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THE LITHIATION OF GEM-BIS (PYRAZOL-1-YL)ALKANES

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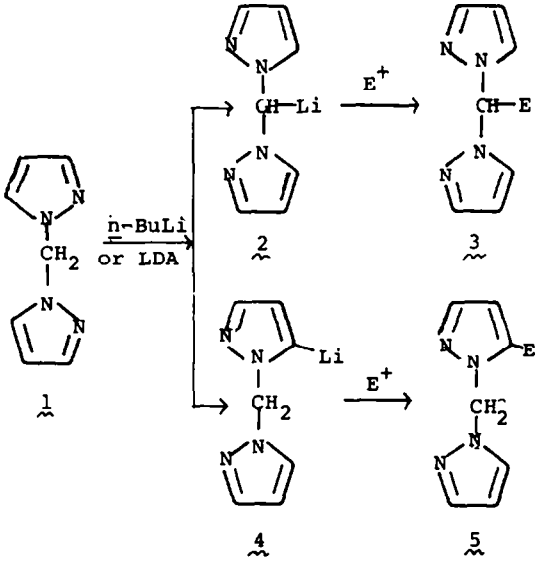
Abstract - The title compounds can be lithiated at the inter-ring carbon atom to give carbanions which react with a variety of electrophiles. Lithiation can also be directed to the 5-position of the ring.

The ring-metallation of azoles in general[1] and pyrazoles in particular[2a] is well-known and the phenyl group of 1-phenylpyrazole can be ortho-metallated.[2b,3] α-Metallation of an N-alkyl group in simple azoles is less familiar although the lithiation of N-methyl groups in indazoles and pyrazoles and subsequent reaction with CO_2 and other electrophiles was first reported in 1971[4] and 1972[5], respectively (c.f. also ref.6).

We recently reported[7] a systematic study of the lithiation of N-benzyl- and N-methylpyrazoles, and showed that whereas N-substituent metallation is kinetically favoured, at higher temperatures the metal rearranges to the 5-position (if this is blocked, ring-opening can evidently occur[8]).

We now report the metallation of some gem-bis(pyrazol-1-yl)alkanes, having reasoned that the double activation of the C-H bonds would facilitate both the ease of preparation and the stability of these compounds.

Indeed, bis(pyrazol-1-yl)methane 1[9] on treatment with n-butyllithium at 25°C, followed by reaction with MeI or $PhCH_2Cl$ gave the expected 1-substituted bis(pyrazol-1'-yl)-methanes 3b, 3c (70, 81%) (Table I). But surprisingly, reaction with carbonyl electrophiles under the same conditions gave the products from ring lithiation 5a, 5d, 5e, 5h, 5i, (17-60%) (Table II).



a	D	f	p-$CH_3C_6H_4CO$
b	CH_3	g	PhCO
c	$PhCH_2$	h	CH_3CO
d	p-$CH_3C_6H_4CH(OH)$	i	$Ph_2C(OH)$
e	n-PrCH(OH)	j	PhC(=NH)

SCHEME I

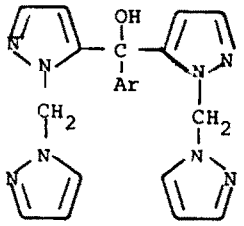
Table I

Preparation and physical characteristics of 1,1-bis(pyrazol-1-yl)alkanes.

Comp.		Methylene Subst.			m.p. or b.p.	crystal	recryst.	Yield	Required (%)				Found (%)		
No.	Electrophile	R^1	R^2[a]	Method	(°C)	form	solvent	(%)	C	H	N	Formula	C	H	N
3b	CH_3I	H	CH_3	A	70-71[b]	oil	-	70	-	-	-	$C_8H_{10}H_4$[c]	-	-	-
3c	$PhCH_2Cl$	H	$PhCH_2$	A	107-108	needles	pet.ether[d]	81	70.59	5.88	23.53	$C_{14}H_{14}N_4$	71.09	5.90	23.86
3d	p-$CH_3C_6H_4CHO$	H	p-$CH_3C_6H_4CH(OH)$	B	127-128	plates	C_6H_6	61	67.16	5.97	20.89	$C_{15}H_{16}N_4O$	67.28	5.97	20.69
3f	p-$CH_3C_6H_4CO_2Et$	H	p-$CH_3C_6H_4CO$	B	125-126	needles	C_6H_6/pet.ether[d]	56	67.67	5.26	21.05	$C_{15}H_{14}N_4O$	67.57	5.19	20.92
3i	Ph_2CO	H	$Ph_2C(OH)$	B	228-229	needles	C_6H_6	68	72.73	5.45	16.97	$C_{20}H_{18}N_4O$	72.59	5.49	16.75
8	PhCN	-	$=CPhNH_2$	B	129-130	needles	pet.ether[d]	29	66.93	5.17	27.89	$C_{14}H_{13}N_5$	66.61	5.24	28.17
10a	D_2O	Ph	D	C	63-64	needles	pet.ebher[d]	90[e]	-	-	-	$C_{13}H_{11}DN_4$[f]	-	-	-
10b	CH_3I	Ph	CH_3	C	140-145[g]	oil	-	50	-	-	-	$C_{14}H_{14}N_4$[h]	-	-	-
10c	$PhCH_2Cl$	Ph	$PhCH_2$	C	91-92	prisms	pet.ether[d]	43	76.43	5.73	17.83	$C_{20}H_{18}N_4$	76.66	5.94	17.96
10g	PhCOCl	Ph	PhCO	C	169-170	needles	C_6H_6	67	73.17	4.87	17.07	$C_{20}H_{16}N_4O$	73.01	5.03	17.19

[a] Derived from electrophile. [b] b.p., 1.5 mmHg. [c] Mass spectrum m/z 162.090 ($C_8H_{10}N_4$ requires 162.090; M^+). [d] Boiling range 37-57°C.
[e] Estimated from integration of ^1H NMR. [f] Mass spectrum m/z 225; M^+. [g] b.p., 1.3 mmHg. [h] Mass spectrum m/z 238.121 ($C_{14}H_{14}N_4$ requires 238.121; M^+).

In two examples, reaction with PhCOCl and p-$CH_3C_6H_4CO_2Et$, the ketones 5f, 5g were not isolated but reacted with a second equivalent of the lithio derivative 4 to give the bis-(pyrazol-5-yl) alcohols 6f and 6g in low yield (30, 37% respectively).



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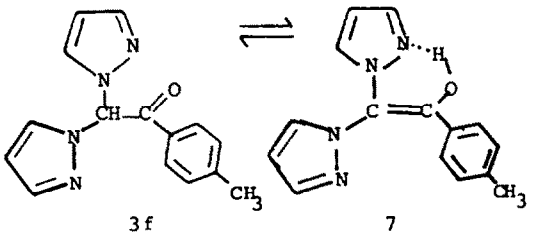
Ar	
f	p-$CH_3C_6H_4$
g	Ph

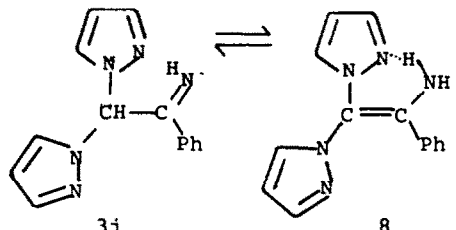
However, when lithium diisopropylamide (LDA) is used as the base, under reverse addition conditions at 0°C, exclusive α-addition occurs to give 3d, 3f, 3i, 8 (29 - 68%) by trapping of the α-lithio derivative 2 with either p-tolualdehyde, ethyl p-toluate, benzophenone or benzonitrile as electrophile.

The derivatives 3f and 3j, which could potentially exist in two tautomeric forms 3f ⇌ 7, 3j ⇌ 8, are shown by spectral evidence (^1H, ^{13}C NMR and IR Tables III, V and VII) to exist as the ketone 3f and enamine 8 respectively.

In particular, for 3f: the IR spectrum ($CHBr_3$) shows νC=O at 1700 cm^{-1} and no νOH; ^1H NMR ($CDCl_3$) 8.13 p.p.m. (s, 1H, CH-), 6.40 p.p.m. (dd, 2H, H-3-pyrazole) and ^{13}C NMR ($CDCl_3$) shows 186.9 (C=O), 75.9 p.p.m. (CH-). For 8, the ^1H NMR spectrum shows a broad 2H peak for NH_2 at 5.13 p.p.m. In the ^{13}C NMR spectrum no signal is found near 75 p.p.m. (absence of N-CH-N), whereas a singlet at 137.6 p.p.m. is assigned to =CPhNH$_2$ (Tables III, IV).

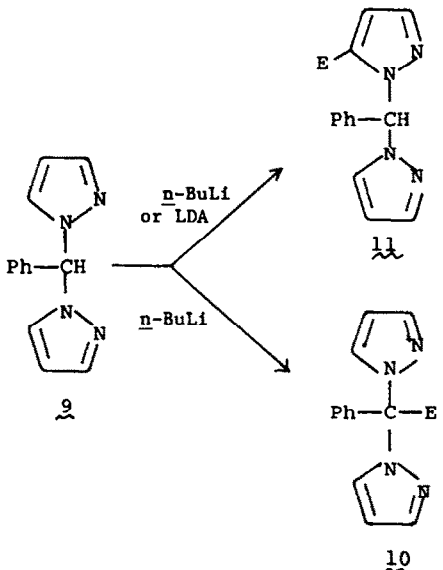


3f 7



3j 8

Phenylbis(pyrazole-1'-yl)methane (9), prepared by refluxing pyrazole, $PhCHCl_2$ and aqueous sodium hydroxide with a phase transfer catalyst, underwent smooth lithiation with n-butyllithium at -78 °C. The lithio derivative was trapped with D_2O, CH_3J, benzyl chloride or benzoyl chloride to give the expected 1-substituted compounds 10a, 10b, 10c and 10g (Table I). However, reaction with benzophenone afforded, under various reaction conditions, the ring substituted product 11i (Table II).



9 11

10

See Scheme I for designation of E.

SCHEME II

Table II

Preparation and physical characteristics of 1-(5-substituted pyrazol-1-yl)-1-(pyrazol-1-yl)alkanes.

Comp.		Methylene Subst.			m.p. or b.p.	crystal	recryst.	Yield	Required (%)				Found (%)		
No.	Electrophile	R^1	R^2	Method	(°C)	form	solvent	(%)	C	H	N	Formula	C	H	N
5a	D_2O	H	D[a]	A	108	-	-	90[b]	-	-	-	$C_7H_7DN_4$[c]	-	-	-
5d	p-$CH_3C_6H_4CHO$	H	p-$CH_3C_6H_4CH(OH)$	A	75-76	plates	C_6H_6	77	67.16	5.97	20.89	$C_{15}H_{16}N_4O$[d]	67.35	6.03	20.63
5e	$CH_3(CH_2)_2CHO$	H	$CH_3(CH_2)_2CH(OH)$	A	97-98	needles	C_6H_6/pet.ether[e]	60	60.00	7.27	25.45	$C_{11}H_{16}N_4O$	59.60	7.26	25.08
5h	$(CH_3CO)_2O$	H	CH_3CO	A	59-60	needles	pet.ether[e]	17	56.84	5.26	29.47	$C_9H_{10}N_4O$[f]	56.87	5.26	31.49
5i	Ph_2CO	H	$Ph_2C(OH)$	A	117-118	plates	C_6H_6/pet.ether[e]	20	72.73	5.45	16.97	$C_{20}H_{20}N_4O$	72.89	5.81	17.41
11i	Ph_2CO	Ph	$Ph_2C(OH)$	B/C	161-162	plates	C_6H_6/pet.ether[e]	33	76.85	5.42	13.79	$C_{26}H_{22}N_4O$	76.55	5.39	13.52

[a] Identified by ^1H NMR spectrum, loss of 4-H peak (δ 6.3). [b] By integration. [c] Mass spectrum m/z 149; M^+. [d] Mass spectrum m/z 268.134 ($C_{15}H_{16}N_4O$ requires 268.132; M^+), 267.125 (for $C_{15}H_{15}N_4O$ requires 267.125; M^+-1). [e] Boiling range 37-57°C. [f] Mass spectrum m/z 190.085 (for $C_9H_{10}N_4O$ requires 190.085; M^+).

Table III

^{1}H NMR spectra[a] (p.p.m.) of 1,1-bis(pyrazol-1-yl)alkanes.

Comp.	Methylene Subst.		R^1 (1H)			Pyrazole	Aromatic[b]		Other
No.	R^1	R^2	δ	m[d]	J[e]	(2H)	δ	H[c]	Signals
1[f]	H	H	6.30	s	-	6.3 m	7.6 - 7.5	4	-
3b	H	Me	6.60	q	7	6.3-6.0 dd[g]	7.7 - 7.3	4	h
3c	H	$PhCH_2$	6.60	t	7	6.4-6.2 dd[i]	7.7 - 7.1	9	j
3d	H	p-$CH_3C_6H_4CH(OH)$	6.56	d	5	6.2 dd[i]	7.8 - 7.1	8	k
3f	H	p-$CH_3C_6H_4CO$	8.13	s	-	6.33 dd[i]	7.9 - 7.2	8	l
3i	H	$Ph_2C(OH)$	6.35	s	-	6.35[m], 6,15 dd[g,n]	8.1 - 7.1	14	o
8	-	$=CPhNH_2$	-	-	-	6.29 dd[g], 6.09 dd[g,n]	7.7 - 7.2	9	p
9	Ph	H	7.75	s	-	6.38 dd[g]	7.7 - 7.0	9	-
10a	Ph	D	-	-	-	6.38 dd[g]	7.7 - 7.0	9	-
10b	Ph	Me	-	-	-	6.31 dd[g]	7.7 - 6.7	9	q
10c	Ph	$PhCH_2$	-	-	-	6.33 dd[i]	7.8 - 6.58	14	r
10g	Ph	PhCO	-	-	-	6.38 dd[g]	7.9 - 7.2		s

[a] In $CDCl_3$, referenced to $(CH_3)_4Si$. [b] Pyrazole 3,5-H and others. [c] Integration. [d] Multiplicity, s=singlet, d=doublet, dd=double doublet, t=triplet, q=quartet, m=multiplet. [e] Coupling constant (Hz). [f] From ref.9. [g] $J_{3,4}=J_{4,5}=2$Hz. [h] Also 2.20 p.p.m. (d, 3H, J=7Hz, CH_3). [i] $J_{3,4}=1.7$Hz, $J_{4,5}=2.4$Hz. [j] Also 3.90 p.p.m. (d, 2H, J=7Hz, $-CH_2Ph$). [k] Also 5.7 p.p.m. (dd, 1H, $J_{H,OH}=J_{H,CH}=5$Hz, PhCH(OH); after D_2O-exchange: d, 1H, J=5Hz); 5.20 p.p.m. (d, 1H, J=5Hz, OH); 2.23 p.p.m. (s, 3H, CH_3). IR ($CHBr_3$) 3120 cm^{-1} (OH). [l] Also 2.36 p.p.m. (s, 3H, CH_3); IR ($CHBr_3$) 1700 cm^{-1} (C=O). [m] Coincident with $-CH_2-$ peak. [n] Pyrazole rings dissymmetric due to H-bonding to pyrazole nitrogen. [o] OH in aromatic region; IR ($CHBr_3$) 3210 cm^{-1} (OH). [p] Also 5.13 p.p.m. (br. s, 2H, NH_2). [q] Also 2.70 p.p.m. (s, 3H, CH_3). [r] Also 4.60 p.p.m. (s, 2H, $-CH_2-$). [s] IR ($CHBr_3$) 1700 cm^{-1} (C=O).

^{1}H NMR Spectra. The CH_2 of the parent compound 1 appears as a singlet at 6.3 p.p.m. which in the methylene-substituted products 3 is replaced by a 1H signal of the correct multiplicity at 6.3 - 6.6 p.p.m. except in 3f where it is shifted to 8.13 p.p.m. by the adjacent carbonyl group (Table III). Usually clearly distinguishable are the 4- and 4'-pyrazole proton signals which occur as multiplets in the same region. Similarly, compounds 10 show the loss of the original CH signals at 7.75 p.p.m.; now the 4- and 4'-pyrazole signals show clearly as double doublets ($J_{3,4}=J_{4,5}=2$Hz and $J_{3,4}=1.7$Hz, $J_{4,5}=2.4$Hz, respectively), indicating C-unsubstituted pyrazole rings.

Table IV

^{1}H NMR spectra [a] (p.p.m.) of 1-(5-substituted pyrazol-1'-yl)-1-(pyrazol-1''-yl)alkanes (5).

Comp.	Pyrazol-5'-Subst.		R^1 (2H)		Pyrazole	Aromatic[b]		Other
No.	R^1 (2H)	R^2	δ	m[d]	4'-H, 4''-H (2H)	δ	H[c]	Signals
5a	H	D	6.40	s	6.40 m	7.7-7.6	3	-
5d	H	p-$CH_3C_6H_4CH(OH)$	6.30	s	5.98 d[e], 6.30	7.8-7.2	7	f
5e	H	n-PrCH(OH)	6.40	s	6.3-6.2 m	7.8-7.4	3	g
5h	H	CH_3CO	6.77	s	6.90 d[e], 6.28 dd[h]	7.8-7.6	3	i
5i	H	$Ph_2C(OH)$	6.10	s	5.68 d[e], 6.31 dd[h]	7.7-7.3	13	j
11i	Ph/H	$Ph_2C(OH)$	7.98	s	5.73 d[e], 6.23 dd[h]	7.7-7.0	18	k

[a] - [d] See Table III. [e] J=2Hz. [f] Also 6.15 (s, 1H, PhCH(OH)), 2.36 p.p.m. (s, 3H, CH_3), OH not observed; IR ($CHBr_3$) 3225 cm^{-1} (OH). [g] Also 5.36 (d, 1H, J=3Hz, OH), 5.1-4.9[(m, 1H, -CH-OH) after D_2O-exchange: 5.0 (t, 1H, J=6Hz)], 2.0-1.3 (m, 4H, $-CH_2CH_2-$), 0.97 p.p.m. (t, 3H, J=6Hz, CH_3). [h] $J_{3,4}=J_{4,5}=$ 2Hz. [i] Also 2.55 p.p.m. (s, 3H, CH_3 ; IR ($CHBr_3$) 1690 cm^{-1} (C=O). [j] OH in aromatic region. [k] Also 6.58 (s, 1H, OH); IR ($CHBr_3$) 3200 cm^{-1} (OH).

Table V

^{13}C NMR spectra [a] (p.p.m.) of 1,1-bis(pyrazol-1'-yl)alkanes (pyrazole carbons excluded).

Comp.	Methylene Subst.			Phenyl (R^1)				α-C	Aryl (R^2)				
No.	R^1	R^2	1-C	1	2	3	4	(R^2)	1	2	3	4	p-CH_3
1[b]	H	H	65.1	-	-	-	-	-	-	-	-	-	-
3d	H	p-$CH_3C_6H_4CH(OH)$	75.0	-	-	-	-	78.3	138.0	129.6[c]	126.1[c]	130.6	21.2
3f	H	p-$CH_3C_6H_4CO$	75.9	-	-	-	-	186.9	145.2	129.9[c]	128.6[c]	131.2	21.7
3i	H	$Ph_2C(OH)$	77.8	-	-	-	-	80.6	143.1	128.0[c]	125.2[c]	127.1[c]	-
8	-	=CPhNH$_2$	d	-	-	-	-	137.6	135.6	128.3[c]	127.6[c]	128.8[c]	-
9	Ph	H	77.7	136.1	128.7[c]	126.8[c]	129.2[c]	-	-	-	-	-	-
10c	Ph	$PhCH_2$	85.7	138.4	131.7[c]	128.0[c]	127.4[c]	44.9	134.9	128.7[c]	127.7[c]	125.9[c]	-
10g	Ph	PhCO	87.3	135.8	128.5[c]	127.8[c]	129.6[c]	190.0	136.7	128.5[c]	127.9[c]	131.7[c]	-

[a] In $CDCl_3$, referenced to $CDCl_3$ except where otherwise stated. [b] Ref. 9. [c] Tentative assignments. [d] Not observed.

By contrast, compounds 5 retain the CH_2 signal near 6.20 p.p.m. In several cases the 4'-pyrazole ring proton signal is now found as a doublet (J=2Hz), whereas the 4''-signal occurs as the usual double doublet. In 3d and 5e the OH-proton is coupled with the neighbouring methine proton (3d: $J_{OH,\ H}$ = 5Hz, 5e: $J_{OH,\ H}$ = 3Hz). After D_2O exchange this coupling is removed and the methine protons appear as a doublet (3d) or triplet (5e) (Tables III, IV).

^{13}C NMR Spectra. In the parent compound 1, the CH_2 group gives rise to a signal at 65.1 p.p.m.[9] and shows signals for the (equivalent) pyrazole rings at 140.6, 107.0, and 129.5 p.p.m. (for C-3, C-4 and C-5 respectively). In compound 3, the pyrazole ring signals are little affected; 140.6-141.1 p.p.m. (C-3), 107.0-107.5 p.p.m. (C-4) and 129.5-133.3 p.p.m. (C-5). However, in 3i and 8, the hydrogen-bonding of OH or NH_2 to the pyrazole nitrogen renders the pyrazole rings non-equivalent, and thus gives rise to extra signals in the ^{13}C NMR (Table VII). In compounds 5, by contrast, six peaks are now observed for the pyrazole carbons. The substituted ring carbons are shifted downfield at 140.2-141.0 p.p.m. (C-3), 106.7-113.4 p.p.m. (C-4) and 145.6-153.7 p.p.m. (C-5). The unsubstituted ring, as before, is little affected.

Conclusions. The easy lithiation of 1 and its conversion to derivatives 3 in high yield is noteworthy. We are now investigating the hydrolytic conversion of 3 into E.CHO and other potential synthetic applications of this work.

ACKNOWLEDGEMENT

We thank Dr. M. Lopez-Rodriguez for ^{13}C NMR spectra.

EXPERIMENTAL

IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer. ^1H NMR spectra were recorded with a Varian EM 360 L spectrometer and a JEOL FX-100 spectrometer was used for ^{13}C NMR spectra. Mass spectra were taken on a AEI MS20 spectrometer. Elemental analyses were carried out by Dr. R. King in this department. Melting points were taken on a Hoover Uni-melt capilliary apparatus and are uncorrected.

Solvents and all reagents were carefully dried, THF being distilled from Na/benzophenone[10] immediately prior to use. The molarity of n-BuLi was checked regularly by titration[11]. Reagents were routinely distilled and stored on 4 Å molecular sieves.

Bis(pyrazol-1-yl)methane (1) was prepared[9] (92%) from pyrazole and CH_2Cl_2, mp 108 °C (lit.[9], 111°C).

Phenylbis(pyrazol-1-yl)methane (9) was prepared by refluxing, with vigorous stirring, pyrazole (4g, 0.06 mol), tetrabutylammonium hydrogen sulphate (1g, 0.003 mol), NaOH (21 M, 40 ml, 0.4 mol) and benzal chloride (10 ml, 0.1 mol) for 8 hours. The mixture was extracted with Et_2O (2 x 30 ml), washed with H_2O (20 ml) and dried over $MgSO_4$ (anhyd.). Evaporation of Et_2O in vacuo gave an oil, which was distilled in vacuo. The fraction boiling at 150-155°C, (2.2 mmHg) gave the desired product (9, 45%) as colourless needles on trituration with petroleum ether (40-60), mp 62-63°C (lit.[12], 61.5-62°C).

General Methods of Lithiation.- Method A with n-BuLi. To 1 g (6mmol) of 1,1-bis(pyrazol-1'-yl)methane in freshly distilled THF (20 ml) under nitrogen at ambient temperature was added n-BuLi (2.5 M in hexane, 2 ml, 6 mmol) and

Table VI

^{13}C NMR spectra [a] (p.p.m.) of 1-(5-substituted pyrazol-1'-yl)-1-(pyrazol-1''-yl)alkanes (5) (pyrazole carbons excluded).

Comp.	Pyrazole-5-Subst.		R^2			Aryl (R^2)				
No.	R^1 (2H)	R^2	1-C	α-C	β-C	1	2	3	4	p-CH_3
5d	H	p-$CH_3C_6H_4CH(OH)$	66.7	62.7	-	138.3	129.2[b]	125.2[b]	137.5	21.2
5h	H	CH_3CO	63.9	[c]	28.4	-	-	-	-	-
5i	H	$Ph_2C(OH)$	63.3	[c]	-	[c]	128.1[b]	127.0[b]	127.5[b]	-
11i	Ph	$Ph_2C(OH)$	74.6	76.7	-	145.2	-	-	-[d]	-
						144.8	-	-	-[d]	

[a] In $CDCl_3$, referenced to $CDCl_3$ except where otherwise stated. [b] Tentative assignments. [c] Not observed. [d] Also 134.6 (*s*, C-1, R^1), not assigned: 128.6, 128.1, 128.0, 127.3, 127.1.

Table VII

^{13}C NMR spectra [a] (p.p.m.) Of 1,1-bis(pyrazol-1-yl)alkanes and 1-(5-substituted pyrazol-1-yl)-1-(pyrazol-1-yl)alkanes (pyrazol carbons).

Comp.	Methylene Subst.		Pyrazol-	Pyrazole	Pyrazole Ring Carbons		
No.	R^1	R^2	5-Subst.	Ring	3	4	5
1[b]	H	H	H	both	140.6	107.0	129.5
3d	H	p-$CH_3C_6H_4CH(OH)$	H	both	140.1	106.6	129.3
3f	H	p-$CH_3C_6H_4CO$	H	both	140.8	107.5	129.5
3i	H	$Ph_2C(OH)$	H	-	140.7 139.5	107.1 106.2	130.9[c]
8	-	=$CPhNH_2$	H	-	141.1 139.4	106.3 105.5	133.9[c]
5d	H	H	p-$CH_3C_6H_4CH(OH)$	unsubst. subst.	140.2 141.0	106.7 108.0	130.3 145.8
5h	H	H	CH_3CO	unsubst. subst.	139.6 140.8	106.3 113.4	130.2 153.7
5i	H	H	$Ph_2C(OH)$	unsubst. subst.	139.5 140.7	106.4 110.7	130.3 145.6
9	Ph	H	H	both	140.7	106.5	129.6
10c	Ph	$PhCH_2$	H	both	140.0	106.2	130.3
10g	Ph	PhCO	H	both	140.0	106.6	132.4
11i	Ph	H	$Ph_2C(OH)$	unsubst. subst.	139.3 139.5	105.9 109.1	129.6 149.5

[a] In $CDCl_3$, referenced to $CDCl_3$. [b] Ref. 9. [c] Pyrazole rings dissymmetric due to H-bonding to pyrazole nitrogen.

the mixture was stirred for 1h. The electrophile (6 mmol) in dry THF (20 ml) was added and stirring was continued for a further 12 hours. Water (2 ml) was added, the reaction mixture was evaporated to dryness, then triturated with CH_2Cl_2 (20 ml). The CH_2Cl_2 was then filtered and evaporated to dryness to give the product after recrystallisation from a suitable solvent (Tables I, II).

Method B, reverse addition with LDA. A solution of LDA (0.6 g, 6 mmol) in THF (10 ml) was prepared by adding n-BuLi (2.5 M, 2 ml, 6 mmol) to dry diisopropylamine (0.8 g, 8 mmol) in THF under N_2 at -78°C. The solution was allowed to warm to -10°C and transferred by syringe, to the flask containing 1 (1g, 6 mmol) and the electrophile (6 mmol) in THF (20 ml) under N_2 at 0°C. The reaction mixture was stirred for 3 hours at 0°C and at ambient temperature for a further 12 hours. Water, (2 ml) was added, the mixture was evaporated to dryness in vacuo, and the solid residue was extracted with CH_2Cl_2. After filtering, the CH_2Cl_2 solution, drying over $MgSO_4$ (anhyd.) and evaporation in vacuo the α-addition products were isolated as white solids or as oils which gave solids on trituration with pet. ether (40-60).

In the preparation of 3f and 8 2 equivalents of LDA were used.

Method C with n-BuLi. Phenyl-1,1-bis[pyrazol-1'-yl]methane (9) (1.3 g, 6 mmol) in freshly destilled THF (20 ml) was treated with n-BuLi (2.5 M in hexane, 2 ml, 6 mmol) under N_2. The solution was stirred for 60 min. at -78°C and the electrophile (6 mmol) was added at 0°C. Stirring was continued for 12 h at 23°C. The work-up was as in Method A.

1-(4-Methylphenyl)-1,1-bis[1'-(pyrazol-1''-ylmethylene)pyrazol-5'-yl]methanol (6f).- Prepared by reaction of 1 with n-BuLi (Method A) with ethyl p-toluate as electrophile to give 6f as white prisms, m.p. 134-135°C, (0.4 g, 35%) from EtOAc/pet. ether (40-60): IR ($CHBr_3$) 3180 cm^{-1} (νOH); ^1H NMR, 8.57 (s, 1H, OH), 8.07-7.03 (m, 11H, arom.), 6.38 (s, 4H, $-CH_2-$), 6.20 (dd, 2H, $J_{3,4}=J_{4,5}=2Hz$, pyrazole 4'-H), 5.55 (d, 2H, J=2Hz, pyrazole 4-H), 2.3 p.p.m. (s, 3H, $-CH_3$).

Anal. Calcd. for $C_{22}H_{22}N_8O$: C, 63.76; H, 5.30; N, 27.05. Found: C, 63.72; H, 5.30; N, 27.50.

1-Phenyl-1,1-bis[1'-(pyrazol-1''-ylmethylene)pyrazole-5'-]methanol (6g).- Prepared by the reaction of 1 with n-BuLi (Method A) with PhCOCl as the electrophile to give 6g as white needles, m.p. 145-147°C (0.44 g, 37%), from EtOAc: IR ($CHBr_3$) 3200 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 8.93 (br. s, 1H, OH), 7.9-7.3 (m, 10H, arom.), 6.66 (br. s, 4H, $-CH_2-$), 6.5 (m, 2H, pyrazole 4'-H), 5.73 p.p.m. (m, 2H, pyrazole 4-H); ^{13}C NMR ($CDCl_3$) 146.0 (s, pyrazole C-5), 143.3 (s, C-1 benzene), 140.0 (d, pyrazole C-3), 139.3 (d, pyrazole C'-3), 129.9 (d, pyrazole C'-5), 128.2, 126.4, 108.8 (d, pyrazole C-4), 106.1 (d, pyrazole C'-4), 72.1 (s, C-OH), 63.5 (tr, NCH_2N); mass spectrum, m/z (relative intensity) 400 (2), 264 (7), 175 (8), 105 (10), 81 (100), 53 (26), 28 (37).

Anal. Calcd. for $C_{21}H_{20}N_8O$: C, 63.0; H, 5.04; N, 28.0. Found: C, 63.23; H, 5.13; N, 28.42.

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