S,S-Dimethyl Dithiocarbonate: A Convenient Reagent for the Synthesis of Symmetrical and Unsymmetrical Ureas

Man-kit Leung,* Jun-Liang Lai, King-Hang Lau, Hsiao-hua Yu, and Hsiang-Ju Hsiao

Department of Chemistry, National Taiwan University, Taipei, Taiwan, Republic of China

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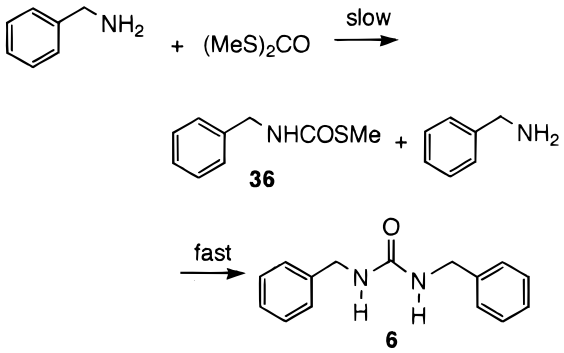
The condensation of primary amines with phosgene or isocyanates is a classic method for the synthesis of organic ureas.[1] However, due to their high toxicity and reactivity, phosgene and isocyanates are difficult to handle in the laboratory. Although several substitutes for phosgene such as triphosgene and carbonyldiimidazole have been developed during the last few decades,[2,3] these reagents are themselves prepared from phosgene. Alternative methods involving drastic reaction conditions, such as direct reactions of amines with dialkyl carbonates at high temperature[4] and the reaction of amines with *N,N′*-diphenylurea in the presence of Et_3N in refluxing DMF,[5] have been reported previously. Our efforts are therefore directed toward the development of mild reagents that can be used instead of phosgene or its derivatives in urea synthesis. Since *S,S*-dimethyl dithiocarbonate (DMDTC) is structurally similar to phosgene and can be prepared from methanol, carbon disulfide, and dimethyl sulfate by a two-step sequence,[6] DMDTC was deemed an appropriate candidate for our investigation. Although dimethyl sulfate is a suspected human carcinogen, the substance is relatively nonvolatile (bp 188 °C) and can be handled safely with care in the laboratory.

To explore the feasibility of using DMDTC in urea synthesis, we first reacted DMDTC with 2 equiv of primary alkyl amines **1**, **3**, and **5** using methanol or ethanol as the solvent at 60 °C and obtained, respectively, the desired symmetrical ureas **2**, **4**, and **6** as the only products (Table 1). No incorporation of methanol or ethanol into the products occurred according to the ^1H NMR analyses. While the above procedure is quite successful for primary alkylamines, we discovered that DMDTC is relatively sensitive to steric environment and the nucleophilicity of the amino group. Thus, α-substituted amines **7** and **9** react with DMDTC at much slower rates. Furthermore, reaction of *tert*-butylamine with DMDTC does not proceed under the same conditions. Although piperidine (**11**) is considered to be a good nucleophile, it only reacts with DMDTC at a moderate rate, affording thiocarbamate **12** as the product. Attempts to extend our procedure to less nucleophilic aromatic amines such as aniline were unsuccessful, resulting in recovery of the starting materials. From the above observations, we concluded that DMDTC is a very selective reagent toward amines. By taking advantage of its selectivity, we successfully obtained the bisaniline **14** directly from DMDTC and 4-aminobenzylamine (**13**) without the need for protection and deprotection procedures. Furthermore, heating DMDTC with 2 equiv of 3-aminopropanol (**15**) in methanol afforded a mixture of bis(3-hydroxypropyl)urea **16** and the cyclic urethane **17** in a ratio of 7:3. More interesting is the fact that **16** is a highly crystalline compound which was readily purified by recrystallization from chloroform. Nevertheless, because of the proximity of the amino group and the hydroxy group, preparation of bis(2-hydroxyethyl)urea (**19**) in methanol was less successful, rendering oxazolidone (**20**) as the major product. Since the product ratio of the symmetrical urea to the cyclic carbamate is dependent on the reaction concentration of the corresponding amino alcohol, we carried out the synthesis at higher concentration, obtaining the desired symmetrical bis(hydroxyalkyl)ureas **16** and **19** in satisfactory yields.

Further experiments with DMDTC (Table 2) revealed that aliphatic amines bearing a hydroxy or an amino substituent at the β or γ position react in dilute solution to provide predominantly cyclic ureas or carbamates. In particular, reaction of (±)-3-aminopropane-1,2-diol (**21**) with DMDTC afforded exclusively 5-(hydroxymethyl)oxazolidin-2-one (**22**), the kinetically favored isomer. On the other hand, 1,3-diamino-2-propanol (**23**) reacted under the same conditions to give **24** as the major product. Also formed was 5-(aminomethyl)oxazolidin-2-one (**25**) as a minor component. We attribute the regioselectivity of the cyclization to the greater nucleophilicity of the amino group, which favors the six-membered ring closure over oxazolidone formation.

In an effort to ascertain the scope of DMDTC application to the synthesis of unsymmetrical ureas, we examined the possibility of preparing *N*-alkyl-*S*-methyl thiocarbamate by mono aminolysis of DMDTC. First, benzylamine was allowed to react with excess DMDTC (1.6 molar equiv), affording *N*-benzyl-*S*-methyl thiocarbamate (**36**) and dibenzylurea (**6**) in a ratio of 1:30. This result implies that the formation of dibenzylurea (**6**) at the second stage of the reaction is faster than *N*-benzyl-*S*-methyl thiocarbamate (**36**) formation from DMDTC. To



prevent thiocarbamate **36** from converting to dibenzylurea, we carried out the reaction under basic conditions, in the course of which **36** should be deprotonated immediately after being formed. Since the anion **37** is relatively stable toward nucleophilic substitution at ambient temperature and will not react further to give

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(2) Staab, H. A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 531.
(3) Eckert, H.; Forster, B. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 894.
(4) Flyes, T. M.; James, T. D.; Pryhitka, A.; Zojsji, M. *J. Org. Chem.* **1993**, *58*, 7456.
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(6) (a) Degani, I.; Fochi, R.; Regondi, V. *Synthesis* **1980**, 375. (b) Degani, I.; Fochi, R.; Regondi, V. *Synthesis* **1981**, 149.

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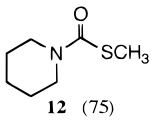
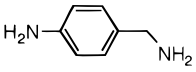
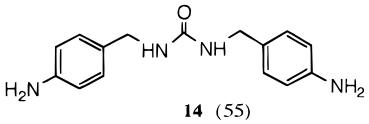
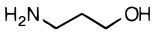
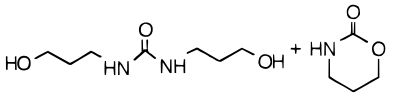
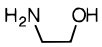
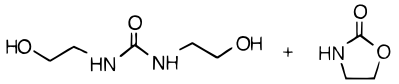
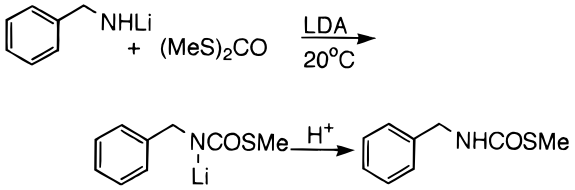
Table 1. Preparation of Symmetrical Ureas from Condensation of Various Amines with DMDTC

$$2RNH_2 + (MeS)_2CO \rightarrow RNHCONHR$$

entry	starting amine	solvent (conc.)[a]	product (yield, %)[b]
1	isobutylamine (**1**)	MeOH (1M)	*N, N'*-diisobutylurea (**2**) (92)
2	allylamine (**3**)	MeOH (1M)	*N, N'*-diallylurea (**4**) (80)
3	benzylamine (**5**)	MeOH (1M)	*N, N'*-dibenzylurea (**6**) (85)
4	1-methylpropylamine (**7**)	no solvent	*N, N'*-bis(1-methylpropyl)urea (**8**) (70)
5	cyclohexylamine (**9**)	no solvent	*N, N'*-dicyclohexylurea (**10**) (65)
6	 **11**	MeOH (1M)	 **12** (75)
7	 **13**	MeOH (1M)	 **14** (55)
8	 **15**		 **16** : **17**
		MeOH (2 M)	70 : 30
		MeOH (4.5 M)	90 : 10
		no solvent	(70)
9	 **18**		 **19** + **20**
		MeOH (0.4 M)	5 : 95
		no solvent	75 (55) : 25

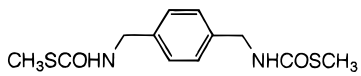
[a] Initial concentration of the starting amine. [b] Isolated yield.

dibenzylurea (**6**), quenching of **37** led to the thiocarbamate **36** in high yield. Further condensation of **36** with



37 **36**

tetrahydrofurfurylamine furnished the unsymmetrical urea **38** (Table 3). This synthetic strategy was extended to the preparation of bisureas, a new class of guest−host molecules that has been developed recently for molecular recognition,[7] by using bisthiocarbamate **39** as the key intermediate.



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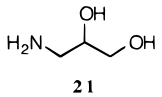
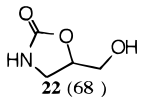
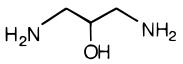
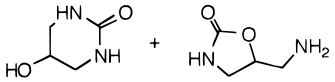
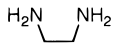
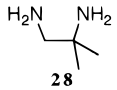
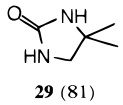
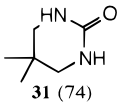
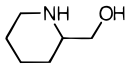
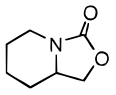
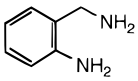
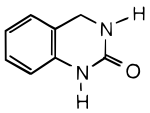
The foregoing methodology offers a new approach to the synthesis of symmetrical and unsymmetrical ureas. It is particularly attractive for the preparation of hydroxy- and amino-substituted ureas that are not easy to obtain by conventional methods. In addition, unsymmetrical ureas have been prepared from DMDTC and two different amines through a two-step sequence. This method is especially useful when the corresponding isocyanates are unavailable.

Experimental Section

Materials. Amines (Aldrich, Janssan, Tokyo Kasei) were commercially available and used as received. *S,S*-Dimethyl dithiocarbonate (DMDTC) was prepared according to the procedures reported in the following section. Carbon disulfide is highly toxic, while benzene and dimethyl sulfate are suspected human carcinogens; these reagents should be handled in a properly ventilated fume hood, and rubber gloves should be worn.

Preparation of *S,S*-Dimethyl Dithiocarbonate (DMDTC). To a suspension of granulated KOH (21.5 g, 0.33 mol) in anhydrous Et_2O and benzene (1:1, 140 mL) was added methanol (10.5 g, 0.33 mmol), followed by dropwise addition of a solution of CS_2 (24.7 g, 0.33 mol) in benzene (15 mL) at 0 °C. The reaction mixture was kept at 0 °C for 5 h, and Me_2SO_4 (41 g, 0.33 mol) was added. The reaction was allowed to react at ambient temperature for 20 h. The organic layer then was decanted, washed sequentially with dilute HCl solution and saturated NaCl solution, dried over anhydrous Na_2SO_4, and

Table 2. Condensation of Various Diamines or Amino Alcohols with DMDTC

entry	starting amine	solvent (conc.)[a]	product (yield, %)[b]
1	 **21**	MeOH (1 M)	 **22** (68)
2	 **23**	MeOH (0.7 M)	 **24** (70) + **25** (< 5)
3	 **26**	MeOH (0.5 M)	 **27** (80)
4	 **28**	MeOH (1M)	 **29** (81)
5	 **30**	MeOH (1M)	 **31** (74)
6	 **32**	no solvent	 **33** (55)
7	 **34**	MeOH (1M)	 **35** (40)

[a] Initial concentration of the starting amine. [b] Isolated yield.

concentrated using simple distillation to afford crude *O,S*-dimethyl dithiocarbonate (39 g). The oily crude product was then subjected to thermal rearrangement at 100−110 °C, using tetrabutylammonium iodide (3 mol %) as a catalyst. After being heated for 18 h, the yellowish crude oil was fractionally distilled under reduced pressure to give DMDTC as a colorless oil (25 g, 58%): bp 60−62 °C (20 mmHg) (lit.[6] bp 58−59 °C, 16 Torr); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.43 (s, 6H) (lit.[6] ^{1}H NMR (CCl_4) δ 2.40 (s, 6H)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.8, 12.7.

Typical Synthetic Procedures for Symmetrical Ureas. *N,N′*-Bis(isobutyl)urea (2) (Method A). To a stirred solution of isobutylamine (**1**) (0.18 g, 2.6 mmol) in methanol (1.5 mL) was added DMDTC (0.16 g, 1.3 mmol). The mixture was heated at 60 °C for 24 h. The released malodorous methyl sulfide by product was absorbed and oxidized by NaOCl solution. When the reaction was complete, the reaction mixture was concentrated under reduced pressure, providing a crude solid which was further purified by recrystallization from methanol−H_2O (1:1) to give **2** as colorless crystals (92%): mp 130−132 °C (lit.[8] 128−130 °C); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.54 (broad triplet, 2H), 2.91 (t, J = 6.1 Hz, 4H), 1.72−1.56 (m, 2H), 0.84 (d, J = 6.6 Hz, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 47.7, 29.0, 20.1; IR (KBr) cm^{-1} 3347, 1623, 1572; MS (EI, 70 eV) *m/e* 172 (M^+, 100), 157 ($M^+ - CH_3$, 20), 129 ($M^+ - C_3H_7$, 25), 72 (29), 58 (81); HRMS calcd for $C_9H_{20}N_2O$ 172.1576, obsd 172.1573. Anal. Calcd for $C_9H_{20}N_2O$: C, 62.75; H, 11.70; N: 16.26. Found: C, 62.49; H, 11.67; N; 16.21.

***N,N′*-Diallylurea (4):** colorless crystals; mp 93−95 °C (lit.[9] mp 92−94 °C).

***N,N′*-Dibenzylurea (6).** Recrystallization from $CHCl_3$−hexane yielded **6** as colorless crystals: mp 166−168 °C (lit.[10] mp 167−170 °C).

***N,N′*-Cyclohexylurea (10).** Recrystallization from MeOH yielded **10** as colorless crystals: mp 230−231 °C (lit.[1b] mp 229−230 °C from MeOH).

***S*-Methyl 1-Piperidinecarbothioate (12).** Flash chromatography on silica gel, using MeOH−CH_2Cl_2 (1:7) as the eluent, afforded **12** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.52−3.40 (m, 4H), 2.32 (s, 3H), 1.70−1.49 (m, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.1, 45.7 (broad peak), 25.6, 24.4, 12.8; IR (neat, NaCl) cm^{-1} 1734; MS (EI, 70 eV) *m/e* 159 (M^+, 28), 112 ($M^+ - CH_3S$, 81), 69 (100); HRMS (EI, 70 eV) calcd for $C_7H_{13}NOS$ 159.0719, obsd 159.0722.

***N,N′*-Bis(4-aminobenzyl)urea (14).** Flash chromatography on silica gel, using MeOH−$CHCl_3$ (1:20) as the eluent afforded **14** as colorless crystals: mp 200−202 °C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 6.90 (d, J = 8.2 Hz, 4H), 6.50 (d, J = 8.2 Hz, 4H), 6.04 (broad triplet, 5.6 Hz, 2H), 4.90 (bs, 4H), 4.02 (d, J = 5.6 Hz, 4H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 158.2, 147.4, 128.2, 127.8, 113.9, 43.0; IR (KBr) cm^{-1} 3416, 3318, 1606, 1560; MS (EI, 70 eV) *m/e* 270 (M^+, 40), 177 (32), 164 (61), 121 (100), 106 (45), 94 (20); HRMS (EI, 70 eV) calcd for $C_{15}H_{18}N_4O$ 270.1480, obsd 270.1479. Anal. Calcd for $C_{15}H_{18}N_4O$: C, 66.64; H, 6.71; N, 20.72. Found: C, 66.34; H, 6.67; N, 20.59.

***N,N′*-Bis(2-hydroxyethyl)urea (19) (Method B).** Excess ethanolamine and DMDTC were mixed and heated at 60 °C for 15 h. The released malodorous methyl sulfide by product was absorbed and oxidized by NaOCl solution. When the reaction was complete, the unreacted ethanolamine was removed under reduced pressure by simple distillation, providing a crude

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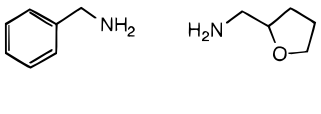
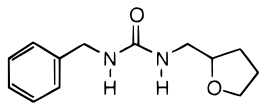
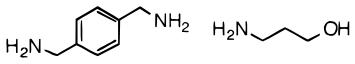
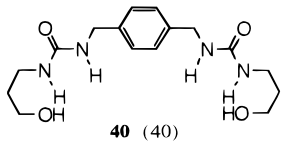
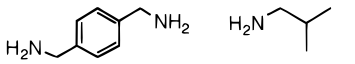
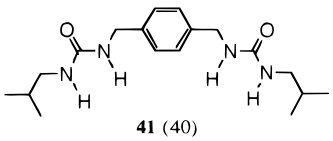
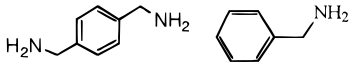
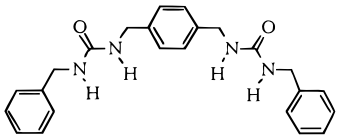
(9) Laufer, D. A.; Al-Farhan, E. *J. Org. Chem.* **1991**, *56*, 891.
(10) Pihuleac, J.; Bauer, L. *Synthesis* **1989**, 61.

Table 3. Preparation of Unsymmetrical Ureas from DMDTC

$$R^1NHLi + (MeS)_2CO \xrightarrow[(2)\ H^+]{(1)\ LDA} R^1NHCOSMe \xrightarrow{R^2NH_2} R^1NHCONHR^2$$

entry	R^1NH_2	R^2NH_2	product (yield, %)[a]
1			 **38** (65)
2			 **40** (40)
3			 **41** (40)
4			 **42** (43)

[a] Overall isolated yield.

mixture of oxazolidone and bis(2-hydroxyethyl)urea which was further purified by recrystallization from methanol−ethyl acetate (1:4.5) to give **19** as colorless crystals: mp 82−84 °C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 5.96 (broad triplet, 2H), 4.62 (bs, 2H), 3.33 (bs, 4H), 3.02 (q, J = 6 Hz, 4H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.4, 60.8, 42.1; IR (KBr) cm^{-1} 3343, 1621; MS (EI, 70 eV) *m/e* 149 (M^+ + H, 5), 148 (M^+, 2), 118 (100), 117 (60), 70 (40); HRMS (EI, 70 eV) calcd for $C_5H_{12}N_2O_3$ 148.0848, obsd 148.0842. Anal. Calcd for $C_5H_{12}N_2O_3$: C, 40.53; H, 8.17; N, 18.91. Found: C, 40.08; H, 8.16; N, 18.78.

***N,N′*-Bis(3-hydroxypropyl)urea (16).** Recrystallization from MeOH−$CHCl_3$ provided **16** as colorless crystals: mp 83−86 °C (lit.[4] mp 93−94 °C from CH_3CN); ^{1}H NMR (200 MHz, DMSO-d_6) δ 5.82 (t, J = 6.0 Hz, 2H), 4.00−4.50 (bs, 2H), 3.38 (t, J = 6.0 Hz, 4H), 3.00 (q, J = 6 Hz, 4H), 1.48 (quintet, J = 6 Hz, 4H) (lit.[4] ^{1}H NMR (90 MHz, D_2O) δ 3.5 (t, J = 7.0 Hz, 4H), 3.1 (q, J = 7 Hz, 4H), 1.6 (m, 4H)); ^{13}C NMR (50 MHz, DMSO-d_6) δ 158.5, 58.4, 36.4, 33.2 (lit.[4] ^{13}C NMR (62.89 MHz, D_2O) δ 160.7, 59.2, 36.7, 31.8); IR (KBr) cm^{-1} 3339 (br), 1613, 1584; MS (EI, 70 eV) *m/e* 176 (M^+, 20), 146 (65), 132 (90), 102 (40), 74 (100), 57 (91); HRMS (EI, 70 eV) calcd for $C_7H_{16}N_2O_3$ 176.1161, obsd 176.1155.

***N,N′*-Bis(1-methylpropyl)urea (8).** Recrystallization from $CHCl_3$−hexane yielded **8** as colorless crystals: mp 131−132.5 °C (lit.[8] mp 135 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.30 (bs, 2H), 3.62 (m, 2H), 1.48 (m, 4H), 1.07 (d, J = 6.7 Hz, 6H), 0.87 (t, J = 7.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.6, 47.3, 30.3, 21.0, 10.3; IR (KBr) cm^{-1} 3339 (br), 1613, 1584; MS (EI, 70 eV) *m/e* 172 (M^+, 12), 143 ($M^+ - C_2H_5$, 63), 72 (20), 58 (100); HRMS (EI, 70 eV) calcd for $C_9H_{20}N_2O$ 172.1576, obsd 172.1573. Anal. Calcd for $C_9H_{20}N_2O$: C, 62.74; H, 11.70; N, 16.26. Found: C, 62.49; H, 11.57; N, 16.39.

Typical Synthetic Procedures for Cyclic Ureas and Carbamates. **5-(Hydroxymethyl)oxazolidin-2-one (22).** To a stirred solution of 3-aminopropane-1,2-diol (**21**) in methanol was added DMDTC. After being heated at 60 °C for 24 h, the reaction mixture was concentrated under reduced pressure, providing a crude oil which was further purified by flash chromatography, using MeOH−CH_2Cl_2 (1:10) as the eluent to give **22** as colorless oil: ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.38 (bs, 1H), 5.06 (t, J = 5.6 Hz, 1H), 4.45−4.57 (m, 1H), 3.33−3.58 (m, 3H), 3.21 (dd, J = 8.4, 6.6 Hz, 1H) (lit.[9] ^{1}H NMR (CD_3OD) δ 4.8 (bs, 2H), 4.6 (m, 1H), 3.25−3.80 (m, 4H)); ^{13}C NMR (50 MHz, DMSO-d_6) δ 159.4, 76.4, 62.3, 41.6 (lit.[11] ^{13}C NMR (CD_3OD) δ 78.5, 63.5, 42.9); IR (KBr) cm^{-1} 3320 (br), 3297, 1731; MS (EI, 20 eV) *m/e* 118 (M^+ + H, 5), 100 (M^+ − OH, 24), 86 ($M^+ - CH_2$-OH, 100); HRMS (EI, 70 eV) calcd for $C_4H_7NO_3$ 117.0426, obsd 117.0420.

Tetrahydro-5-hydroxy-2(1*H*)-pyrimidinone (24). Recrystallization of the crude product from MeOH−acetone afforded **24** as colorless crystals: mp 210−213 °C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 6.16 (bs, 2H), 5.07 (d, J = 4 Hz, 1H), 3.79−3.82 (m, 1H), 3.05−3.20 (m, 2H), 2.80−3.00 (m, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 156.1, 60.4, 46.2; IR (KBr) cm^{-1} 3344, 3297, 3217, 1645; MS (EI, 20 eV) *m/e* 116 (M^+, 90), 88 (30), 59 (100); HRMS (EI, 70 eV) calcd for $C_4H_8N_2O_2$ 116.0586, obsd 116.0583. Anal. Calcd for $C_4H_8N_2O_2$: C, 41.37; H, 6.94; N, 24.13. Found: C, 41.03; H, 6.84; N, 23.99.

4,4-Dimethyl-2-imidazolidinone (29). Recrystallization from CH_2Cl_2−hexane (4:1) afforded **29** as colorless crystals: mp 139−141 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.63 (bs, 2H), 3.20 (s, 2H), 1.33 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.5. 54.9, 53.8, 28.1; IR (KBr) cm^{-1} 3281, 1704, 1688; MS (EI, 70 eV) *m/e* 114 (M^+, 10), 99 (100), 56 (30); HRMS (EI, 70 eV) calcd for $C_5H_{10}N_2O$ 114.0793, obsd 114.0787. Anal. Calcd for $C_5H_{10}N_2O$: C, 52.61; H, 8.83; N, 24.54. Found: C, 52.28; H, 8.81; N: 24.42.

Tetrahydro-5,5-dimethyl-2(1*H*)-pyrimidinone (31). Recrystallization of **31** from CH_2Cl_2−hexane afforded colorless crystals: mp 254−256 °C (lit.[12] 255−257 °C); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.19 (bs, 2H), 2.94 (d, J = 2.2 Hz, 4H), 1.05 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 157.0, 52.3, 28.3, 24.7; IR (KBr) cm^{-1} 3228, 1697; MS (EI, 70 eV) *m/e* 128 (M^+, 70), 113 ($M^+ - CH_3$), 56 (100); HRMS (EI, 70 eV) calcd for $C_6H_{12}N_2O$ 128.0950, obsd 128.0950. Anal. Calcd for $C_6H_{12}N_2O$: C, 56.23; H, 9.44; N, 21.86. Found: C, 55.96; H, 9.40; N, 21.76.

Hexahydro-3*H*-oxazolo[3,4-*a*]pyridin-3-one (33). Flash chromatography on silica gel, using MeOH−CH_2Cl_2 as the

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eluent, yielded **33** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.38 (t, 8.1 Hz, 1H), 3.88−3.96 (m, 2H), 3.50−3.70 (m, 1H), 2.90−2.70 (m, 1H), 1.78−1.98 (m, 2H), 1.66−1.75 (m, 1H), 1.20−1.55 (m, 3H) (lit.[13] ^{1}H NMR (neat) δ 4.8 (m, 1H), 4.2 (m, 3H), 3.25 (m, 1H), 2.1 (m, 6H)); ^{13}C NMR (50 MHz, $CDCl_3$) δ 156.8, 67.9, 54.2, 41.1, 30.2, 24.0, 22.3; IR (neat, NaCl) cm^{-1} 1739; MS (EI, 70 eV) *m/e* 141 (M^+, 100), 126 (20), 97(30), 83 (95), 69 (40), 55 (55); HRMS (EI, 70 eV) calcd to $C_7H_{11}NO_2$ 141.0790, found 141.0799.

3,4-Dihydro-2(1*H*)-quinazolinone (35). Recrystallization of **35** from MeOH−CH_2Cl_2 led to colorless crystals: mp 222−223 °C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.98 (bs, 1H), 7.03−7.14 (m, 2H), 6.78−6.87 (m, 3H), 4.28 (s, 2H) (lit.[14] ^{1}H NMR (DMSO-d_6) δ 9.08 (bs, 1H), 6.80−7.50 (m, 5H), 4.40 (s, 2H)); ^{13}C NMR (50 MHz, DMSO-d_6) δ 154.8, 138.3, 127.8, 125.9, 121.1, 118.3, 113.7, 42.7; IR (KBr) cm^{-1} 3248, 1718; MS (EI, 70 eV) *m/e* 148 (M^+, 100), 147 (M^+ − H, 90), 104 (20); HRMS (EI, 70 ev) calcd for $C_8H_8N_2O$ 148.0637, obsd 148.0638. Anal. Calcd for $C_8H_8N_2O$: C, 64.85; H, 5.54; N: 18.91. Found: C, 64.68; H: 5.42; N: 18.90.

Typical Synthetic Procedures for *S*-methyl *N*-Alkylthiocarbamates. *S*-Methyl *N*-Benzylthiocarbamate (36). To a solution of benzylamine (0.93 g, 0.87 mmol) and diisopropylamine (0.89 g, 8.8 mmol) in THF (20 mL) at −78 °C under nitrogen atmosphere was added *n*-BuLi (1.6 M, 10.9 mL, 17.5 mmol) in hexane. After addition, the solution was stirred at -78 °C for 0.5 h, followed by addition of a solution of DMDTC (1.07 g, 8.8 mmol). The solution was then allowed to react at room temperature for 20 h. The reaction was quenched by pouring it into a mixture of ice−dilute HCl solution. The crude solid was dissolved into EtOAc, washed with aqueous Na_2CO_3 and brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and recrystallized from hexane to provide **36** as colorless crystals (0.95 g, 62%): mp 76−79 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20−7.34 (m, 5H), 5.67 (bs, 1H), 4.45 (d, J = 6 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 137.7, 128.45, 127.4, 127.3, 45.1, 12.2; IR (KBr) cm^{-1} 3305, 1639; MS (EI, 70 eV) 181 (M^+, 30), 133 (30), 91 (100); HRMS (EI, 70 eV) calcd for $C_9H_{11}NOS$ 181.0562, obsd 181.0559. Anal. Calcd for $C_9H_{11}NOS$: C, 59.64; H, 6.12; N, 7.73. Found: C, 59.65; H, 6.12; N, 7.78.

***S*-Methyl *N,N′*-(*p*-Xylylene)bis(thiocarbamate) (39).** Recrystallization from EtOAc−hexane yielded **39** as colorless crystals: mp 201−203 °C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.64 (broad triplet, J = 6.0 Hz, 2H), 7.17 (s, 4H), 4.25 (d, J = 6.0 Hz, 4H), 2.20 (s, 6H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 166.4, 137.8, 127.3, 43.7, 11.6; IR (KBr) cm^{-1} 3244, 1629; MS (EI, 70 eV) 284 (M^+, 1), 236 (10), 193 (46), 188 (16), 180 (37), 146 (100), 91 (48); HRMS (EI, 70 eV) calcd for $C_{12}H_{16}N_2O_2S_2$ 284.0653, obsd 284.0652. Anal. Calcd for $C_{12}H_{16}N_2O_2S_2$: C, 50.70; H, 5.68; N, 9.86. Found: C, 51.30; H, 5.74; N, 9.70.

Typical Synthetic Procedures for Unsymmetrical Ureas from *S*-Methyl *N*-Alkylthiocarbamates. *N*-Benzyl-*N′*-tetrahydrofurfurylurea (38). To a stirred solution of *S*-methyl *N*-benzylthiocarbamate **(36)** (0.11 g, 0.63 mmol) in methanol (2 mL) was added tetrahydrofurfurylamine (0.12 g, 1.1 mmol). After being heated at 60 °C for 24 h, the reaction mixture was concentrated under reduced pressure, providing a crude solid. Recrystallization of the solid from $CHCl_3$−hexane gave **38** as colorless crystals (0.14 g, 88%): mp 78−80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18−7.30 (m, 5H), 5.86 (broad triplet, 1H), 5.55 (broad triplet, 1H), 4.27 (d, J = 6 Hz, 2H), 3.90 (m, 1H), 3.60−3.80 (m, 2H), 3.39 (m, 1H), 3.03 (m, 1H), 1.75-1.95 (m, 3H), 1.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 139.3, 128.5, 127.4, 127.2, 78.8, 68.0, 44.5, 44.4 28.2, 25.9; IR (KBr) cm^{-1} 3339, 1615; MS (EI, 70 eV) 234 (M^+, 31), 190 (17), 164 (40), 151 (20), 106 (58), 91 (80), 71 (100); HRMS calcd for $C_{13}H_{18}N_2O_2$ 234.136, obsd 234.1369. Anal. Calcd for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.95. Found: C, 66.67; H, 7.75; N, 11.93.

***N,N″*-(*p*-Xylylene)bis[*N′*-(3-hydroxypropyl)urea] (40).** Recrystallization of **40** from DMSO−EtOAc afforded colorless crystals: mp 219−221 °C dec; ^{1}H NMR (200 MHz, DMSO-d_6) δ 7.16 (s, 4H), 6.28 (t, J = 6.0 Hz, 2H), 5.89 (t, J = 6.0 Hz, 2H), 4.45 (t, J = 6.0 Hz, 2H), 4.15 (d, J = 6.0 Hz, 4H), 3.35−3.42 (q, J = 6.0 Hz, 4H), 3.05 (q, J = 6.0 Hz, 4H), 1.50 (quintet, J = 6.0 Hz, 4H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.2, 139.2, 126.9, 58.4, 42.7, 36.4, 33.2; IR 3325, 1606, 1574; FAB (NBA) 339.2 (M^+ + H). Anal. Calcd for $C_{14}H_{22}N_4O_4$: C, 56.78; H, 7.74; N, 16.55. Found: C, 56.55; H, 7.87; N, 16.50.

***N,N″*-(*p*-Xylylene)bis[*N′*-(2-methylpropyl)urea] (41).** Recrystallization from DMSO−EtOAc afforded **41** as colorless crystals: mp 237−240 °C dec; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.15 (s, 4H), 6.19 (broad triplet, 2H), 5.92 (broad triplet, 2H), 4.14 (d, J = 6 Hz, 4H), 2.82 (t, J = 6 Hz, 4H), 1.60 (m, 2H), 0.81 (d, J = 6.6 Hz, 12 H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 158.1, 139.2, 126.9, 46.8, 42.6, 28.6, 20.0; IR (KBr) cm^{-1} 3318, 1613, 1562; FAB (NBA) 335.2 (M^+ + H). Anal. Calcd for $C_{18}H_{30}N_4O_2$: C, 64.64; H, 9.04; N, 16.75. Found: C, 64.36; H, 8.97; N, 16.70.

***N,N″*-(*p*-Xylylene)bis(*N′*-benzylurea) (42).** Recrystallization from DMSO−EtOAc afforded **42** as colorless crystals: mp 258−261 °C dec; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.20−7.33 (m, 10H), 7.17 (s, 4H), 6.39 (m, 4H), 4.21 (d, J = 6 Hz, 4H), 4.19 (d, J = 6 Hz, 4H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 158.0, 140.9, 139.2, 128.2, 128.1, 127.0, 126.6, 42.9, 42.7; IR (KBr) cm^{-1} 3319, 1619; FAB (NBA) 403.2 (M^+ + H). Anal. Calcd for $C_{24}H_{26}N_4O_2$: C, 71.62; H, 6.51; N, 13.91. Found: C, 71.52; H, 6.50; N, 13.90.

Acknowledgment. We thank the National Science Council of the Republic of China for the financial support (NSC 85-2113-M-002-013 and NSC 85-2815-C002-01-010M).

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of DMDTC and compounds **4**, **6**, **8**, **12**, **14**, **16**, **19**, **22**, **24**, **29**, **31**, **33**, **35**, **36**, and **38**−**42** (38 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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