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AMINOMETHYLATION OF FORMONONETIN AND CLADRIN BY PRIMARY AMINES

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*The reaction of natural isoflavones formononetin and cladrin with primary amines and formalin in the presence of a base catalyst was studied. Several novel substituted 9,10-dihydro-4*H*,8*H*-chromeno [8,7-e][1,3]oxazin-4-ones containing alkyl, benzyl, or heterylalkyl substituents in the N-9 position were synthesized.*

Key words: isoflavone, formononetin, cladrin, electrophilic substitution, 9,10-dihydro-4*H*,8*H*-chromeno [8,7-*e*][1,3]oxazin-4-one.

Flavonoids, some representatives of which are present in practically all plant species, are the most widely distributed natural compounds of plant origin [1].

Isolation of the natural isoflavone formononetin (4′-methoxy-7-hydroxyisoflavone) from leaves of *Genista* [2] and cladrin (3′,4′-dimethoxy-7-hydroxyisoflavone) from *Cladrastis lutea* [3] has been reported.

Isoflavonoids containing a methoxy group in the *p*-position of ring B are used as natural anti-oxidants [4] and for treatment of cardiovascular diseases [5] and breast [6] and prostate [7] cancers. Formononetin exhibits hypolipidemic activity [8] and lowers the level of cholesterol and triglycerides in blood, phospholipids, and β-lipoproteins [9, 10]. Considering these factors, modification of the natural isoflavones formononetin and cladrin seemed interesting from both chemical and biological points of view.

We have previously studied the reaction of natural isoflavones and their analogs with aminal reagents and prepared a series of 8-aminomethyl derivatives containing secondary amines [11, 12].

Mannich reaction conditions with the appropriate ratio of substrate, amine, and formaldehyde in the presence of a base catalyst [KOH, *N*,*N*-dimethylaminopyridine (DMAP)] is known to produce through electrophilic substitution derivatives of 3,4-dihydro-1,3-benzooxazines [13-17]. Annelation of an oxazine ring to the coumarin core by reaction of 7-hydroxycoumarins and synthesized beforehand *N*,*N-bis*(hydroxymethyl)amines in the presence of DMAP forms derivatives of 9,10-dihydro-2*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-2-one [18] whereas isomeric derivatives of 9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one are formed by condensation of isoflavone derivatives with esters of α-amino acids and an excess of formalin [19].

In continuation of research on the synthesis and reactivity of isoflavonoids, we studied the reaction of formononetin and cladrin with primary aliphatic amines and formalin and obtained new derivatives of these natural isoflavones that may exhibit biological activity.

As it turned out, heating 7-hydroxyisoflavones **1** and **2** with equivalent amounts of primary amines and a two-fold excess of formalin in propan-2-ol in the presence of a catalytic amount of DMAP formed derivatives of 9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one in satisfactory yields without prelimiary preparation of the *N*,*N-bis*(hydroxymethyl)amines. Thus, simultaneous C- and O-aminomethylation of the benzopyran-4-one core produced derivatives of 9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-ones **3**-**16** containing alkyl, benzyl, or heterylalkyl substituents in the 9-position.

It was shown earlier that the 3,4-dihydro-1,3-oxazine ring is smoothly annelated to a benzopyron-2-one ring by using *N*,*N-bis*(hydroxymethyl)amines that were synthesized beforehand from aliphatic amines, benzylamines, and *p*-substituted anilines. The 9,10-dihydro-2*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-2-ones were not formed if anilines containing strong electron-accepting or bulky substitutents in the *o*-position to the amine were used [18].

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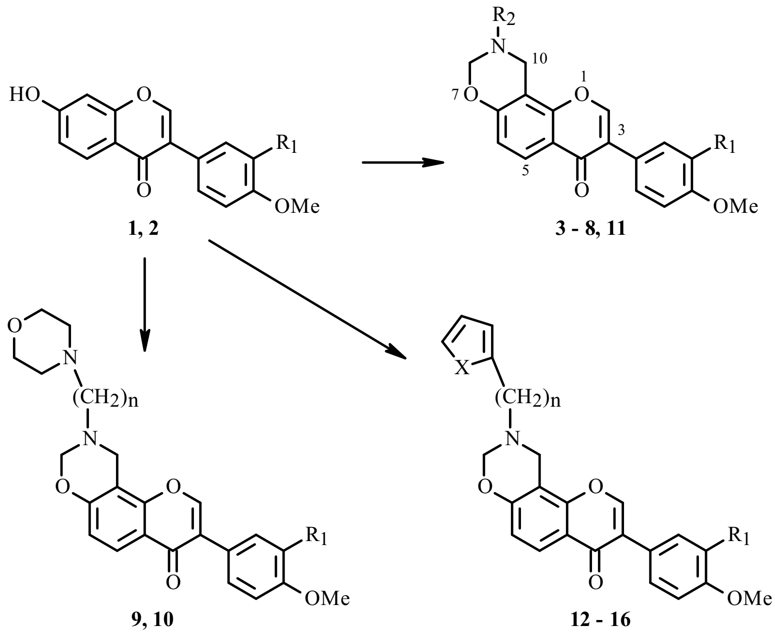

1, 3, 4, 7, 9, 11, 12, 15: R_1 = H; **2, 5, 6, 8, 10, 13, 14, 16:** R_1 = OMe; **3:** R_2 = cyclopropyl; **4:** R_2 = sulfolan-3-yl
5: R_2 = $MeOCH_2CH_2$; **6:** R_2 = $MeO(CH_2)_3$; **7:** R_2 = 2-$MeOC_6H_4CH_2CH_2$; **8:** R_2 = $Ph(CH_2)_3$; **11:** R_2 = 4-picolyl
9, 11 – 14: n = 1; **10, 15, 16:** n = 2; **12, 13:** X = O; **14 – 16:** X = S

Derivatives of 9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-ones were synthesized in 65-84% yields without preparation beforehand of *N*,*N*-*bis*(hydroxymethyl)amines by reaction of 7-hydroxyisoflavones **1** and **2** with aliphatic amines and benzyl- or heterylalkylamines regardless of their structure. As expected, reacting 4-methoxyaniline with formononetin formed **17** in satisfactory yield. Reaction of the 7-hydroxyisoflavones with 2-methoxy- and 2-(trifluoromethyl)anilines did not give the desired result. Difficultly separated mixtures of products were produced.

Structures of synthesized derivatives **3**–**17** were confirmed using NMR spectroscopy. Thus, the resonance of H-8 in the chromone ring disappeared and resonances of the CH_2-10 and CH_2-8 methylenes at 4.21–4.28 and 4.93–5.07 ppm, respectively, and of the amine protons appeared in the PMR spectra.

Thus, we studied the reaction of the natural isoflavones formononetin (**1**) and cladrin (**2**) with primary amines and formalin in the presence of a base catalyst. Several new substituted 9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-ones (**3-17**) containing alkyl, aryl, benzyl, or heterylalkyl substituents in the N-9 position were synthesized.

EXPERIMENTAL

The course of reactions and purity of products were monitored by TLC on Sorbfil UV-254 (Russia) and Merck (Germany) plates with elution by $CH_3C_6H_5$:EtOH (9:1 and 95:5). PMR spectra were measured in $CDCl_3$ on a VXR-300 instrument (Varian, 300 MHz) relative to TMS (internal standard) on the δ-scale. Elemental analyses of all compounds agreed with those calculated.

Starting **1** and **2** were prepared as before [20, 21].

General Method for Synthesizing 3–17. A hot solution of the appropriate 7-hydroxyisoflavone (**1** or **2**, 2 mmol) in propan-2-ol (20 mL) was treated with primary amine (2.2 mmol), formalin (1.2 mL, 37%), and DMAP (5 mg), refluxed for 3-5 h (end of reaction determined by TLC), cooled, and evaporated in vacuo. The solid was crystallized from the appropriate solvent.

3-(4-Methoxyphenyl)-9-cyclopropyl-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (3). $C_{21}H_{19}NO_4$. Yield 65%, mp 150–151°C (toluene:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.84 (3H, s, OMe-4′), 4.27 (2H, s, CH_2-10), 4.99 (2H, s, CH_2-8), 6.90 (1H, d, ^3J = 8.7, H-6), 6.97 (2H, d, ^3J = 9, H-3′, H-5′), 7.50 (2H, d, ^3J = 9, H-2′, H-6′), 7.93 (1H, s, H-2), 8.09 (1H, d, ^3J = 8,7, H-5); amine protons: 0.61 [4H, m, $(CH_2)_2$], 2.39 (1H, m, NCH).

3-(4-Methoxyphenyl)-9-(1,1-dioxytetrahydrothien-3-yl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (4). $C_{22}H_{21}NO_6S$. Yield 69%, mp 203–204°C (propan-2-ol:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.85 (3H, s, OMe-4′), 4.19, 4.34 (each 1H, d, $^3J = 18$, CH_2-10), 5.0, 5.06 (each 1H, d, $^3J = 9.0$, CH_2-8), 6.87 (1H, d, $^3J = 8.7$, H-6), 6.98 (2H, d, $^3J = 9$, H-3′, H-5′), 7.49 (2H, d, $^3J = 9$, H-2′, H-6′), 7.92 (1H, s, H-2), 8.10 (1H, d, $^3J = 8.7$, H-5); sulfolane protons: 2.26, 2.53 (each 1H, m, CH_2-4), 3.08, 3.45 (each 2H, m, CH_2-2, CH_2-5), 3.80 (1H, m, CH-3).

3-(3,4-Dimethoxyphenyl)-9-(2-methoxyethyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (5). $C_{22}H_{23}NO_6$. Yield 73%, mp 103–104°C (toluene:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.91, 3.93 (each 3H, s, OMe-3′, OMe-4′), 4.26 (2H, s ,CH_2-10), 5.01 (2H, s, CH_2-8), 6.88 (1H, d, $^3J = 8.7$, H-6), 6.93 (1H, d, $^3J = 8.3$, H-5′), 7.05 (1H, dd, $^3J = 8.3$, $^4J = 2.0$, H-6′), 7.21 (1H, d, $^4J = 2.0$, H-2′), 7.95 (1H, s, H-2), 8.08 (1H, d, $^3J = 8.7$, H-5); amine protons: 2.99, 3.60 [each 2H, m, N(9)-$(CH_2)_2$], 3.41 (3H, s, OMe).

9-(3-Methoxypropyl)-3-(3,4-dimethoxyphenyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (6). $C_{23}H_{25}NO_6$. Yield 81%, mp 107–108°C (toluene:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.91, 3.93 (each 3H, s, OMe-3′, OMe-4′), 4.18 (2H, s, CH_2-10), 4.97 (2H, s, CH_2-8), 6.87 (1H, d, $^3J = 8.7$, H-6), 6.93 (1H, d, $^3J = 8.3$, H-5′), 7.05 (1H, dd, $^3J = 8.3$, $^4J = 2.0$, H-6′), 7.21 (1H, d, $^4J = 2.0$, H-2′), 7.94 (1H, s, H-2), 8.08 (1H, d, $^3J = 8.7$, H-5); amine protons: 2.86, 1.86, 3.47 [each 2H, m, N(9)-$(CH_2)_3$], 3.34 (3H, s, OMe).

3-(4-Methoxyphenyl)-9-[2-(2-methoxyphenyl)ethyl]-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (7). $C_{27}H_{25}NO_5$. Yield 84%, mp 120–121°C (propan-2-ol:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.84 (3H, s, OMe-4′), 4.24 (2H, s, CH_2-10), 4.99 (2H, s, CH_2-8), 6.97 (2H, d, $^3J = 9$, H-3′, H-5′), 7.50 (2H, d, $^3J = 9$, H-2′, H-6′), 7.92 (1H, s, H-2), 8.07 (1H, d, $^3J = 8.7$, H-5); amine protons: 2.87-3.06 [4H, m, N(9)-$(CH_2)_2$], 3.78 (3H, s, OMe-2), 6.87, 7.17 (5H, 2m, H-6, Ar′).

3-(3,4-Dimethoxyphenyl)-9-(3-phenylpropyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (8). $C_{28}H_{27}NO_5$. Yield 75%, mp 99–100°C (propan-2-ol:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.92, 2.70, 2.78 [each 2H, m, N-$(CH_2)_2$], 3.91, 3.93 (each 3H, s, OMe-3′, OMe-4′), 4.18 (2H, s, CH_2-10), 4.98 (2H, s, CH_2-8), 6.87 (1H, d, $^3J = 8.7$, H-6), 6.93 (1H, d, $^3J = 8.3$, H-5′), 7.04 (1H, dd, $^3J = 8.3$, $^4J = 2.4$, H-6′), 7.21, 7.29 (6H, 2m, Ph, H-2′), 7.95 (1H, s, H-2), 8.08 (1H, d, $^3J = 8.7$, H-5).

3-(4-Methoxyphenyl)-9-(2-morpholin-4-ylethyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (9). $C_{24}H_{26}N_2O_5$. Yield 79%, mp 176–177°C (propan-2-ol:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.84 (3H, s, OMe-4′), 4.24 (2H, s, CH_2-10), 5.0 (2H, s, CH_2-8), 6.86 (1H, d, $^3J = 8.7$, H-6), 6.97 (2H, d, $^3J = 9$, H-3′, H-5′), 7.49 (2H, d, $^3J = 9$, H-2′, H-6′), 7.92 (1H, s, H-2), 8.08 (1H, d, $^3J = 8.7$, H-5); amine protons: 2.61, 2.93 [each 2H, m, N(9)-$(CH_2)_2$], 2.48 [4H, m, N$(CH_2)_2$], 3.71 [4H, m, O$(CH_2)_2$].

3-(3,4-Dimethoxyphenyl)-9-(3-morpholin-4-ylpropyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (10). $C_{26}H_{30}N_2O_6$. Yield 72%, mp 112–113°C (propan-2-ol:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.91, 3.93 (each 3H, s, OMe-3′, OMe-4′), 4.19 (2H, s, CH_2-10), 4.97 (2H, s, CH_2-8), 6.87 (1H, d, $^3J = 8.7$, H-6), 6.93 (1H, d, $^3J = 8.3$, H-5′), 7.04 (1H, dd, $^3J = 8.3$, $^4J = 2.0$, H-6′), 7.21 (1H, d, $^4J = 2.0$, H-2′), 7.95 (1H, s, H-2), 8.08 (1H, d, $^3J = 8.7$, H-5); amine protons: 1.78, 2.81 [each 2H, m, N(9)-$(CH_2)_3$], 2.45 [6H, m, 4H of morpholine N$(CH_2)_2$ and 2H of N(9)-$(CH_2)_3$], 3.72 [4H, m, O$(CH_2)_2$].

3-(4-Methoxyphenyl)-9-(pyridin-4-ylmethyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (11). $C_{24}H_{20}N_2O_4$. Yield 78%, mp 163–164°C (propan-2-ol). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.83 (3H, s, OMe-4′), 4.16 (2H, s, CH_2-10), 5.0 (2H, s, CH_2-8), 6.92 (1H, d, $^3J = 8.7$, H-6), 6.96 (2H, m, H-3′, H-5′), 7.47 (2H, m, H-2′, H-6′), 7.86 (1H, s, H-2), 8.11 (1H, d, $^3J = 8.7$, H-5); amine protons: 3.97 [2H, s, N(9)CH_2], 7.34 (2H, m, H-3″, H-5″), 8.61 (2H, m, H-2″, H-6″).

3-(4-Methoxyphenyl)-9-(2-furylmethyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (12). $C_{23}H_{19}NO_5$. Yield 73%, mp 146–147°C (propan-2-ol:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.84 (3H, s, OMe-4′), 3.94 [2H, s, N(9)-CH_2], 4.22 (2H, s, CH_2-10), 4.99 (2H, s, CH_2-8), 6.91 (1H, d, $^3J = 8.7$, H-6), 6.97 (2H, d, $^3J = 9$, H-3′, H-5′), 7.49 (2H, d, $^3J = 9$, H-2′, H-6′), 7.91 (1H, s, H-2), 8.10 (1H, d, $^3J = 8.7$, H-5); furan protons: 6.30, 6.36, 7.44 (each 1H, m).

3-(3,4-Dimethoxyphenyl)-9-(2-furylmethyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (13). $C_{24}H_{21}NO_6$. Yield 78%, mp 141–142°C (propan-2-ol). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.91, 3.93 (each 3H, s, OMe-3′, OMe-4′), 3.94 [2H, s, N(9)-CH_2], 4.22 (2H, s, CH_2-10), 4.98 (2H, s, CH_2-8), 6.91 (1H, d, $^3J = 8.4$, H-5′), 6.93

(1H, d, $^3J = 9.0$, H-6), 7.04 (1H, dd, $^3J = 8.4$, $^4J = 2.0$, H-6′), 7.21 (1H, d, $^4J = 2.0$, H-2′), 7.94 (1H, s, H-2), 8.10 (1H, d, $^3J = 9.0$, H-5); furan protons: 6.30, 6.37, 7.44 (each 1H, m).

3-(3,4-Dimethoxyphenyl)-9-(thien-2-ylmethyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (14). $C_{24}H_{21}NO_5S$. Yield 76%, mp 177–178°C (toluene:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.91, 3.93 (each 3H, s, OMe-3′, OMe-4′), 4.14 [2H, s, N(9)-CH_2], 4.23 (2H, s, CH_2-10), 5.01 (2H, s, CH_2-8), 7.21 (1H, d, $^4J = 2.0$, H-2′), 7.92 (1H, s, H-2), 8.11 (1H, d, $^3J = 8.7$, H-5); H-6, H-5′, H-6′, and thiophene protons: 6.90-7.08 (5H, m), 7.32 (1H, m).

3-(4-Methoxyphenyl)-9-(2-thien-2-ylethyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (15). $C_{24}H_{21}NO_4S$. Yield 65%, mp 136–137°C (toluene:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.10 [4H, m, N(9)-$(CH_2)_2$], 3.84 (3H, s, OMe-4′), 4.23 (2H, s, CH_2-10), 4.99 (2H, s, CH_2-8), 6.87 (1H, d, $^3J = 8.7$, H-6), 6.97 (2H, d, $^3J = 9$, H-3′, H-5′), 7.50 (2H, d, $^3J = 9$, H-2′, H-6′), 7.91 (1H, s, H-2), 8.08 (1H, d, $^3J = 8.7$, H-5); thiophene protons: 6.85, 6.93, 7.15 (each 1H, m).

3-(3,4-Dimethoxyphenyl)-9-(2-thien-2-ylethyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (16). $C_{25}H_{23}NO_5S$. Yield 70%, mp 140–141°C (propan-2-ol:hexane). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.10 [4H, m, N(9)-$(CH_2)_2$], 3.91, 3.93 (6H, 2s, OMe-3′, OMe-4′), 4.23 (2H, s, CH_2-10), 5.00 (2H, s, CH_2-8), 6.84-6.96 (4H, m, H-6, H-2′, H-5′, H-6′), 7.95 (1H, s, H-2), 8.09 (1H, d, $^3J = 9.0$, H-5); thiophene protons: 7.05, 7.15, 7.21 (each 1H, m).

3,9-bis(4-Methoxyphenyl)-9,10-dihydro-4*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-4-one (17). $C_{25}H_{21}NO_5$. Yield 68%, mp 137–138°C (propan-2-ol). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.75, 3.84 (each 3H, s, OMe-4″, OMe-4′), 4.73 (2H, s, CH_2-10), 5.39 (2H, s, CH_2-8), 6.82 (2H, d, $^3J = 8.7$, H-3″, H-5″), 6.89 (1H, d, $^3J = 9.0$, H-6), 6.97 (2H, d, $^3J = 9.0$, H-3′, H-5′), 7.11 (2H, d, $^3J = 8.7$, H-2″, H-6″), 7.48 (2H, d, $^3J = 9.0$, H-2′, H-6′), 7.91 (1H, s, H-2), 8.08 (1H, d, $^3J = 9.0$, H-5).

REFERENCES

1. A. L. Kazakov, V. P. Khilya, V. V. Mezheritskii, and D. Litkei, *Natural and Modified Isoflavonoids* [in Russian], Izd. RGU, Rostov-on-Don, 1985.
2. E. T. Bailey, *Aust. J. Agric. Res.*, **22**, 731 (1971).
3. M. Shamma, *Tetrahedron*, **25**, 3887 (1969).
4. J. Torel, J. Gillard, and P. Gillard, *Phytochemistry*, **25**, 383 (1986).
5. P. Da Re, L. Verlicchi, and I. Setniker, *J. Med. Chem.*, **10**, 266 (1966).
6. C. Ito, M. Itoigawa, H. T. W. Tan, H. Tokuda, X. Y. Mou, T. Mukainaka, T. Ishikawa, H. Nishino, and H. Furukawa, *Cancer Lett.*, **152**, 187 (2000).
7. L. Denis, M. S. Morton, and K. Griffiths, *Eur. Urol.*, **35**, 377 (1999).
8. M. T. Siddiqui and M. Siddiqui, *Lipids*, **11**, 243 (1976).
9. S. Yahara, T. Ogata, and R. Saijo, *Chem. Pharm. Bull.*, **37**, 979 (1989).
10. G. N. Dorofeenko, A. L. Shinkarenko, L. I. Lisevitskaya, V. V. Mezheritskii, A. L. Kazakov, and Yu. A. Zhdanov, *Nauchn. Dokl. Vyssh. Shk. Biol. Nauki*, **3**, 35 (1975).
11. S. P. Bondarenko, M. S. Frasinyuk, and V. P. Khilya, *Khim. Prir. Soedin.*, 273 (2003).
12. S. P. Bondarenko, M. S. Frasinyuk, and V. P. Khilya, *Khim. Prir. Soedin.*, 277 (2003).
13. M. Tramontini, *Synthesis*, **12**, 703 (1973).
14. R. B. Desai, *J. Org. Chem.*, **26**, 5251 (1961).
15. M. G. Patel and S. Sethna, *J. Indian Chem. Soc.*, **39**, 595 (1962).
16. D. R. Shridhar, C. V. R. Sastry, B. Lal, G. S. Raddi, K. K. Bhopale, R. S. Khokar, and K. Tripathi, *Indian J. Chem., Sect. B*, **19**, 1065 (1980).
17. J. N. Gadre and P. S. Raote, *Indian J. Chem., Sect. B*, **32**, 1285 (1993).
18. I. V. Nagorichna, M. M. Garazd, Ya. L. Garazd, and V. P. Khilya, *Khim. Prir. Soedin.*, 14 (2007).
19. M. M. Garazd, Ya. L. Garazd, A. S. Ogorodniichuk, V. V. Shilin, A. M. Zhivolup, A. V. Turov, and V. P. Khilya, *Khim. Prir. Soedin.*, 632 (1998).
20. A. Pelter and S. Foot, *Synthesis*, **5**, 326 (1976).
21. A. S. Kukla and T. R. Seshadri, *Indian J. Chem.*, **1**, 343 (1963).