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2-(3-ETHYL-2,2-DIMETHYLCYCLOBUTYL-METHYL)-4(3H)-QUINAZOLINONES

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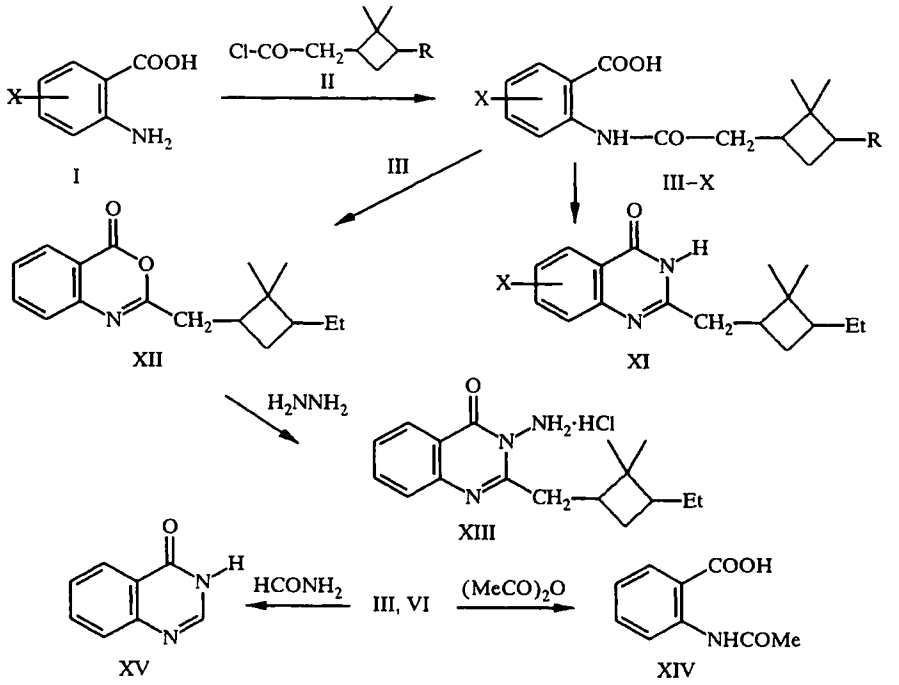
Anthranilic acid and its 5-bromo and 4-chloro derivatives react with pinanoic and pinonoic acid chlorides to give the corresponding N-acyl derivatives. The pinanoyl derivatives give the corresponding 2-(3-ethyl-2,2-dimethyl-cyclobutylmethyl)-4-(3H)-quinazolinones when refluxed in formamide. Pinanoylanthranilic acid reacts with dicyclohexylcarbodiimide to give 2-(3-ethyl-2,2-dimethyl-cyclobutylmethyl)benz-3,1-oxazin-4(H)-one and subsequently with hydrazine hydrate to give 3-amino-2-(3-ethyl-2,2-dimethylcyclobutylmethyl)-4(3H)-quinazolinone. Refluxing of the pinanoyl- and pinonoylanthranilic acids with acetic anhydride gives acetylanthranilic acid, and pinonoylanthranilic acid gives 4(3H)-quinazolinone with formamide.

2,3-Substituted 4(3H)-quinazolinones show various biological activity and interest in this aspect has increased in recent years [1-21]. Series of theoretical synthetic problems there were solved [22-25]. The structural fragment of 2,3-substituted 4-(3H)-quinazolinones are included in the skeleton of the majority of quinazoline



I, XI a X = H, b X = 5-Br, c X = 4-Cl; II a R = Et, b R = COMe; III X = H, R = Et; IV X = 5-Br, R = Et; V X = 4-Cl, R = Et; VI X = H, R = COMe; VII X = 5-Br, R = COMe; VIII X = 4-Cl, R = COMe; IX X = H, R = C(NOH)Me; X X = H, R = NHCOMe

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TABLE 1. IR and PMR Spectra of Anthranilic Acid Amides (III-X) and 4(3H)-Quinazolinones (XI-XIII).

Compound	IR Spectrum, ν, cm^{-1}	PMR Spectrum, δ, ppm ($CDCl_3$)
1	2	3
III	1710, 1692, 1682, 1610, 1588, 1535 3250-3150, 2600	0.72 (3H, t, J = 7 Hz, CH_3); 0.88 (3H, s, β-CH_3); 1.02 (3H, s, α-CH_3); 1.22-2.38 (8H, m, $-CH_2CHCH_2CHCH_2-$) 7.03 (1H, dt, ^4J = 2, ^3J = 8 Hz, Ar); 7.54 (1H, dt, ^4J = 2, ^3J = 8 Hz, Ar); 8.09 (1H, dd, ^4J = 8, ^3J = 2 Hz, Ar); 10.1 (1H, br. s, NH) 11.04 (1H, br. s, OH)
IV	1705-1698, 1680, 1589, 1575, 1520 3250	0.76 (3H, t, J = 7 Hz, CH_3); 0.89 (3H, s, β-CH_3); 1.03 (3H, s, α-CH_3); 1.24-2.36 (8H, m, $-CH_2CHCH_2CHCH_2-$);7.58 (1H, dd, ^3J = 8, ^4J = 2 Hz, Ar); 8.23 (1H, d, ^4J = 2 Hz, Ar); 8.69 (1H, d, ^3J = 8 Hz, Ar); 10.84 (1H, br. s, NH); 11.27 (1H, br. s, OH)
V	1710, 1680-1670, 1604, 1590, 1580 1532; 3150-3250, 3120, 2600	0.73 (3H, t, J = 7 Hz, CH_3); 0.89 (3H, s, β-CH_3); 1.02 (3H, s, α-CH_3); 1.19-2.30 (8H, m, $-CH_2CHCH_2CHCH_2-$) 4.40 (H_2O + COOH); 7.12 (1H, dd, ^4J = 2, ^3J = 8 Hz, Ar); 7.96 (1H, d, ^3J = 8 Hz, Ar); 8.60 (1H, d, ^4J = 2 Hz, Ar) 11.17 (1H, br. s, NH)
VI	1706, 1695, 1687, 1650, 1606, 1590 1530-1520; 3300-3150, 2600	0.89 (3H, s, β-CH_3); 1.31 (3H, s, α-CH_3); 2.03 (3H, s, $COCH_3$); 1.50-2.48 (5H, m, $-CH_2CHCH_2-$); 2.88 (1H, t, ^3J = 9 Hz, C_3–H) 7.02 (1H, t, ^3J = 8 Hz, Ar); 7.49 (1H, t, ^3J = 8 Hz, Ar); 8.07 (1H, dd, ^3J = 8, ^4J = 1.5 Hz, Ar); 8.62 (1H, dd, ^3J = 8, ^4J = 1.5 Hz, Ar) 10.53 (1H, br. s, NH); 11.16 (1H, br. s, OH)
VII	1710-1685, 1638, 1602, 1578, 1510 3250-3150, 2560	0.94 (3H, s, β-CH_3); 1.36 (3H, s, α-CH_3); 1.61-2.44 (5H, s, m, $-CH_2CHCH_2-$); 2.07 (3H, s, CH_3); 2.95 (1H, t, J = 9 Hz, C_3–H) 7.62 (1H, dd, J = 2 Hz, Ar); 8.21 (1H, d, ^4J = 2 Hz, Ar); 8.69 (1H, d, ^3J = 8 Hz, Ar); 8.72 (1H, br. s, NH); 10.87 (1H, br. s, OH)
VIII	1680, 1610, 1586, 1556 3380, 2650-2550	0.89 (3H, s, β-CH_3); 1.34 (3H, s, α-CH_3); 1.61-2.39 (5H, m, $-CH_2CHCH_2-$); 2.03 (3H, s, CH_3); 2.91 (1H, t, J = 9 Hz, C_3–H) 6.98 (1H, dd, ^3J = 8, ^4J = 2 Hz, Ar); 7.50 (1H, br. s, OH); 7.94 (1H, d, ^3J = 8 Hz, Ar); 8.72 (1H, d, ^4J = 2 Hz, Ar) 11.42 (1H, br. s, NH)
IX	1700, 1682, 1655, 1606, 1590, 1550 1534, 1500; 3260, 2600	0.89 (3H, s, β-CH_3); 1.24 (3H, s, α-CH_3); 1.77 (3H, s, $COCH_3$); 1.95-2.37 (5H, m, $-CH_2CHCH_2-$); 2.56 (1H, t, ^3J = 9 Hz, C_3–H) 7.05 (1H, td, ^3J = 8, ^4J = 1.5 Hz, Ar); 7.50 (1H, br. s, OH); 7.9 (1H, td, ^3J = 8, ^4J = 1.5 Hz, Ar); 8.01 (1H, dd, ^4J = 1.5 Hz, Ar) 8.67 (1H, dd, ^3J = 8, ^4J = 1.5 Hz, Ar); 9.38 (2H, br. s, NH + OH); 11.33 (1H, br. s, OH)

TABLE 1 (continued)

1	2	3
X	1698, 1688, 1664, 1590, 1575, 1534 3320, 3260, 3130	0.81 (3H, s, β-CH_3); 1.05 (3H, s, α-CH_3); 1.80 (3H, s, $COCH_3$); 1.52-2.51 (5H, m, –CH_2CHCH_2–); 3.80 (1H, m, C_3–H) 7.13 (1H, t, ^3J = 8 Hz, Ar); 7.51 (1H, t, ^3J = 8 Hz, Ar); 7.69 (1H, d, J = 5 Hz, NH); 7.99 (1H, dd, ^3J = 8, ^4J < 1.5 Hz, Ar) 8.49 (1H, dd, ^3J = 8, ^4J < 1.5 Hz, Ar); 11.08 (1H, br. s, OH)
XIa	1674, 1614, 1564, 1504, 3170, 3130	0.69 (3H, t, J = 7 Hz, CH_3); 0.99 (3H, s, β-CH_3); 1.07 (3H, s, α-CH_3); 1.22-2.28 (8H, m, –$CH_2CHCH_2CHCH_2$–) 7.32-7.66 (3H, m, C_6H_4); 8.22 (1H, dd, ^3J = 8, ^4J < 1.5 Hz, Ar); 12.00 (1H, br. s, NH)
XIb	1686, 1620, 1604, 1500, 3180, 3100	0.76 (3H, t, J = 7 Hz, CH_3); 1.02 (3H, s, β-CH_3); 1.11 (3H, s, α-CH_3); 1.17-2.73 (8H, m, –$CH_2CHCH_2CHCH_2$–) 7.54 (1H, d, ^3J = 8 Hz, Ar); 7.81 (1H, dd, ^3J = 8, ^4J = 2 Hz, Ar); 8.37 (1H, d, ^4J = 2 Hz, Ar); 11.81 (1H, br. s, NH)
XIc	1674, 1615, 1604, 1558, 1502 3170, 3120	0.70 (3H, t, J = 7 Hz, CH_3); 0.97 (3H, s, β-CH_3); 1.06 (3H, s, α-CH_3); 1.18-2.70 (8H, m, –$CH_2CHCH_2CHCH_2$–) 7.30 (1H, dd, J = 8, J = 2 Hz, Ar); 7.65 (1H, d, J = 2 Hz, Ar); 8.09 (1H, d, J = 8 Hz, Ar); 11.76 (1H, br. s, NH)
XII	1762, 1642, 1608, 1576, 1560	0.74 (3H, t, J = 7 Hz, CH_3); 0.93 (3H, s, β-CH_3); 1.04 (3H, s, α-CH_3); 1.20-2.83 (8H, m, –$CH_2CHCH_2CHCH_2$–) 7.38-7.85 (3H, m, Ar); 8.13 (1H, dd, ^3J = 8, ^4J = 1,5 Hz, Ar)
XIII	1738, 1642, 1610, 1572, 1538 3420, 3250, 3140	0.74 (3H, t, J = 7 Hz, CH_3); 1.01 (3H, s, β-CH_3); 1.10 (3H, s, α-CH_3); 1.15-2.47 (8H, m, –$CH_2CHCH_2CHCH_2$–) 5.68 (2H, br. s, NH_2); 7.59-8.87 (4H, m, Ar)

TABLE 2. Anthranilic Acid Amides III-X and 4(3H)-Quinazolinones XI-XIII

Compound	Empirical formula	Found, % / Calculated, %				mp, °C	R_f	Yield, %
		C	H	N	Hal			
III	$C_{17}H_{23}NO_3$	70.33 / 70.56	7.88 / 8.01	4.65 / 4.84		Syrup	0.68	70
IV	$C_{17}H_{22}BrNO_3$	55.40 / 55.44	5.95 / 6.02	3.75 / 3.80	21.70 / 21.70	161-162	0.66	69
V	$C_{17}H_{22}ClNO_3$	63.11 / 63.05	6.80 / 6.85	4.22 / 4.32	11.50 / 10.95	159-160	0.65	84
VI	$C_{17}H_{21}NO_4$	67.10 / 67.31	7.14 / 6.98	4.44 / 4.62		Syrup	0.62	91
VII	$C_{17}H_{20}BrNO_4$	53.31 / 53.42	5.25 / 5.27	3.61 / 3.66	21.60 / 20.90	170-171	0.66	92
VIII	$C_{17}H_{20}ClNO_4$	60.25 / 60.44	6.00 / 5.97	4.29 / 4.15	10.62 / 10.49	228-229	0.65	73
IX	$C_{17}H_{22}N_2O_4$	63.94 / 64.13	6.76 / 6.96	8.72 / 8.80		168-169	0.50	34
X	$C_{17}H_{22}N_2O_4$	64.04 / 64.13	7.05 / 6.96	8.62 / 8.80		223-225	0.41	67
XIa	$C_{17}H_{22}N_2O$	72.46 / 72.55	8.15 / 8.20	10.19 / 10.36		135-136	0.71	70
XIb	$C_{17}H_{21}BrN_2O$	58.50 / 58.46	5.95 / 6.06	7.88 / 8.02	23.14 / 22.88	164-165	0.66	93
XIc	$C_{17}H_{21}ClN_2O$	67.00 / 66.97	7.00 / 6.94	9.24 / 9.19	12.50 / 11.63	155-156	0.56	70
XII	$C_{17}H_{21}NO_3$	75.11 / 75.24	7.75 / 7.80	5.01 / 5.16		120-123	0.62	63
XIII	$C_{17}H_{24}ClN_3O$	63.46 / 63.44	7.65 / 7.52	13.13 / 13.06	11.10 / 11.02	180-181	0.66	91

alkaloids [26]. Experience of work in the area of cyclobutanecarboxylic acids [27-30] and modified 4(3H)-quinazolinones containing 1,3-cyclanedione fragments [31-33] stimulated us to synthesize 4(3H)-quinazolinones having 2,2-dimethyl-3-ethyl- and 3-acetyl-2,2-dimethylcylobutylmethyl groups as the substituent.

Reactions of anthranilic acid (Ia) and its 5-bromo (Ib) and 4-chloro derivative (Ic) with pinanoyl (IIa) and pinonoyl (IIb) chlorides gave the corresponding N-acyl derivatives III-VIII. The action of hydroxylamine on the pinonoylamide VI using method [34] gave oxime IX, Beckmann rearrangement of which according to [35] afforded 3-acetylamino-2,2-dimethylcyclobutylacetylanthranilic acid (X).

Refluxing of the pinanoyl derivatives III-V in formamide gives 2-(2,2-dimethyl-3-ethylcyclobutylmethyl)-4(3H)-quinazolinones XI. Treatment of the pinanoyl derivative III with dicyclohexylcarbodiimide gives 2-(2,2-dimethyl-3-ethylcyclobutylmethyl)benz-3,1-oxazin-4(H)-one (XII), which reacts with hydrazine to give 3-amino-2-(2,2-dimethyl-3-ethylcyclobutylmethyl)-4(3H)quinazolinone (XIII). Refluxing of the pinanoyl- and pinonoyl derivatives III, VI in acetic anhydride gives the transacylation product – acetylanthranilic acid and the compound VI in formamide under reflux gives the 4(3H)-quinazolinone (XV).

The structure of the synthesized compounds was confirmed by IR and PMR data (Table 1). PMR spectra of compounds III-XIII are complex, hence a clear assignment is not possible for all resonance signals. In their PMR spectra, the aliphatic part of compounds III-XIII contains signals for the geminal α- and β- methyl groups at C_2 of the cyclobutane ring. Previously it was found that the β-CH_3 group at equatorial position absorbs at higher field (0.88-1.01 ppm) than the α-CH_3 group at axial position (1.02-1.36 ppm) [40, 41].

In the spectra of compounds VI-X there can also be identified triplet signals for the methine C_3–H protons (2.56-3.80 ppm $^3J_{HH}$ = 9 Hz) and singlet for the acetyl groups at 1.70-2.07 ppm. The OH and NH group protons appear as broadened singlets in the region from 10-12 ppm. Although the lowest field signal was assigned to the proton of the carboxyl group, it is possible that these may be reversed.

EXPERIMENTAL

IR spectra were taken on a Specord IR-75 instrument for suspension in vaseline oil (region 1800-1500 cm^{-1}) and hexachlorobutadiene (region 3600-2000 cm^{-1}); the absorptions for the C–H stretching vibrations in the region 3050-2800 cm^{-1} are not given. PMR Spectra were recorded on a Bruker WH-90/DS spectrometer for solutions in $CDCl_3$, DMSO-d_6 with internal standard TMS. Monitoring of the reaction course and the purity of the products was carried out by TLC on Silufol UV-254 in the system $CHCl_3$–C_2H_5OH (9:1); visualization by UV light or chlorine and subsequent treatment with KI-benzidine reagent.

***cis*(±)-3-Ethyl-2,2-dimethylcyclobutylacetic (Pinanonic) Acid Chloride (IIa) and *cis*(±)-3-Acetyl-2,2-dimethylcyclobutylacetic (Pinonoic) Acid Chloride (IIb)** were obtained according to [36, 37]. Methods [34-36] were used for preparation of pinanoyl- (III-V) and pinonoylanthranilic acids (VI-VIII). As an example we report the synthesis of amide III. The characteristics for III-XIII are given in Table 2.

Pinanoylanthranilic Acid (III). A solution of pinanoic acid chloride (3.00 g, 14.8 mmol) in anhydrous benzene (20 ml) was added slowly with stirring to a solution of anthranilic acid (2.03 g, 14.8 mmol) and triethylamine (2.07 ml, 14.8 mmol) in anhydrous benzene (40 ml) at 20°C. Reaction mixture stirred for a further 3 h was washed with dilute hydrochloric acid (1:5, 30 ml) and water (3 × 30 ml) to neutrality and dried over anhydrous magnesium sulfate. Benzene was distilled off to give amide III (4.36 g, 97%) as a viscous, yellow material. Attempts to vacuum distil it led to decomposition in all cases. Distillation of solvent after column chromatography led to the same thick oil. Compound VI is also a thick liquid. Amides IV, VIII were recrystallized from acetonitrile and V, VII from nitromethane.

3-(1-Hydroxyiminoethyl)-2,2-dimethylcyclobutylacetylanthranilic Acid (IX). Hydroxylamine hydrochloride (1.60 g, 23.0 mmol) in water (5 ml) and a hot solution of sodium acetate (2.80 g, 22.7 mmol) in water (10 ml) were added to a solution of pinonoylanthranilic acid (VI, 4.98 g, 15.7 mmol) in ethanol (50 ml). The reaction mixture was left for 12h at room temperature (20°C). The product was diluted with water (150 ml) and the precipitated IX filtered off and recrystallized from nitromethane.

3-Acetylamino-2,2-dimethylcyclobutylacetylanthranilic Acid (X). Oxime IX (1.05 g, 3.3 mmol) and PPA (6.0 g) were heated at 90-95°C for 3 h. The product was cooled, suspended in water (30 ml), and extracted with ethyl acetate (3 × 20 ml). The combined extracts were dried over anhydrous magnesium sulfate, ethyl acetate was evaporated, and the residue was recrystallized from diethyl ether.

2-(3-Ethyl-2,2-dimethylcyclobutylmethyl)-4(3H)-quinazolinone (XIa). A mixture of amide III (4.41 g, 15.2 mmol) and formamide (2.95 g, 65.5 mmol) was heated for 4 h at 175±3°C. The product cooled and suspended in water (30 ml) containing sodium bicarbonate (1.30 g, 15.5 mmol) was extracted with ethyl acetate (3 × 15 ml). The combined extract was dried over anhydrous magnesium sulfate and the solvent was evaporated. The solid residue was recrystallized from nitromethane. Quinazolinones XIb and XIc obtained similarly from amides IV and V were recrystallized from acetonitrile.

2-(3-Ethyl-2,2-dimethylcyclobutylmethyl)benz-3,1-oxazin-4(H)-one (XII). Amide III (5.93 g, 20.5 mmol) and dicyclohexylcarbodiimide (5.08 g, 24.6 mmol) were refluxed for 2 h in anhydrous benzene (40 ml). The product was cooled, the precipitate filtered off and washed with anhydrous benzene (3 × 15 ml), and the benzene extracts added to the benzene filtrate. Benzene was distilled off and the residue was distilled in vacuo to give oxazine XII (3.50 g, 63%); bp 120-123°C/1 mm Hg, $n_D^{15.5}$ 1.5354, d_4^{20} 1.0646, and R_f 0.62.

3-Amino-2-(3-ethyl-2,2-dimethylcyclobutylmethyl)-4(3H)-quinazolinone Hydrochloride (XIII). Oxazine XII (1.45 g, 5.3 mmol) and hydrazine hydrate (0.50 g, 10.0 mmol) in anhydrous pyridine (15 ml) were refluxed for 2 h. The product was cooled, poured into concentrated hydrochloric acid (7.0 ml) and crushed ice (20 g), and allowed to stand overnight. The precipitated hydrochloride XIII was filtered off and recrystallized from a mixture of ethyl acetate and *n*-hexane (3:1).

Reaction of pinonoylanthranilic acid VI with acetic anhydride was performed by refluxing of the acid VI (10 mmol) with the anhydride (10 ml) for 20 h. Acetic anhydride was evaporated and the oily product was treated with hot *n*-heptane (3 × 10 ml). The extracts were combined, heptane distilled off, and the residue recrystallized from nitromethane. The melting point of the acetylanthranilic acid obtained was 180-181°C; it was not depressed by a known sample [38].

Treatment of Pinanoylanthranilic Acid III with Acetic Anhydride was carried out similarly and also led to the acid XIV.

Treatment of Pinonoylanthranilic Acid VI with Formamide. A mixture of VI (5.05 g, 16.6 mmol) and formamide (20 ml) was held for 6 h at 150±5°C. After cooling, it was suspended in water (50 ml) containing sodium bicarbonate (3.0 g, 35.7 mmol) and extracted with ethyl acetate (3 × 20 ml). Ethyl acetate was evaporated and the residue was recrystallized from nitromethane to give the 4(3H)-quinazolinone (XV) (1.68 g, 65%); mp 214-215°C. The melting point was not depressed by a known sample [39].

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REFERENCES

1. Kh. M. Shakhidoyatov, *Quinazol-4-ones and their Biological Activity* [in Russian], Federal Academy of Sciences, Tashkent (1988), p. 138.
2. P. K. Naithani, G. Ralit, V. K. Srivastava, and K. Shanker, *Indian J. Chem.*, **28B**, No. 9, 745 (1989).
3. B. Srivastava, J. S. Shukla, Y. S. Prabhabar, and A. K. Saxena, *Indian J. Chem.*, **30B**, No. 3, 332 (1991).
4. S. Saxena, M. Verma, A. K. Saxena, G. P. Gupta, and K. Shanker, *Indian J. Chem.*, **30B**, No. 4, 453 (1991).
5. M. Hori, T. Iemura, H. Hara, A. Ozaki, T. Sukamoto, and H. Ohtaka, *Chem. Pharm. Bull.*, **38**, No. 3, 681 (1990).
6. M. Hori, R. Iemura, H. Hara, T. Sukamoto, K. Ito, and H. Ohtaka, *Chem. Pharm. Bull.*, **39**, No 2, 367 (1991).
7. J. F. Wolfe, T. L. Rathman, M. C. Slewi, J. A. Campbell, and T. D. Greenwood, *J. Med. Chem.*, **33**, No. 1, 161 (1990).
8. H. Y. Hassan, A. A. Ismael, and El-Sherief Hah, *Eur. J. Med. Chem.*, **26**, 743 (1991).
9. A. I. Mikhalev, M. E. Konshin, O. A. Yanborisova, A. S. Zaks, and V. V. Yushkov, *Khim.-Farm. Zh.*, **25**, No 10, 37 (1991).
10. I. N. Nesterova, T. P. Radkevich, and V. G. Granik, *Khim.-Farm. Zh.*, **25**, No. 11, 28 (1991).
11. B. Pramella, E. Rajanarender, and A. K. Murthy, *Indian J. Heterocycl. Chem.*, **2**, No. 2, 115 (1992).
12. S. I. Kovalenko, R. S. Sinyak, I. A. Mazur, I. F. Belenichev, and P. N. Stevlyuk, *Farm. Zh. (Kiev)*, No. 5-6, 38 (1992).
13. A. R. R. Rao and Y. M. Reddy, *Pharmazie*, **47**, No 10, 794 (1992).
14. P. B. Trivedi, N. K. Undevia, A. M. Dave, K. N. Bhatt, and N. C. Desai, *Indian J. Chem.*, **32B**, No. 4, 497 (1993).
15. A. R. R. Rao and V. M. Reddy, *Arzneim.-Forsch.*, **43**, No. 6, 663 (1993).
16. Chia Chung Cheng, Dun Fu Liu, and Ting Chao Chou, *Heterocycles*, **35**, No. 2, 775 (1993).
17. E. E. Allen, S. E. de Laszlo, S. X. Huang, C. S. Quagliato, W. J. Geenlee, R. S. L. Chang, T. B. Chen, K. A. Faust, and V. J. Lotti, *Bioorg. Med. Chem. Lett.*, **3**, No. 6, 1293 (1993).
18. G. Daidone, B. Maggio, D. Ralfa, S. Plescia, M. L. Bajardi, A. Caruso, V. M. C. Cutuli, and M. Amico-Roxas, *Eur. J. Med. Chem.*, **29**, No. 3, 707 (1994).
19. A. I. Mazur, T. S. Sinyak, S. I. Kovalenko, I. F. Belenichev, V. V. Muzilev, G. V. Litinskaya, and D. V. Ivanova, *Ukr. Khim. Zh.*, **61**, No. 7-8, 54 (1995).
20. J. K. Padia, H. Chilvers, P. Daum, R. Pinnock, N. Suman-Chauhan, L. Webdale, and B. K. Trivedi, *Bioorg. Med. Chem. Lett.*, **7**, No. 7, 805 (1997).
21. S. A. Shiba, A. A. El-Khamry, M. F. Shaban, and K. S. Atia, *Pharmazie*, **52**, No. 3, 189 (1997).
22. R. S. Atkinson and P. J. Williams, *J. Chem. Soc., Perkin Trans. I*, 1951 (1996).
23. K. Smith, G. A. El-Hiti, M. F. Abdel-Megeed, and M. A. Abdo, *J. Org. Chem.*, **61**, No. 2, 647 (1996).
24. K. Smith, G. A. El-Hiti, M. F. Abdel-Megeed, and M. A. Abdo, *J. Org. Chem.*, **61**, No. 2, 656 (1996).
25. S. Eguchi, T. Suzuki, T. Okawa, Y. Matsushita, E. Yashima, and Y. Okamoto, *J. Org. Chem.*, **61**, No. 21, 7316 (1996).

26. A. L. V'yakonov and M. V. Telezhenetskaya, *Khim. Prirod. Soedin.*, No. 3, 297 (1997).
27. F. M. Avotin'sh, *Usp. Khim.*, **62**, No. 9, 949 (1993).
28. O. Daugulis and F. Avotin'sh, *Latv. Khim. Zh.*, No. 1, 115 (1994).
29. O. Daugulis and F. Avotin'sh, *Latv. Khim. Zh.*, No. 5, 612 (1994).
30. O. Daugulis and F. Avotin'sh, *Latv. J. Chem.*, No. 1, 102 (1997).
31. A. Ya. Strakov, T. F. Kozlovskaya, A. A. Krasnova, I. A. Strakova, and M. V. Petrova, *Latv. Khim. Zh.*, No. 3, 344 (1993).
32. A. Ya. Strakov, A. A. Krasnova, A. A. Aleksandrov, and M. V. Petrova, *Latv. Khim. Zh.*, No. 1, 106 (1994).
33. A. Ya. Strakov, A. A. Krasnova, and M. V. Petrova, *Latv. Khim. Zh.*, No. 3-4, 114 (1995).
34. E. Yu. Gudriniece, F. M. Avotin'sh, and E. O. Bizdena, *Izv. Akad. Nauk Latv. SSR.*, Ser. Khim., No. 5, 598 (1969).
35. E. Yu. Gudriniece, E. O. Bizdena, F. M. Avotin'sh, and I. I. Shtaka, Russian Patent 386931, *Byul. Izobr.*, No. 27, 65 (1973).
36. Z. F. Bore, F. M. Avotin'sh, and E. Yu. Gudriniece, *Izv. Akad. Nauk Latv. SSR., Ser. Khim.*, No. 5, 583 (1973).
37. M. Harispe, P. Ham, and R. Charonnat, *Bull. Soc. chim. Fr.*, No. 5, 732 (1958).
38. A. Kaufmann, *Chem. Ber.*, **42**, 3482 (1909).
39. R. Anschütz, O. Schmidt, and A. Griffenberg, *Chem. Ber.*, **35**, 3480 (1902).
40. E. E. Liepin'sh, R. B. Kampare, and F. M. Avotin'sh, *Izv. Akad. Nauk Latv. SSR., Ser. Khim.*, No. 1, 89 (1975).
41. L. R. Subramanian and G. S. Krishna Rao, *Tetrahedron*, **25**, No. 8, 1749 (1969).