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AMINOMETHYLATION OF CYTISINE BY 3-HETARYL-7-HYDROXYCHROMONES

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8-Aminomethyl derivatives of 7-hydroxychromones were prepared by reaction of methylene-bis-cytisine with substituted 7-hydroxychromones. The structures of the synthesized compounds were investigated using NMR spectroscopy.

Key words: cytisine, alkylation, 3-hetaryl-7-hydroxychromones, aminomethylation, Mannich bases.

The alkaloid cytisine (**1**) is used in medicine as a respiratory analeptic [1] known as cytiton and as an anti-smoking drug. Because cytisine contains a secondary amine group, it is promising for chemical modification. Among the known methods for chemical modification, the one most commonly used is alkylation by various reagents [2-12]. Acylation [13], the Kabachnik—Fields reaction [14], synthesis of cyanomethyl derivatives using hydroxyacetonitrile [15], and reactions with amides and formalin [16] have also been reported.

Research on the aminomethylation of cytisine has recently begun. It was found that cytisine reacts under Mannich reaction conditions with barbituric and thiobarbituric acid derivatives substituted in the 5-position [17, 18]. According to our results, 3-hetaryl-7-hydroxycoumarins can be aminomethylated using aminals, including those synthesized using cytisine [19].

In continuation of research on modification of analogs of natural isoflavanoids and taking into account results on the synthesis of aminomethyl derivatives of benzopyrones, we prepared aminomethyl derivatives of heteroatomic analogs of isoflavones with cytisine as the amine. The type of derivative was selected based on the fact that cytisine retains the properties of an amine and the presence of spatially close amine and phenol groups facilitates the formation of H-bonds up to the formation of a betaine, which favorably affects the solubility of these compounds.

Considering research on aminomethylation of isofoavones and the possible reaction mechanism [19, 20], we chose the route using the aminal (**2**) (methylene-*bis*-cytisine), which was prepared from cytisine and formalin, to synthesize the Mannich bases containing cytisine.

The structures of Mannich adducts **6**-**8** were established using PMR and ^{13}C NMR. Because both proton and carbon spectra were rather complicated, signals in the proton spectra were assigned using spin coupling between protons that was revealed using COSY two-dimensional (2D) spectra. Signals of C atoms were assigned using HMQC and HMBC 2D heteronuclear correlations. Signals of all protonated C atoms except those with chemical shifts 60.5 and 60.7 ppm (**6**) could be assigned using HMQC spectra. Although it was clear that these signals belonged to N–CH_2 groups of the aminomethylene moiety, they could be assigned the values given in Table 1 or the alternate assignment.

We used HMBC methods to assign signals of quaternary C atoms of **6** based on couplings through 2-3 chemical bonds. Thus, the signal at 164.3 ppm was assigned to the C-2 carbonyl C atom based on its correlations with signals for H-3 and H-4 of the pyridone ring; that at 149.6 ppm, to bridging atom C-6 based on corrleations with signals for H-4 and H-5. Analogous arguments were used to assign signals of other quaternary C atoms. A correlation between the methylene protons of the 6′-ethyl in the isoflavone and bridging C atom C-4′ at 116.6 ppm in the 2D HMBC spectrum was unexpected. We explain this through ω-coupling. This correlation can be used to confirm the assignment of the C-4a signal.

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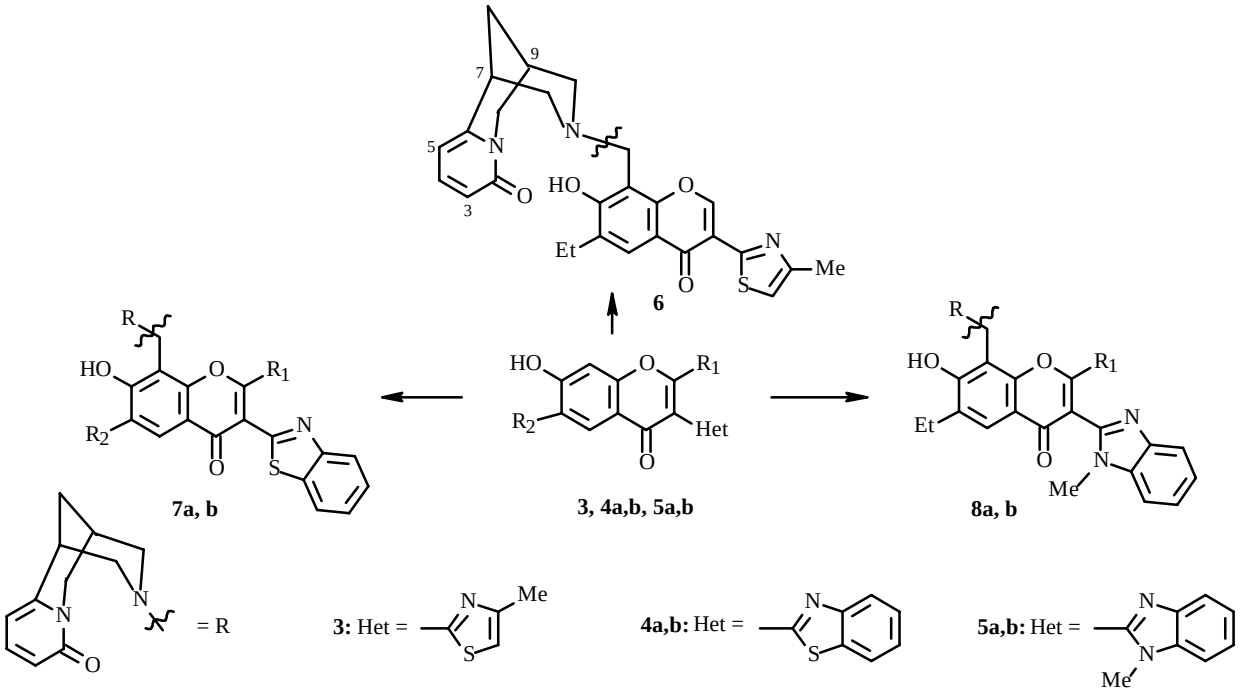
TABLE 1. PMR and ^{13}C NMR Spectra of Compound **6** with Correlations Found in 2D Spectra

C atom	δ_H	HMQC	HMBC
3	6.56 (dd, J = 8.7, J = 1.2)	118.6	164.3, 106.0
4	7.28 (dd, J = 8.7, J = 6.9)	139.5	164.3, 149.6
5	5.97 (dd, J = 6.9, J = 1.2)	106.0	149.6, 35.6, 118.6
7	3.09	35.6	-
2H-8	1.92, 2.02	26.4	-
9	2.52	28.5	26.4
10ax	3.92 (m, J = 16.0)	50.2	28.5
10eq	4.20 (m, J = 16.0)	50.2	149.6, 60.5, 28.5, 26.4
11ax	2.60	60.5*	50.2
11eq	3.02	60.7	-
13ax	2.60	60.7*	-
13eq	3.17	60.5	-
2′	8.92	153.9	174.8, 157.8, 154.1, 116.6
5′	7.96	125.3	174.8, 162.5, 23.3, 154.1
$\underline{C}H_2$-6′	2.49	23.3	116.6, 132.3, 125.3, 14.3
$C\underline{H}_3CH_2$-6′	1.13 (t, J = 7.7)	14.3	132.3
CH_2-8′	3.95	54.0	116.6, 107.0, 162.5, 154.1, 60.5, 60.7
CH_3-4″	2.49	17.8	152.2, 116.5
5″	6.99	116.5	157.8, 152.2, 17.8



3, 4a, 7a: R_1 = H; **4b, 5a, 7b, 8a:** R_1 = Me; **5b, 8b:** R_1 = $CHMe_2$

3, 4a, 5a, 5b, 7a, 8a, 8b: R_2 = Et; **4b, 7b:** R_2 = H

Practically the same correlations were observed for **7a** as for **6**. The chemical shifts for common structural fragments turned out also to be very similar. This indicated that the type of heterocyclic substituent in the chromone 3′-position had practically no effect on the electron-density distribution in this moiety.

Signals in the C framework were assigned in the same way as that described for **6**. Certain difficulties did arise in assigning signals for the benzothiazole substituent of **7a** because of the overlap of chemical shifts for H-4″ and H-7″. However, based on a comparison of correlations in HMBC and COSY spectra, the problem was rather convincingly solved. The empirical rule that correlations in HMBC spectra through three bonds in aromatic compounds are significantly stronger those through two bonds if the mixing time is selected so that maximum correlations are observed for SSCC = 8 Hz was a great help.

TABLE 2. PMR and ^{13}C NMR Spectra of Compounds **7a** and **7b** with Correlations Found in 2D Spectra

Atom	**7a**			**7b**		
	δ_H	HMQC	HMBC	δ_H	HMQC	HMBC
3	6.56 (dd, J = 8.7, J = 1.2)	118.1	105.5, 163.8	6.14 (dd, J = 8.7, J = 1.2)	116.2	162.8, 104.5
4	7.30 (dd, J = 6.9, J = 8.7)	139.0	163.8, 149.1	7.24 ((dd, J = 6.9, J = 8.7)	139.4	162.8, 152.0
5	5.98 (dd, J = 6.9, J = 1.2)	105.5	149.1, 118.1, 35.1	6.01 (dd, J = 6.9, J = 1.2)	104.5	152.0, 116.2, 35.0
7	3.09	35.1		3.02	35.0	
8	1.91; 2.02	26.4		1.71, 1.79	25.5	
9	2.57	27.9	35.1	2.39	27.9	
10	3.91, 4.21 (m, J = 16.0)	49.7	27.9, 26.4, 60.0, 149.1	3.67, 3.80 (m, J = 16.0)	50.1	152.0, 162.8, 60.4, 25.5, 27.9, 59.7
11	2.57, 3.03	60.4	49.7, 26.4	2.43, 2.85	60.4	50.1, 59.7
13	2.57, 3.16	60.0	149.1	2.39, 2.96	59.7	152.0, 50.1
2′	9.11	155.2	153.6, 174.4, 159.3, 147.8			
5′	7.99	124.9	174.4, 153.6, 162.2, 22.9	7.86	126.3	174.6, 163.0, 155.2
6′				6.87	115.7	163.0, 155.2, 115.0, 109.9
CH_2-8′	3.95	53.5	162.2, 153.6, 124.9, 116.1, 106.6, 60.4, 60.0	3.78	51.0	60.4, 163.0, 59.7 109.9, 155.2,163.0
4″	7.99	122.5	151.8, 124.9	8.09	122.2	151.7, 126.6
5″	7.38	126.3	136.4, 122.5	7.41	125.6	151.7, 123.1, 135.7
6″	7.49	124.9	151.8, 121.9	7.49	126.6	151.7, 122.2
7″	7.99	124.9	136.4, 126.3	7.99	123.1	125.5, 135.7
CH_3CH_2-6′	1.14	13.8	22.9			
$CH_3\underline{C}H_2$-6′	2.54	22.9	13.8, 162.2, 124.9			
CH_3-2′				2.88	22.4	144.6, 160.6, 169.5

It also seemed interesting to synthesize the Mannich bases from the more sterically hindered heterocyclic isoflavone analogs. An additional chiral axis can arise in these compounds owing to hindered rotation between the chromone core and the 3-hetaryl substituent. Because the aminomethyl fragment in these compounds is not inherently chiral, diastereomers can arise for these compounds and be detected in NMR spectra. For this, we studied **7b**, **8a**, and **8b**, in which steric hindrances increase successively between the chromone and the 3″-hetaryl substituent. Table 2 lists assignments for signals of **7b**, which differ from those of **7a** mentioned above because the chromone has a methyl in the 2′-position. These spectra were measured in DMSO-d_6 in order to determine the magnitude of the solvent effect on the chemical shifts. As it turned out, differences in PMR spectra were greatest for protons of the aminomethylene moiety that were located near the pyridine N atom. The signals in DMSO shifted to strong field. In this instance, solvent probably associated with the carbonyl O atom and decreased the polarization of the carbonyl bond, which led to diamagnetic shifts of the nearest signals. This was also confirmed by the decrease in the chemical shift of the carbonyl C atom by more than 1 ppm compared with **6**.

The pattern of observed correlations in the HMBC spectrum of **7b** (Table 2) was practically the same as that in spectra of **6** and **7a**. This enabled all signals in the PMR and ^{13}C NMR spectra to be assigned. The only unusual correlation was that through four bonds between the Me-2′ methyl and the benzothiazole C-2″. This correlation enabled the signal at 160.6 ppm to be assigned to C-2″.

As it turned out, this compound did not have diastereomers that were due to axial chirality.

Spectra of *N*-methylbenzimidazole derivative **8a** showed that certain signals were broadened in its ^{13}C NMR spectrum. As before, signals were assigned using HMQC and HMBC spectra (Table 3).

A correlation between the chromone Me-2′ protons that resonated at 2.43 ppm and benzimidazole C-2″ at 148.0 ppm was unexpected. The appearance of this correlation through four chemical bonds indicated that the conformation of the benzimidazole moiety was rather rigidly fixed.

TABLE 3. PMR and ^{13}C NMR Spectra of Compounds **8a** and **8b** with Correlations Found in 2D Spectra

Atom	**8a**			**8b**		
	δ_H	HMQC	HMBC	δ_H	HMQC	HMBC
3	6.54 (dd, J = 8.7, J = 1.2)	118.0	104.5, 163.7	6.55 (dd, J = 8.7, J = 1.2)	118.1	163.8, 105.5
4	7.30 (dd, J = 8.7, J = 6.9)	138.9	163.7, 149.2	7.30 (dd, J = 8.7, J = 6.9)	139.0	149.1, 163.8
5	5.98 (dd, J = 6.9, J = 1.2)	104.5	35.0, 118.0, 149.2	5.98 (dd, J = 6.9, J = 1.2)	105.5	149.1, 118.1, 35.0
7	3.07	35.0		3.10	35.0	
8	1.98; 1.90	25.8		1.91; 2.01	25.8	
9	2.18	27.9		2.52	28.0	
10	3.92; 4.18 (m, J = 16)	49.7	59.9, 27.9, 25.8, 149.2, 60.3	3.91; 4.20 (m, J = 16)	49.7	28.0, 60.5
11	2.58; 3.14	59.9	161.9	2.52; 3.10	60.5	
13	2.58; 3.01	60.4	149.2	2.58; 3.20	60.0	149.1
5′	7.85	124.7	22.9, 106.2, 175.3, 161.9, 153.5	7.85	124.9	175.8, 161.8, 153.5, 106.5, 22.9
CH_2-8′	3.94	53.5	161.9, 153.5, 105.4	3.95	53.5	161.8, 105.5, 153.5
4″	7.78	119.9	122.9, 136.1	7.80	120.1	136.2, 122.8
5″	7.30	122.1	143.1, 109.9	7.30	122.1	142.3, 120.1
6″	7.30	122.9	136.1, 109.8	7.30	122.8	136.2, 109.8
7″	7.41	109.8	122.1, 143.1	7.41	109.8	142.3, 122.1
$\underline{C}H_3CH_2$-6′	1.12	13.9	22.9, 131.3	1.13	14.0	131.4, 22.9
$CH_3\underline{C}H_2$-6′	2.53	22.9	13.9	2.52	22.9	161.8
CH_3-2′	2.43	19.8	148.0, 143.9, 167.1	-	-	-
N-CH_3	3.68	31.1	148.0, 136.1	3.67	30.8	175.8, 147.8, 136.2
2′-C-CH_3 (a)				1.40	21.0	173.4, 31.9, 21.0
2′-C-CH_3 (b)				1.13	21.4	173.4, 21.0, 31.9

Signal assignments in the ^{13}C NMR spectrum showed that the signals for the aminomethylene N–CH_2 groups (C-11 and C-13) that resonated at 59.9 and 60.4 ppm and that for pyridone H-5 in that moiety with chemical shift 104.5 ppm were broadened. Because the most important factor that distinguishes the structure of **8a** from that of **6** and **7** is the presence of steric hindrance to free rotation between the chromone and the 3-hetaryl substituent, the signal broadening is obviously due to the generation of diastereomers and the broadening of signals for atoms located near the asymmetric centers of the aminomethylene substituent.

Steric hindrance is even greater in **8b**, which contains an isopropyl substituent in the chromone 2-position. The presence of diastereomers is evident even in the PMR spectrum. Signals for the isopropyl methyls differ from one another by 0.35 ppm. The ^{13}C NMR spectrum shows differences in the chemical shifts of the isopropyl C atoms of about 1 ppm and doublets for the *N*-methyls of the aminomethylene moiety at 60.0 and 60.5 ppm. The magnitude of the signal splitting here was 0.7 ppm. Small splitting was also observed for the pyridine H-5 proton. The pattern of heteronuclear correlations for **8b** differed little from those for **6**, **7a**, **7b**, and **8a**. Figure 1 shows signal assignments and heteronuclear correlations in the HMBC spectrum of **8b**, which was the basis for the assignments.

The only quaternary C atom for which no correlation with protons was observed was benzimidazole C-2″. Its chemical shift was established by exclusion and was close to that of the corresponding signal in **8a**.

Thus, the developed aminomethylation methods can be used to synthesize compounds containing cytisine moieties, which may be promising in biological research, open new chemical pathways for modifying cytisine, and broaden the scope of its reactivity. Their structures were proved convincingly using PMR and ^{13}C NMR and 2D COSY and NOESY spectra and HMQC and HMBC heteronuclear correlations.

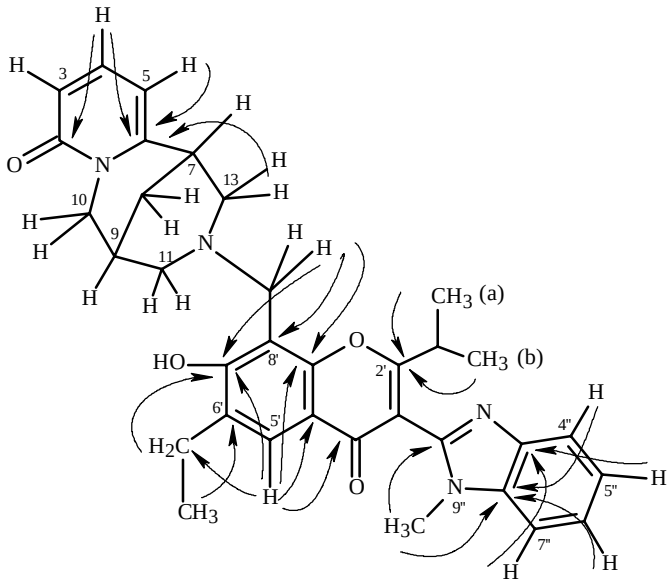


Fig. 1. Assignment of peaks in PMR and ^{13}C NMR spectra of **8b**.

EXPERIMENTAL

The course of reactions and purity of products were monitored using TLC on Merck plates (Germany) with elution by $CHCl_3$:CH_3OH:Et_2NH (88:10:2). Elemental analyses of all compounds agreed with those calculated.

General Method for Preparing 3-(2-Hetaryl)-7-hydroxy-8-(cytisyl-12)methylchromones 6-8. A boiling solution of the appropriate 3-(2-hetaryl)-7-hydroxychromone (**4a-4c**, 2 mmol) [21-23] in absolute dioxane (30 mL) was treated with aminal (2.5 mmol). The mixture was boiled for 2 h (completion of reaction determined by TLC), cooled, and evaporated in vacuo. The solid was crystallized from propan-2-ol or propan-2-ol:hexane.

(1*R*,5*S*)-3-{[7-Hydroxy-3-(4-methyl-1,3-thiazol-2-yl)-6-ethyl-4-oxo-4*H*-chromen-8-yl]methyl}-1,2,3,4,5,6-hexahydro-8*H*-1,5-methanepyrido[1,2-*a*][1,5]diazocin-8-one (6), $C_{27}H_{27}N_3O_4S$, yield 48%, mp 229-230°C (propan-2-ol:hexane).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): cytisine: 164.3 (C-2), 118.6 (C-3), 139.5 (C-4), 106.0 (C-5), 149.6 (C-6), 35.6 (C-7), 26.4 (C-8), 28.5 (C-9), 50.2 (C-10), 60.7 (C-11), 60.5 (C-13); chromone: 153.9 (C-2′), 148.6 (C-3′), 174.8 (C-4′), 116.6 (C-4a′), 125.3 (C-5′), 132.3 (C-6′), 162.5 (C-7′), 107.0 (C-8′), 154.1 (C-8a′), 23.0, 14.3 (6′-CH_2CH_3), 54.0 (CH_2-8′); thiazole: 157.8 (C-2″), 152.2 (C-4″), 116.5 (C-5″), 17.8 (Me-4″).

(1*R*,5*S*)-3-{[3-(1,3-Benzothiazol-2-yl)-7-hydroxy-6-ethyl-4-oxo-4*H*-chromen-8-yl]methyl}-1,2,3,4,5,6-hexahydro-8*H*-1,5-methanepyrido[1,2-*a*][1,5]diazocin-8-one (7a), $C_{30}H_{27}N_3O_4S$, yield 72%, mp 170-171°C (propan-2-ol).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): cytisine: 163.8 (C-2), 118.1 (C-3), 139.0 (C-4), 105.5 (C-5), 149.1 (C-6), 35.1 (C-7), 26.4 (C-8), 27.9 (C-9), 49.7 (C-10), 60.4 (C-11), 60.0 (C-13); chromone: 155.2 (C-2′), 147.8 (C-3′), 174.4 (C-4′), 116.1 (C-4a′), 124.9 (C-5′), 132.1 (C-6′), 162.2 (C-7′), 106.5 (C-8′), 153.6 (C-8a′), 22.9, 13.8 (6′-CH_2CH_3), 53.5 (CH_2-8′); benzothiazole: 159.3 (C-2″), 136.4 (C-3a″), 122.5 (C-4″), 126.3 (C-5″), 124.9 (C-6″), 124.9 (C-7″), 151.8 (C-7a″).

(1*R*,5*S*)-3-{[3-(1,3-Benzothiazol-2-yl)-7-hydroxy-2-methyl-4-oxo-4*H*-chromen-8-yl]methyl}-1,2,3,4,5,6-hexahydro-8*H*-1,5-methanepyrido[1,2-*a*][1,5]diazocin-8-one (7b), $C_{29}H_{25}N_3O_4S$, yield 77%, mp 199-200°C (propan-2-ol).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): cytisine: 162.8 (C-2), 116.2 (C-3), 139.4 (C-4), 104.5 (C-5), 152.0 (C-6), 35.0 (C-7), 25.5 (C-8), 27.9 (C-9), 50.1 (C-10), 60.4 (C-11), 59.7 (C-13); chromone: 169.5 (C-2′), 144.6 (C-3′), 174.6 (C-4′), 115.0 (C-4a′), 126.3 (C-5′), 115.7 (C-6′), 163.0 (C-7′), 109.9 (C-8′), 155.2 (C-8a′), 22.4 (2′-CH_3), 51.0 (CH_2-8′); benzothiazole: 160.6 (C-2″), 135.7 (C-3a″), 122.2 (C-4″), 125.6 (C-5″), 126.6 (C-6″), 123.1 (C-7″), 151.7 (C-7a″).

(1*R*,5*S*)-3-{[7-Hydroxy-2-methyl-3-(1-methyl-1*H*-benzimidazol-2-yl)-6-ethyl-4-oxo-4*H*-chromen-8-yl]methyl}-1,2,3,4,5,6-hexahydro-8*H*-1,5-methanepyrido[1,2-*a*][1,5]diazocin-8-one (8a), $C_{32}H_{32}N_4O_4$, yield 43%, mp 256-257°C (propan-2-ol:hexane).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): cytisine: 163.7 (C-2), 118.0 (C-3), 138.9 (C-4), 104.5 (C-5), 149.2 (C-6), 35.0 (C-7), 25.8 (C-8), 27.9 (C-9), 49.7 (C-10), 59.9 (C-11), 60.4 (C-13); chromone: 167.1 (C-2′), 143.9 (C-3′), 175.3 (C-4′), 106.2 (C-4a′), 124.7 (C-5′), 131.3 (C-6′), 161.9 (C-7′), 105.4 (C-8′), 153.5 (C-8a′), 19.8 (2′-CH_3), 22.9, 13.9 (6′-CH_2CH_3), 53.5 (CH_2-8′); benzimidazole: 31.1 (1″-CH_3), 148.0 (C-2″), 143.1 (C-3a″), 119.2 (C-4″), 122.1 (C-5″), 122.9 (C-6″), 109.8 (C-7″), 136.1 (C-7a″).

(1*R*,5*S*)-3-{[7-Hydroxy-2-isopropyl-3-(1-methyl-1*H*-benzimidazol-2-yl)-6-ethyl-4-oxo-4*H*-chromen-8-yl]methyl}-1,2,3,4,5,6-hexahydro-8*H*-1,5-methanepyrido[1,2-*a*][1,5]diazocin-8-one (8b), $C_{34}H_{36}N_4O_4$, yield 68%, mp 255-256°C (propan-2-ol:hexane).

^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): cytisine: 163.8 (C-2), 118.1 (C-3), 139.0 (C-4), 105.5 (C-5), 149.1 (C-6), 35.0 (C-7), 25.8 (C-8), 28.0 (C-9), 49.7 (C-10), 60.7, 60.3 (C-11), 60.4, 60.0 (C-13); chromone: 173.4 (C-2′), 115.4 (C-3′), 175.8 (C-4′), 106.5 (C-4a′), 124.9 (C-5′), 131.4 (C-6′), 161.8 (C-7′), 105.5 (C-8′), 153.5 (C-8a′), 31.9, 21.0 [2′-$CH(CH_3)_2$], 22.9, 14.0 (6′-CH_2CH_3), 53.5 (CH_2-8′); benzimidazole: 30.8 (1″-CH_3), 147.8 (C-2″), 142.3 (C-3a″), 120.1 (C-4″), 122.1 (C-5″), 122.8 (C-6″), 109.8 (C-7″), 136.2 (C-7a″).

REFERENCES

1. M. D. Mashkovskii, *Medicinal Preparations* [in Russian], Vol. 1, Torsing, Khar′kov (1997).
2. E. E. Tamelen and J. S. Baran, *J. Am. Chem. Soc.*, **80**, 4659 (1958).
3. C. C. Boido and F. Sparatore, *Farmaco*, **54**, 7, 438 (1999).
4. C. C. Boido, B. Tasso, V. Boido, and F. Sparatore, *Farmaco*, **58**, 3, 265 (2003).
5. O. Nicolotti, C. Boido, S. F. Canu, and A. Carotti, *Farmaco*, **57**, 6, 469 (2002).
6. S. Ohmiya and K. Higashiyama, *Phytochemistry*, **18**, 645 (1979).
7. S. Takamatsu, K. Saito, S. Ohmiya, N. Ruangrungsi, and I. Murakoshi, *Phytochemistry*, **30**, 11, 3793 (1991).
8. I. Murakoshi, M. Watanabe, T. Okuda, E. Kidoguchi, J. Haginiwa, et al., *Phytochemistry*, **24**, 11, 2707 (1985).
9. R. A. Shaimardanov, S. Iskandarov, and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 383 (1971).
10. O. A. Nurkenov, A. M. Gazaliev, K. M. Turdybekov, A. B. Bukeeva, and I. V. Kulakov, *Zh. Obshch. Khim.*, **73**, 6, 1015 (2003).
11. T. V. Khakimova, O. A. Pukhlyakova, G. A. Shavalaeva, A. A. Fatykhov, E. V. Vasil′eva, and L. V. Spirikhin, *Khim. Prir. Soedin.*, 301 (2001).
12. O. A. Pukhlyakova, N. Z. Baibulatova, I. O. Maidanova, T. V. Khakimova, V. A. Dokichev, and M. S. Yunusov, *Zh. Org. Khim.*, **36**, 9, 1404 (2000).
13. P. Ing, *J. Chem. Soc.*, 1774 (1936).
14. S. D. Fazylov, A. M. Gazaliev, L. M. Vlasova, R. Z. Kasenov, and V. K. Byistro, *Zh. Obshch. Khim.*, **66**, 2, 238 (1996).
15. O. A. Nurkenov, A. M. Gazaliev, K. M. Turdybekov, A. B. Shalbaeva, A. Aubakirova, and M. Zh. Zhurinov, *Zh. Obshch. Khim.*, **69**, 4, 675 (1999).
16. Y.-H. Wang, J.-S. Li, H. Kubo, K. Higashiyama, H. Komiya, and S. Ohmiya, *Chem. Pharm. Bull.*, **47**, 9, 1308 (1999).
17. K. A. Krasnov, V. G. Kartsev, and A. S. Gorovoi, *Khim. Prir. Soedin.*, 152 (2000).
18. K. A. Krasnov, V. G. Kartsev, A. S. Gorovoi, and V. N. Khrustalev, *Khim. Prir. Soedin.*, 367 (2002).
19. M. S. Frasinyuk, A. V. Turov, V. I. Vinogradova, and V. P. Khilya, *Khim. Prir. Soedin.*, 145 (2007).
20. M. Tramontini, *Synthesis*, **12**, 703 (1973).
21. V. G. Pivovarenko and V. P. Khilya, *Khim. Geterotsikl. Soedin.*, **5**, 625 (1991).
22. N. V. Gorbulenko, N. N. Shimko, and V. P. Khilya, *Dokl. Akad. Nauk Ukr. SSR, Ser. B*, No. 5, 117 (1991).
23. M. S. Frasinyuk, N. V. Gorbulenko, and V. P. Khilya, *Khim. Geterotsikl. Soedin.*, **9**, 1237 (1997).