Selective Lithiation of Bis(azol-1-yl)methanes

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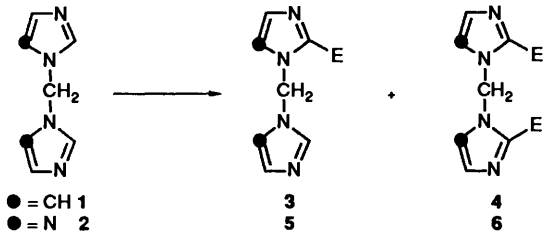
Lithiation of bis(azol-1-yl)methanes and subsequent reaction with electrophiles yields selectively mono- and di-ring-substituted derivatives. The regioselectivity observed is explained in terms of the structure of the substrate, the hard and soft acids and bases principle, and the nature of the electrophile used.

Bis(azol-1-yl)methanes **1**, **2** and **7**, are widely used as complexation agents. The presence of substituents in the ring or on the bridge provides interesting modifications in the structure of the formed complexes.[1,2] Direct incorporation of substituents may be performed by lithiation and subsequent reaction with electrophiles.[3,4] Lithiation of 1-benzylimidazole and 1-benzyl-1,2,4-triazole has been reported.[5,6] The incorporation of electrophiles occurs at the ring positions. However, electrophiles for which pentaco-ordination is required in the transition state (for instance, benzyl chloride) are incorporated at the benzylic methylene. Deprotonation of bis(pyrazol-1-yl)methane with butyllithium or lithium diisopropylamide (LDA) at 25 °C and subsequent reaction with electrophiles yield ring- or bridge-substituted derivatives depending on the electrophile and the nature of the base.[7]

The aim of this paper is the study of the lithiation of bis(imidazol-1-yl)methane **1**, bis(1,2,4-triazol-1-yl)methane **2** and bis(pyrazol-1-yl)methane **7** and the subsequent reaction with methyl iodide, dimethyl disulfide, trimethylsilyl chloride and paraformaldehyde.

Results and Discussion

Reactions were performed in two steps: deprotonation with butyllithium at 0 °C for 1 h and subsequent reaction with the electrophile at room temperature for 14 h. Results are gathered in Tables 1 and 2. Bis(imidazol-1-yl)methane **1** and bis(1,2,4-triazol-1-yl)methane **2** afford exclusively ring-substitution products (Table 1 and Scheme 1). However, bis(pyrazol-1-yl)methane **7** affords seven of the eight possible products, their nature and proportions depending on the electrophile used (Table 2 and Scheme 2).



E: **a**; Me; **b**; SMe; **c**; $SiMe_3$; **d**; CH_2OH

Scheme 1

The regioselectivity observed is explained by considering the structure of the substrate. Position 5 in bis(pyrazol-1-yl)-methane **7** is α-activated by N-1, position 5 in bis(1,2,4-triazol-1-yl)methane **2** is α-activated by both N-2 and N-4, while position 2 in bis(imidazol-1-yl)methane **1** is activated by both N-1 and N-3. Moreover, the 'benzylic' positions in compounds **2** and **7** are β-activated by N-2 (Fig. 1). Thus, bis(1,2,4-triazol-1-yl)methane **2** presents an intermediate situation between those of substrates **1** and **7**.

Table 1 Reactions of compounds **1** and **2**

Entry	Electrophile	1 or 2:BuLi:E	3 (%)[a]	4 (%)[a]	5 (%)[a]	6 (%)[a]
1	MeI	1:1:1	53	31	56	25
2	MeI	1:2.1:2.1	0	100	11	77
3	MeSSMe	1:1:1	57	14	67	14
4	MeSSMe	1:1:1[b]	58	12		
5	MeSSMe	1:1:1[c]	50	16		
6	MeSSMe	1:2.4:2.4	12	75	20	79
7	Me_3SiCl	1:1:1	57	43	80	0
8	Me_3SiCl	1:2.1:2.1	38	62	23	77
9	$(H_2CO)_n$	1:1:1	55	12	39	15
10	$(H_2CO)_n$	1:2.1:2.1	36	64	33	67

[a] Determined by ^1H NMR spectroscopy. [b] Base, LDA. [c] At 60 °C.

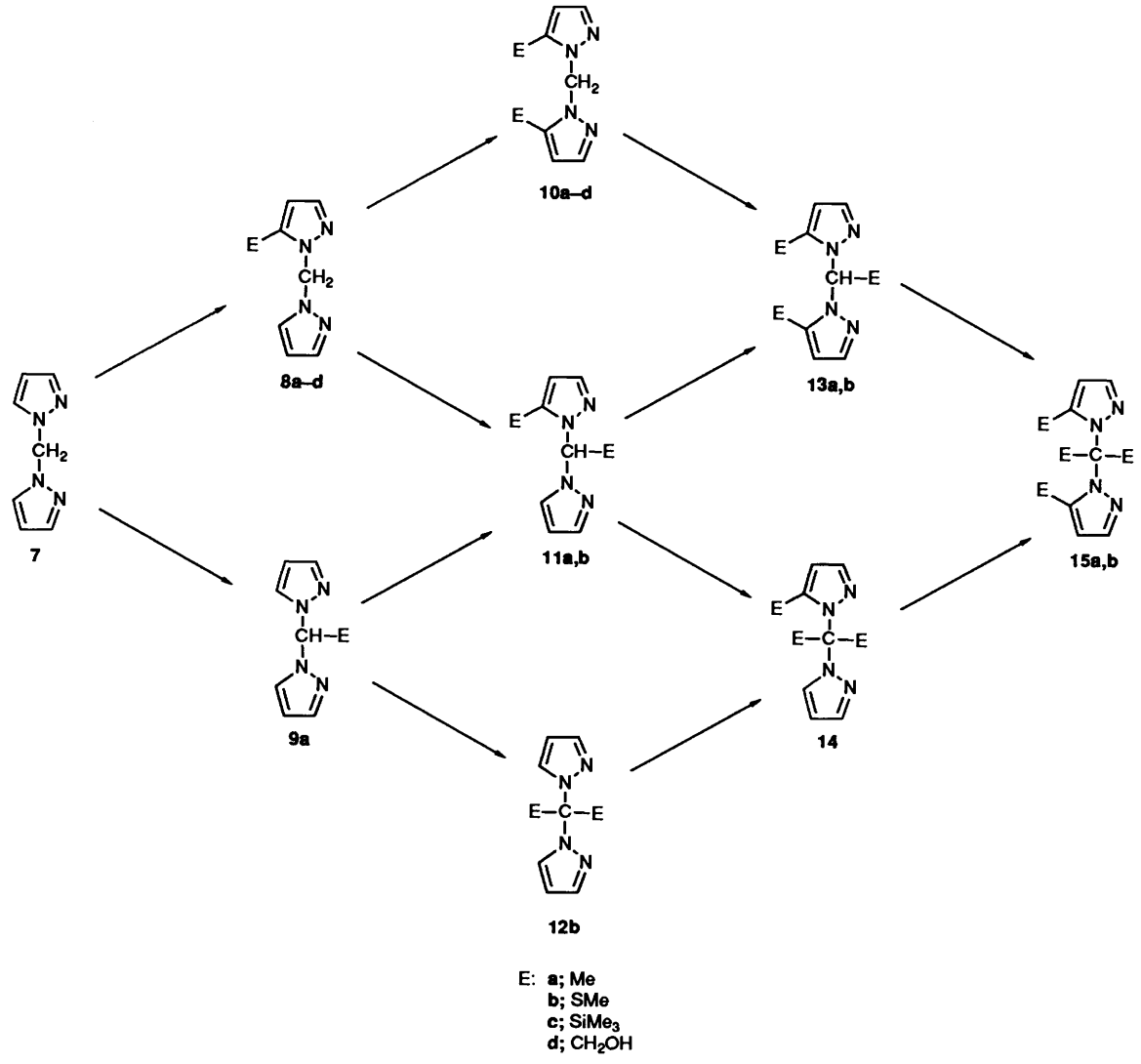
Table 2 Reactions of compound **3**

Entry	Electrophile	7:BuLi:E	8[a]	9[a]	10[a]	11[a]	12[a]	13[a]	15[a]
1	MeI	1:1:1	28	20	6	13			
2	MeI	1:2.1:2.1	11		34	24			
3	MeI	1:4.2:4.2						85	15
4	MeSSMe	1:1:1	54						
5	MeSSMe	1:2.4:2.4	7		14		12		19
6	MeSSMe	1:2.4:2.4[b]	17		23	7		5	10
7	MeSSMe	1:4.2:4.2	5		8		8		40
8	Me_3SiCl	1:1:1	80						
9	Me_3SiCl	1:2.1:2.1	35		65				
10	$(H_2CO)_n$	1:1:1	27		13				
11	$(H_2CO)_n$	1:2.1:2.1	23		45	4			

[a] Determined by ^1H NMR spectroscopy. [b] Base, LDA.

Results obtained with bis(azol-1-yl)methanes **1** and, especially, **2**, show that α-lithiation is preferred over β-lithiation whatever the nature of the electrophile. The fact that LDA or an increase in the temperature produces results similar to those with butyllithium or at room temperature shows that α-lithiation is both kinetically and thermodynamically favoured (Table 1, entries 3–5).

With bis(pyrazol-1-yl)methane **7** the nature and the product proportions depend on the nature of the electrophile. 'Hard' electrophiles (trimethylsilyl chloride or paraformaldehyde) afford only ring-substitution products, whereas the use of methyl iodide or dimethyl disulfide ('soft' electrophiles) afforded mixtures of ring- and bridge-substituted products. These results are explained in terms of the 'hard and soft acids and bases' (HSAB) principle and confirm the existence of two deprotonation sites with different natures, the bridge position having the 'soft' site and the ring position the 'hard' centre, as previous literature results suggest.[7]



Scheme 2

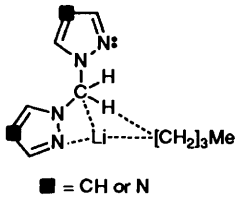


Fig. 1

Bridge-disubstituted derivatives are mainly obtained using dimethyl disulfide, whereas bridge monosubstitution is observed with methyl iodide. The incorporation of an electron-withdrawing substituent, such as methylthio, in the bridge increase the acidity of the remaining hydrogen atom and a second deprotonation is then favoured. On the other hand, the methyl group, an electron-donor substituent, impedes the second deprotonation.

The use of the non-cordinative LDA increases the ring-substitution ratio and confirms that α-metallation is kinetically favoured (Table 2, entry 6). Finally, the presence of bridge-substituted products permits the selective preparation of tetrasubstituted products, **15a** and **15b**, by using an excess of base and electrophile. ^1H and ^{13}C NMR data for the products are presented in Tables 3 and 4.

Experimental

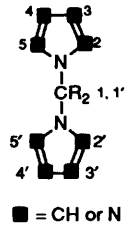
M.p.s were determined with a Gallenkamp capillary apparatus and are uncorrected. Microanalyses were performed at the Centro Nacional de Química Orgánica, CSIC, Madrid, Spain. IR spectra were recorded with a Philips PU 9500 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded in a Varian Unity 300 (300 MHz) spectrometer. Silica gel 60 (70–230 mesh) (Merck) was used in column chromatography.

General Procedure.—In a Schlenk tube, the appropriate bis(azol-1-yl)methane (2 mmol) was dissolved in dry tetrahydrofuran (THF) (35 cm^3) and the solution was cooled to 0 °C. Under nitrogen, a 1.6 mol dm^{-3} solution of butyllithium in hexane (Tables 1 and 2) was added dropwise during 5–10 min and the solution was stirred for 1 h. The electrophile (Tables 1 and 2) was added and the mixture was stirred at room temperature for 14 h. The reaction was quenched with ammonium chloride. After removal of solvents, the crude residue was elaborated as indicated.

Bis(imidazol-1-yl)methane **1**. (a) *Reaction with dimethyl sulfate.** Neutralization with potassium hydrogen carbonate

* The isolation of the substitution products was performed by using dimethyl sulfate because, in the reaction with methyl iodide, the presence of lithium iodide impedes the isolation.

Table 3 ^{1}H NMR spectra of compounds **3–6**, **8–15** [δ relative to $SiMe_4$; J (Hz); solvent $CDCl_3$]



Comp.	1-H	1'-H	2-H	2'-H	3-H	3'-H	4-H	4'-H	5-H	5'-H	Other
3a	5.90 (s)	5.90 (s)	2.43 (s) (Me)	7.60 (s)			6.9–7.0 (m)	7.10 (d) *J* 1.1	6.9–7.0 (m)	6.9–7.0 (m)	
4a	5.82 (s)	5.82 (s)	2.43 (s) (Me)	2.43 (s) (Me)			6.93 (d) *J* 1.5	6.93 (d) *J* 1.5	6.83 (d) *J* 1.5	6.83 (d) *J* 1.5	
3b	5.99 (s)	5.99 (s)	2.62 (s) (MeS)	7.79 (s)			7.10 (d) *J* 1.5	7.10 (d) *J* 1.5	7.07 (d) *J* 1.5	7.07 (d) *J* 1.5	
4b	5.97 (s)	5.97 (s)	2.62 (s) (MeS)	2.62 (s) (MeS)			7.17 (d) *J* 1.5	7.17 (d) *J* 1.5	7.07 (d) *J* 1.5	7.07 (d) *J* 1.5	
3c	6.07 (s)	6.07 (s)	0.22 (s) ($SiMe_3$)	7.75 (s)			7.53 (br s)	7.19 (br s)	7.10 (d) *J* 0.6	6.86 (br s)	
4c	6.06 (s)	6.06 (s)	0.24 (s) ($SiMe_3$)	0.24 (s) ($SiMe_3$)			7.33 (br s)	7.33 (br s)	7.22 (d) *J* 0.9	7.22 (d) *J* 0.9	
3d[a]	6.31 (s)	6.31 (s)	4.73 (s) (CH_2OH)	7.95 (br s)			7.25 (d) *J* 1.6	7.36 (d) *J* 1.2	6.90 (d) *J* 1.6	6.99 (d) *J* 1.2	OH 4.78 (s)
4d[a]	6.38 (s)	6.38 (s)	4.75 (s) (CH_2OH)	4.75 (s) (CH_2OH)			7.29 (d) *J* 1.6	7.29 (d) *J* 1.6	6.90 (d) *J* 1.6	6.90 (d) *J* 1.6	OH 4.78 (s)
5a	6.34 (s)	6.34 (s)			7.77 (s)	7.92 (s)			2.66 (s) (Me)	8.39 (s)	
6a	6.22 (s)	6.22 (s)			7.72 (s)	7.72 (s)			2.64 (s) (Me)	2.64 (s) (Me)	
5b	6.33 (s)	6.33 (s)			7.98 (s)	7.87 (s)			2.74 (s) (MeS)	8.40 (s)	
6b	6.22 (s)	6.22 (s)			7.88 (s)	7.88 (s)			2.73 (s) (MeS)	2.73 (s) (MeS)	
5c	6.5 (s)	6.5 (s)			7.98 (s)	7.90 (s)			0.47 (s) ($SiMe_3$)	8.33 (s)	
6c	6.4 (s)	6.4 (s)			7.9 (s)	7.9 (s)			0.52 (s) ($SiMe_3$)	0.52 (s) ($SiMe_3$)	
5d[a]	6.71 (s)	6.71 (s)			7.99 (s)	7.88 (s)			4.95 (s) (CH_2OH)	8.73 (s)	OH 4.76 (s)
6d[a]	6.85 (s)	6.85 (s)			7.94 (s)	7.94 (s)			5.02 (s) (CH_2OH)	5.02 (s) (CH_2OH)	OH 4.85 (s)
8a	6.25 (s)	6.25 (s)			7.43 (d) *J* 1.6	7.51 (d) *J* 1.6	6.03 (d) *J* 1.6	6.27 (t) *J* 1.8	2.43 (s) (Me)	7.62 (d) *J* 2.4	
9a	2.17 (d) *J* 7.2 (Me)	6.59 (q) *J* 7.2			7.51 (d) *J* 1.6	7.51 (d) *J* 1.6	6.24 (dd) *J* 1.6, 2.8	6.24 (dd) *J* 1.6, 2.8	7.56 (d) *J* 2.8	7.56 (d) *J* 2.8	
10a	6.23 (s)	6.23 (s)			7.40 (d) *J* 1.8	7.40 (d) *J* 1.8	6.01 (d) *J* 1.5	6.01 (d) *J* 1.5	2.48 (s) (Me)	2.48 (s) (Me)	
11a	2.15 (d) *J* 7.2 (Me)	6.59 (q) *J* 7.2			7.3–7.5 (m)	7.3–7.5 (m)	5.9–6.1 (m)	6.23 (t) *J* 2.1	2.13 (s) (Me)	7.3–7.5 (m)	
13a	2.16 (d) *J* 7.2 (Me)	6.7 (q) *J* 7.2			7.37 (d) *J* 1.6	7.37 (d) *J* 1.6	5.97 (d) *J* 1.6	5.97 (d) *J* 1.6	2.13 (s) (Me)	2.13 (s) (Me)	
15a	1.64 (s) (Me)	1.64 (s) (Me)			7.35 (s)	7.35 (s)	6.02 (s)	6.02 (s)	2.16 (s) (Me)	2.16 (s) (Me)	
8b	6.41 (s)	6.41 (s)			7.52 (d) *J* 2.1	7.51 (d) *J* 1.5	6.30 (d) *J* 2.1	6.25 (t) *J* 2.1	2.36 (s) (MeS)	7.66 (d) *J* 2.4	
10b	6.44 (s)	6.44 (s)			7.48 (d) *J* 1.5	7.48 (d) *J* 1.5	6.25 (d) *J* 1.5	6.25 (d) *J* 1.5	2.41 (s) (MeS)	2.41 (s) (MeS)	
12b	2.07 (s) (MeS)	2.07 (s) (MeS)			7.55 (d) *J* 1.8	7.55 (d) *J* 1.8	6.34 (dd) *J* 1.8, 2.6	6.34 (dd) *J* 1.8, 2.6	7.77 (d) *J* 2.6	7.77 (d) *J* 2.6	
15b	1.87 (s) (MeS)	1.87 (s) (MeS)			7.53 (d) *J* 2.1	7.53 (d) *J* 2.1	6.24 (d) *J* 2.1	6.24 (d) *J* 2.1	2.35 (s) (MeS)	2.35 (s) (MeS)	
8c	6.33 (s)	6.33 (s)			7.47 (d) *J* 1.6	7.55 (d) *J* 2.4	6.39 (d) *J* 2.1	6.22 (t) *J* 2.1	0.28 (s) ($SiMe_3$)	7.43 (d) *J* 2.4	
10c	6.41 (s)	6.41 (s)			7.52 (d) *J* 0.9	7.52 (d) *J* 0.9	6.42 (d) *J* 0.9	6.42 (d) *J* 0.9	0.37 (s) ($SiMe_3$)	0.37 (s) ($SiMe_3$)	
8d[a]	6.60 (s)	6.60 (s)			7.62 (d) *J* 1.5	7.69 (d) *J* 1.5	6.45 (d) *J* 1.5	6.48 (t) *J* 2.1	5.03 (s) (CH_2OH)	8.01 (d) *J* 1.5	OH 5.0 (s)
10d[a]	6.67 (s)	6.67 (s)			7.61 (d) *J* 1.8	7.61 (d) *J* 1.8	6.44 (d) *J* 1.5	6.44 (d) *J* 1.5	5.07 (s) (CH_2OH)	5.07 (s) (CH_2OH)	OH 5.03 (s)

[a] Solvent CD_3OD.

Table 4 ^{13}C NMR spectra of compounds **3–6**, **8–10** [δ relative to $SiMe_4$; J (Hz); solvent $CDCl_3$]

Comp.	C-1	C-2	C-2′	C-3	C-3′	C-4	C-4′	C-5	C-5′	1,1′-R	2,2′-R	5,5′-R
4a	55.27	144.34	144.34			128.46	128.46	118.66	118.66		13.29	
3b	55.51	136.87	130.65*			130.86*	130.97*	120.35	118.31		16.65	
4b	54.43	142.85	142.85			130.22	130.22	120.52	120.52		16.68	
3c	57.09	130.01	135.90			140.32*	130.72	141.27*	117.46		−0.89	
4c	58.39	129.63	129.63			140.31*	140.31*	140.71*	140.71*		−0.82	
6a	57.98			151.13	151.13			153.60	153.60			11.99
5b	58.74			152.48*	152.85*			154.84	143.91			15.88
6b	57.88			152.31	152.31			154.95	154.95			16.02
6d[a]	57.44			149.81	149.81			155.44	155.44			54.19
8a	62.93			140.08*	140.2*	106.80	107.08	139.54	129.31			11.10
10a	60.92			139.77	139.77	106.51	106.51	139.37	139.37			11.16
8b	62.25			140.33*	140.75*	110.70	106.77	137.05	129.46			19.50
10b	59.47			140.85	140.85	110.24	110.24	137.53	137.53			19.78
15b	97.94			137.96	137.96	108.15	108.15	140.42	140.42	13.23		17.85
8c	65.68			139.54*	140.14*	116.06	106.71	143.85	128.66			−0.90
10c	66.09			139.48	139.48	115.99	115.99	143.81	143.81			−0.42
8d[a]	64.66			142.13*	142.79*	108.69**	108.88**	145.75	132.87			56.46
10d[a]	62.36			142.03	142.03	108.73	108.73	146.07	146.07			56.38

[a] Solvent CD_3OD. * or **, interchangeable.

and flash chromatography [$CHCl_3$–MeOH (8:1)] afforded bis-(2-methylimidazol-1-yl)methane **4a**, m.p. 168–170 °C; ν_{max}-(KBr)/cm^{-1} 1526 (Found: C, 61.1; H, 7.1; N, 31.8. Calc. for $C_9H_{12}N_4$: C, 61.3; H, 6.8; N, 31.8%).

(b) *Reactions with dimethyl disulfide.* Extraction with ethanol (2 × 50 cm^3) and flash chromatography [$CHCl_3$–EtOH (7:2)] gave bis(2-methylthioimidazol-1-yl)methane **4b**, b.p. 170 °C/10^{-4} mbar;* ν_{max}(liquid)/cm^{-1} 1508 and 1448 (Found: C, 45.1; H, 5.1; N, 23.4. Calc. for $C_9H_{12}N_4S_2$: C, 44.9; H, 5.3; N, 23.3%) and imidazol-1-yl(2-methylthioimidazol-1-yl)methane **3b**, b.p. 170 °C/10^{-4} mbar; ν_{max}(liquid)/cm^{-1} 1508 and 1437 (Found: C, 49.9; H, 5.4; N, 28.4. Calc. for $C_8H_{10}N_4S$: C, 49.5; H, 5.1; N, 28.8%).

(c) *Reactions with trimethylsilyl chloride.* Extraction with chloroform (4 × 50 cm^3) and flash chromatography [$CHCl_3$–MeOH (20:1)] gave bis(2-trimethylsilylimidazol-1-yl)methane **4c**, m.p. 75–77 °C (from light petroleum 50–70 °C); ν_{max}-(KBr)/cm^{-1} 1515, 1249, 863 and 761 (Found: C, 53.5; H, 8.1; N, 19.1. Calc. for $C_{13}H_{24}N_4Si_2$: C, 53.4; H, 8.3; N, 19.1%) and imidazol-1-yl(2-trimethylsilylimidazol-1-yl)methane **3c**, b.p. 175 °C/10^{-4} mbar; ν_{max}(liquid)/cm^{-1} 1508, 1252, 846 and 758 (Found: C, 54.2; H, 7.3; N, 25.8. Calc. for $C_{10}H_{16}N_4Si$: C, 54.5; H, 7.3; N, 25.4%).

Bis(1,2,4-*triazol*-1-*yl*)*methane* **2**. (a) *Reactions with methyl iodide.* Crude reaction product was dissolved in water (50 cm^3). Extraction with methylene dichloride (4 × 50 cm^3), drying of the extract over $MgSO_4$, removal of solvent, and flash chromatography [$CHCl_3$–MeOH (10:1)] afforded bis(5-methyl-1,2,4-triazol-1-yl)methane **6a**, m.p. 114–116 °C (from toluene); ν_{max}(KBr)/cm^{-1} 1529 (Found: C, 47.2; H, 5.9; N, 46.8. Calc. for $C_7H_{10}N_6$: C, 47.2; H, 5.7; N, 47.2%). 5-Methyl-1,2,4-triazol-1-yl(1,2,4-triazol-1-yl)methane **5a** was identified by ^1H NMR spectroscopy.

(b) *Reactions with dimethyl disulfide.* Extraction with chloroform (4 × 50 cm^3) and flash chromatography [light petroleum–ethyl acetate (1:5)] gave bis(5-methylthio-1,2,4-triazol-1-yl)methane **6b**, m.p. 154–155 °C (sublimation at 115 °C/10^{-4} mbar); ν_{max}(KBr)/cm^{-1} 1524 and 1406 (Found: C, 34.9; H, 4.0; N, 34.2. Calc. for $C_7H_{10}N_6S_2$: C, 34.7; H, 4.2; N, 34.7%) and 5-methylthio-1,2,4-triazol-1-yl(1,2,4-triazol-1-yl)-methane **5b**, m.p. 108–109 °C (sublimation at 100 °C/10^{-4} mbar); ν_{max}(KBr)/cm^{-1} 1506 and 1412 (Found: C, 36.4; H, 3.9; N, 42.6. Calc. for $C_6H_8N_6S$: C, 36.7; H, 4.1; N, 42.8%).

(c) *Reaction with paraformaldehyde.* Flash chromatography [$CHCl_3$–EtOH (4:1)] gave bis(5-hydroxymethyl-1,2,4-triazol-1-yl)methane **6d**, m.p. 128–129 °C (from ethanol–hexane); ν_{max}(KBr)/cm^{-1} 3137, 3097, 1525 and 1285 (Found: C, 39.8; H, 5.0; N, 39.9. Calc. for $C_7H_{10}N_6O_2$: C, 40.0; H, 4.8; N, 40.%). 5-Hydroxymethyl-1,2,4-triazol-1-yl(1,2,4-triazol-1-yl)methane **5d** was identified by ^1H NMR spectroscopy.

Bis(*pyrazol*-1-*yl*)*methane* **7**. (a) *Reactions with methyl iodide.* Molar proportions (1:1:1). Extraction with chloroform (4 × 50 cm^3) and flash chromatography [light petroleum–ethyl acetate (6:1)] gave 5-methylpyrazol-1-yl(pyrazol-1-yl)methane **8a**, m.p. 68–69 °C (sublimation at 48 °C/10^{-4} mbar); ν_{max}(KBr)/cm^{-1} 1546 (Found: C, 58.9; H, 6.1; N, 34.4. Calc. for $C_8H_{10}N_4$: C, 59.2; H, 6.2; N, 34.6%).

Molar proportions (1:2.4:2.4). Extraction with chloroform (4 × 50 cm^3) and flash chromatography [light petroleum–ethyl acetate (2:1)] gave bis(5-methylpyrazol-1-yl)methane **10a**, m.p. 95–96 °C (sublimation at 80 °C/10^{-4} mbar); ν_{max}(KBr)/cm^{-1} 1546 (Found: C, 61.3; H, 6.9; N, 31.5. Calc. for $C_9H_{12}N_4$: C, 61.3; H, 6.9; N, 31.8%).

Compounds **9a**, **11a**, **13a** and **15a** were identified by ^1H NMR spectroscopy.

(b) *Reactions with dimethyl disulfide.* Molar proportions (1:2.4:2.4). Extraction with chloroform (4 × 50 cm^3) and flash chromatography [light petroleum–ethyl acetate (1:2)] gave 5-methylthiopyrazol-1-yl(pyrazol-1-yl)methane **8b**, m.p. 42–44 °C (b.p. 160 °C/10^{-4} mbar); ν_{max}(KBr)/cm^{-1} 1575 and 1427 (Found: C, 49.4; H, 5.4; N, 28.6. Calc. for $C_8H_{10}N_4S$: C, 49.4; H, 5.2; N, 28.9%). Bis(5-methylthiopyrazole-1-yl)methane **10b** was identified by ^1H NMR spectrocopy.

Molar proportions (1:4.2:4.2). Extraction with chloroform (4 × 50 cm^3) and flash chromatography [light petroleum–ethyl acetate (1:2)] gave bis(methylthio)bis(5-methylthiopyrazol-1-yl)methane **15b**, m.p. 154–156 °C (from toluene–light petroleum); ν_{max}(KBr)/cm^{-1} 1491 and 1426 (Found: C, 39.4; H, 4.9; N, 16.7. Calc. for $C_{11}H_{16}N_4S_4$: C, 39.7; H, 4.9; N, 16.9%).

Compounds **11b**, **12b** and **13b** were identified by ^1H NMR spectroscopy.

(c) *Reactions with trimethylsilyl chloride.* Molar proportion (1:1:1). Extraction with chloroform (4 × 50 cm^3) and flash chromatography [light petroleum–ethyl acetate (2:1)] gave pyrazol-1-yl(5-trimethylsilylpyrazol-1-yl)methane **8c**, m.p. 64–66 °C (b.p. 120 °C/10^{-4} mbar) (Found: C, 54.5; H, 7.3; N, 25.0. Calc. for $C_{10}H_{16}N_4Si$: C, 54.5; H, 7.3; N, 25.4%).

* 1 mbar = 10^2 Pa.

Molar proportions (1:2.1:2.1). Extraction with chloroform (4 × 50 cm^3) and flash chromatography [light petroleum–ethyl acetate (20:1)] gave bis(5-trimethylsilylpyrazol-1-yl)-methane **10c**, m.p. 90–92 °C (sublimation at 100 °C/10^{-4} mbar); ν_{max}(KBr)/cm^{-1} 1246, 842 and 760 (Found: C, 53.6; H, 7.9; N, 19.4. Calc. for $C_{13}H_{24}N_4Si_2$: C, 53.4; H, 8.3; N, 19.2%).

(c) *Reactions with paraformaldehyde.* The crude product was dissolved in water (25 cm^3). Extraction with chloroform (4 × 50 cm^3), drying of the extract over $MgSO_4$, removal of the solvent, and flash chromatography [light petroleum–ethyl acetate (1:1)] afforded 5-hydroxymethylpyrazol-1-yl(pyrazol-1-yl)methane **8d**, m.p. 111–113 °C (from toluene–light petroleum); ν_{max}(KBr)/cm^{-1} 3302 and 1268 (Found: C, 53.8; H, 5.5; N, 31.1. Calc. for $C_8H_{10}N_4O$: C, 53.9; H, 5.6; N, 31.5%). Elution with ethyl acetate then afforded bis(5-hydroxymethylpyrazol-1-yl)methane **10d**, m.p. 167–168 °C (from $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3300, 1544 and 1270 (Found: C, 51.8; H, 5.6; N, 26.2. Calc. for $C_9H_{12}N_4O_2$: C, 51.9; H, 5.8; N, 26.9).

Acknowledgements

Financial support by Spanish CICYT (Project PB88–0363) is gratefully acknowledged.

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Paper 2/05842A
Received 2nd *November* 1992
Accepted 4th *December* 1992