Fused Heterocycles. Part 3.[1] Synthesis and Stereochemistry of Benzopyrano- and Benzothiapyrano-[4,3-*c*]Pyrazoles

Gábor Tóth* and Áron Szöllösy
Technical Analytical Research Group of the Hungarian Academy of Sciences, Technical University, H-1111 Budapest, Gellért tér 4, Hungary
Tamás Lóránd, Tibor Kónya, and Dezsö Szabó
Department of Chemistry, University Medical School, P.O.B. 99, H-7601 Pécs, Hungary
András Földesi
Central Research Laboratory, University Medical School, P.O.B. 99, H-7601 Pécs, Hungary
Albert Lévai
Department of Organic Chemistry, Kossuth L. University, P.O.B. 20, H-4010 Debrecen, Hungary

Several tricyclic benzopyrano[4,3-*c*]pyrazole derivatives have been studied by ^1H and ^{13}C n.m.r. spectroscopy. They were prepared by treating 3-benzylidene-chromanones and -1-thiochromanones with semicarbazide or thiosemicarbazide: reactions which give only the *cis* 3-H,3a-H stereoisomers.

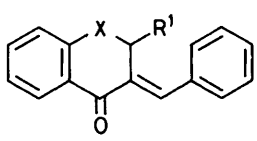
Recently we reported on the synthesis and stereochemical investigations of various dihydropyrazoles substituted with fused ring systems.[1-3] Owing to the interesting biological activities of this type of compound increasing attention has been focused on this ring system. Thus 1,4-dihydro[1]-benzothiopyrano[4,3-*c*]pyrazole has antimicrobial activity,[4] the 2-one derivatives are immunosuppressive agents,[5,6] and benzopyranopyrazoles have been prepared and used as CNS depressants.[7] Some of our previously synthesized dihydropyrazole derivates were found to possess antimicrobial effects.[8] This prompted us to extend our studies to the synthesis of newer dihydropyrazoles containing fused ring systems. In this paper reactions of exocyclic α,β-unsaturated ketones with semicarbazide and thiosemicarbazide, and the stereochemistry of the compounds prepared are reported.

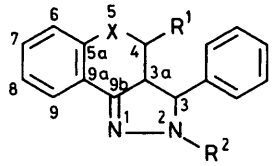
Results and Discussion

There are various synthetic routes to benzo(thio)pyranopyrazoles. Intramolecular cycloaddition of nitrile imides gives such compounds.[9] Other synthetic methods involve reactions of 3-formylchroman-4-one,[7,10] 4-chloro-3-formylcoumarins,[11] 3-benzylidenechroman-4-one,[1,3,12] 3-benzylidene-1-thiochromanone,[1,3] and hydrazine derivatives. Stereochemical investigations of benzopyrano[4,3-*c*]dihydropyrazoles and related compounds have been reported by Sangwan [12,13] and by us.[1-3] Reaction of 3-benzylidene-chroman-4-one (**1**), -flavanone (**2**), -1-thiochroman-4-one (**3**), -1-thiochroman-4-one 1,1-dioxide (**4**), and -1-thioflavanone (**5**) with semicarbazide or thiosemicarbazide in hot ethanol in the presence of hydrochloric acid gave the dihydropyrazoles (**7**)–(**15**) (Scheme). Theoretically, this reaction may result in the formation of 3-H,3a-H *cis* and *trans* isomers. Moreover, in the case of compounds (**9**), (**10**), and (**15**), depending on the relative configuration of C-4, formation of two other diastereoisomers can be expected. In the event, the reactions gave only one isomer in relatively good yield. For the determination of the structure of the compounds isolated [(**7**)–(**15**)] ^1H and ^{13}C n.m.r. spectra and homonuclear proton–proton n.O.e. difference measurements were utilized. Compound (**16**) was prepared by the above-mentioned procedure and its spectroscopic data were correlated with those of its previously synthesized *trans* isomer[1] (**16a**). Characteristic ^1H chemical-shift data and coupling constants are summarized in Table 1 where data for the previously prepared[1] 2-methyl-3-phenyl-2,3,3a,4-tetrahydro[1]benzopyrano[4,3-*c*]pyrazole (**17**) of *trans* configuration are included as well.

While studying the benzopyrano[4,3-*c*]pyrazoles it was found that the chemical shift value of 3-H is considerably higher in the *cis* compound than in the *trans*.[2,12,13] This is understandable since 3-H is quasi-equatorial in the *cis* isomer and quasi-axial in the *trans*. In the case of (**16**) and (**16a**) the difference is reflected well in the measured values (5.46 and 4.62 p.p.m.). In spite of this finding, the *cis* or *trans* configuration cannot be determined solely from the chemical shift of 3-H since the $\delta_{3\text{-H}}$ is considerably dependent on substituents R^1 and R^2, moreover it is influenced, to a small extent, by the X group a well. Owing to the diamagnetic effect of the phenyl group, a 0.2–0.3 p.p.m. upfield shift was measured in the presence of an equatorial 4-Ph. When the substituent $R^2 = CONH_2$ was replaced by $CSNH_2$, the chemical shift was increased by 0.2–0.5 p.p.m. In the case of thiocarbamoyl group delocalization is so pronounced that rotation around the N-2–$CSNH_2$ bond is hindered even at room temperature which is corroborated by the appearance of two NH signals of different chemical shift and the increased linewidth of the signal of the phenyl *ortho* protons.

It has been observed that, owing to the diamagnetic effect of the neighbouring phenyl group, $\delta_{3a\text{-H}}$ characteristically decreased (*ca.* 0.5 p.p.m.) in the 3-H,3a-H *trans* isomers compared with that measured in the *cis* compounds. On the basis of chemical shifts (3.73 and 3.25 p.p.m.) measured in model compounds (**16**) and (**16a**) this difference is 0.48 p.p.m. Incorporation of substituent R^1 = Ph results in a higher alteration, *e.g.*, in compound pairs (**7**), (**9**), (**8**), (**10**), and (**12**), (**15**) the difference is 0.62, 0.70, and 0.86 p.p.m. which also reflects the paramagnetic effect of the phenyl group. On this basis it can be assumed that along bond C-4—Ph a conformer predominates in which C-4—Ph_{ax} and the phenyl ring are coplanar. This is corroborated by the fact that downfield shifts of 1.43, 1.46, and 1.92 p.p.m. were measured on the 4-H_{ax} signal of substances (**9**), (**10**), and (**15**). As far as the influence of substituent R^2 is concerned, the $CONH_2 \longrightarrow CSNH_2$ modification resulted only in a 0.1–0.2 p.p.m. downfield shift. The chemical shift of 3a-H is slightly influenced by the X heteroatom, except for the X = SO_2 derivatives (**13**) and (**14**), in which a downfield shift, originating from the effect of the *peri*-positioned S=O group,[14] was detected. From all of this information it appears that for a single isomer $\delta_{3a\text{-H}}$ is of little





(**1**) X = P R^1 = H
(**2**) X = O R^1 = Ph
(**3**) X = S R^1 = H
(**4**) X = SO_2 R^1 = H
(**5**) X = S R^1 = Ph
(**6**) X = CH_2 R^1 = H

(**7**) X = O R^1 = H R^2 = $CONH_2$
(**8**) X = O R^1 = H R^2 = $CSNH_2$
(**9**) X = O R^1 = Ph R^2 = $CONH_2$
(**10**) X = O R^1 = Ph R^2 = $CSNH_2$
(**11**) X = S R^1 = H R^2 = $CONH_2$
(**12**) X = S R^1 = H R^2 = $CSNH_2$
(**13**) X = SO_2 R^1 = H R^2 = $CONH_2$
(**14**) X = SO_2 R^1 = H R^2 = $CSNH_2$
(**15**) X = S R^1 = Ph R^2 = $CSNH_2$
(**16**),(**16a**) X = CH_2 R^1 = H R^2 = Ph
(**17**) X = O R^1 = H R^2 Me

Scheme.

Table 1. ^{1}H n.m.r. chemical shifts and characteristic coupling constants (Hz) of compounds (**7**)–(**17**) in [$^2H_6$]Me_2SO

	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)[a]	(16a)[a]	(17)[a]
3-H	5.62	6.13	5.32	5.83	5.88	6.05	5.74	6.20	5.86	5.46	4.62	3.78
3a-H	4.02	4.18	4.64	4.84	4.03	4.18	4.47	4.60	5.04	3.73	3.25	3.57
4-H_{ax}	2.98	2.97	4.41	4.43	2.09	2.07	2.45	2.44	3.99	1.05	1.94	4.15
4-H_{eq}	4.24	4.27			2.69	2.76	3.60	3.61		1.80	2.29	4.48
5-H_{ax}										2.92	2.90	
5-H_{eq}										2.80		
6-H	6.88	6.90	6.90	6.92	7.18	7.21	7.82	7.86	7.22	*b*	7.15	6.88
7-H	7.30	7.36	7.34	7.40	7.28	7.29	7.67	7.73	7.37	*b*	7.37	7.22
8-H	7.02	7.05	7.09	7.12	7.16	7.19	7.76	7.78	7.26	*b*	7.24	6.97
9-H	7.82	7.89	7.93	8.00	8.14	8.24	8.29	8.40	8.36	8.16	8.06	7.80
2′6′-H	7.05	7.04	6.60	6.58	7.07	7.03	7.07	7.03	6.48	7.12	7.46	7.44
3′5′-H	7.30	7.30	7.08	7.08	7.31	7.31	7.32	7.32	7.02	*b*	7.39	7.39
4′-H	7.23	7.22	7.17	7.17	7.24	7.24	7.27	7.26	7.13	*b*	7.31	7.34
2″6″-H			7.06	7.08					7.08	7.08[c]	7.07[c]	
3″5″-H			7.30	7.31					7.27	*b*	7.15[c]	
4″-H			7.38	7.38					7.32	6.74[c]	6.81[c]	
NH_2	6.51	7.79	6.49	7.60	6.63	7.95	6.82	8.23	7.98			2.81[d]
		8.08		8.06		8.09		8.34	8.07			
$J_{3,3a}$	11.2	10.7	11.1	10.7	11.4	11.0	11.4	11.0	10.5	11.5	12.1	13.5
$J_{3a,4}$	13.0	12.9	12.3	12.5	12.8	12.8	13.3	13.2	13.0	13.5	12.1	12.2
	5.9	6.1			4.6	4.7	4.5	4.5		4.8	4.9	5.8
$J_{4,4}$	−10.5	−10.4			−13.0	−13.0	−13.3	−13.2		−12.7	−13.2	−10.2

[a] Measured in $CDCl_3$. [b] Overlapped signals between 7.17–7.37 p.p.m. [c] These data are referred to the NPh group. [d] NMe.

diagnostic value. In isomers (**16**) and (**16a**) a characteristic upfield shift can be observed for signals due to 4-H_{ax} and 4-H_{eq} of the *cis* compound, caused by the effect expected by the neighbouring 3-Ph group (Δδ 0.89 and 0.49 p.p.m.) and this is valuable information when comparing *cis–trans* isomeric pairs. Furthermore, complete assignment of the ^{1}H spectra has been performed which was necessary, above all, to the evaluation of the two-dimensional ^{13}C–^{1}H correlation maps utilized for the assignment of the ^{13}C signals. It is noteworthy that the signal due to the *ortho* phenyl protons underwent a *ca.* 0.5 p.p.m. diamagnetic shift as a result of the incorporation of a phenyl substituent (R^1 = Ph).

On the basis of former studies it can be concluded that the $J_{3,3a}$ coupling constants can be used only tentatively to determine the *cis–trans* isomerism, since these values are very similar.[1,2,12,13] In the case of model compounds (**16**) and (**16a**) these values are 11.5 and 12.1 Hz. It should be mentioned that in some cases an opposite tendency was observed.[1,12,13,15] Expected coupling constants were calculated by means of the modified Karplus equation[16] taking into account the electronegativity of the substituents. However, values calculated for the *cis* and *trans* isomers hardly differed from each other. Moreover, calculated values differed considerably from the measured data for both isomers. On this basis it was concluded that *cis* and *trans* isomers cannot be differentiated by means of the $J_{3,3a}$ coupling constants. On the other hand, stereoposition

Table 2. Results of proton–proton 1D n.O.e. difference experiments on selected compounds

Compound	Proton irradiated	N.O.e. observed (%)
(**9**)	3-H	3a-H (6), 2′,6′-H (7), 2″6″-H (1)
	3a-H	3-H (9), 2″,6″-H (11)
	4-H_{ax}	2′,6′-H (3), 2″,6″-H (8)
(**11**)[a]	3-H	3a-H (15), 2′,6′-H (13)
	3a-H	3-H (15), 4-H_{eq} (5)
(**15**)	3-H	3a-H (5), 2″,6″-H (1)
	3a-H	3-H (6), 2″,6″-H (10)
(**16**)[b]	3-H	3a-H (6), 2″,6″-H (11)
	3a-H	3-H (9), 4-H_{eq} (3), 5-H_{ax} (2)
(**16a**)[b]	3-H	4-H_{ax} (4), 2′,6′-H (6), 2″,6″-H (7)
	3a-H	4-H_{eq} (3), 5-H_{ax} (2), 2′,6′-H (2)
(**17**)	3-H	4-H_{ax} (6), 2′,6′-H (10), NMe (5)
	3a-H	4-H_{eq} (4), 2′,6′-H (6)

[a] Measured at 250 MHz. [b] In this case 2″6″-H belongs to the NPh group.

Table 3. ^{13}C N.m.r. chemical shifts for compounds (**7**)–(**16a**) in $[^2H_6]Me_2SO$

Carbon	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)[a]	(16a)[a]
3	61.5	65.0	62.4	65.6	63.5	66.9	63.1	66.4	67.1	66.6	73.3
3a	45.3	45.3	49.6	49.5	48.2	48.2	44.7	44.8	52.4	49.1	56.4
4	66.7	67.0	79.7	79.8	26.7	26.7	49.6	49.7	45.0	24.1	27.4
5										29.6	29.4
5a	155.8	156.5	156.6	157.3	134.7	135.9	136.1	137.8	137.1	137.6	138.1
6	117.3	117.4	117.5	117.5	126.9	127.0	123.1	123.2	126.3	128.8	129.0
7	131.9	132.9	132.0	133.0	130.0	130.8	131.0	131.9	131.2	128.8	129.1
8	121.6	121.6	121.9	121.8	125.0	125.2	133.0	133.1	125.6	126.5	126.7
9	124.5	125.0	124.5	124.9	126.0	126.6	126.3	125.9	126.8	124.3	124.4
9a	115.7	114.9	115.8	114.9	124.9	125.8	125.4	125.8	125.2	128.4	128.2
9b	146.4	150.9	146.9	151.3	147.8	152.2	143.3	147.5	152.9	148.2	150.5
R^2	154.2	175.3	154.2	175.2	154.2	175.5	154.0	176.3	175.3	*b*	*c*
1′	137.2	136.6	136.7	136.0	137.4	136.9	137.0	135.8	136.1[d]	136.9	142.2
2′, 6′	125.2	125.3	126.6	126.9	125.1	125.1	125.9	126.0	127.1	126.9	129.3
3′, 5′	128.6	128.5	128.0	128.2	128.5	128.5	128.7	128.6	127.7	128.9[d]	126.1
4′	127.5	127.4	127.6	127.4	127.4	127.4	127.8	127.7	127.5	127.5	127.7
1″			136.4	135.8					136.0[d]		
2″, 6″			128.2	127.8					128.1		
3″, 5″			128.5	128.4					128.5		
4″			129.2	129.3					128.5		

[a] Measured in $CDCl_3$. [b] C_{ipso} 144.0, C_{ortho} 112.9, C_{meta} 128.6, [d] C_{para} 118.2. [c] C_{ipso} 146.9, C_{ortho} 114.9, C_{meta} 128.7, C_{para} 120.0. [d] Tentative assignments.

Table 4. Observed ^1H–^{13}C long-range correlations for compound (**10**)

	^2J	^3J
3-H	C-3a	C-9b
3a-H	C-4, C-9b	C-1′
4-H	C-1″	C-9b
6-H		C-8, C-9a
8-H		C-9a
2″,6″-H		C-4″

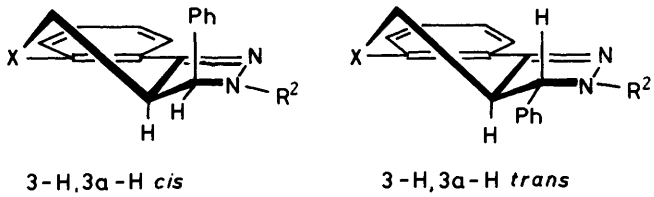


Figure.

of substituent R^1 can unequivocally be determined from $J_{3a,4}$ since the antiperiplanar position of the 3a-H and 4-H_{ax} is verified by the measured *ca.* 12 Hz coupling constants. Homonuclear proton–proton n.O.e. difference spectroscopy[17] makes possible the unambiguous identification of *cis* and *trans* isomerism, as structure elucidation based on the ^1H chemical shift and $J_{3,3a}$ coupling constant data do not, since an n.O.e. effect can be expected between the neighbouring 3-H and 3a-H protons of the *cis* isomer which is absent in the *trans* isomer. Thus it is possible to determine the relative configuration of a single isomer without using a reference compound. As regards the structure elucidation, n.O.e. measurements provided important information toward the assignment of the ^1H signals, by simplifying the strongly overlapping signals in the normal ^1H n.m.r. spectra so that they can be analysed. In accordance with the 3-H,3a-H *cis* configuration in the case of compounds (**9**), (**11**), (**15**), and (**16**), irradiation of 3-H caused an enhancement in the intensity of the 3a-H signal or of the 3-H signal if 3a-H was saturated (see Table 2). A further feature is that in compounds (**16**) and (**17**) saturation of the 3a-H signal results in an n.O.e. only on 4-H_{eq} of the 4-H_2 methylene protons. The equatorial position of substituent R^1 is corroborated by the fact that no intensity enhancement was detected on the 4-H signal in substances R^1 = Ph. In *trans*-(**16a**) and -(**17**), 3-H and 4-H_{ax} and 3a-H and 4-H_{eq} are in spatial proximity which was unequivocally proved by the n.O.e. measurements.

The structures deduced above were further corroborated by ^{13}C n.m.r. investigations. Characteristic ^{13}C chemical-shift data are summarized in Table 3. Assignments were based on 2D ^{13}C–^1H correlation maps[18] and on different substituent effects[19] caused by the heteroatoms. In the case of compounds (**9**) and (**10**), for an unambiguous assigment of the quaternary carbon atoms, COLOC spectra[20] optimized for 6 Hz long-range ^{13}C–^1H couplings were also measured. In this way it was possible to differentiate C-1′ and C-1″, the signals of which were very close together (136.7 and 136.4 p.p.m.), of substance (**9**) since a cross-peak with the 3a-H proton was detected only at C-1′. Assignment of the 146.7 p.p.m. signal to C-9b was corroborated by its cross-peak with 3-H and 4-H. Characteristic ^2J(C, H) and ^3J(C, H) connectivities observed in the case of compound (**10**), which confirm our assignment, are summarized in Table 4. On the basis of our more recent studies it became evident that our assignments of the C-4 and C-5 signals of compound (**16a**)[1] should be interchanged (see Table 3). The basic difference between the 3-H,3a-H *cis* and *trans* structures is that 3-Ph is quasi-axial in the former and quasi-equatorial in the latter (Figure). This results in characteristically different α, β, and γ substituent effects[21] which is well illustrated by the (**16**), (**16a**) isomeric pair. When the 3-Ph group was transferred from the equatorial to the axial position, diamagnetic shifts of 6.7 p.p.m. on the α-positioned C-3 atom, 7.3 p.p.m. on the β C-3a, and 3.3 and 2.3 p.p.m., respectively, on the γ C-4 and C-9b atoms were observed. Similarly characteristic is the upfield shift on the C-1′ signal which is certainly connected with the γ_{gauche} interaction between C-1′ and C-4 instead of the previously assumed N-2 lone-pair electron effect.[2] (The latter can be excluded if the delocalization of the aniline- and amide-type N-2 atom is taken into consideration.) Owing to the different electronic effects of the carbamoyl and thiocarbamoyl groups, characteristic differences can be observed if the pairs (**7**) and (**8**), (**9**) and (**10**), (**11**) and (**12**), and (**13**) and (**14**) are compared. The $CONH_2 \longrightarrow CSNH_2$ exchange resulted in a 3.2–3.5 p.p.m. paramagnetic shift on C-3, 4.2–4.5 p.p.m. on C-9b, 0.7–1.7 p.p.m. on C-5a, and in a characteristic 0.8–1.0 p.p.m. shift in the case of the very remote C-7. Slight, opposing changes were detected in the C-1′ signals.

Table 5. Physical constants, analytical and i.r. spectral data of compounds (7)–(16)

Compound	M.p./ °C	Yield (%)	ν Amide/thioamide/ cm^{-1}	Overall formula	Required (%) C	Required (%) H	Required (%) N	Found (%) C	Found (%) H	Found (%) N
(7)	258	39.0	1 675	$C_{17}H_{15}N_3O_2$	69.6	5.15	14.3	69.7	5.3	14.5
(8)	269	34.1	1 360	$C_{17}H_{15}N_3OS$	66.0	4.8	13.5	66.0	4.5	13.6
(9)	279	27.2	1 675	$C_{23}H_{19}N_3O_2$	74.7	5.1	11.3	74.5	5.6	11.2
(10)	228	26.0	1 370	$C_{23}H_{19}N_3OS$	71.6	4.9	10.9	71.4	4.7	10.7
(11)	235	38.3	1 660	$C_{17}H_{15}N_3OS$	66.0	4.8	13.5	66.2	4.9	13.6
(12)	236	56.4	1 340	$C_{17}H_{15}N_3S_2$	62.7	4.6	12.9	62.8	4.6	12.8
(13)	287	62.0	1 665	$C_{17}H_{15}N_3O_3S$	59.8	4.4	12.3	60.0	4.5	12.0
(14)	245	84.0	1 380	$C_{17}H_{15}N_3O_2S_2$	57.1	4.2	11.7	57.1	4.5	11.6
(15)	272	26.1	1 375	$C_{23}H_{19}N_3S_2$	68.8	4.7	10.4	68.7	5.0	10.4
(16)	146	59.0	—	$C_{23}H_{20}N_2$	85.1	6.2	8.6	84.6	6.4	8.8

Replacement of S by SO_2 change gave rise to characteristic alterations in the chemical shift values of some carbon atoms, *e.g.* the 3.5 p.p.m. upfield shift on the C-3a signals was caused by the S=O group in γ_{gauche} position.[22] Changes observed in the fused aromatic ring in positions C-7 and C-9 are in accordance with the known substituent effects.[19,23,24]

During the course of our stereochemical studies we have developed procedures that selectively afford 3-H,3a-H *cis* and *trans* isomers: *viz.* the reaction carried out in hot pyridine gives the *trans*[1,3] isomer, while that in hot ethanol, in the presence of hydrochloric acid, gives the *cis* isomer. Studies on the reaction mechanism are in progress and their results will be published elsewhere.

Experimental

I.r. spectra were recorded on a Specord 75 IR-type spectrometer in KBr pellets. The n.m.r. spectra were recorded on Bruker AM-400 and AC-250 spectrometers at room temperature. Chemical shifts are given in δ. In the 1D measurements 32 K data points were used for the FID. For homonuclear n.O.e. experiments a delay time of 3 s and an irradiation time of 1.5 s (*ca.* $1 \times T_1$) was applied. N.O.e. difference and two-dimensional carbon–proton correlated experiments were recorded by using the Bruker software package. In the 2D experiments 1 K × 1 K data matrices were transformed. M.p.s were determined on a Boetius hot-plate apparatus and are uncorrected.

Starting materials (**1**)–(**3**) were prepared as reported previously by us[25,26] and compounds (**4**) and (**5**) according to known methods.[27,28]

General Procedure for the Synthesis of Compounds (**7**)–(**16**).— A mixture of the starting α,β-unsaturated ketone (**1**)–(**6**) (10 mmol) and semicarbazide hydrochloride or thiosemicarbazide (20 mmol), and concentrated hydrochloric acid (10.0 ml) was refluxed in ethanol (100 ml) or, to maintain an appropriate temperature, in propanol in the case of (**15**). The course of the reaction was monitored by t.l.c. Crystalline materials precipitated when the reaction was cooled were filtered off and washed with water to remove acid. A second fraction separated when the mother liquor was poured into water, and was treated in a similar way. Crude materials were crystallized from methanol. Physical constants, analytical and i.r. spectroscopic data of compounds prepared are summarized in Table 5.

Acknowledgements

The authors are grateful to the OTKA program of the Hungarian Academy of Science and to the Hungarian Ministry of Health and Welfare for financial support. One of us (G. T.) thanks the A.v. Humboldt Stiftung for a fellowship (Ruhr University, Bochum, FRG). We wish to thank Mr. Ohmacht and Mrs. M. Ott for the analyses and i.r. spectra. Special thanks are due to Miss E. Tóth, Miss I. Semmelroth, Mrs. E. Bleszity, and Mrs. E. Hajnal for their technical assistance.

References

1 Part 2: A. Lévai, Á. Szöllösy, and G. Tóth, *J. Chem. Res.* (*S*), 1985, 392.
2 T. Lóránd, D. Szabó, A. Földesi, L. Párkányi, A. Kálmán, and A. Neszmélyi, *J. Chem. Soc., Perkin Trans. 1*, 1985, 481.
3 A. Lévai, G. Tóth, and Á. Szöllösy, 'Flavonoids and Bioflavonoids,' eds. L. Farkas, M. Gábor, and F. Kállay, Akadémiai Kiadó, Budapest, 1985, 47.
4 K. Ramalingam, G. X. Thyvelikakath, K. D. Berlin, R. W. Chesnut, R. A. Brown, N. N. Durham, A. E. Ealick, and D. van der Helm, *J. Med. Chem.*, 1977, **20**, 847.
5 J. G. Lombardino and I. G. Otterness, *J. Med. Chem.*, 1981, **24**, 830.
6 I. G. Lombardino, I. G. Otterness, and J. F. Muren, U.S. P. 4,268,516 (*Chem. Abstr.*, 1981, **95**, 62201).
7 R. E. Brown and J. Shavrel, Jr., U.S. P. 3,624,102 (*Chem. Abstr.*, 1972, **76**, 59618).
8 T. Lóránd, in preparation.
9 T. Shimizu, Y. Hayashi, Y. Nagamo, and K. Teramura, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 429.
10 F. M. Dean and S. Murray, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1706.
11 S. R. Moorty, V. Sundaramurthy, and N. V. S. Rao, *Indian J. Chem.*, 1973, **11**, 854.
12 N. K. Sangwan and S. H. Rastogi, *Indian J. Chem., Sect. B*, 1981, **20**, 135.
13 N. K. Sangwan, *J. Chem. Res.* (*S*), 1987, 22.
14 A. H. Fawcett, K. J. Ivin, and C. D. Stewart, *Org. Magn. Reson.*, 1978, **11**, 360.
15 A. Hassner and M. J. Michelson, *J. Org. Chem.*, 1962, **27**, 3974.
16 L. A. G. Haasnoot, F. A. A. M. de Leeuw, and C. Altona, *Tetrahedron*, 1980, **36**, 3783.
17 J. K. M. Saunders and J. D. Mersh, *Prog. Nucl. Magn. Reson. Spectrosc.*, 1982, **15**, 353.
18 A. Bax, *J. Magn. Reson.*, 1983, **53**, 517.
19 E. Pretsch, T. Clerc, J. Seibl, and W. Simon, 'Tabellen zur Strukturaufklärung organischer Verbindungen mit Spektroskopischen Methoden,' Springer Verlag, Berlin, 1976, pp. C 10 and C 120.
20 H. Kessler, C. Griesinger, J. Zarbock, and H. R. Loosli, *J. Magn. Reson.*, 1984, **57**, 413.
21 M. J. Cook and K. A. Nasri, *Magn. Reson. Chem.*, 1987, **26**, 644.
22 E. L. Eliel and K. M. Pietrusiewicz, 'Topics in Carbon-13 Spectroscopy,' ed. G. C. Levy, vol. 3, Wiley–Interscience, New York, 1979, p. 197.
23 M. S. Chauhan and I. W. J. Still, *Can. J. Chem.*, 1975, **53**, 2880.
24 D. F. Ewing, *Org. Magn. Reson.*, 1979, **12**, 49.

25 A. Lévai and E. H. Hetey, *Pharmazie*, 1978, **33**, 378.
26 A. Lévai and J. B. Schág, *Pharmazie*, 1979, **34**, 749.
27 F. Arndt, W. Fleming, E. Scholz, and V. Löwenson, *Ber. Dtsch. Chem. Ges.*, 1923, **56**, 1269.
28 F. Arndt, W. Fleming, E. Scholz, V. Löwenson, G. Kallner, and B. Eistert, *Ber. Dtsch. Chem. Ges.*, 1925, **58**, 1612.

Received 5*th April* 1988; *Paper* 8/01329B