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3-PHENYLPYRAZOLO(4,3-c)PYRIDINE AND DERIVATIVES: STRUCTURE DETERMINATION

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ABSTRACT

The structures of 3-phenylpyrazolo(4,3-c)pyridine (1) and 5-methyl-3-phenyl-4,5,6,7-tetrahydropyrazolo(4,3-c)pyridine (2) are determined by detailed ^{1}H and ^{13}C NMR analysis and theoretical calculations in comparison with their *N*-methyl derivatives as fixed models. CNDO/2 and PPP calculations are performed on the three prototropic forms admissible for the tautomeric system 1. By comparison of the ^{13}C NMR and UV spectra of 1 with those of its three fixed *N*-methyl derivatives and of the UV spectra calculated for the tautomers of 1 with that experimentally obtained in the range 200–450 nm, 3-phenylpyrazolo(4,3-c)pyridine (1) is established to exist entirely in the 1H tautomeric form 1A.

By ^{13}C NMR investigations of 5-methyl-3-phenyl-4,5,6,7-tetrahydropyrazolo(4,3-c)-pyridine (2), in comparison with its fixed 1-methyl-1H derivative 9 and other substituted pyrazoles, 2 is determined to be a mixture of the 1H- (2A) and 2H- (2B) tautomers with 2A largely predominating. The compounds investigated are described here for the first time.

INTRODUCTION

The tautomerism of pyrazolopyridines, with three tautomeric forms possible, has not been investigated [1], whereas considerable scientific efforts have been directed to the study of tautomeric equilibria in related indazoles and monoazaindoles [2]. The latter compounds are known to undergo *N*-alkylation with the formation of isomers [2, 3].

This paper describes the structure of 3-phenylpyrazolo(4,3-c)pyridine, 5-methyl-3-phenyl-4,5,6,7-tetrahydropyrazolo(4,3-c)pyridine and their *N*-methylation products as determined by ^{1}H and ^{13}C NMR investigations and theoretical calculations.

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EXPERIMENTAL

Methods and materials

All NMR spectra were recorded on a Bruker WM-250 spectrometer supplied with an Aspect 2000 Data System with an internal D lock. The spectra were measured using approx. 0.5 M solutions in DMSO-d_6 at ambient temperature unless otherwise stated. Chemical shifts were determined from the central peak of the solvent using the following relations:

$$\delta^{H}_{TMS} = \delta^{H}_{DMSO\text{-}d_6} + 2.49 \pm 0.002 \text{ ppm}$$

$$\delta^{C}_{TMS} = \delta^{C}_{DMSO\text{-}d_6} + 39.6 \pm 0.05 \text{ ppm}$$

Typical recording conditions for the ^{1}H NMR spectra were: 250.13 MHz, 5 mm o.d. tubes, spectral width 2.5 kHz, pulse width 4 μs (ca. 70°), data memory 16K, 16 scan.

The ^{13}C NMR spectra were measured at 62.89 MHz in 10 mm o.d. tubes. The recording conditions for the proton-noise decoupled spectra were as follows: spectral width 12.5 kHz, pulse width 15 μs (ca. 30°), pulse repetition time 2.5 s, data memory 16K, decoupling power 1.5 W.

Thin-layer chromatography was performed on Alumina TLC-Cards with fluorescent indicator (layer thickness 0.2 mm, Fluka); 2 μl of ca. 1% solutions in chloroform were applied 1.5 cm from the edge and the chromatograms were developed with hexane: chloroform (20:80) without saturation of the tank over a run distance of 10 cm, UV light (254 nm) detection. The R_f values are means of four determinations. Aluminium oxide S, neutral (Brockman activity II, Riedel-de Haën) was used for column chromatography.

3-Phenylpyrazolo(4,3-c)pyridine (1)

To a stirred solution of 4-chloro-3-pyridinyl phenyl ketone (3) hydrochloride [4] (12.71 g, 0.05 mol) in absolute ethanol (50 ml) was added hydrazine (12.7 ml, 0.40 mol). The solution was heated under reflux for 2 h, cooled, the product filtered off and washed consecutively with water and methanol to give 7.23 g (74%) of 1 as colorless crystals: m.p. 266–267°C; IR (Nujol) 2900(br), 1640(sh), 1620, 1590, 1570, 1520, 1490, 1420, 1360, 1320, 1250 cm^{-1}; ^{1}H NMR (DMSO-d_6) δH4', 7.44t, 1H; 2H3', 7.54t, 2H; H7, 7.57d, 1H; 2H2', 8.05d, 2H; H6, 8.35d, 1H; H4, 9.41s, 1H and HN, 13.63s, 1H. M.S. (EI, 70 eV) *m/e* 195(M^+, 100%), 168 (M^+—HCN, 4), 139(M^+—$H_4C_2N_2$, 2) and 77($C_6H_5^+$, 7); M.S. (CI, iso-C_4H_{10}) *m/e* 196(M + 1, 100%).

Analysis was obtained on the picrate salt which was formed in EtOH and recrystallized from EtOH, m.p. 242–244°C. Calculated for $C_{18}H_{12}N_6O_7$: C, 50.95; H, 2.85; N, 19.81; found: C, 51.23; H, 3.21; N, 20.15.

1-Methyl-3-phenyl-1H-pyrazolo(4,3-c)pyridine (4) (see footnote * on p. 103)

To a stirred suspension of crushed potassium hydroxide pellets (100 mg) in dry dimethyl sulfoxide (2 ml) 1 (50 mg, 0.25 mmol) was added. After 45 min methyl iodide (0.03 ml, 0.50 mmol) was added and stirring was continued for 1.5 h. The mixture was diluted with water (2 ml) and ether (2 ml), stirred for an additional 10 min, the ether evaporated and the product filtered off, washed with cold water and dried over phosphorus pentoxide (49 mg, 90%, m.p. 89—91°C). R_f 0.70; IR ($CHCl_3$) 3030, 1645, 1620, 1570, 1495, 1460, 1405, 1370, 1315 cm^{-1}; ^1H NMR (DMSO-d_6) δ H_3CN1, 4.11 s, 3H; H4′, 7.44t, 1H; 2H3′, 7.51t, 2H; H7, 7.70d, 1H, 2H2′, 8.04d, 2H; H6, 8.42d, 1H; H4, 9.40s, 1H. M.S. (EI, 70 eV) *m/e* 209(M^+, 100%), 181 (2.5), 139(1.5), 104(2), 77(4) and 51(2); M.S. (CI, iso-C_4H_{10}) *m/e* 210 (M + 1, 100%).

Analysis was obtained on the picrate salt which was formed in EtOH and recrystallized from EtOH, m.p. 216—217°C. Calculated for $C_{19}H_{14}N_6O_7$: C, 52.06; H, 3.22; N, 19.17; found: C, 52.32; H, 3.53; N, 19.20.

2-Methyl-3-phenyl-2H-pyrazolo(4,3-c)pyridine (5)

This compound was obtained along with the 1-methyl-1H isomer 4 from 1. A stirred suspension of 1 (781 mg, 4.0 mmol) in methanol (25 ml) was treated with an etheric diazomethane solution in excess. After 2 h at ambient temperature complete solution occurred. The mixture was evaporated to dryness, the residue was treated with dichloromethane, cooled and the insoluble material filtered off to recover 428 mg (54.9%) of unreacted 1. The filtrate was chromatographed over Al_2O_3 with hexane:chloroform (75:25) as eluent to give 348 mg (41.6%) of a 1.25:1 mixture (as determined by ^1H NMR) of the isomers 4 and 5, respectively. A pure sample of 5 was obtained by preparative TLC on aluminium oxide DG, neutral (Riedel-de Haën) with 0.2% fluorescent indicator F_{254} (Merck) and hexane:chloroform (20:80) as eluent as a colorless oil: R_f 0.58; M.S. (EI, 70 eV) *m/e* 209 (M^+, 100%), 181(1), 139(2.5); ^1H NMR ($CDCl_3$/TMS) δ H_3CN2, 4.22s, 3H, C_6H_5, 7.6m, 5H; H7, 7.60d, 1H; H6, 8.33d, 1H, H4, 9.08s, 1H.

5-Methyl-3-phenylpyrazolo(4,3-c)pyridinium iodide (6)

A stirred mixture of 1 (1.95 g, 10.0 mmol) and methyl iodide (10 ml) was allowed to stand for 48 h at ambient temperature. Excess methyl iodide was evaporated and the solid residue was recrystallized from aqueous EtOH to give 3.20 g (95%) of 6: m.p. 249—250°C (decomp.); ^1H NMR (DMSO-d_6) δ HN, 3.63br.s, 1H; H_3CN5, 4.41s, 3H; 2H3′ and H4′, 7.58m, 3H; 2H2′, 8.08d, 2H; H7, 8.18d, 1H; H6, 8.59d, 1H; H4, 9.95s, 1H.

Analysis calculated for $C_{13}H_{12}N_3I$: C, 46.31; H, 3.59; N, 12.46; found: C, 46.51; H, 3.81; N, 12.67.

1,5-Dimethyl-3-phenyl-1H-pyrazolo(4,3-c)pyridinium iodide (7) (see footnote ** on p. 103)

The compound was prepared from 4 by the same procedure as shown above for the preparation of 6 to give a 97% yield of 7: m.p. 301—302°C

(decomp.); ^{1}H NMR (DMSO-d_6) δ H_3CN1, 4.26s, 3H; H_3CN5, 4.40s, 3H; 2H3′ and H4′, 7.60m, 3H; 2H2′, 8.08d, 2H; H7, 8.35d, 1H; H6, 8.67d, 1H; H4, 9.93s, 1H.

Analysis calculated for $C_{14}H_{14}N_3I$: C, 47.88; H, 4.02; N, 11.97; found: C, 48.16; H, 4.04; N, 11.98.

5-Methyl-3-phenyl-5H-pyrazolo(4,3-c)pyridine (8)

A solution of 6 (1.69 g, 5.0 mmol) in hot water (20 ml) was made alkaline by addition of concentrated aqueous potassium carbonate solution. The product was filtered off, washed with water and dried. The crude product was recrystallized from methanol:ether to give 1.03 g (98%) of 8: m.p. 246—248°C; IR (Nujol) 3340(br), 3200(br), 1695, 1680, 1635, 1605, 1345 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ H_3CN5, 4.17s, 3H; H7, 7.35d, 1H; 2H3′, 7.47t, 2H; H4′, 7.70t, 1H; H6, 7.82d, 1H; 2H2′, 8.05d, 2H; H4, 9.36s, 1H. M.S. (EI, 70 eV) *m/e* 209(M^+, 100%), 181(2), 180(3), 166(7), 152(1.5), 140(2.5), 139(10).

Analysis calculated for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08; found: C, 74.52; H, 5.34; N, 20.20.

5-Methyl-3-phenyl-4,5,6,7-tetrahydropyrazolo(4,3-c)pyridine (2) [8]

A solution of 6 (4.21 g, 12.5 mmol) in hot methanol (100 ml) was prepared and allowed to cool to ambient temperature while stirring. Sodium borohydride powder (0.94 g, 25.0 mmol) was added in small portions and stirring was continued for 3 h. The solution was concentrated and diluted with cold water to turbidity. The product was filtered off, washed with cold water and recrystallized from ethanol:water to give 1.62 g (61%) of 2 as colorless crystals: m.p. 70—72°C; ^{1}H NMR (DMSO-d_6) δ H_3CN5, 2.39s, 3H; 2H6 and 2H7, 2.68m, 4H; 2H4, 3.53s, 2H; H4′, 7.28t, 1H; 2H3′, 7.41t, 2H; 2H2′, 7.57d, 2H; HN, 12.71 br.s, 1H. M.S. (EI, 70 eV) *m/e* 213 (M^+, 10%), 212 (M^+—H, 13), 170 (M^+—CH_3N=CH_2, 100 — Retro-Diels-Alder), 77 ($C_6H_5^+$, 2) and 42 (CH_2=N=CH_2^+, 3).

Analysis calculated for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70, found: C, 73.35; H, 7.34; N, 19.66.

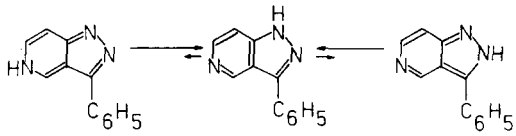
1,5-Dimethyl-3-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo(4,3-c)pyridine (9)

A solution of 7 (1.23 g, 3.5 mmol) in hot methanol (70 ml) was prepared and allowed to cool to ambient temperature while stirring. Sodium borohydride powder (0.24 g, 6.5 mmol) was added in small portions and the solution was additionally stirred for 3 h. The solution was concentrated, diluted with water and extracted with dichloromethane. The dichloromethane extracts were filtered through a short pad (~2 cm) of activated alumina, concentrated and treated with dry ether. The product was filtered off and dried over phosphorus pentoxide (0.41 g, 52%, m.p. 49—51°C). ^{1}H NMR (DMSO-d_6) δ H_3CN5, 2.38s, 3H; 2H6 and 2H7, 2.65m, 4H; 2H4, 3.50s, 2H; H_3CN1, 3.69s, 3H; H4′, 7.27t, 1H; 2H3′, 7.38t, 2H; 2H2′, 7.57d,

2H. M.S. (EI, 70 eV) *m/e* 227(M^+, 8%), 226(M^+—H, 8), 184(M^+—$CH_3N{=}CH_2$, 100 — Retro-Diels-Alder), 77 ($C_6H_5^+$, 2) and 42 ($CH_2{=}N{=}CH_2^+$, 6).

RESULTS

We prepared 3-phenylpyrazolo(4,3-c)pyridine (1) from 4-chloro-3-pyridinyl phenyl ketone (3) [4] and hydrazine. For the tautomeric system in 1 three prototropic forms are admissible: 1H (1A), 2H (1B) and 5H (1C) (Scheme 1). From 1 with methyl iodide/solid potassium hydroxide/dimethyl

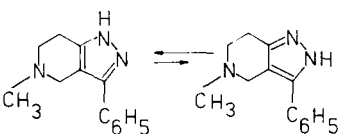


1C 1A 1B

Scheme 1

sulfoxide at ambient temperature the 1-methyl-1H derivative 4 was obtained*. The methylation of 1 with etheric diazomethane solution in methanol at ambient temperature proceeded with formation of a 1.25:1 mixture (as determined by ^1H NMR) of the 1-methyl-1H and the 2-methyl-2H isomers 4 and 5, respectively.

The pyrazolopyridines 1 and 4 with methyl iodide were quaternized at the 5-nitrogen atom to give the *N*5 methiodides of 1 and 4—6 and 7, respectively**. Treatment of the methiodide 6 with potassium carbonate in aqueous solution afforded the 5-methyl-5H derivative 8. The quaternary salts 6 and 7 were reduced selectively with sodium borohydride in methanol to give the corresponding 3-phenyl-4,5,6,7-tetrahydropyrazolo(4,3-c)pyridines 2 and 9. For the tautomeric system in 2 two prototropic forms are possible: 1H (2A) and 2H (2B) (Scheme 2).

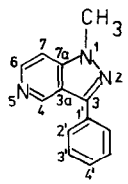


2A 2B

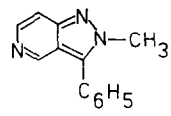
Scheme 2

*The 1-methyl-1H derivative 4 was also prepared (93%) from 4-chloro-3-pyridinyl phenyl ketone (3) and methylhydrazine at ambient temperature in ether.

**With methyl iodide and sodium methoxide by heating in methanol 1 is converted quantitatively (95%) to the 5-methiodide of 4, i.e. to 7, as a result of simultaneous N1 methylation and N5 quaternization.



4



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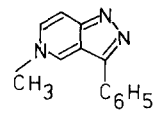
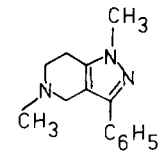


8



9

NMR investigations

For structure determination purposes the ^{1}H NMR spectra of the compounds prepared were recorded. The position of the *N*-methyl group is confirmed to be *N*1 for 4 by a NOESY spectrum, and *N*5 for 8 by NOE difference experiments.

In order to determine the position of the tautomeric equilibrium for the pyrazolopyridine 1 (Scheme 1) the ^{13}C NMR spectra of 1 and the fixed *N*-methyl derivatives 4 (1H), 5 (2H) and 8 (5H) in DMSO-d_6 were recorded (See Table 1). Assignment of the signals is based on the gated decoupling spectra and selective decoupling experiments. In order to distinguish between the signals of the carbon atoms C3 and C7a the corresponding coupling constants J(C3—H2′) and J(C7a—H6) in the gated decoupling spectra were selectively removed (by low power irradiation, $\gamma H_2 \sim 20$ Hz).

Compared with the fixed model **9**, the signals for C3, C7a and C1′ in the ^{13}C NMR spectrum of the tetrahydropyrazolopyridine **2** are broadened, giving evidence for a prototropic exchange between the 1H (**2A**) and 2H (**2B**) forms (Scheme 2). After addition of sulfuric acid the exchange is accelerated and average signals for all C atoms are observed. In order to determine the position of the tautomeric equilibrium for **2** its ^{13}C NMR spectrum in dichloromethane at 193 K was recorded (See Table 1). In these conditions the predominance (~80%) of one of the tautomers **2A**, or **2B** is evident.

Theoretical calculations

From the three prototropic forms admissible for the pyrazolo(4,3-c)-pyridine system in 1 (Scheme 1) the 5H-tautomer **1C** was ruled out by comparison of the theoretically calculated UV absorbtion spectra for the tautomers **1A**, **1B** and **1C** using the CNDO/2 method with the experimental ones of the model compounds 4 (1H), 5 (2H) and 8 (5H) taken in ethanol (Table 2). The planarity of the conjugated systems of the 1H- and 2H-tautomers allowed us to consider the PPP scheme calculations sufficiently correct and quantum chemical calculations for the two tautomers **1A** and **1B** were consequently carried out by the PPP method. Ideal geometry (R = 1.4 Å) and parameters: $I_{\dot{N}}$ = —22.69 eV; $I_{\dot{N}}$ = —14.11 eV; I_C =

TABLE 1

^{13}C NMR chemical shifts[a] for compounds 1, 2, 4, 5, 8, 9

C Atom	1	4	5	8		2		9
Solvent:	DMSO-d_6	DMSO-d_6	DMSO-d_6	DMSO-d_6	DMSO-d_6	DMSO-d_6	CH_2Cl_2[c]	DMSO-d_6
3	144.37	143.82[d]	148.23	150.67	—[e]	141.58	144.99	144.02
3a	117.93	118.22	118.56	118.38	115.25	108.50	110.10	112.13
4	144.99	145.06	146.66	139.97	51.64	51.05	50.90	52.07
6	143.51	143.55	142.04	130.51	52.04		50.19	51.14
7	105.68	104.98	110.50	111.55	22.56	21.01	19.33	21.3
7a	144.37	143.28[d]	137.19	147.37	—[e]	140.55	137.00	138.13
CH_3	—	35.55	38.96	45.21	45.38	43.66	44.30	45.19[f] 35.59[g]
1′	132.62	132.19	127.97	134.36	—[e]	131.85	132.56	134.10
2′	127.26	127.08	129.68	126.23	125.71	125.89	125.26	125.80
3′	129.26	129.19	129.39	128.77	128.75	128.90	127.76	128.90
4′	128.72	128.66	129.68	127.11	127.09	127.54	126.29	126.90

[a]In ppm downfield from TMS. [b]After addition of a drop of sulfuric acid. [c]For the predominating tautomer at 193 K. [d]Assignment could be reversed. [e]Not observed. [f]For CH_3N5. [g]For CH_3N1.

TABLE 2

Comparison of UV absorption spectra wavelengths and results from quantum chemical calculations for compounds 1, 2, 4, 5, 8, 9

Parameter	UV absorption spectra												PPP Calculations	
	1		4		5		8		2		9		1A	1B
	a	b	a	b	a	b	a	b	a	b	a	b		
λ_{max} [nm]														
I	293	318	303	326	310	340	368	324	305	312	255	252	292	344
II	235	235	236	236	240	262[c]	294[c]	232	253	251	—[d]	—[d]	243	258
III	220	213[c]	226	215[c]	214	246[c]	252[c]	205	—[d]	—[d]	—	—	212	216
IV	—	—	—	—	—	224	236	—	—	—	—	—	—	—
V	—	—	—	—	—	204	203	—	—	—	—	—	—	—
log ϵ														
I	3.94	3.74	3.94	3.77	3.86	3.78	3.59	3.71	2.40	2.55	4.18	4.18		
II	4.10	4.16	4.09	4.20	3.86	3.55	3.52	4.26	4.10	4.11	—[d]	—[d]		
III	4.02	3.85	4.09	3.92	4.38	3.90	4.16	4.50	—[d]	—[d]	—	—		
IV	—	—	—	—	—	4.35	4.30	—	—	—	—	—		
V	—	—	—	—	—	4.30	4.37	—	—	—	—	—		

[a] 1×10^{-4} M solutions in EtOH. [b] 1×10^{-4} M solutions in EtOH after addition of a drop of 37% hydrochloric acid. [c] Inflexion. [d] Not determined.

-11.22 eV; $\gamma_N = -12.92$ eV; $\gamma_C = -10.84$ eV; $\beta_{NN} = -2$ eV; $\beta_{C\dot{N}} = -2.35$ eV; $\beta_{C\dot{N}} = -2.58$ eV; $\beta_{CC} = -2.318$ eV were assumed. The theoretically obtained UV spectra yielded the values 292 and 344 nm, respectively for the longest wavelength transitions of **1A** and **1B** (see Table 2).

DISCUSSION

A comparison of: (a) the ^{13}C NMR spectrum of the tautomeric system 1 (Scheme 1) with the ^{13}C NMR spectra of the fixed models 4 (1H), 5 (2H) and 8 (5H) (see Table 1); (b) the UV spectrum of the tautomeric system 1 with the UV spectra of the fixed models 4, 5 and 8 (see Table 2); and (c) the theoretically obtained UV spectra of tautomers **1A** and **1B** with the UV spectrum of **1** taken in the range 200–450 nm with ethanol as the solvent (see Table 2) show that 3-phenylpyrazolo(4,3-c)pyridine is a pure 1H-tautomer **1A**, not a tautomeric mixture. Hence, for pyrazolo(4,3-c)pyridines, as for indazoles [5], the 1H-tautomer (1A) with retained aromatic electron sextet is considerably more stable than the quinonoid types (1B and 1C).

For 5-methyl-3-phenyl-4,5,6,7-tetrahydropyrazolo(4,3-c)pyridine (2) (Scheme 2) in dichloromethane at 193 K, we conclude, by comparison of its ^{13}C NMR spectrum with ^{13}C NMR spectra of the fixed model 9 (1H) (see Table 1) and of a series of substituted pyrazoles [6, 7], that the predominating tautomer must be the 1H-tautomer **2A**.

CONCLUSIONS

The structures of 3-phenylpyrazolo(4,3-c)pyridine and 5-methyl-3-phenyl-4,5,6,7-tetrahydropyrazolo(4,3-c)pyridine are determined by detailed ^1H and ^{13}C NMR analysis and theoretical calculations in comparison with their *N*-methyl derivatives as fixed models. 3-Phenylpyrazolo(4,3-c)pyridine is established to exist entirely in the 1H tautomeric form. 5-Methyl-3-phenyl-4,5,6,7-tetrahydropyrazolo(4,3-c)pyridine is a mixture of the 1H and 2H tautomers with the 1H tautomer largely predominating.

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REFERENCES

1 C. R. Hardy, Adv. Heterocycl. Chem., 36 (1984) 343.
2 J. Elguero, C. Marzin, A. R. Katritzky and P. Linda, The Tautomerism of Heterocycles, Adv. Heterocycl. Chem. Suppl. 1, Academic Press, New York, 1976, pp. 291, 528.
3 (a) M. H. Palmer, R. H. Findlay, S. M. F. Kennedy and P. S. McIntyre, J. Chem. Soc., Perkin Trans. 2, (1975) 1695.

(b) G. A. Jaffari and A. J. Nunn, J. Chem. Soc., Perkin Trans. 1, (1973) 2371.
4 R. Radinov, M. Haimova and E. Simova, Synthesis, (1986) 886.
5 P. Bouchet, A. Fruchier, G. Joncheray and J. Elguero, Org. Magn. Reson., 9 (1977) 716.
6 J. E. Elguero, C. Marzin and J. D. Roberts, J. Org. Chem., 39 (1974) 357.
7 P. Cabildo, R. M. Claramunt and J. Elguero, Org. Magn. Reson., 22 (1984) 603.
8 G. Winters, A. Sala and D. Barone, U.S. Patent 4,500,525 (1985) to Gruppo Lepetit SpA; G. Winters, A. Sala, D. Barone and E. Baldoli, J. Med. Chem., 28 (1985) 934.