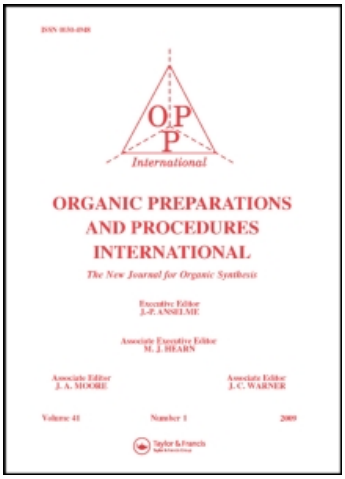

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A ONE-POT PREPARATION OF DIMETHYL N-ALKYLIMINODITHIOCARBONATES

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A ONE-POT PREPARATION OF DIMETHYL N-ALKYLIMINODITHIOCARBONATES

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The dialkyl N-(alkyl)iminodithiocarbonates (**2**) are of great interest in organic synthesis because of their synthetic equivalence to the azaallyl anion $^{-}$C-N=C. The use of metallated N-(alkyl)iminodithiocarbonates as transfer agents of the $^{-}$C-N=C synthon to saturated and unsaturated electrophiles is of broad synthetic utility, such as the homologation of aldehydes and ketones to thiiranes or S-vinylthiocarbamates,[1] the alkylation of 2-azaallyl anions derived from dialkyl N-(benzyl)iminodithiocarbonates,[2] and the preparation of β-mercaptoalcohols,[3] α-branched α-aminoacids,[4] azetidinones,[5] 2-alkyl (and 2-aryl)imino-1,3-oxathiolanes,[6] 3-aryl-2-(methylthiocarbonylamino)-acrylates,[7] thiazoles,[8] and oxazoles.[9]

Dialkyl N-(alkyl)iminodithiocarbonates have been usually obtained in a two-step procedure by the condensation from primary amines, carbon disulfide, methyl or ethyl iodide and triethylamine in homogeneous phase to give the intermediate N-(alkyl)dithiocarbamate which was isolated.[4,10,11-13]. The dimethyl N-(p-tosylmethyl)iminodithiocarbonate has also been obtained in a two-step procedure;[14] the intermediate methyl N-(p-tosylmethyl)iminodithiocarbonate, obtained in 73% yield by a Mannich condensation from methyl dithioformate, sodium p-toluenesulfinate, formaldehyde, formic acid and ammonia, was converted (93%) to the iminodithiocarbonate by methylation with methyl fluorosulfonate. An one-pot synthesis of dimethyl N-cyanoiminodithiocarbonate by using a phase-transfer catalyst in a two-phase system has been described.[15] However, this reference describes a single compound and the experimental procedure is difficult to reproduce. This paper describes a simple, rapid and very efficient one-pot synthesis of dimethyl N-(alkyl)iminodithiocarbonates.

The reaction is performed in a one-pot procedure from the primary amine **1**, carbon disulfide and methyl iodide using benzyltriethylammonium chloride (TEBA) as phase-transfer catalyst and NaOH-water/benzene in a two-phase system.

$$\underset{\mathbf{1}}{\text{R-NH}_2} \xrightarrow[\text{2. MeI, PhH, TEBA, 20°}]{\text{1. CS}_2\text{, NaOH, PhH}} \underset{\mathbf{2}}{\text{R-N=C(SMe)}_2}$$

a) R= 2 pyridylmethyl; b) 2-thienylmethyl; c) 2-furylmethyl; d) 2-(1-methylpyrrolyl)ethyl; e) (ethoxycarbonyl)methyl; f) benzyl; g) 3-(4-morpholyl)propyl; h) cyclohexyl; i) 2,2-dimethoxyethyl; j) allyl

Our procedure has some advantages over previously described methods because the experimental procedure is simple and rapid (20 min. at room temperature), the yields are fair to good

(39-86%), and the products obtained can be used directly without further purification (98%) (Table 1). The low yield observed for **2e** may be caused by a partial hydrolysis of the ester group under the reaction conditions.

TABLE 1. Dimethyl N-Alkyliminodithiocarbonates (**2**)

Product **2**[a]	a	b	c	d	e	f	g	h	i	j
Yield (%)	74	72	85	62	39	74	65	79	72	86

a) All products were isolated as liquids, except **2a** which was a solid, (EtOAc-hexane), mp. 46-47°; b) Lit.[4] yield: 77%; c) Lit.[11] yield: 52%.

The purity of all compounds was checked by tlc on silica gel (9:1 ethyl acetate-hexane), IR and ^{1}H NMR. The analytical samples were obtained by a flash chromatography on silica gel (9:1 ethyl acetate-hexane), and satisfactory combustion analysis were obtained (Table 2).

The structural assignments were carried out with the help of IR, ^{1}H NMR, and ^{13}C NMR spectra and comparison with **2e**[11] and **2f**[4], compounds previously described, or with the calculated values for similar compounds. The assignment of signals to carbons was made from DEPT spectra.[16] The IR data support the presence of an imino group (1570-1590 cm^{-1}),[4,11] and the ^{1}H NMR data establishes the presence of two methylthio groups bound to an sp^2 carbon.[17] The ^{13}C NMR data support the proposed structure for **2a-2j**. The assignment of signals to the two methylthio groups is proposed by comparison with the chemical shifts reported by us for methylthio groups to a C=N group.[7-9] Furthermore, the assignment of signals to CH_2-N= and C=N carbons is unambiguous by comparison of the observed chemical shifts with the tabulated values for similar carbons.

EXPERIMENTAL SECTION

Glycine ethyl ester hydrochloride, benzylamine, 2-(aminomethyl)pyridine, 2-(aminomethyl)-thiophene, 2-(aminomethyl)furan, 2-(2-aminoethyl)-1-methylpyrrole, and *N*-(3-amino-propyl)morpholine were purchased from Aldrich Chemical Co; cyclohexylamine and methyl iodide from Fluka; allylamine, 2-aminoacetaldehyde dimethylacetal, triethylbenzylammonium chloride, and potassium *tert*-butoxide from Merck, and carbon disulfide from Probus. ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR 300S spectrometer (^{1}H: 300 MHz; ^{13}C: 75 MHz) in $CDCl_3$, and chemical shifts are reported as δ values from tetramethylsilane as internal reference. Solutions in $CDCl_3$ at 303°K were used and chemical shifts are quoted in δ values. Infrared (IR) spectra were recorded on a Perkin Elmer 781 spectrophotometer. Analytical TLC plates were purchased from Merck (silica gel 60 F_{254}). The melting point of **2a** was determined using a Buchi apparatus and is uncorrected. Microanalytical data were determined by Centro de Investigacion y Desarrollo C. S. I. C. (Barcelona, Spain). The IR spectra were recorded on a Perkin Elmer 781 spectrometer.

Dimethyl *N*-Alkyliminodithiocarbonates (2). General Procedure.- To the amine (**1a-1j**, 18.5

TABLE 2. Elemental Analysis of the Iminodithiocarbonates **2**

Compound	Molecular formula	Found (Calcd.) C	H	N	S
2a	$C_9H_{12}N_2S_2$	51.05 (50.91)	5.62 (5.70)	12.82 (13.20)	30.58 (30.20)
2b	$C_8H_{11}NS_3$	44.29 (44.20)	5.18 (5.10)	6.72 (6.44)	43.81 (44.25)
2c	$C_8H_{11}NOS_2$	47.80 (47.73)	5.40 (5.51)	7.01 (6.96)	31.62 (31.85)
2d	$C_{10}H_{16}N_2S_5$	52.48 (52.59)	7.31 (7.06)	12.07 (12.27)	28.14 (28.08)
2e	$C_7H_{13}NO_2S_2$	40.32 (40.55)	6.25 (6.32)	7.04 (6.76)	31.02 (30.93)
2f	$C_{10}H_{13}NS_2$	57.03 (56.83)	6.09 (6.20)	6.45 (6.63)	30.43 (30.34)
2g	$C_{10}H_{10}N_2OS_2$	48.20 (48.35)	7.98 (8.11)	11.39 (11.28)	26.09 (25.81)
2h	$C_9H_{17}NS_2$	53.01 (53.15)	8.16 (8.43)	6.96 (6.89)	31.87 (31.53)
2i	$C_7H_{15}NO_2S_2$	39.86 (40.16)	7.03 (7.22)	6.79 (6.69)	30.73 (30.63)
2j	$C_6H_{11}NS_2$	44.57 (44.68)	6.83 (6.87)	8.79 (8.68)	39.81 (39.76)

mmol) in a round-bottomed flask fitted with a magnetic stirrer was added aqueous NaOH (12.4 mL, 20 M); stirred suspension was cooled in an ice-bath. After 5 min, a solution of carbon disulfide (1.11 g, 18.5 mmol) in benzene (2.9 mL) was added, followed by a solution of methyl iodide (7.88 g, 55.5 mmol) in benzene (3.3 mL). The mixture was stirred at room temperature for 5 min, and benzyltriethylammonium chloride (0.42 g, 1.8 mmol) was added. After further stirring at room temperature for 20 min, the organic phase was separated and the aqueous layer was extracted with Et_2O (3 x 50 mL). The organic extracts were combined with the organic phase, washed with water (3 x 50 mL), and dried (Na_2SO_4, 12 hrs). Evaporation of solvent gave the crude product **2** in a purity greater than 98%.

Dimethyl *N*-(2-pyridylmethyl)iminodithiocarbonate (2a), white solid (2.9 g, 74%), mp. 46-47°

(EtOAc-hexane). IR (KBr): 3120, 3060, 1585, 770, 730 cm^{-1}. ^1H NMR: δ 2.47 (s, 3H, SCH_3), 2.58 (s, 3H, SCH), 4.75 (s, 2H, CH_2-N=C), 7.15 (td, 1H, J 6.2, 0.9 Hz, H-5, pyridine ring), 7.57 (dd, 1H, J 7.8 0.6 Hz, H-3, pyridine ring), 7.67 (td, 1H, J 7.8, 1.6, H-4, pyridine ring), 8.54 (dd,1H,J 4.8, 0.9 Hz, H-6, pyridine ring); ^{13}C NMR: δ 14.5 (CH_3, 2 SCH_3), 57.7 (CH_2), 121.3, 121.4 (C-5, C-3, pyridine ring), 136.2 (C-4, pyridine ring), 148.6 (C-6, pyridine ring), 159.9, 160.1 (C-2, C=N, pyridine ring and iminodithiocarbonate group).

Dimethyl *N*-(2-thienylmethyl)iminodithiocarbonate (2b), colorless liquid (2.76 g, 72%). IR (film): 3110, 1585, 920, 710 cm^{-1}. ^1H NMR: δ 2.43 (s, 3H, SCH_3), 2.57 (s, 3H, SCH_3), 4.77 (s, 2H, CH_3), 6.94-6.96 (m, 2H, H-3 and H-4, thiophene ring), 7.11-7.20 (m, 2H, H-1 and H-5, thiophene ring); ^{13}C NMR: δ 14.6 (CH_3, 2 SCH_3), 51.5 (CH), 123.3, 123.8 (C-3, C-4, thiophene ring), 126.4 (C-5,thiophene ring), 144.1 (C-2, thiophene ring), 159.8 (C=N).

Dimethyl *N*-(2-furylmethyl)iminodithiocarbonate (2c), colorless liquid (3.52 g, 85%). IR (film): 3120, 1580, 920, 750 cm^{-1}. ^1H NMR: δ 2.39 (s, 3H, SCH_3), 2.57 (s, 3H, SCH_3), 4.59 (s, 2H, CH_3), 6.23 (dd, 1H, J 3.2, 0.8 Hz, H-3, furan ring), 6.33 (dd, 1H, J 3.2, 2.0 Hz, H-4, furan ring), 7.36 (m, 1H, H-5, furan ring); ^{13}C NMR: δ 14.4 (SCH_3), 14.6 (SCH_3), 49.7 (CH_3), 106.2 (C-4, furan ring), 110.0 (C-3, furan ring), 141.4 (C-5, furan ring), 153.3 (C-2, furan ring), 160.5 (C=N).

Dimethyl *N*-[2-(1-methylpyrrolyl)ethyl]iminodithiocarbonate (2d), colorless liquid (2.28 g, 62%). IR (film): 3120, 3010, 1570, 1500, 730, 720 cm^{-1}. ^1H NMR: δ 2.36 (s, 3H, SCH_3), 2.52 (s, 3H, SCH_3), 2.91 (t, 2H, J 7.8 Hz, CH_2-CH-N=), 3.57 (s, 3H, N-CH_3), 3.64 (t, 2H, J 7.8 Hz, CH_2-N=), 5.93 (m, 1H, H-3, pyrrole ring), 6.04 (t, 1H, J 3.2 Hz, H-4, pyrrole ring), 6.52 (t, 1H, J 2.3 Hz, H-5, pyrrole ring); ^{13}C NMR: δ 14.3 (SCH_3), 14.4 (SCH_3), 27.4 (CH_2CH_2N), 33.5 (N-CH_3), 52.7 (CH_2-N=C), 106.0, 106.4 (C-3, C-4, pyrrole ring), 120.9 (C-5, pyrrole ring), 131.2 (C-2, pyrrole ring), 160.0 (C=N).

Dimethyl *N*-(Ethoxycarbonylmethyl)iminodithiocarbonate (2e), colorless liquid (1.16 g, 39%). IR (film): 1750, 1580, 1020, 900 cm^{-1}. ^1H NMR: δ 1.23 (t, 3H, J 7.14 Hz, CH_3CH_2), 2.40 (s, 3H, SCH_3), 2.54 (s, 3H, SCH_3), 4.17 (q, 2H, J 7.14 Hz, CH_3CH_2), 4.18 (s, 2H, CH_2C=N); ^{13}C NMR: δ 13.4 (CH_3CH_2), 13.7 (SCH_3), 14.0 (SCH_3), 53.3 (CH_2N), 59.9 (CH_2CH_3), 161.9 (C=N), 169.0 (CO_2Et).

Dimethyl *N*-(Phenylmethyl)iminodithiocarbonate (2f), colorless liquid (2.92 g, 74%). IR (film): 3060, 3020, 1580, 1500, 920 cm^{-1}. ^1H NMR: δ 2.35 (s, 3H, SCH_3), 2.46 (s, 3H, SCH_2), 4.46 (s, 2H, CH_2), 7.11 (m, 5H, Ph); ^{13}C NMR: δ 13.9 (2 SCH_3), 55.4 (CH_2), 125.8 (*ortho*-C), 126.8 (*para*-C), 127.5 (*meta*-C), 139.5 (*ipso*-C), 158.3 (C=N).

Dimethyl *N*-[3-(4-Morpholinyl)propyl]iminodithiocarbonate (2g), colorless liquid (2.24 g, 65%). IR (film): 1595, 1155, 1135, 770 cm^{-1}. ^1H NMR: δ 1.80 (quintuplet, 2H, J 6.8 Hz, H-2), 2.29 (s, 3H, SCH_3), 2.38-2.43 (m, 4H, CH_2-N, morpholine ring), 2.48 (s, 3H, SCH_3), 3.36 (t, 2H, J 6.8 Hz, CH_2-N=C), 3.66 (dd, 2H, J 4.8, 4.5 Hz, CH_2-N, morpholine ring); ^{13}C NMR: δ 14.2 (SCH_3), 14.3 (SCH_3), 27.4 ($CH_2CH_2CH_2$), 50.6 (N-CH_2-CH_2-CH_2-N=C), 53.5 (NCH_2, morpholine ring), 56.8 (CH_2-N=C),

66.7 (OCH_2, morpholine ring), 153.7 (C=N).

Dimethyl *N*-Cyclohexyliminodithiocarbonate (2h), colorless liquid (3.24 g, 79%). IR (film): 1595 cm^{-1}. ^1H NMR: δ 1.26-1.46 (m, 6H, H-3, H-4, H-5, cyclohexyl ring), 1.68-1.79 (m, 4H, H-2, H-6, cyclohexyl ring), 2.35 (s, 3H, SCH_3), 2.53 (s, 3H, SCH_3), 3.56-3.65 (m, 1H, H-1, cyclohexyl ring); ^{13}C NMR: δ 14.4 (SCH_3), 4.5 (SCH_3), 24.3 (C-3, cyclohexyl ring), 25.7 (C-4, cyclohexyl ring), 33.1 (C-2, cyclohexyl ring), 61.0 (C-1, cyclohexyl ring), 153.7 C=N).

Dimethyl *N*-(2,2-Dimethoxyethyl)iminodithiocarbonate (2i), colorless liquid (2.87 g, 72%). IR(film): 1600, 1200, 1150, 1110, 1080, 1040, 740 cm^{-1}. ^1H NMR: δ 2.38 (s, 3H, SCH_3), 2.53 (s, 3H, SCH_3), 3.42 (s, 6H, $2OCH_3$), 3.53 (d, 2H, J 5.4 Hz, CH_2N=C), 4.67 (t, 1H, J 5.4 Hz, $CH(OMe)_2$); ^{13}C NMR: δ 14.2 (SCH), 14.4 (SCH_3), 53.7 (OCH_3), 54.9 (CH_2-N=C), 104.3 (CH), 159.6 (C=N).

Dimethyl *N*-Allyliminodithiocarbonate (2j), colorless liquid (4.85 g, 86%). IR(film): 3090, 3020, 1660, 1590, 1010, 930, 770 cm^{-1}. ^1H NMR: δ 2.40 (s, 3H, SCH_3), 2.55 (s, 3H, SCH_3), 4.06 (dt, 2H, J 5.1, 1.8 Hz, CH_2-N), 5.12 (dq, 1H, J 10.2, 1.8 Hz, *trans*-H *versus* CH_3), 5.29 (dq,1H,J 17.1, 1.8, *cis*-H *versus* CH_2), 5.96-6.08 (m, 1H, *gem*-H *versus* CH_2); ^{13}C NMR: δ 14.3 (SCH_3), 14.4 (SCH_3), 54.7 (CH_2), 114.8 (CH_2=), 135.4 (CH), 158.6 (C=N).

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