Synthesis and NMR Spectroscopy (¹H, ¹³C) of 1-(2'-Benzothiazolyl)-3(5),4-polymethylenepyrazoles and Related Compounds

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Received November 30, 1991

A series of 3(5),4-trimethylene and 3(5),4-tetramethylenepyrazoles (tetrahydroindazoles) have been prepared from 2-acylcyclanones using two methods: direct reaction with a substituted hydrazine and through an NH-pyrazole followed by nucleophilic substitution. The results mainly concern the 2-benzothiazolyl substituent, but 2,4-dinitrophenyl derivatives were also studied for comparison. The orientation of the reactions (isomer ratio), the deshielding in ¹H nmr of the 5-methyl and 5-methylene signals when a benzothiazolyl residue is at position 1, and the ring strain effect on heterocyclic carbons chemical shifts, are discussed.

This work results from the confluence of studies aimed at the understanding of the reactivity between heterocyclic hydrazines and β-dicarbonyl compounds [1-6] and those reporting the use of 2-acylcyclanones for the synthesis of pyrazoles [7,8].

Scheme 1 contains the compounds studied. Pyrazoles **1d, 1e, 2a, 2b, 2c, 2d, 2e, 3a, 3d, 3e, 4a, 4d**, and **4e** were

Scheme 1
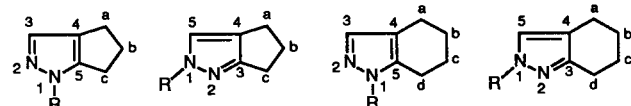
R = 2',4'-dinitrophenyl:

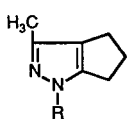**1d**   **1e**

R = H: **2a**
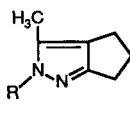
R = 2'-benzothiazolyl:

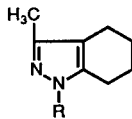**2b**   **2c**

R = 2',4'-dinitrophenyl:

2d   **2e**

R = H: **3a**

R = 2'-benzothiazolyl:

3b   **3c**

R = 2'-(5'-methylbenzothiazolyl):

3b'

R = 2',4'-dinitrophenyl:

3d   **3e**

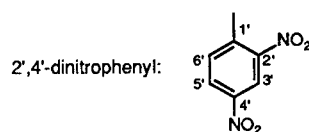R = H: **4a**
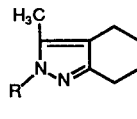
R = 2'-benzothiazolyl:

4b   **4c**

R = 2'-(5'-methylbenzothiazolyl):

4b'   **4c'**

R = 2',4'-dinitrophenyl:
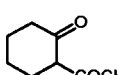
4d   **4e**
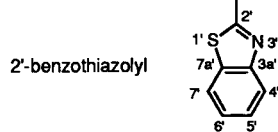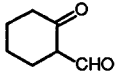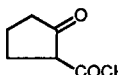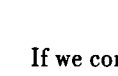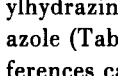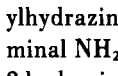
2',4'-dinitrophenyl: 2'-benzothiazolyl

already known [7-9]. When samples were not available, they were reprepared according to reported methods. As the melting points were identical, only the nmr spectroscopy will be discussed, ¹H nmr in the experimental part and ¹³C nmr in the discussion. Thus, the new compounds are: **3b, 3b', 3c, 4b, 4b', 4c** and **4c'**.

To synthesize them we first use the reaction between 2-hydrazinobenzothiazole (or its 6'-methyl derivative) and, respectively, 2-acetylcyclopentanone and 2-acetylcyclohexanone. Two isomers were generally obtained whose ratio was determined by ¹H nmr on the reaction crude (Table I).

Table I

Percentages of Isomers Obtained from
2-Acylcyclanones and Hydrazines

	2,4-dinitrophenyl hydrazine			2-hydrazinobenzo-thiazole		
	95%	**2d**	(86%)	65%	**2b**	(68%)
	5%	**2e**	[7]	35%	**2c**	
	80%	**3d**	(81%)	95%	**3b**	(64%
	20%	**3e**	[8]	5%	**3c**	
	25%	**4d**	(33%)	15%	**4b**	(26%)
	75%	**4e**	[8]	85%	**4c**	

If we compare the results obtained with 2,4-dinitrophenylhydrazine with those obtained with 2-hydrazinobenzothiazole (Table I) some differences are observed. These differences can be explained assuming that 2,4-dinitrophenylhydrazine reacts almost quantitatively (95%) by the terminal NH₂ in the first step (yielding **d** isomers) whereas in 2-hydrazinobenzothiazole, both nitrogen atoms compete in the first step although the NH₂ (yielding **b** isomers) is still the more reactive (75%). To obtain isomer distribu-

tion consistent with the experimental results, it is necessary to assume that compared with the endocyclic carbonyl group, the reactivity of the exocyclic one decreases in the order:
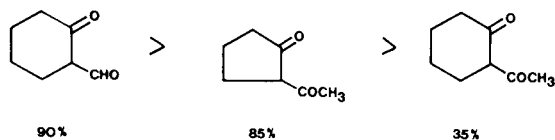
The percentages between parentheses in Table I are obtained with these values, i.e.. 75% x 35% = 26% for **4b**. Only in the case of **3b** the agreement is not satisfactory.

The reaction of aromatic or heteroaromatic halides with pyrazoles yields a mixture of isomers whose ratio depends on steric effects (Table II). In the case of 1-fluoro-2,4-dinitrobenzene, the increase of **e** isomers between series **3** and **4** was assigned [8] to an increase in the steric requirements of the methylene group from a five-membered ring (C_c-H_2 in **3a**) to a six-membered ring (C_d-H_2 in **4a**). The results obtained with 2-chlorobenzothiazole confirm that this conclusion is still true but with much lower steric requirements of the heterocycle. For instance, the C-CH$_3$ group of compound **4a** appears larger than the C_d-H_2 when opposed to the 1-(2',4'-dinitrophenyl) substituent (75% of **4d**) and smaller when opposed to 1-(2'-benzothiazolyl) (10% of **4b**). However, the differences in energy, which are proportional to the natural logarithms of the ratios, experience the same variation ($\Delta \ln R = 3.3$).

Table II

Percentages of Isomers Obtained from N-Substitution of 3(5)-Methyl-5(3),4-polymethylenepyrazoles

Pyrazole	1-fluoro-2,4-dinitrobenzene [8]	2-chlorobenzothiazole
3a	98% **3d**	65% **3b**
	R = 49, ln R = 3.89	R = 1.86, ln R = 0.62
	2% **3e**	35% **3c**
	75% **4d**	10% **4b**
4a	R = 3, ln R = 1.1	R = 0.11, ln R = 2.2
	25% **4e**	90% **4c**

Proton nmr studies have become routine and only two points will be discussed here, the rest is to be found in the experimental part: i) the assignment of methylene protons because they will be used to assign methylene carbons; ii) the anisotropic effects of the substituent at position 1 on protons of the position 5 of pyrazole.

i) ^{1}H-^{1}H COSY and NOESY experiments were performed on compounds **3a** and **4a**. Both kinds of bidimensional spectra show interaction spots corresponding to methyl-methylene a; methylene a-methylene b; methylene b-methylene c (only for **3a**), and methylene c-methylene d (only for **4a**).

ii) With regard to 1-(2',4'-dinitrophenyl)pyrazoles, the corresponding 1-(2'-benzothiazolyl) derivatives show a large deshielding effect on the methyl and methylene of the position 5 (C_c-H_2 in **3b** and C_d-H_2 in **2b** and **4b**). These relative deshieldings are similar to those observed for H$_5$ in 5-unsubstituted pyrazoles [1,4] (for instance, in **2c**, δ H$_5$ = 8.15 whereas in **2e**, δ H$_5$ = 7.43) and are due to differences in conformation (atropoisomerism) between both series of derivatives. In 1-(2',4'-dinitrophenyl)pyrazoles, series **d** and **e**, the 2'-nitro group is on the same side as the N$_2$ atom [10], whereas in 1-(2'-benzothiazolyl)pyrazoles, series **b** and **c**, like in bipyridine and 1-heteroarylpyrazoles, both nitrogen atoms are antiperiplanar:
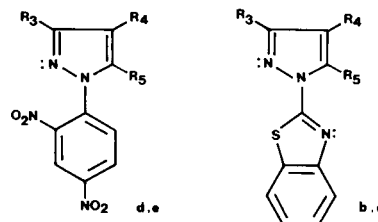
It results that in **d** and **e** series the R^5 substituent (CH$_3$ or CH$_2$) is unaffected by the anisotropy of the NO$_2$ group. On the contrary, the lone pair of N$_{3'}$, strongly deshielded the protons of R^5: δ = 3.20 for the methylenes of **2b**, **3b** and **4b**, and δ = 2.65 for the methyles of **3c** and **4c**.

Carbon-13 NMR Results.

Literature reports on polymethylenepyrazoles are very scarce. Only the carbon-13 nmr spectrum of compound **2a** has been previously described [11]. Two kinds of assignment problems are found in these compounds: i) the assignment of methylene carbons C_a and C_c (series **1** and **3**) or C_a and C_d (series **2** and **4**), that is, the sp^3 carbons linked to positions 3(5) and 4 of the pyrazole ring; ii) the assignment of carbons C_3 and C_5 when both are quaternary (series **3** and **4**).

The first problem was solved through bidimensional experiments using ^{1}J(^{1}H-^{13}C) correlation spectra (HETCOR). Since the methylene protons have been assigned without ambiguity so are the corresponding carbons. These experiments were carried out on compounds **3a**, **4a**, **3b** and **4c**.

The solution of the second problem comes from the ^{1}H-^{13}C coupled spectra. The carbon bearing the methyl group gives rise to a quartet with a ^{2}J coupling constant of 6.6 Hz whereas the carbon bearing the methylene appears as a triplet with a ^{2}J = 3.3 Hz. The difference between these two values is probably related to the fact that the methyl group is free to rotate whereas the methylene protons are in a fixed position with regard to the carbon atom, position that seems to correspond to low values of ^{2}J.

These experiments together with literature data on pyrazoles [4,12], 1-(2',4'-dinitrophenyl) derivatives [13] and benzothiazoles [14,15], lead to the values of Table III.

Table III

13C-NMR Chemical Shifts (ppm) of Compounds 1-4 (Solvent: deuteriochloroform)

Compound	C_3	C_4	C_5	C_a	C_b	C_c	C_d	3(5)-CH_3	$C_{1'}$	$C_{2'}$	$C_{3'}$	$C_{4'}$	$C_{5'}$	$C_{6'}$	$C_{7'}$	C_{3a}	C_{7a}	6'-CH_3
1d	138.24	131.72	150.47	22.94	30.97	25.31	—	—	137.43	142.97	121.05	145.01	127.16	125.02	—	—	—	—
1e	167.66	130.41	122.47	22.75	30.96	24.37	—	—	137.61	142.01	121.04	144.16	127.23	124.43	—	—	—	—
2a [a]	131.7	114.8	143.2	20.5	23.6	22.1	23.2	—	—	—	—	—	—	—	—	—	—	—
2b	141.76	120.41	141.00	20.75	22.69	22.69	24.33	—	—	161.32	—	122.30	126.12	124.38	121.27	151.64	132.69	—
2c	154.43	120.48	124.68	20.68	23.08	23.08	23.67	—	—	160.71	—	121.98	126.37	124.31	121.49	151.29	132.96	—
2d	141.87	119.61	139.55	20.30	22.30	22.30	22.52	—	137.42	144.58	120.87	145.45	127.33	127.10	—	—	—	—
2e	154.95	121.31	124.38	20.50	22.91	22.91	23.34	—	137.33	141.88	120.97	144.17	127.28	125.69	—	—	—	—
3a	133.62 [b]	122.56	159.53 [c]	22.08	30.40	24.31	—	10.40 [d]	—	—	—	—	—	—	—	—	—	—
3b	147.50	130.13	151.59	22.32	30.28	26.58	—	12.97	—	160.19	—	121.99	126.10	124.04	121.30	150.98	132.77	—
3b'	147.26	129.97	150.92	22.23	30.28	26.48	—	12.67	—	159.43	—	121.55	127.51	134.09	121.19	149.58	132.88	21.25
3c	165.29	128.66	134.92	22.13	29.68	24.67	—	13.36	—	161.50	—	122.01	125.95	124.05	121.05	151.70	132.65	—
3d	148.04 [e]	131.33	150.73 [f]	22.45	30.94	25.80	—	12.55 [g]	137.36	142.05	121.16	144.15	127.18	124.41	—	—	—	—
3e	165.43	127.74	133.04	22.37	29.74	24.60	—	11.05	138.08	145.23	120.89	145.51	128.61	127.18	—	—	—	—
4a	139.27 [h]	113.38	143.32 [i]	18.83	21.06	21.72	22.17	9.38 [j]	—	—	—	—	—	—	—	—	—	—
4b	150.00	119.47	141.31	20.20	22.50	22.59	24.37	11.86	—	160.91	—	122.01	126.02	124.04	121.13	n.o.	132.66	—
4c	151.73	118.49	137.34	20.16	22.98	22.98	23.55	12.03	—	161.73	—	122.10	125.96	124.09	121.08	153.34	132.74	—
4c'	149.75	118.38	137.28	20.26	23.05	23.57	24.35	12.01	—	160.98	—	121.70	127.41	134.16	121.05	153.19	132.87	21.45
4d	150.85	118.70	139.98	19.88	22.20	22.37	22.50	11.53	137.53	144.18	120.94	144.91	127.05	127.05	—	—	—	—
4e	153.26	117.54	135.75	20.31	22.96	22.96	23.34	9.91	138.23	145.29	120.79	145.84	127.05	128.93	—	—	—	—

[a] From reference [10], exchanging the methylene carbons C_a and C_b. [b] $2J(^1H\text{-}^{13}C) = 6.5$ Hz. [c] $2J(^1H\text{-}^{13}C) = 3.2$ Hz. [d] $1J(^1H\text{-}^{13}C) = 127.8$ Hz. [e] $2J(^1H\text{-}^{13}C) = 6.6$ Hz. [f] $2J(^1H\text{-}^{13}C) = 3.6$ Hz. [g] $1J(^1H\text{-}^{13}C) = 127.9$ Hz. [h] $2J(^1H\text{-}^{13}C) = 6.7$ Hz. [i] $2J(^1H\text{-}^{13}C) = 3.4$ Hz. [j] $1J(^1H\text{-}^{13}C) = 128.7$ Hz.

We will discuss the chemical shifts of Table III according to the following points: i) a comparison of dinitrophenyl (DNP) and benzothiazolyl derivatives regarding the heterocyclic and the methylene signals; ii) the substituent chemical shifts produced by the methyl group at positions 3 or 5; iii) the effect of the pyrazole nature on the signals of the substituent at position 1 and, particularly, on the carbon C_2, of the dinitrophenyl group.

i) Defining $\Delta\delta$ as δ(DNP) - δ(benzothiazolyl), *i.e.* δd - δb or δe - δc, it is possible to calculate the effect of replacing a dinitrophenyl by a benzothiazolyl group at position 1 on the signals of the pyrazole carbons (sp^2 and sp^3). The only important effects are observed for carbon C_5 and for it directly bonded methylene or methyl carbon:

	2b-2d	**2c-2e**	**3b-3d**
$\Delta\delta$ (C_5)	-1.4	-0.3	-0.9
$\Delta\delta$ ($C_\blacksquare$)	-1.8	---	-0.8
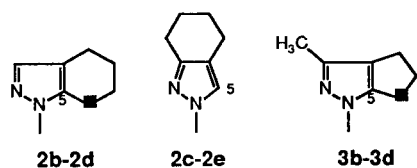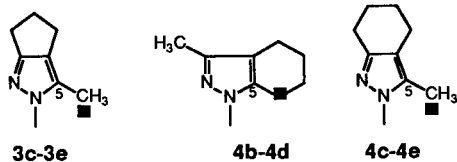
|	**3c-3e**	**4b-4d**	**4c-4e**
	-1.9	-1.3	-1.6
	-2.3(CH$_3$)	-1.9	-2.1(CH$_3$)

A methyl group or a six-membered methylene at position 5 is deshielded by the benzothiazolyl residue by a mechanism probably similar to that observed in ^{1}H nmr (anisotropy of the $N_{3'}$ lone pair). The methylene of the five-membered ring, more removed, is much less affected (**3d/3b** pair). Carbon C_5 signal is deshielded only when the first effect is observed.

This deshielding of 5-methyl carbon by the 1-(2'-benzothiazolyl) residue produces a breakdown of the rule that in pyrazoles δ CH$_3$-4 < δ CH$_3$-5 < δ CH$_3$-3 (for instance, in 1,3,4,5-tetramethylpyrazole δ CH$_3$-4 = 7.9, δ CH$_3$-5 = 9.2 and δ CH$_3$-3 = 11.5 [12]). This rule is followed in the case of 1-(2',4'-dinitrophenyl) derivatives, δ CH$_3$-5 < δ CH$_3$-3, even for the methylene carbons: δ CH$_2$-4 < δ CH$_2$-5 < δ CH$_2$-3. On the contrary, in the benzothiazolyl derivatives of Table III, δ CH$_3$-3 < δ CH$_3$-5 and δ CH$_2$-4 < δ CH$_2$-3 < δ CH$_2$-5.

ii) The methyl substituent effects are similar to those observed for other pyrazoles [12] but larger on C_{ipso}. The averaged values for 3-methyl and 5-methyl are:
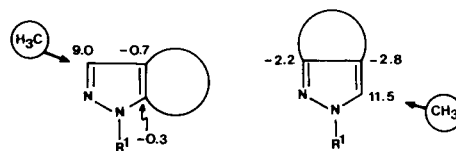
The main interest of these effects is that they provide a complementary proof of the consistency of Table III assignments.

iii) It is known that the chemical shifts of *ortho* carbons in *N*-arylazoles can be used as a measure of interannular conjugation [13]. In the case of 1-(2',4'-dinitrophenyl) derivatives, it is better to use $C_{2'}$, than $C_{6'}$, since $C_{2'}$ is far from the effects of the substituent at position 5 on the pyrazole ring. Taking the chemical shift of $C_{2'}$ as a measure of the dihedral angle between the pyrazole ring and the dinitrophenyl substituent, the conclusion that the angle increases in the following order is obtained: 5-unsubstituted (δ = 141.9) < five-membered ring (δ = 142.5) < six-membered ring (δ = 144.4) < 5-methyl group (δ = 145.3), order which correspond to the steric effects we have discussed in the reactivity part (Table II).

EXPERIMENTAL

Melting points were recorded in open capillaries and are uncorrected. The ^{1}H nmr spectra were recorded at 293 K on a Bruker AM-200 spectrometer operating at 200 MHz or a Varian XL-300 instrument operating at 300 MHz, in both cases TMS was used as internal standard. The ^{13}C nmr spectra were recorded on the Bruker instrument operating at 50 MHz. Mass spectra were recorded on a Varian MAT-212 mass spectrometer.

2'-(Dihydro-3-methyl-1(*H*)-cyclopentapyrazolyl)benzothiazole (3b).

Method A.

A mixture of 2-hydrazinobenzothiazole [16] (825 mg, 5 mmoles) and 2-acetylcyclopentanone (630 mg, 5 mmoles) in ethanol (20 ml) containing 0.3 ml of hydrochloric acid was refluxed for 2 hours. On cooling a solid separated out, which was filtered and crystallized from ethanol, mp 153-154°, yield 900 mg (70%); ms: m/z 255 (100%) (M$^+$); ^{1}H nmr (deuteriochloroform): δ ppm 2.25 (s, 3H, C$_3$-CH$_3$), 2.57-2.68 (m, 4H, C$_a$-CH$_2$ and C$_b$-CH$_2$), 3.19 (m, 2H, C$_c$-CH$_2$), 7.27 (t, 1H, C$_{6'}$-H), 7.41 (t, 1H, C$_{5'}$-H), 7.69 (d, 1H, C$_{7'}$-H), 7.81 (d, 1H, C$_{4'}$-H) (J$_{45}$ = 8.3, J$_{46}$ = 1.1, J$_{47}$ = 0.5, J$_{56}$ = 1.4 and J$_{67}$ = 7.7 Hz).

Anal. Calcd. for C$_{14}$H$_{13}$N$_3$S: C, 65.88; H, 5.10; N, 16.47. Found: C, 65.81; H, 5.07; N, 16.13.

In a similar manner **3b'** (the 6'-methyl derivative) was prepared by refluxing 2-hydrazino-6-methylbenzothiazole [17] (895 mg, 5 mmoles) and 2-acetylcyclopentanone (630 mg, 5 mmoles) in ethanol (30 ml) containing 0.3 ml of hydrochloric acid, mp 158-159° (ethanol), yield 1.1 g (82%); ms: m/z 269 (100%) (M$^+$); ^{1}H nmr (deuteriochloroform): δ ppm 2.25 (s, 3H, C$_3$-CH$_3$), 2.43 (s, 3H, C$_{6'}$-CH$_3$), 2.50-2.75 (m, 4H, C$_a$-CH$_2$ and C$_b$-CH$_2$), 3.00-3.30 (m, 2H, C$_c$-CH$_2$), 7.18 (dd, 1H, C$_{5'}$-H), 7.55 (d, 1H, C$_{7'}$-H), 7.74 (d, 1H, C$_{4'}$-H) (J$_{45}$ = 8.2 and J$_{57}$ = 1.8 Hz).

Anal. Calcd. for $C_{15}H_{15}N_3S$: C, 66.91; H, 5.88; N, 15.61. Found: C, 66.80; H, 5.85; N, 15.56.

Method B.

To a solution of **3a** (0.5 g, 0.004 mole) in anhydrous acetone (25 ml) and sodium hydroxide (0.15 g, 0.004 mole), 2-chlorobenzothiazole (0.7 g, 0.004 mole) was added. The reaction mixture was refluxed for 4 hours. The solid was filtered off and the organic phase was evaporated under reduced pressure. The residue, which was the mixture of the two isomers **3b** and **3c**, was chromatographed on silica gel (70-230 mesh) column using chloroform:hexane (10:1) as eluent, to give 2'-(dihydro-3-methyl-2*H*-cyclopentapyrazolyl)benzothiazole (**3c**), mp 148-149° (methanol), yield 200 mg (20%); ¹H nmr (deuteriochloroform): δ ppm 2.33 (m, 2H, C_b-CH₂), 2.54 (m, 2H, C_a-CH₂), 2.65 (s, 3H, CH₃), 2.68 (m, 2H, C_c-CH₂), 7.20 (d, 1H, $C_{6'}$-H), 7.33 (t, 1H, $C_{5'}$-H), 7.70 (d, 1H, $C_{7'}$-H), 7.75 (d, 1H, $C_{4'}$-H) ($J_{45} = 7.9$, $J_{46} = 1.4$, $J_{47} = 0.6$, $J_{56} = 7.3$, $J_{57} = 1.3$ and $J_{67} = 7.3$ Hz).

Anal. Calcd. for $C_{14}H_{13}N_3S$: C, 65.88; H, 5.10; N, 16.47. Found: C, 66.10; H, 5.29; N, 16.70.

From the second column fraction, it was possible to isolate **3b** after evaporation *in vacuo* of the organic solvent, mp 162-163° (methanol), yield 400 mg (38%).

2'-(Tetrahydro-3-methyl-1*H*-indazol-1-yl)benzothiazole (**4b**) and 2'-(Tetrahydro-3-methyl-2*H*-indazol-2-yl)benzothiazole (**4c**).

Method A.

A mixture of 2-hydrazinobenzothiazole [16] (1.65 g, 0.01 mole) and 2-acetylcyclohexanone (1.40 g, 0.01 mole) in ethanol (50 ml) containing 0.5 ml of hydrochloric acid was refluxed for 3 hours. The reaction mixture was concentrated and left at room temperature for 4-5 hours. The crude solid which separated out was filtered, washed with little cold ethanol and dried. The crude solid (yield 89%) indicated the formation of two isomeric products. The column chromatographic separation using hexane:ethylacetate (100:2.5) as eluent afforded **4c**, mp 159° (hexane), yield 1.45 g (54%); ms: m/z 269 (100%) (M⁺); ¹H nmr (deuteriochloroform): δ ppm 1.80 (m, 4H, C_b-CH₂ and C_c-CH₂), 2.48 (t, 2H, C_a-CH₂), 2.68 (s, 3H, CH₃), 2.73 (t, 2H, C_d-CH₂), 7.28 (t, 1H, $C_{6'}$-H), 7.40 (t, 1H, $C_{5'}$-H), 7.79 (d, 1H, $C_{7'}$-H), 7.83 (d, 1H, $C_{4'}$-H) ($J_{45} = 9.2$, $J_{46} = 1.4$, $J_{47} = 0.6$, $J_{56} = 7.6$, $J_{57} = 1.4$ and $J_{67} = 8.8$ Hz).

Anal. Calcd. for $C_{15}H_{15}N_3S$: C, 66.91; H, 5.58; N, 15.61. Found: C, 66.70; H, 5.79; N, 15.52.

The minor isomer **4b** could not be separated even after repeated column chromatography.

In a similar manner **4c'** was synthesized by refluxing 2-hydrazino-6-methylbenzothiazole [17] (895 mg, 5 mmoles) and 2-acetylcyclohexanone (700 mg, 5 mmoles) in ethanol (30 ml) containing 0.3 ml of hydrochloric acid. The crude solid indicated the formation of two isomeric products (90:10), which after column chromatographic separation afforded **4c'**, mp 148° (methanol), yield 680 mg (48%); ms: m/z 283 (100%) (M⁺); ¹H nmr (deuteriochloroform): δ ppm 1.60-1.95 (m, 4H, C_b-CH₂ and C_c-CH₂), 2.30-2.56 (m, 5H, C_a-CH₂ and $C_{6'}$-CH₃), 2.56-2.85 (m, 5H, C_d-CH₂ and C_3-CH₃), 7.20 (dd, 1H, $C_{5'}$-H), 7.56 (d, 1H, $C_{7'}$-H), 7.74 (d, 1H, $C_{4'}$-H) ($J_{45} = 8.2$ and $J_{57} = 1.8$ Hz).

Anal. Calcd. for $C_{16}H_{17}N_3S$: C, 67.84; H, 6.00; N, 14.84. Found: C, 67.69; H, 5.81; N, 14.71.

Method B.

To a solution of **4a** (1.8 g, 0.013 mole) in anhydrous acetone (40 ml) and sodium hydroxide (0.5 g, 0.013 mole), 2-chlorobenzothiazole (2.3 g, 0.013 mole) was added. The reaction mixture was refluxed for 4 hours. After cooling to room temperature, the solid was filtered off, and the organic phase was evaporated *in vacuo*. The residue which was a mixture of the two possible isomers, was chromatographed on silica gel (70-230 mesh) column eluting with chloroform:hexane (10:1). From the first fraction it was possible to isolate **4c**, mp 159° (hexane), yield 1.3 g (36%).

The minor isomer **4b**, could not be separated even after repeated column chromatography, although it was possible to obtain a very enriched mixture in **4b**, that was able to perform the nmr experiments; ¹H nmr (deuteriochloroform): δ ppm 2.16 (s, 3H, CH₃), 3.20 (t, 2H, C_d-CH₂).

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