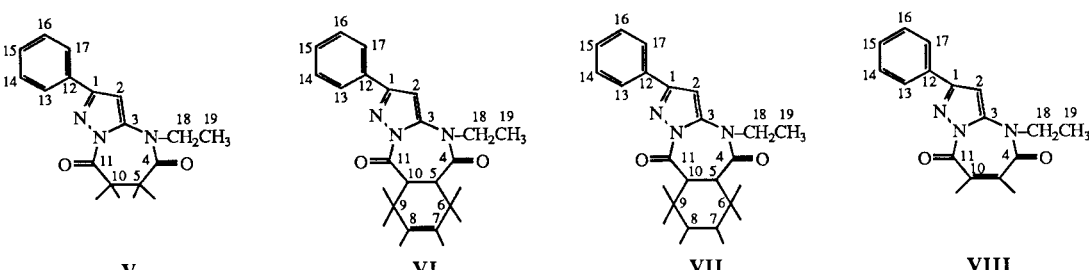


Table 1
C-13 NMR Chemical Shifts


Compound No.	1	2	3	4	5	6	7	8	9	10
V	154.81	97.26	143.54	166.48	30.33					33.10
VI	154.95	97.05	143.02	168.88 [a]	37.78	26.57 [c]	123.78 [b]	125.99 [b]	25.57 [c]	44.81
VII	154.87	97.74	143.04	170.33 [a]	41.04	27.33 [b]	26.41 [b]	25.09 [b]	22.08 [b]	48.38
VIII	155.58	95.25	142.06	158.30 [a]	129.19					134.09

Compound No.	11	12	13	14	15	16	17	18	19
V	169.79	130.71	128.57	126.27	129.60	126.27	128.57	44.62	12.77
VI	169.92 [a]	130.77	128.47	126.12	129.42	126.12	128.47	44.98	12.82
VII	170.72 [a]	130.91	128.53	126.23	129.43	126.23	128.53	45.02	12.96
VIII	159.71 [a]		128.64	126.53	129.82	126.53	128.64	45.91	11.91

[a] [b] [c] Assignments may be reversed.

on treatment with glacial acetic acid at reflux [9].

Compound **II** was suspended in diethyl ether and reduced with lithium aluminum hydride to 5-ethylamino-3-phenylpyrazole **IV** [10], which was reacted with a series of dicarboxylic acid anhydrides, namely succinic, maleic, 4-cyclohexenedicarboxylic and cyclohexanedicarboxylic acid anhydrides. The reaction was carried out in tetrahydrofuran in the presence of 1,3-dicyclohexylcarbodiimide, according to a method employed in a peptide synthesis procedure [11]. The above condensation affords bicyclic and tricyclic derivatives of the pyrazolo[1,5-a][1,3]diazepine system, although in low yield. Alternative synthetic routes, such as isolation of reaction intermediates between **IV** and the above-mentioned carboxyanhydrides, which are then cyclized, proved unsuccessful, either because of the low reactivity of the reagents, or because of the formation of intractable tars.

Structure assignments to the products are based on spectral data, ir, ^1H - and ^{13}C -nmr (see Experimental). It is apparent that the amino group of **I** must be mono-blocked, since carboxyanhydrides are known to react smoothly with aminopyrazoles to yield imidopyrazoles [11].

Some compounds, were tested in preliminary experi-

ments, to investigate their behavioural reactions according to Irwing technique, to be a useful indication of their systemic effects [12].

Compounds **V**, **VI**, **VII** were administered p.o. in a 1% carboxymethylcellulose suspension (0.1 ml/10 g) up to dose of 1 g/Kg to Swiss male rats weighing 20 ± 2 g. In Irwin's test none of the tested compounds showed any particular symptomatology.

EXPERIMENTAL

Melting points were determined with a Buchi 510 apparatus, and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 681 spectrophotometer, in Nujol mulls. The ^1H -nmr spectra were measured with a Varian EM 60 spectrometer and chemical shifts are expressed in δ (ppm) downfield from TMS as an internal standard. Multiplicity is indicated by: s, singlet, d, doublet, t, triplet, m, multiplet, bs, broad singlet which exchanges with deuterium oxide. The ^{13}C -nmr spectra were run at 20 MHz on a Varian FT 80-A spectrometer. The temperature of measures was 38° and the concentration of samples was 10% (v/v) in DMSO- d_6 . Chemical shifts are reported relative to TMS as internal standard. The purity of samples was determined by means of tlc., which was performed using Merk (Darmstadt) silica gel 60 F 254 plates. The mass spectra were obtained with a VG 70-70 EQ in-

strument (VG Analytical, Manchester, U.K.) in D.E.I. (Direct Electro Impact) at $M/\Delta M = 1500$ mass resolution (10% valley definition) and a run speed of 2 s per decade. The data were processed on a Digital PDP8/A computer system.

Bis(3-phenylpyrazol-5-yl)amine III.

A solution of 5 g of **I** in 10 ml of acetic acid was refluxed for 3 hours. The solution was diluted with 30 ml of water and the resulting precipitate was collected by filtration and recrystallized from 95% ethanol (yield 78%); colourless crystals, mp 276-277°; pmr (deuteriodimethyl sulfoxide): 8.10 (4 H, m, *ortho* H), 7.78 (3 H, b s, 3 NH, exchangeable), 7.50 (6 H, m, *meta, para* H), 6.90 (1 H, s, pyrazole H), 6.68 (1 H, s, pyrazole H) ppm; ms: m/z 286 ($M + \text{-NH}$) (base peak), 246.

Anal. Calcd. for $C_{18}H_{15}N_5$: C, 71.74; H, 5.02; N, 23.24. Found: C, 71.50; H, 5.00; N, 23.54.

5-Ethyl-3-phenylpyrazole IV.

To a suspension of 1.6 g (0.042 mole) of lithium aluminum hydride in 50 ml of dry ether, 5 g (0.020 mole) of **II** was added in small portions and stirred at room temperature for 1 hour. The mixture was gently refluxed for 4 hours, under cooling then some drops of water were carefully added. The mixture was washed with water and the ether layer was dried (sodium sulfate) and evaporated to give a colourless residue, which recrystallized from water, (yield 75%), mp 98-100°; pmr (deuteriochloroform): 7.50 (5 H, m, aromatic protons), 6.85 (2 H, b s, 2 NH, exchangeable), 5.85 (1 H, s, pyrazole H), 3.20 (2 H, q, CH_2), 1.20 (3 H, t, CH_3) ppm.

Anal. Calcd. for $C_{11}H_{13}N_3$: C, 70.56; H, 6.99; N, 22.44. Found: C, 70.68; H, 6.86; N, 22.56.

General Procedure for the Preparation of Bicyclic and Tricyclic Derivatives of Pyrazolo[1,5-a][1,3]diazepines V, VI, VII, VIII.

To a solution of equimolar amounts (0.010 mole) of **IV** and suitable anhydrides in 30 ml of dry tetrahydrofuran was added a solution of 1,3-dicyclohexylcarbodiimide (0.010 mole) in 10 ml of the same solvent. After the mixture had been stirred for 2 days at room temperature, a white precipitate was filtered and the tetrahydrofuran was evaporated under reduced pressure. The residue was taken up in isopropyl ether and collected by filtration. The crude products were further purified by recrystallization.

The ^{13}C -nmr chemical shifts of all compounds are reported in Table I and positional numbering of carbon atoms is arbitrary, as indicated in the structure diagrams.

4-Ethyl-5,6,7,8-tetrahydro-2-phenylpyrazolo[1,5-a][1,3]diazepin-5,8-dione V.

According to the general procedure, using succinic anhydride, white crystals were obtained from isopropyl ether-cyclohexane, (yield 6%), mp 153-155°; ir: cm^{-1} 1740, 1690, 1590, 1570, 1210, 770; pmr (deuteriochloroform): 7.90 (2 H, m, *ortho* H), 7.50 (3 H, m, *meta, para* H), 6.50 (1 H, s, pyrazole H), 4.00 (2 H, d, N-CH_2), 3.10 (4 H, m, CH_2 at 6- and 7-positions), 1.20 (3 H, t, CH_3) ppm.

Anal. Calcd. for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.75; H, 5.56; N, 15.75.

5,10-Dihydro-4-ethyl-2-phenylpyrazolo[1,5-a][1,3]-7-cyclohexendiazepin-5,10-dione VI.

According to the general procedure using 4-cyclohexanedicarboxylic acid 1,2-anhydride; white crystals were obtained from isopropyl ether-cyclohexane (yield 30%), mp 185-187°; ir: cm^{-1}

1720, 1680, 1590, 1570, 1300, 760; pmr (deuteriochloroform): 7.90 (2 H, m, *ortho* H), 7.50 (3 H, m, *meta, para* H), 6.50 (1 H, s, pyrazole H), 5.98 (2 H, m, 2 CH), 2.60 (4 H, m, CH_2 at 6- and 9-positions), 1.29 (3 H, t, CH_3) ppm.

Anal. Calcd. for $C_{15}H_{15}N_3O_2$: C, 71.00; H, 5.95; N, 13.07. Found: C, 71.12; H, 6.00; N, 13.12.

5,10-Dihydro-4-ethyl-2-phenylpyrazolo[1,5-a][1,3]cyclohexandiazepin-5,10-dione VII.

According to the general procedure, using 1,2-cyclohexanedicarboxylic anhydride, white crystals were obtained from isopropyl ether-cyclohexane (yield 15%), mp 168-170°; ir: cm^{-1} 1720, 1680, 1590, 1570, 1520, 1350, 1220, 760; pmr (deuteriochloroform): 7.90 (2 H, m, *ortho* H), 7.45 (3 H, m, *meta, para* H), 6.45 (1 H, s, pyrazole H), 3.95 (2 H, m, N-CH_2), 3.20 (2 H, m, 2 CH), 1.80 (8 H, m, 4 CH_2 at 6-, 7-, 8-, and 9-positions), 1.30 (3 H, t, CH_3) ppm.

5,8-Dihydro-4-ethyl-2-phenylpyrazolo[1,5-a][1,3]diazepin-5,8-dione VIII.

As above general procedure, using maleic anhydride, yellow crystals were obtained from isopropyl ether-cyclohexane (yield 1%), mp, 160-164°; ir: cm^{-1} 1700, 1660, 1620, 1560, 1200, 760; pmr (deuteriochloroform): 7.90 (2 H, m, *ortho* H), 7.50 (3 H, m, *meta, para* H), 6.95 (2 H, s, $\text{C}_6\text{H}=\text{C}_7\text{H}$), 6.50 (1 H, s, pyrazole H), 4.20 (2 H, q, N-CH_2), 1.40 (3 H, t, CH_3) ppm.

Anal. Calcd. for $C_{15}H_{13}N_3O_2$: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.32; H, 4.85; N, 15.80.

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