_2-S); 6.99–8.03 (m, 8H, arom.). Elemental analysis calculated for $C_{13}H_{12}N_2O_5S_2$ (340.38): C 45.87, H 3.55, N 8.23; found C 45.87, H 3.49, N 8.05%. MS (EI, 70 eV): m/z = 202, {[(NC)(MeOOC)C=C(SCH_3)(SCH_2)]$^+$, 61}, 188 {[(NC)(MeOOC)C=C(Me)(S)]$^+$, 12}, 152 {[$C_6H_4(NO_2)$-O-CH_2]$^+$, 100}, 122 ([$C_6H_4NO_2$]$^+$, 83), 97 {[(NC)(MeOOC)C]$^+$, 22}. IR (KBr): ν (cm^{-1}) = 2200 (CN), 1705 (COOMe).

4.6 *Methyl 2-cyano-3-methylthio-3-(4,5-diethoxycarbonyl-1-phenyl-imidazol-2-yl-thiomethylthio)acrylate (11)*

A mixture of diethyl 2-mercapto-1-phenylimidazole-4,5-dicarboxylate [12] (3.20 g, 0.01 mol), methyl 3-(chloromethylthio)-2-cyano-3-methylthioacrylate (**5b**; 2.38 g, 0.01 mol) and potassium carbonate (1.38 g, 0.01 mol) in absolute acetone (80 ml) was heated under reflux for 6 h.

The resulting solid was collected by filtration and the solution evaporated. The oily residue crystallized after heating with ethanol (30 ml) to give 1.04 g (20%) of **11**, mp 125–126 °C. ^{1}H NMR (100 MHz, $CDCl_3$): δ 1.03 (t, Me); 1.30 (t, Me); 2.58 (s, SMe); 2.67 (s, SMe); 3.76 (s, COOMe); 4.08 (q, CH_2); 4.30 (q, CH_2); 4.90 (s, S-CH_2-S); 4.97 (s, S-CH_2-S). Elemental analysis calculated for $C_{22}H_{23}N_3O_6S_3$ (521.64): C 50.66, H 4.44, N 8.06; found C 50.44, H 4.42, N 7.89%. MS (EI, 70 eV): m/z = 521 (M^+, 5), 474 (23), 188 (81), 97 (60), 91 (100). IR (KBr): ν (cm^{-1}) = 2205 (CN), 1705 and 1715 (COOMe).

4.7 *Methylenebis[methyl(cyano-methoxycarbonyl-methylene)dithiocarbonate] (12a)*

Dimethylsulfate (5.0 g, 0.04 mol) was added dropwise to a cold (ice-water) and stirred solution of disodium salt **2b** [10] (8.8 g, 0.04 mol) in water (30 ml). After stirring for 3 h at r. t. methylene bromide (8.7 g, 0.05 mol) was added and the mixture was stirred for another 20 h at 40 °C. The solid was filtered off, washed with diethyl ether and recrystallized from ethanol to give 2.1 g (23%) of **12a**, mp 95–97 °C. ^{1}H NMR (100 MHz, $CDCl_3$/DMSO-D_6): δ 2.57–2.59 (m, 3H, SMe); 2.73–2.80 (m, 3H, SMe); 3.81–3.86 (m, 6H, 2 COOMe); 4.71–4.78 (m, 2H, S-CH_2-S). Elemental analysis calculated for $C_{13}H_{14}N_2O_4S_4$ (390.52): C 39.98, H 3.61, N 7.17; found C 39.72, H 3.45, N 6.99%. IR (KBr): ν(cm^{-1}) = 2185 (CN), 1685 (COOMe).

4.8 *Methylenebis[methyl(dicyanomethylene)dithiocarbonate] (12b)*

To a cooled (ice-bath) and stirred solution of malononitrile (**1c**, 6.6 g, 0.1 mol) and sodium methylate (5.4 g, 0.1 mol) in dry methanol (80 ml) carbon disulfide (3.8 g, 0.05 mol) was added dropwise. After 15 min a second portion of sodium methylate (2.7 g, 0.05 mol) in methanol (15 ml) and carbon disulfide (1.9 g, 0.025 mol) was added to the reaction mixture, followed by a third portion of sodium methylate (1.35 g, 0.025 mol) in methanol (15 ml) and carbon disulfide (0.95 g, 0.0125 mol) after an interval of 30 min. The mixture was stirred for another 1 h and dimethylsulfate (11.0 g, 0.0875 mol) was added dropwise maintaining the temperature of the solution below 15 °C. After stirring for 2 h at r.t., the solvent was evaporated under reduced pressure to give **3c** as raw product which is used for the next step without further purification. After adding bromochloromethane (100 ml) and benzyltriethylammonium chloride (1.5 g, 6.6 mmol) vigorous stirring was continued for 20 h at 40 °C. The solid was filtered off, the organic layer washed with water (2 × 100 ml) and dried over calcium chloride. After the evaporation of bromochloromethane, the solid was recrystallized from methanol/benzene to yield 5.8 g (41%) of **12b**, mp 136–137 °C. ^{1}H NMR (200 MHz, acetone-d_6): δ 2.91 (s, 6H, 2Me); 5.13 (s, 2H, CH_2). ^{13}C NMR (50 MHz, acetone-d_6): δ 20.1 (Me); 42.7 (CH_2); 83.4 (C_α); 113.0 (CN); 113.3 (CN); 179.9 (C_β). Elemental analysis calculated for $C_{11}H_8N_4S_4$ (324.47): C 40.72, H 2.49, N 17.27, S 39.53; found C 40.97, H 2.53, N 17.09, S 39.49%. MS (EI, 70 eV): m/z = 324 ($M^{+\cdot}$, 62), 309 (24), 277 (13), 201 (5), 169 (100), 155 (7), 123 (56), 108 (13), 61 (46).

4.9 *Methylenebis[methyl(aminocarbonyl-cyano-methylene)dithiocarbonate] (12c)*

A mixture of **4d** [10] (1.74 g, 0.01 mol) and sodium methylate (0.54 g, 0.01 mol) in dry methanol (10 ml) was stirred for 3 h at r.t. and then evaporated to dryness under reduced pressure. Dry acetone (60 ml) and methylene iodide (1.34 g, 0.005 mol) were added to the residue and stirring was continued for another 10 h at 40 °C. The solid was filtered off, washed with water (2x10 ml) and recrystallized from ethanol to give 0.5 g (28%) of **12c**, mp 174–178 °C. ^{1}H

NMR (100 MHz, DMSO-D_6): δ 2.50 (m, 3H, SMe); 2.66 (m, 3H, SMe); 4.61–4.66 (d, 2H, S-CH_2-S); 7.58 (m, 4H, 2 $CONH_2$). Elemental analysis calculated for $C_{11}H_{12}N_4O_2S_4$ (360.50): C 36.65, H 3.36, N 15.54; found C 36.82, H 3.34, N 15.44%. IR (KBr): ν (cm^{-1}) = 2190 (CN).

4.10 *1,3-Thiazetidines 14a,c,e, Thiazolidines 14b,d,f and Methyl 3-anilino-3-chloromethylthio-2-cyanoacrylate 15; general procedure*

Sodium hydride (0.48 g, 20 mmol) was added portionwise, during 10 min and at −10 °C, to a solution of the corresponding malonic acid derivative **1b,c,e** (10 mmol) in dry dimethylformamide (20 ml) under N_2 atmosphere while stirring. After 10 min phenyl isothiocyanate (1.35 g, 10 mmol) was added dropwise and stirring was continued for 2 h at r. t. Finally, the alkylating agent (10 mmol) was added maintaining the temperature at 0 °C. Stirring was continued for another 3 h at r. t. The reaction mixture was then poured into ice-water (150 ml) and the resulting solid was filtered off and recrystallized.

4.11 *Methyl 2-(3-phenyl-1,3-thiazetidin-2-ylidene)cyanoacetate 14a*

Alkylating agent: dibromomethane; yield: 47%; mp 123–125 °C (methanol). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.78 (s, 3H, Me); 5.17 (s, 2H, SCH_2); 7.26–7.47 (m, 5H, arom.). Elemental analysis calculated for $C_{12}H_{10}N_2O_2S$ (246.29): C 58.52, H 4.09, N 11.37, S 13.02; found C 58.42, H 4.29, N 11.25, S 12.85%. MS (EI, 70 eV): m/z = 246 ($M^{+\cdot}$, 48), 215 (5), 187 (10), 105 (100), 104 (28), 77 (21). IR (KBr): ν(cm^{-1}) = 2955–2915, 2220 (CN), 1680 (COOMe).

4.12 *Methyl 2-(3-phenyl-thiazolidin-2-ylidene)cyanoacetate 14b*

Alkylating agent: 1,2-dibromoethane; yield: 19%; mp 168-170 °C (methanol). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.22 (s, 2H, NCH_2); 3.72 (s, 3H, COOMe); 4.16 (s, 2H, SCH_2); 7.23–7.46 (m, 5H, arom.). Elemental analysis calculated for $C_{13}H_{12}N_2O_2S$ (260.32): C 59.98, H 4.65, N 10.76, S 12.32; found C 59.80, H 4.63, N 10.60, S 12.36%. MS (EI, 70 eV): m/z = 260 ($M^{+\cdot}$, 100), 229 (34), 201 (40), 200 (38), 173 (9), 155 (5), 77 (16).

4.13 *2-(3-Phenyl-1,3-thiazetidin-2-ylidene)malononitrile 14c*

Alkylating agent: bromochloromethane; yield: 42%; mp 140–141 °C (methanol). ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.18 (s, 2H, CH_2); 7.25–7.50 (m, 5H, arom.). Elemental analysis calculated for $C_{11}H_7N_3S$ (213.26): C 61.95, H 3.31, N 19.70, S 15.03; found C 61.59, H 3.38, N 19.50, S 15.08%. MS (EI, 70 eV): m/z = 213 ($M^{+\cdot}$, 64), 167 (3), 105 (100), 104 (31), 77 (37).

4.14 *2-(3-Phenyl-thiazolidin-2-ylidene)malononitrile 14d*

Alkylating agent: 1,2-dibromoethane; yield: 90%; mp 168–170 °C (n-butanol). ^{1}H NMR (200 MHz, $CDCl_3$/DMSO-D_6): δ 3.30 (t, 2H, NCH_2); 4.16 (t, 2H, SCH_2); 7.09–7.32 (m, 5H, arom.). Elemental analysis calculated for $C_{12}H_9N_3S$ (227.29): C 63.41, H 3.99, N 18.49, S 14.11; found C 63.74, H 4.00, N 18.41, S 14.23%. MS (EI, 70 eV): m/z = 227 ($M^{+\cdot}$, 100), 226 (19), 201 (7), 199 (14), 172 (5), 77 (6).

4.15 *Dimethyl 2-(3-phenyl-1,3-thiazetidin-2-ylidene)malonate 14e*

Alkylating agent: dibromomethane; yield: 18%; mp 97–99 °C (diethyl ether/petroleum ether). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.00 (s, 3H, Me); 3.78 (s, 3H, Me); 5.03 (s, 2H, SCH_2); 7.02–7.34 (m, 5H, arom.). ^{13}C NMR (50 MHz, $CDCl_3$): δ 50.3 (COO<u>Me</u>); 51.6 (COO<u>Me</u>); 56.8 (SCH_2); 89.9 (C_α); 120.5, 126.6, 129.2, 141.9 (arom.); 163.6 (<u>C</u>OOMe); 168.2 (<u>C</u>OOMe); 173.0 (C_β). Elemental analysis calculated for $C_{13}H_{13}NO_4S$ (279.32): C 55.90, H 4.69, N 5.01, S 11.48; found C 55.97, H 5.05, N 4.74, S 11.47%. MS (EI, 70 eV): $m/z = 279$ ($M^{+\cdot}$, 38), 247 (31), 217 (8), 202 (7), 188 (8), 143 (16), 105 (100), 104 (36), 77 (26), 59 (11). IR (KBr): ν (cm^{-1}) = 1700 (CO), 1645 (CO).

4.16 *Dimethyl 2-(3-phenyl-thiazolidin-2-ylidene)malonate 14f [13]*

Alkylating agent: 1,2-dibromoethane; yield: 61%; mp 150–151 °C (methanol). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.12 (t, 2H, NCH_2); 3.30 (s, 6H, 2Me); 4.11 (s, 2H, SCH_2); 7.11–7.36 (m, 5H, arom.). ^{13}C NMR (50 MHz, $CDCl_3$): δ 27.0 (SCH_2); 51.2 (2COO<u>Me</u>); 59.1 (NCH_2); 93.3 (C_α); 124.3; 126.3; 129.2; 142.7 (arom.); 166.6 (C_β); 166.8 (2<u>C</u>OOMe). Elemental analysis calculated for $C_{14}H_{15}NO_4S$ (293.35): C 57.32, H 5.15, N 4.77, S 10.93; found C 57.30, H 5.21, N 4.76, S 11.01%. MS (EI, 70 eV): $m/z = 293$ ($M^{+\cdot}$, 22), 262 (10), 234 (97), 233 (72), 230 (63), 202 (100), 175 (48), 160 (12), 146 (14), 104 (11), 103 (16), 91 (18), 77 (80), 59 (57).

4.17 *Methyl 3-anilino-3-chloromethylthio-2-cyanoacrylate 15*

Alkylating agent: bromochloromethane. The ice-water mixture was extracted with chloroform (2 × 70 ml) and the combined organic layers were dried over calcium chloride. The chloroform was then removed under reduced pressure and the resultant oily residue purified by column chromatography on silica gel with petroleum ether/diethyl ether (1:1) to give **15** in 11% yield; mp 83–85 °C (methanol). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.83 (s, 3H, Me); 4.65 (s, 2H, SCH_2); 7.25–7.44 (m, 5H, arom.); 11.51 [s(br), 1H, NH]. Elemental analysis calculated for $C_{12}H_{11}ClN_2O_2S$ (282.75): C 50.98, H 3.92, Cl 12.54, N 9.91, S 11.34; found C 50.77, H 3.95, Cl 12.55, N 9.82, S 11.64%. MS (EI, 70 eV): $m/z = 282$ ($M^{+\cdot}$, 19), 246 (24), 218 (100), 215 (36), 201 (74), 187 (10), 169 (34), 155 (30), 144 (29), 119 (9), 105 (38), 100 (61), 91 (28), 77 (44).

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