Augusto Colombo*, Jordi Frigola, Juan Parés and Blas Andaluz

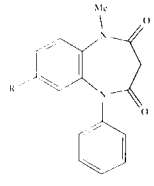
Department of Medicinal Chemistry, Laboratorios Dr. Esteve,
Avda. Mare de Déu de Montserrat, 221, 08026-Barcelona, Spain

Received January 3, 1989

The synthesis and structure elucidation of new pyrazolo[3,4-*b*][1,4]diazepines and pyrazolo[3,4-*b*]pyrazines are reported and the characterisation of isomers and tautomers by proton and carbon-13 nmr are discussed. In some case only NOE experiments allow us to identify the isomeric structure.

J. Heterocyclic Chem., **26**, 949 (1989).

1-Aryl-3-methyl-4,5-diaminopyrazoles are starting materials for two families of condensed heterocycles, the pyrazolo[3,4-*b*][1,4]diazepines and the pyrazolo[3,4-*b*]-pyrazines. Both are related to molecules of biological interest, the first ones to [1,5]benzodiazepines [1], for instance, the antiepileptic drugs clobazam (**1a**) and triflubazam (**1b**), and the second ones, to purines and the corresponding nucleosides [2,3].



1a R = Cl

1b R = CF_3

Pyrazolo[3,4-*b*][1,4]diazepines.

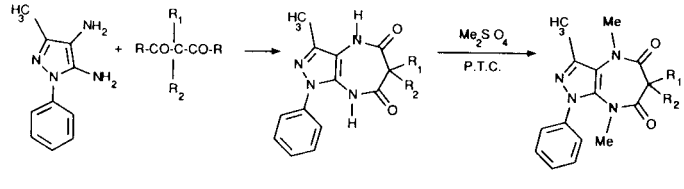
1-Phenyl-3-methylpyrazolo[3,4-*b*][1,4]-diazepine-5,9-diones **4** can be prepared from 1-phenyl-3-methyl-4,5-diaminopyrazole (**2**) and malonyl derivatives **3** (Scheme I). When malonyl dichloride (**3a**) in pyridine was used, **4e** was obtained in good yield but the preparation of this compound by reaction of **2** with diethyl malonate (**3c**) in a variety of solvents like ethanol, acetonitrile, pyridine, toluene or xylene, results in recovery of **2**. The addition of molar amounts of anhydrous sodium acetate or sodium methoxide do not result in the obtention of **4e**. The 6,6-di-*n*-butyl derivative **4d** was obtained, in moderate yield, by reaction of **2** with the corresponding malonyl dichloride (**3a**, $R_1 = R_2 =$ *n*-butyl) in pyridine.

The preparation of **4f** was attempted several times by reaction of **2** with the corresponding dichloride **3a** ($R_1 =$ *n*-butyl, $R_2 =$ H) in pyridine and by reaction of **2** with **3c** ($R_1 =$ *n*-butyl, $R_2 =$ H), but these reactions failed. Finally, the reaction of **2** with bis(2,6-dimethylphenyl)-2-*n*-butyl malonate (**3b**) [4] in an oil bath at 230° results in the formation, with good yield, of **4f**. Methylation of **4f** with dimethyl sulfate in phase transfer conditions afforded the 4,9-dimethyl derivative **5** in poor yield.

Condensation of **2** with benzoyl acetates **6** yields pyrazolo[3,4-*b*][1,4]diazepinones (Scheme II). Two different isomers **7** and **8**, can be obtained, each one with several tautomeric forms, *e.g.*, **9** and **10**, in the case of compound **7**. There is a literature result [5] reporting that the reaction between **2** and ethyl acetoacetate yield only the isomer corresponding to structrue **7**. In our case the reaction works differently depending on the substituents on the aryl groups, **6a-6d**.

The reaction between **6a** and **2** in xylene at reflux yield a 1:1 mixture of **7a** and **8a** in a 44%. The same mixture was obtained in a 33% yield working without solvent (15 minutes in an oil bath at 190°). The reaction between **6b** and **2** yield only **7b** both in xylene at reflux (54%) and without solvent (21%). A similar result, formation exclusively of **7d**, was obtained with ester **6d**, whereas **6c**

Scheme I



2 3 4 5

a) R=Cl
b) R=2,6di Me C_6H_3-O-
c) R=OEt

d) $R_1=R_2=$n Butyl
e) $R_1=R_2=H$
f) $R_1=$n Butyl; $R_2=H$

R_1 = n Butyl; R_2 = H

Scheme II

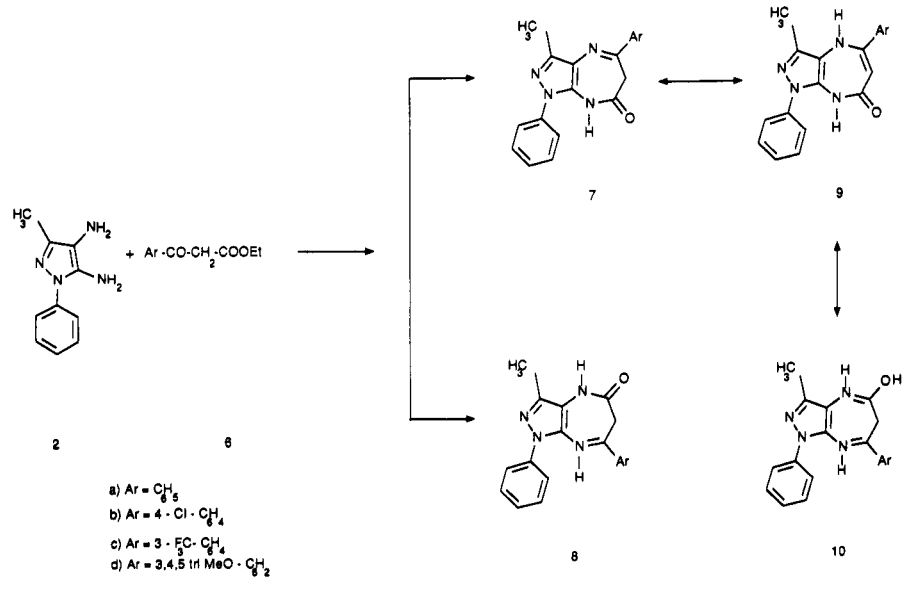


Table 1

Compound	R_1	R_2	Yield %	MP	Analysis % Calcd./Found C	H	N	IR (cm^{-1}) NH	C=O	^{1}H-NMR (DMSO-d_6)
4d	*n*-Bu	*n*-Bu	32	158	68.45 68.32	7.66 7.71	15.20 15.01	3240	1630	0.5-2 (m, 9H, But), 2.5 (s, 3H, Me), 2.6 (m, 1H, CH), 7.4 (m, 5H, Ar)
4e	H	H	80	>290	60.69 60.57	5.09 4.89	21.78 21.93	3230	1690	2.1 (s, 3H, Me), 3.4 (s, 2H, CH_2), 7.35 (m, 5H, Ar)
4f	H	*n*-Bu	69	>290	65.16 64.98	6.75 6.87	17.88 17.63	3260	1690	not soluble enough
5	H	*n*-Bu	7	>290	67.04 67.17	7.10 7.19	16.46 16.60	–	1690	0.7-1.9 (m, 7H, But), 2.2 (m, 5H, Me), 2.9 (s, 3H, Me), 3.1 (s, 3H, Me), 3.4 (m, 1H, CH), 7.4 (m, 5H, Ar)

Table 2

Compound	Ar	Yield %	MP	Analysis % Calcd./Found C	H	N	X	IR (cm^{-1}) NH	C=O	^{1}H-NMR (DMSO-d_6)
7a	Ph	44	239-240	72.13 72.34	5.10 4.90	17.71 18.00	–	3150	1685	2.36 (s, 3H, Me), 3.75 (s, 2H, CH_2), 7.2-8.2 (m, 10H), 10.88 (s, 1H, NH)
8a	Ph	33	234-235	72.13 71.92	5.10 5.07	17.71 17.53	–	3150	1685	2.31 (s, 3H, Me), 3.73 (s, 2H, CH_2), 7.2-8.2 (m, 10H), 10.67 (s, 1H, NH)
7b	4-Cl-C_6H_4	54-21	260-262	65.05 64.79	4.31 4.52	15.97 16.13	10.10	3220	1680	2.35 (s, 3H, Me), 3.75 (s, 2H, CH_2), 7.20-8.20 (m, 9H, Ar), 11.15 (s, 1H, NH)
7c	3-CF_3-C_6H_4	41	196-198	62.50 62.83	3.93 4.19	14.57 14.50	14.83	3125	1695	3.37 (s, 3H, Me), 3.83 (s, 2H), 7.2-8.3 (m, 9H, Ar), 11.23 (s, 1H, NH)
7d	3,4,5 tri MeO-C_6H_2	25	216	65.02 65.19	5.45 5.22	13.78 13.61	–	3160	1680	2.36 (s, 3H, Me), 3.25 (s, 2H, CH_2), 3.75 (s, 3H, Me), 3.9 (s, 6H, Me), 7.6 (m, 7H, Ar), 11.1 (s, 1H, NH)

yield (xylene at reflux) a 5:1 mixture of **7c** and **8c**.

Proton (Table 2) and carbon-13 nmr (Table 6) were used to determine the isomeric structure and the dominant tautomer. The presence of a CH_2 group (both in ^1H and ^{13}C spectra) and the signal near 160 ppm (^{13}C nmr) exclude tautomers **9** and **10**, respectively.

To distinguish between **7** and **8** selective NOE difference experiments were performed. Weak irradiation of the NH singlet (11 ppm) would result in an increase of the *ortho*-phenyl protons signal (7.1-7.5 ppm) in isomer **7** and in an increase of the 3-methyl signal (2.3-2.4 ppm) in isomer **8**.

The mixture of **7a** and **8a** was resolved into its components by hplc. The only significant difference between the ^1H nmr spectra of **7a** and **8a** was the NH proton signal. The first eluted compound (NH = 10.67 ppm) shows an important enhancement of the methyl signal (2.31 ppm) on irradiation of the NH and therefore was assigned the

Table 3

Compound	Ar_1	Ar_2	Time	Solvent	Yield %	MP	Analysis % Calcd./Found C	H	N	X	IR (cm^{-1})		^1H-NMR
12a	Ph	Ph	24	EtOH	91	194-196 [a]	79.53 79.70	5.00 4.89	15.46 15.52	–	1600	1350	2.7 (s, 3H, Me), 7.25 (m, 13H, Ar), 8.1 (m, 2H, Ar), deuteriochloroform
12b	3-Cl-C_6H_4	Ph	3	Toluene	61	207-208	72.63 72.81	4.32 4.19	14.12 14.29	8.93 9.01	1600	1540	3.05 (s, 3H, Me), 7.45-7.95 (m, 12H, Ar), 8.1-8.4 (m, 12H, Ar), DMSO-d_6
12c	3-CF_3-C_6H_4	Ph	12	EtOH Toluene	39	182-184	69.76 69.68	3.98 4.09	13.01 12.89	13.24 13.39	1620	1510	2.7 (s, 3H, Me), 7.3 (m, 12H, Ar), 8.6 (m, 2H, Ar), DMSO-d_6
12d	Ph	4-Cl-C_6H_4	2	P.P.A	79	195-196	66.83 66.92	3.74 3.87	12.99 12.80	16.44 16.32	1600	1495	2.75 (s, 3H, Me), 7.25 (m, 12H, Ar), 8.25 (m, 2H, Ar), deuteriochoroform

[a] Lit mp 183° [6].

Table 4

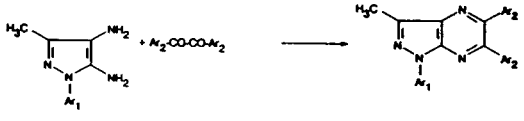
Compound	Ar	Ar_2	Yield %	MP	Analysis % Calcd./Found C	H	N	X	IR (cm^{-1})		^1H-NMR (DMSO-d_6)
15a	Ph	4-ClC_6H_4	37%	203-205	67.40 67.52	4.08 3.87	17.46 17.63	11.05 11.18	1600	1515	2.78 (s, 3H, Me), 7.3-7.6 (m, 5H, Ar), 8.1-8.3 (m, 4H, Ar), 9.15 (s, 1H, C-H) (deuteriochloroform-TFA)
16a	Ph	4-ClC_6H_4	37	135-138	67.40 67.36	4.08 4.14	11.46 11.21	11.05 10.87	1605	1415	3.29 (s, 3H, CH_3), 7.3-7.7 (m, 5H, Ar), 8.2-8.4 (m, 4H, Ar), 9.33 (s, 1H, CH)
15c	3-$CF_3C_6H_4$	Ph	59	170-172	64.40 64.52	3.70 3.58	15.81 15.93	16.09 15.90	1620	1510	3.34 (s, 3H), 7.5-8 (m, 5H), 8.22 (m, 2H), 8.65 (s, 2H), 9.33 (s, 1H)
15d	3-ClC_6H_4	Ph	43	199-201	67.40 67.54	4.08 3.89	17.46 17.32	11.05 11.00	1595	1470	2.91 (s, 3H), 7.4-7.8 (m, 5H), 8.2 (m, 4H), 9.3 (s, 1H)
16d	3-ClC_6H_4	Ph	15	141-143	67.40 67.61	4.08 4.16	17.46 17.51	11.05 11.22	1600	1490	2.64 (s, 3H), 7.6 (m, 5H), 8.3 (m, 4H), 9.3 (s, 1H)

structure **8a**. Similar NOE experiments on the second eluted compound show that on irradiation at 11.10 ppm (NH) only the aromatic protons (7.12 ppm) increase in intensity as expected for isomer **7a**. The same technique was used to determine the structure of **7b** and **7d**. The mixture of isomers **7c** (NH = 11.23 ppm) and **8c** (NH = 10.80 ppm) were assigned by analogy; only isomer **7c** was isolated pure.

Pyrazolo[3,4-*b*]pyrazines.

Pyrazolo[3,4-*b*]pyrazines are relatively unknown substances [6,7] whose pharmacological properties have never been studied. They can be prepared by condensation with 1,2-dicarbonyl compounds. As shown in Scheme III, the reaction of the 3-methyl-1-aryl-4,5-diaminopyrazoles with benzils in refluxing ethanol or toluene during several hours gives 1,5,6-triaryl-3-methyl-1*H*-pyrazolo[3,4-*b*]pyrazine in excellent to moderate yields. In the case of 4,4'-diclorobenzil **12d** we were obliged to use polyphosphoric acid to achieve the condensation.

Scheme III



13 11 12

a) $Ar_1 = Ar_2 = C_6H_5$

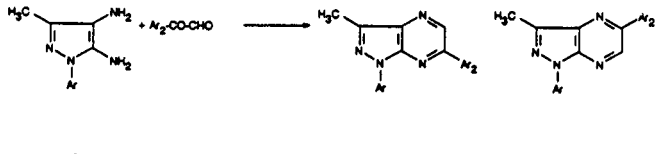
b) $Ar_1 = 3\text{-}Cl\text{-}C_6H_4$; $Ar_2 = C_6H_5$

c) $Ar_1 = 3\text{-}F_3C\text{-}C_6H_4$; $Ar_2 = C_6H_5$

d) $Ar_1 = C_6H_5$; $Ar_2 = 4\text{-}Cl\text{-}C_6H_4$

The reaction between 1-phenyl-3-methyl-4,5-diaminopyrazole **2** and *p*-chlorophenylglyoxal **14b** in ethanol gives, with good yield, a 1:1 mixture of the corresponding regioisomers **15a** and **16a** which were separated by crystallization and characterized by nmr and ir (Scheme IV). When 1-(3-trifluoromethyl)phenyl-3-methyl-4,5-diaminopyrazole **13c** was reacted with phenylglyoxal **14a**, also in refluxing ethanol, we only obtained the product of formula **15c** in moderate yield, this being the result of reaction of the most reactive carbonyl group, the aldehyde, with the more reactive 4-amino group.

Scheme IV



13 14 15 16

a) $Ar = C_6H_5$

b) $Ar = 4\text{-}Cl\text{-}C_6H_4$

c) $Ar = 3\text{-}CF_3\text{-}C_6H_4$

d) $Ar = 3\text{-}Cl\text{-}C_6H_4$

The reaction between the diaminopyrazole **2** and some phenylpyruvic acids **17a-d** Scheme V, in refluxing ethanol gives, in moderate to good yields, insoluble products which proved to be difficult to distinguish between **18** and **20** or their tautomers **19** or **21** by routine spectroscopy and we have recorded ^{13}C nmr spectra with the aim of establishing a spectral method for structural assignment of these ring systems. In view of the ir data of the products in potassium bromide we discarded formulas **19** and **21** due to the presence of an OH absorption and a lack of NH absorption.

The ^1H nmr spectrum of these compounds, in DMSO-d_6, showed a characteristic OH band and the ^{13}C nmr spectrum of one of these products, in DMSO-d_6, showed no

Table 5

Compound	R	Yield %	MP	Analysis % Calcd./Found				IR (cm^{-1})		^1H-NMR (DMSO-d_6), Tautomer **20**
				C	H	N	X	OH	C=N	
21a	Ph	63	>300	75.98 75.73	5.37 5.22	18.65 18.83	–	2760	1660	2.4 (s, 3H, Me), 4.15 (s, 2H, CH_2), 7.3 (m, 8H, Ar), 8.0 (d, 2H, Ar), J = 8 Hz, 12.5 (b, 1H, OH)
21b	4-ClC_6H_4	42	>300	68.16 68.01	4.51 4.60	16.73 16.82	10.59 10.63	2790	1660	2.4 (s, 3H, Me), 4.15 (s, 2H, Me), 7.35 (m, 7H, Ar), 8.0 (d, 2H, Ar), J = 7.9 Hz, 12.65 (b, 1H, OH)
21c	3-ClC_6H_4	48	>300	68.16 67.92	4.51 4.40	16.73 16.85	10.59 10.68	2780	1660	2.4 (s, 3H, Me), 4.2 (s, 2H, CH_2), 7.4 (m, 7H, Ar), 8.0 (d, 2H, Ar), J = 9 Hz, 12.4 (b, 1H, OH)
21d	2-ClC_6H_4	36	>300	68.16 68.41	4.51 4.60	16.73 17.60	10.59 10.72	2720	1660	2.4 (s, 3H, Me), 4.3 (s, 2H, CH_2), 7.5 (m, 7H, Ar), 7.9 (d, 1H, Ar), J = 6.6 Hz, 12.7 (b, 1H, OH)

Scheme V

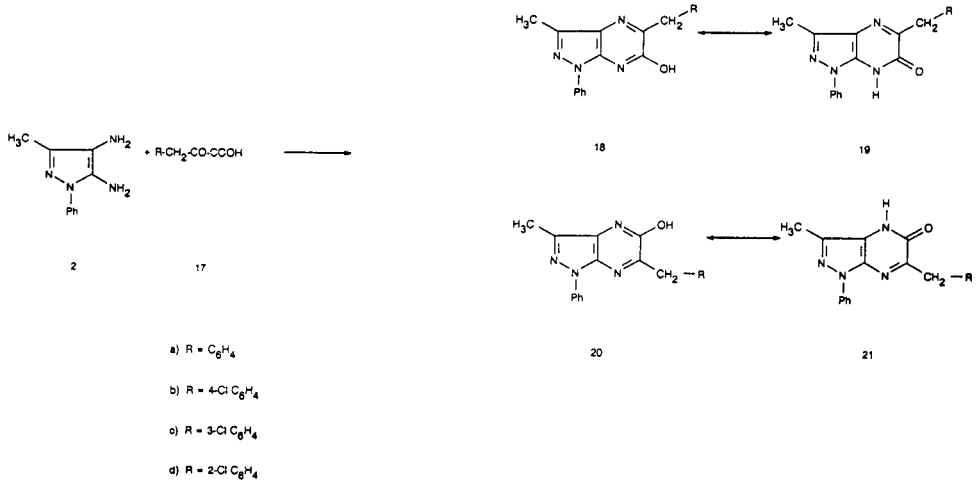
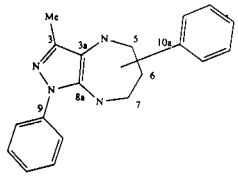
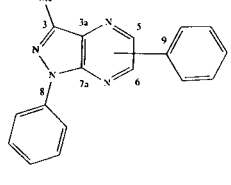


Table 6



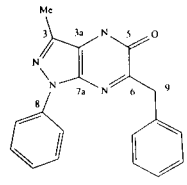
Compound	Me	3	4	5	6	7	8	9	10
7a	10.8	144.5	123.2	151.7	40.6	161.6	127.4	137.9*	138.1*
8a	11.3	139.0	113.7	161.6	41.5	155.3	139.5*	137.1*	138.5
7b	11.3	144.7	123.5	150.6	40.6	161.8	138.2	137.7	135.0
7c	11.3	144.9	123.4	150.2	40.6	161.8	138.9*	138.3*	
7d	11.4	144.7	123.5	151.6	40.9	162.0	140.3	138.4	128.8

Table 7



Compound	Me	3	4	5	6	7	8	9
15a	11.0	141.0	122.8	132.5	139.8	157.7	146.3	136.6
16a	10.6	142.4	126.4	147.6	145.5	144.14	138.5	136.4
15c	11.08	141.3	119.2	133.4	137.8	156.4	146.1	133.4
15d	11.05	141.1	121.7	133.5	138.0	156.4	147.1	136.0
16d	Not registered due to its insolubility							

Table 8



Compound	Me	3	3a	5	6	7a	8	9
20a	9.0	134.7	115.1	166.5	156.7	137.2	133.7	40.6
20b	9.6	134.3	115.0	162.3	156.6	137.0		39.5
20c	9.4	134.9	115.1	164.0	156.7	137.3	134.3	39.8
20d	9.5	134.1	114.8	163.2	156.6	136.9	133.2	38.2

signals attributable to a carbonyl group. This suggests that in DMSO-d_6 the products will have structures **18** or **20**.

The ^{13}C nmr spectra of these sustances in TFAA/deuteriochloroform show an absorption near 165 ppm which is characteristic of a carbonyl group, thus, in these conditions, the most stable tautomers were **19** or **21**.

To distinguish between **19a** and **21a** we performed a NOE transfer experiment in a dilute solution in DMSO-d_6 at 80°. Weak irradiation on the NH signal at 12.6 ppm results in an enhancement of signal at 2.3 ppm, which corresponds to a methyl group and we therefore can discard **19a**. Although the assignments of ^{13}C nmr were made in TFAA/deuteriochloroform, due to the very poor solubility of this compound, and thus would refer to a compound **21**, the solids obtained from the reaction must have the structure **20**.

The products were evaluated for analgesic, antiinflammatory, hypothermal, ataxic and CNS properties and although some of them were active in some tests, their potencies were not sufficient to consider them for further development.

EXPERIMENTAL

All melting points were determined on a Kofler melting point microscope and are uncorrected. The proton magnetic resonance spectra were obtained from Varian AM 360 (60 MHz) or from Bruker A.M. Fourier transform spectrometer operating at 100 MHz and the ^{13}C nmr spectra were obtained from a Bruker AM-100 Fourier transform spectrometer operating at 25.1 MHz. Chemical shifts (δ) are relative to TMS as an internal standard. The infrared spectra were obtained in potassium bromide pellets on a Perkin-Elmer model 177 and the preparative hplc were performed on a Waters Auto 500.

General Procedure for the Preparation of Pyrazolo[3,4-*b*][1,4]diazepines **4d-f**.

A solution of malonyl dichloride **3** (7 g, 27.6 mmoles) in pyridine (20 ml) was treated with 1-phenyl-3-methyl-4,5-diaminopyrazole **2** (5.2 g, 27.6 mmoles) in portions during 30 minutes. After being stirred for 20 hours at room temperature, the solution was treated with water (200 ml), acidified with concentrated hydrochloric acid and extracted with chloroform (3 x 30 ml), dried (sodium sulfate), the solvent evaporated and the residue recrystallized from ethanol/water. Analytical and spectral data are recorded in Table 1.

1-Phenyl-3,4,8-trimethyl-6-butyl-5,7-dioxo-5,6,7,8-tetrahydro-1*H* pyrazolo[3,4-*b*][1,4]diazepine (**5**).

A suspension of compound **4f** (1.2 g, 3.8 mmoles), 50% sodium hydroxide in water (10 ml), benzene (70 ml), triethylbenzylammoniumchloride (TEBA, 50 mg) and dimethylsulfate (1.1 g, 8.5 mmoles) was kept under stirring at room temperature for 20 hours. The mixture was separated and the aqueous phase was extracted with dichloromethane (3 x 5 ml). The organic phases were combined, dried (sodium sulfate), and evaporated. The residue was recrystallized from carbon tetrachloride yielding 100 mg (7%) of **5**, mp >290°. Analytical and spectral data are recorded in Table 1.

1,5-Diphenyl-3-methyl-7-oxo-6,7-dihydro-8*H*-pyrazolo[3,4-*b*][1,4]-diazepine **7a** and 1,7-Diphenyl-3-methyl-5-oxo-5,6-dihydro-8*H*-pyrazolo[3,4-*b*][1,4]diazepine **8a**.

A mixture of **2** (1.9 g, 10 mmoles), **6a** (4.0 g, 20 mmoles) and xylene (100 ml) was refluxed and the falling xylene continuously passed through a soxhlet containing 40 g of 4 Å molecular sieves, for 24 hours. After evaporation of the solvent the residue was crystallized from ethanol yielding 1,4 g (44%) of a compound, mp 203-214°, which was an 1:1 mixture (^1H nmr) of **7a** and **8a**. This mixture was separated by preparative hplc, eluting with a mixture of ethylacetate and petroleum ether (1:1) on a (Pre Pak 500) silica column and the first substance eluted was **7a** mp 240° and the second **8a**, mp 235°. Analytical and spectral data are recorded in Table 1.

By the above procedure using other ethyl-substituted benzoylacetates **6b-d** we obtained the compounds **7b-d**. They were purified by recrystallization from etanol. Analytical and spectral data are recorded in Table 2.

General Procedure for the Preparation of 1,5,6-Triaryl-3-methyl-1*H*-pyrazolo[3,4-*b*]pyrazine **12a-c**.

An equimolar (5 mmoles) mixture of the corresponding 1-aryl-3-methyl-4,5-diaminopyrazole **13** and the corresponding benzil **12** were refluxed in ethanol (20 ml) for 2 hours. The voluminous precipitate was collected and recrystallized from ethanol. Analytical and spectral data are recorded in Table 3.

1-Phenyl-3-methyl-5,6-di(4-chlorophenyl)-1*H*-pyrazolo[3,4-*b*]-pyrazine **12d**.

A mixture of **2** (0.95 g, 5 mmoles) and 4,4'-dichlorobenzil **11d** (1.4 g, 5 mmoles) with polyphosphoric acid (20 g) was heated at 130° on an oil bath, under a nitrogen current for 15 hours. The cold crude mixture was poured over ice-cold water. The solid was collected and recrystallized from acetone: water, yielding 1.7 g (79%) of **12d**. Analytical and spectral data are recorded in Table 3.

1-Phenyl-3-methyl-5-(4'-chlorophenyl)-1*H*-pyrazolo[3,4-*b*]pyrazine **16a** and 1-phenyl-3-methyl-6-(4'-chlorophenyl)-1*H*-pyrazolo[3,4-*b*]-pyrazine **15a**.

A mixture of **2** (1.9 g, 10 mmoles) and *p*-chlorphenylglioxal **14d** in ethanol (20 ml) was refluxed for 30 minutes. The voluminous precipitate was collected and washed with ethanol. The crude product 2.7 g was recrystallized from ethanol (500 ml) yielding 1.2 g (37%) of product **15a**. Compound **16a** (1.2g, 37%) crystallized from the mother liquor.

By the same procedure we obtained product **15c** and by the above procedure, but crystallizing from methanol, we obtained and separated compounds **15d** and **16d**. Analytical and spectral data are recorded in Table 4 and 7.

General Procedure for the Preparation of 1-Phenyl-3-methyl-5-hydroxy-6-chlorobenzyl-1*H*-pyrazolo[3,4-*b*]pyrazines **20a-d**.

A solution of **2** (1.1 g, 6 mmoles) and the corresponding phenylglioxal **17a-d** (6 mmoles) in ethanol (10 ml) was warmed in a water bath for 5 minutes and the voluminous precipitate filtered off and washed with ethanol and acetone. Analytical and spectral data are recorded in Tables 5 and 8.

Acknowledgements.

We would like to thank Dr. F. Sanchez-Ferrando of the Facultad de Ciències, Universitat Autònoma de Barcelona for helpful discusions.

REFERENCES AND NOTES

[1] L. M. Sternbach, *Prog. Drug Res.*, **22**, 229 (1978).

[2] M. Terao, K. Karasawa, N. Tanaka, H. Hyonehara and H. Umegawa, *J. Antibiotic. Ser. A.*, **13**, 401 (1960).

[3] R. A. Sharma, M. Robeck, F. E. Cole and A. Bloch, *J. Med. Chem.*, **16**, 643 (1973).

[4] E. Tiegler and H. Majem, *Monatsh. Chem.*, **89**, 143 (1958).

[5] S. P. Affane-Nguema, J. P. Lavergne and Ph. Viallefont, *J. Heterocyclic Chem.*, **14**, 391 (1977).

[6] I. Grandberg and G. V. Klyucho, *Zh. Obshch. Khim.*, **32**, 1898 (1962).

[7] P. G. Baraldi, D. Simoni, V. Periotto, S. Manfredini and M. Guarnieri, *Synthesis*, 148 (1984).