A Facile Synthesis of Bis(4-amino-5-mercapto-1,2,4-triazol-3-yl)alkanes and Bis(5-mercapto-4*H*-1,2,4-triazol-3-yl)alkanes†

J. Chem. Research (S), 1999, 170–171†

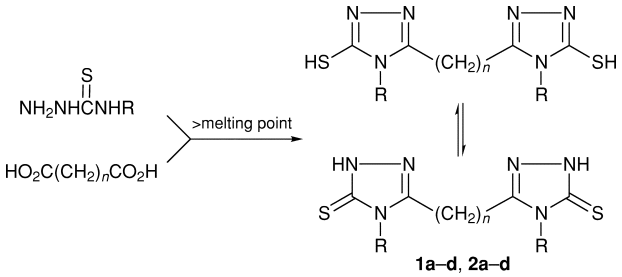
Peng-Fei Xu,* Xiao-Wen Sun, Lin-Mei Zhang and Zi-Yi Zhang

Department of Chemistry, Lanzhou University, Lanzhou 730000, P.R. China

The facile preparation of bis(4-amino-5-mercapto-1,2,4-triazol-3-yl)alkanes **1a–d** and bis(5-mercapto-4*H*-1,2,4-triazol-3-yl)alkanes **2a–d** in one-step is described.

In recent years, attention has been increasingly paid to the synthesis of bisheterocyclic compounds which exhibit various biological activities[1–4] including antibacterial, fungicidal, tuberculostatic and plant growth regulative properties. Our earlier work[5] revealed that bisheterocyclic compounds displayed much better antibacterial activity than heterocyclic compounds. Mohan *et al.*[6] and Dubey and Sangwan[7] prepared bis(4-amino-5-mercapto-1,2,4-triazol-3-yl)phenylenes from benzenedicarboxylic acids following the method of Reid and Heindel, which involved the condensation of dicarboxylic acid hydrazides and carbon disulfide and potassium hydroxide to yield the potassium dithiocarbazates and then performing ring closure with an excess of hydrazine hydrate. The traditional synthetic route to 3-substituted 5-mercapto-4*H*-1,2,4-triazoles involved the initial reaction of acid hydrazides and potassium thiocyanate and the subsequent intramolecular cyclization of the formed substituted thiosemicarbazides in refluxing sodium hydroxide solution. In the present paper we describe a facile one-step synthesis of bis(4-amino-5-mercapto-1,2,4-triazol-3-yl)alkanes **1a–d** and bis(5-mercapto-4*H*-1,2,4-triazol-3-yl)alkanes **2a–d**.

The one-step reaction between aliphatic dicarboxylic acids and two molar equivalents of thiocarbohydrazide at the melting temperature for 30 min afforded bis(4-amino-5-mercapto-1,2,4-triazol-3-yl)alkanes **1a–d** in good yields (Scheme 1). In comparison with the Reid and Heindel procedure, this method avoids the many steps for preparing the starting materials and leads to higher overall yields and shorter working time. As would be anticipated, the corresponding bis(5-mercapto-4*H*-1,2,4-triazol-3-yl)alkanes **2a–d** were obtained by directly treating aliphatic dicarboxylic acids with thiosemicarbazide following this procedure. Structure elucidation of **1a–d** and **2a–d** was accomplished on the basis of their elemental analyses and spectral data. Their IR spectra showed a characteristic absorption band in the region 3080–3286 cm^{-1} due to N–H stretching vibration. The presence of an absorption band in the range 1220–1265 cm^{-1} corresponding to C=S function confirmed



Scheme 1 $n = 1$–4; R = NH_2 **1a–d**, R = H **2a–d**

that they existed preferably in the thione rather than in the thiol forms. The ^{1}H NMR spectra of **1a–d** displayed two singlets for NH and NH_2 protons at δ 13.46–13.62 and 5.33–5.51, respectively. However, in the ^{1}H NMR spectra of **2a–d** the four NH protons appeared as two singlets at δ 13.20–13.37 and 13.08–13.25, respectively. Their mass spectra showed the expected molecular peaks in high intensity.

Experimental

Melting points were determined on a Kofler melting point apparatus and are uncorrected. Elemental analyses were carried out on a 1106 analyzer. IR spectra were obtained in KBr disc on a Nicolet FT-IR 170SX spectrometer. MS were taken on a HP-5988A instrument (EI at 70 eV) or Zabspec Tofspec Platform-ESI instrument (FAB). ^{1}H NMR spectra [$(CD_3)_2SO$] were performed on a Bruker FT-AC 80 spectrometer.

General Procedure for the Preparation of Bis(4-*amino*-5-*mercapto*-1,2,4-*triazol*-3-*yl*)*alkanes* (**1a–d**).—A mixture of aliphatic dicarboxylic acid (0.01 mol) and thiocarbohydrazide (0.02 mol) was warmed carefully until melting occurred and then it was kept at 170 °C for 30 min. The reaction mixture was then cooled and mixed with water (50 ml). The precipitate was filtered off, washed with water and 95% ethanol, and finally recrystallized from DMF.

General Procedure for the Preparation of Bis(5-*mercapto*-4H-1,2,4-*triazol*-3-*yl*)*alkanes* (**2a–d**).—A mixture of aliphatic dicarboxylic acid (0.01 mol) and thiosemicarbazide (0.02 mol) was warmed carefully until melting occurred and then it was kept at 180 °C for 1 h. The reaction mixture was cooled and mixed with water (50 ml). The precipitate was filtered off, washed with carbon disulfide and finally recrystallized from DMF.

Table 1 Preparation and analytical data of compounds **1** and **2**

Compound	Yield (%)	Mp/°C	Formula	Found (required) (%)		
				C	H	N
1a	80	>300	$C_5H_8N_8S_2$	24.72 (24.59)	3.31 (3.28)	45.62 (45.90)
1b	83	220–221	$C_6H_{10}N_8S_2$	28.02 (27.91)	4.00 (3.88)	43.11 (43.41)
1c	70	201–203	$C_7H_{12}N_8S_2$	30.69 (30.88)	4.70 (4.41)	41.01 (41.18)
1d	75	221–222	$C_8H_{14}N_8S_2$	33.50 (33.57)	5.12 (4.90)	38.88 (39.16)
2a	56	288–290	$C_5H_6N_6S_2$	27.86 (28.04)	2.93 (2.80)	39.70 (39.25)
2b	57	>300	$C_6H_8N_6S_2$	31.34 (31.58)	3.60 (3.51)	37.06 (36.84)
2c	46	>300	$C_7H_{10}N_6S_2$	34.68 (34.71)	4.14 (4.13)	34.86 (34.71)
2d	62	>300	$C_8H_{12}N_6S_2$	37.28 (37.50)	4.48 (4.69)	32.94 (32.81)

*To receive any correspondence.

†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 2 Spectral data of compounds **1** and **2**

Compound	IR (KBr, cm^{-1})	^1H NMR [$(CD_3)_2SO$, ppm]	MS (*m/z*, %)
1a	3256, 3119 (N–H), 1625 (C=N), 1230 (C=S)	13.62 (s, 2H, 2NH), 5.33 (s, 4H, $2NH_2$), 4.03 (s, 2H, CH_2)	
1b	3286, 3156 (N–H), 1614 (C=N), 1246 (C=S)	13.62 (s, 2H, 2NH), 5.47 (s, 4H, $2NH_2$), 3.07 (s, 4H, $2CH_2$)	258 (EI, M^+, 19)
1c	3266, 3159 (N–H), 1618 (C=N), 1241 (C=S)	13.51 (s, 2H, 2NH), 5.40 (s, 4H, $2NH_2$), 2.71 (m, 4H, $2CH_2$), 2.00 (m, 2H, CH_2)	272 (EI, M^+, 100)
1d	3247, 3118 (N–H), 1613 (C=N), 1234 (C=S)	13.46 (s, 2H, 2NH), 5.51 (s, 4H, $2NH_2$), 2.66 (m, 4H, $2CH_2$), 1.69 (m, 4H, $2CH_2$)	286 (EI, M^+, 100)
2a	3080 (N–H), 1587 (C=N), 1265 (C=S)	13.37 (s, 2H, 2NH), 13.25 (s, 2H, 2NH), 3.88 (s, 2H, CH_2)	215 (FAB, M + 1, 100)
2b	3101 (N–H), 1597 (C=N), 1222 (C=S)	13.25 (s, 2H, 2NH), 13.09 (s, 2H, 2NH), 2.68 (s, 4H, $2CH_2$)	
2c	3104 (N–H), 1602 (C=N), 1220 (C=S)	13.22 (s, 2H, 2NH), 13.08 (s, 2H, 2NH), 2.55 (m, 4H, $2CH_2$), 1.93 (m, 2H, CH_2)	
2d	3104 (N–H), 1597 (C=N), 1221 (C=S)	13.20 (s, 2H, 2NH), 13.08 (s, 2H, 2NH), 2.72 (m, 4H, $2CH_2$), 1.59 (m, 4H, $2CH_2$)	

This project (No. 29802004) was supported by the National Natural Science Foundation of P.R. China and Gansu Province Natural Science Foundation.

Received, 28th October 1998; Accepted, 19th November 1998
Paper E/8/08351G

References

1 H. Singh, L. D. S. Yadav and B. K. Bhattacharya, *J. Indian Chem. Soc*., 1979, **56**, 1013.
2 N. C. Desai, *Indian J. Chem., Sect. B*, 1993, **32**, 343.
3 X. M. Feng, R. Chen, X. C. Liu and Z. Y. Zhang, *Chin. J. Appl. Chem*., 1991, **8**, 28.
4 P. S. Upadhyay, R. N. Vansdadia and A. J. Baxi, *Indian J. Chem. Sect. B*, 1990, **29**, 793.
5 Z. Y. Zhang, X. Chen, L. L. Wei and Z. L. Ma, *Chem. Res. Chin. Univ*., 1991, **7**, 129.
6 J. Mohan, G. S. R. Anjaneyulu, S. Sudhir and D. R. Arora, *J. Indian Chem. Soc*., 1989, **66**, 330.
7 A. K. Dubey and N. K. Sangwan, *Indian J. Heterocycl. Chem*., 1994, **3**, 277.