Chemistry of Heterocyclic Compounds, Vol. 41, No. 8, 2005

N-MONOSUBSTITUTED 6-AMINOMETHYLENE-5-OXO-2-PHENYL-5,6,7,8-TETRAHYDROQUINAZOLINES

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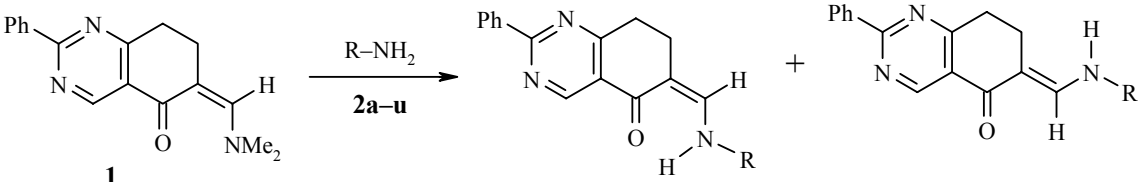
We have obtained the corresponding N-monosubstituted 6-aminomethylene-5-oxo-2-phenyl-5,6,7,8-tetrahydroquinazolines by transamination of 6-dimethylaminomethylene-5-oxo-2-phenyl-5,6,7,8-tetrahydroquinazoline with histamine, tryptamine, 3-(1-imidazolyl)- and 3-(4-morpholyl)-propylamines, 4-amino-1-benzylpiperidine, 2-(1-naphthylamino)ethylamine, 2-pyridylmethylamine, 4-chlorobenzylamine, ethanolamine, 1-aminoadamantane, remantadine, 2-aminodimedone, aniline, 3-trifluoromethylaniline, 4-aminoantipyrine, 2-aminobenzimidazole, 2-amino-5-methylbenzothiazole, 7-amino-4-methylcoumarin, 1-amino-4-methylpiperazine, 2-(2-aminophenyl)benzimidazole, 3-(4-aminophenylamino)-2-cyano-5,5-dimethylcyclohex-2-en-1-one, and 3-amino-2-(2-hydroxyethyl)-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydroindazole.

Keywords: N-monosubstituted 6-aminomethylene-5-oxo-1-phenyl-5,6,7,8-tetrahydroquinazolines, transamination.

In an extension of [1, 2], we have carried out transamination of 6-dimethylaminomethylene-5-oxo-2-phenyl-5,6,7,8-tetrahydroquinazolines **1**. For the transamination, we used ethylamines and propylamines having a heterocyclic or functional group substituent at the β- or γ-position. We selected these amines on the one hand in order to search for agonists and antagonists of H_3 histamine receptors, the rationale for which is given in [3-6] (also see the citations in [2]).



1 ***Z*-3 a–v** ***E*-3m, r, t, u**

2,3 a R = 2-(4-imidazolyl)ethyl; **b** R = 2-(3-indolyl)ethyl; **c** R = 3-(1-imidazolyl)propyl; **d** R = 3-(N-morpholyl)propyl; **e** R = 3-(N-benzylpiperidyl)-4; **f** R = 2(1-naphthylamino)ethyl; **g** R = (2-pyridyl)methyl; **h** R = *p*-chlorobenzyl; **i** R = 2-(hydroxyethyl); **j** R = 1-adamantyl; **k** R = 1-(1-adamantylethyl); **l** R = 5,5-dimethyl-1,3-cyclohexanedion-2-yl; **m** R = phenyl; **n** R = 3-trifluoromethylphenyl; **o** R = 2,3-dimethyl-1-phenylpyrazolin-5-on-4-yl; **p** R = 2-benzimidazolyl; **q** R = 5-methyl-2-benzothiazolyl; **r** R = 4-methyl-6-coumarinyl; **s** R = 4-methyl-1-piperazinyl; **t** R = 2-(2-benzimidazolyl)-1-phenyl; **u** R = 4-(2-cyano-5,5-dimethylcyclohex-1-en-3-on-1-yl)amino-1-phenyl; **v** R = 2-(2-hydroxyethyl)-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydro-3-indazolyl

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On the other hand, quinazoline derivatives containing aminoalkyl, aminocycloalkyl, aminoaryl, or aminohetaryl substituent groups exhibit various types of biological activity [7-17].

In the cases of histamine (**2a**), tryptamine (**2b**), 2-(1-naphthylamino)ethylamine (**2f**), 1-aminoadamantane (**2j**), and remantadine (**2k**), we used their hydrochlorides and the reactions were carried out by boiling in pyridine. The reaction with the hydrochloride of 2-aminodimedone (**2l**) was carried out by boiling in ethanol in the presence of an equimolar amount of piperidine. In the rest of the cases, we used the free amines and boiled equimolar amounts of the reagents in methanol (**2c-e,h,i**), ethanol (**2m,n**), butanol (**2o,p,q,v**), or pyridine (**2g,t,u**). After the reaction had gone to completion and the solvent was completely removed, each time the residue was crystallized twice with addition of activated carbon. In the ^{1}H NMR spectra of compounds **3a-v** (Table 1), we observe signals from protons of all the structural fragments in the expected regions of the spectrum, including the characteristic fragment =CH–NH– with *trans* hydrogen atoms ($^3J_{CHNH}$ ~12-14 Hz). In each of them, as a result of formation of an intramolecular hydrogen bond, the six-membered chelate ring is closed (*Z*-**3**), and the signal from its chelated proton is found in the 10.10-14.08 ppm region and the frequency of the C=O group in the IR spectra is found in the 1660-1632 cm^{-1} region. Compounds **3m,r,t,u** in solutions are a mixture of *Z*-**3** and *E*-**3** isomers and are characterized by a double set of signals from the *trans* fragment =CH–NH–.

TABLE 1. Spectral Characteristics of N-Monosubstituted 6-Aminomethylene-5-oxo-2-phenyl-5,6,7,8-quinazolines **3a-v**

Compound	IR spectrum, ν, cm^{-1} (CO, NH, OH, C≡N)	^{1}H NMR spectrum ($CDCl_3$ and DMSO-d_6*), δ, ppm (*J*, Hz)
1	2	3
3a	1651; 3270, 3120	2.49 (2H, m, CH_2); 2.94 (4H, m, 2CH_2); 3.64 (2H, m, CH_2); 6.91 (1H, d, ^3J = 13, =CH–); 6.99 (1H, s, =CH–); 7.38 (3H, m, C_6H_5); 8.35 (2H, m, C_6H_5); 8.53 (1H, s, =CH–); 9.01 (1H, s, NH); 10.10 (1H, br. m, NH)
3b	1640; 3350, 3220	2.55 (2H, t, ^3J = 7, CH_2); 3.05 (4H, m, 2CH_2); 3.59 (2H, q, ^3J = 7, CH_2); 6.75 (1H, d, ^3J = 12.8, =CH–); 7.07–7.24 (3H, m, C_6H_4, =CH–); 7.37 (1H, d, ^3J = 8, C_6H_4); 7.49 (3H, m, C_6H_5); 7.59 (1H, d, *J* = 8, C_6H_4); 8.20 (1H, br. s, NH); 8.50 (2H, m, C_6H_5); 9.21 (1H, s, =CH–); 10.39 (1H, br. m, NH)
3c	1641; 3230	2.45 (2H, t, ^3J = 6.5, CH_2); 2.67 (2H, t, ^3J = 7, CH_2); 3.06 (2H, t, ^3J = 7, CH_2); 3.38 (2H, q, ^3J = 6.5, CH_2); 3.74 (2H, t, ^3J = 6.5, CH_2); 6.94 (1H, d, ^3J = 13.5, =CH–); 7.49 (3H, m, C_6H_5); 8.51 (2H, m, C_6H_5); 9.21 (1H, s, =CH–); 10.32 (1H, br. m, NH)
3d	1639; 3250	1.85 (2H, m, CH_2); 2.52 (6H, m, 3CH_2); 2.67 (2H, t, ^3J = 7, CH_2); 3.06 (2H, t, ^3J = 7, CH_2); 3.41 (2H, q, ^3J = 6, CH_2); 3.80 (4H, m, 2CH_2); 6.95 (1H, d, ^3J = 12, =CH–); 7.50 (3H, m, C_6H_5); 8.50 (2H, m, C_6H_5); 9.21 (1H, s, =CH–); 10.32 (1H, br. m, NH)
3e	1649; 3270	1.70-2.20 (6H, m, 3CH_2); 2.67 (2H, t, ^3J = 7, CH_2); 2.87 (6H, m, CH_2); 3.06 (2H, t, ^3J = 7, CH_2); 3.21 (1H, m, CH); 3.55 (2H, s, CH_2); 6.99 (1H, d, ^3J = 12.7, =CH–); 7.33 (5H, m, C_6H_5); 7.50 (3H, m, C_6H_5); 8.51 (2H, m, C_6H_5); 9.22 (1H, s, =CH–); 10.43 (1H, dd, ^3J = 7, ^3J = 12.7, NH)
3f	1640; 3220	2.55 (2H, t, ^3J = 7, CH_2); 2.96 (2H, t, ^3J = 7, CH_2); 3.61 (4H, m, 2CH_2); 4.65 (1H, br. s, NH); 6.64 (1H, m, $C_{10}H_7$); 6.75 (1H, d, ^3J = 13, =CH–); 7.27-7.83 (9H, m, $C_{10}H_7$, C_6H_5); 8.54 (2H, m, C_6H_5); 9.25 (1H, s, =CH–); 10.38 (1H, br. m, NH)
3g	1653; 3250	2.71 (2H, t, ^3J = 7, CH_2); 3.08 (2H, t, ^3J = 7, CH_2); 4.61 (2H, d, ^3J = 6, CH_2); 7.05 (1H, d, ^3J = 12.5, =CH–); 7.25 (1H, ddd, ^3J = 7, ^3J = 4.7, ^4J = 0.9, C_5H_4N); 7.32 (1H, d, ^3J = 7.5, C_5H_4N); 7.49 (3H, m, C_6H_5); 7.72 (1H, d, ^3J = 7.5, $^{4.5}J$ = 1.7, C_5H_4N); 8.50 (2H, m, C_6H_5); 8.61 (1H, ddd, ^3J = 4.7, ^4J = 1.7, ^5J = 0.9, C_5H_4N); 9.22 (1H, s, =CH–); 10.63 (1H, br. m, NH)

TABLE 1 (continued)

1	2	3
3h	1647; 3320	2.68 (2H, t, ^3J = 7, CH_2); 3.08 (2H, t, ^3J = 7, CH_2); 4.43 (2H, d, ^3J = 6, CH_2); 6.94 (1H, d, ^3J = 12.6, =CH–); 7.22 (2H, m, ^3J = 8.7, C_6H_4); 7.34 (2H, m, ^3J = 8.7, C_6H_4); 7.50 (3H, m, C_6H_5); 8.51 (2H, m, C_6H_5); 9.21 (1H, s, =CH–); 12.00 (1H, br. m, NH)
3i	1643; 3350-3200	2.21 (1H, br. s, OH); 2.68 (2H, t, ^3J = 7, CH_2); 3.08 (2H, t, ^3J = 7, CH_2); 3.45 (2H, q, ^3J = 6, CH_2); 3.81 (2H, t, ^3J = 6, CH_2); 6.99 (1H, d, ^3J = 14, =CH–); 7.51 (3H, m, C_6H_5); 8.51 (2H, m, C_6H_5); 9.22 (1H, s, =CH–); 10.37 (1H, br. m, NH)
3j	1644	1.65-2.14 (15H, m, H_{Ad}); 2.62 (2H, t, ^3J = 7, CH_2); 3.10 (2H, t, ^3J = 7, CH_2); 7.12 (1H, d, ^3J = 13, =CH–); 7.47 (3H, m, H_{arom}); 8.45 (2H, m, H_{arom}); 9.21 (1H, s, H-4); 10.74 (1H, d, J = 13, NH)
3k	1640	1.22 (3H, d, ^3J = 7, CH_3); 1.49-1.66 (16H, m, H_{Ad} and CH in R); 2.58-3.16 (4H, m, $2CH_2$); 6.92 (1H, d, ^3J = 13, =CH–); 7.52 (3H, m, H_{arom}); 8.52 (2H, m, H_{arom}); 9.25 (1H, s, H-4); 10.53 (1H, m, NH)
3l*	1649, 1629	0.99 (6H, s, $2CH_3$); 2.21 (2H, s, CH_2 in R); 2.47 (2H, s, CH_2 in R); 2.64 (2H, t, ^3J = 7, CH_2); 2.98 (2H, t, ^3J = 7, CH_2); 7.54 (3H, m, H_{arom}); 8.47 (2H, m, H_{arom}); 8.67 (1H, d, ^3J = 13, =CH–); 9.05 (1H, s, H-4); 12.52 (1H, d, ^3J = 13, NH)
3m*	1649; 3280	2.81-3.19 (4H, m, $2CH_2$); 7.01-7.62 (8H, m, H_{arom}); 8.01 and 8.12 (1H, d. d, ^3J = 13, =CH–); 8.25 (2H, m, H_{arom}); 9.16 (1H, s, H-4); 9.42 and 11.91 (1H, dd, ^3J=13, NH)
3n	1656, 3080	2.86 (2H, m, CH_2); 3.16 (2H, m, CH_2); 7.35 (8H, m, 7-H_{arom}, 6-CH); 8.51 (2H, m, H_{arom}); 9.22 (1H, s, H-4); 12.09 (1H, d, ^3J = 13.5, NH)
3o	1665, 1643; 3080	2.29 (3H, s, CH_3); 2.76 (2H, s, CH_2); 3.05 (3H, s, CH_3); 3.08 (2H, m, CH_2); 7.44 (1H, s, =CH–); 7.47 (3H, m, H_{arom}); 8.32 (1H, d, ^3J = 14, =CH–) 8.49 (2H, m, H_{arom}); 9.23 (1H, s, H-4); 12.32 (1H, d, ^3J = 14, NH)
3p*	1666, 3300-3250, 3180	3.07 (4H, m, $2CH_2$); 7.11-7.43 (4H, m, H_{arom} in R); 7.63 (3H, m, H_{arom}); 8.01 (1H, d, ^3J = 13, =CH–); 8.47 (2H, m, H_{arom}); 9.23 (1H, d, ^3J = 13, NH)
3q	1650, 3260, 3080	2.45 (3H, m, CH_3); 2.94-3.16 (4H, m, $2CH_2$); 7.27 (2H, m, H_{arom} in R); 7.54 (3H, m, H_{arom}); 7.71 (1H, d, ^3J = 8, H_{arom} in R); 7.85 (1H, d, ^3J = 12, =CH–); 8.56 (2H, m, H_{arom}); 9.21 (1H, s, H); 12.61 (1H, d, ^3J = 12, NH)
3r	1716, 1650; 3080	2.34 (3H, m, CH_3); 2.76-3.29 (4H, m, $2CH_2$); 6.21 (1H, s, H_{arom} in R); 7.21-7.75 (6H, m, H_{arom}); 7.98 and 8.16 (1H, two dd, ^3J = 13, =CH–); 8.41 (2H, m, H_{arom}); 9.16 (1H, s, H-4); 9.62 and 11.81 (1H, two dd, ^3J = 13, =CH–)
3s	1632; 3060	2.36 (3H, s, CH_3); 2.61 (4H, m, $2NCH_2$); 3.24 (4H, m, $2NCH_2$); 7.52 (3H, m, H_{arom}); 7.83 (1H, s, =CH–); 9.13 (2H, m, H_{arom}); 9.91 (1H, s, 4-H); 13.02 (1H, br. s, NH)
3t*	1656; 3250, 3080	3.18 (4H, center m, $2CH_2$); 7.19-8.56 (14H, m, 9H_{arom}, 4H_{Het}, =CH–); 9.15 and 9.19 (1H, two s, H-4); 13.10 and 14.08 (1H, two d, J = 13.0, NH); 13.18 (1H, br. s, NH)
3u*	1660, 1615; 3240, 3080, 2220	0.94 (6H, s, $2CH_3$); 2.15 (2H, s, CH_2); 2.51 (2H, s, CH_2); 2.72-3.19 (4H, m, $2CH_2$); 7.23-7.52 (7H, m, H_{arom}); 7.96 and 8.12 (1H, two d, J = 13.0, =CH–); 8.49 (2H, m, H_{arom}); 9.21 (1H, s, H-4); 9.54 and 11.88 (1H, two d, J = 13.0, NH); 10.02 (1H, br. s, NH)
3v	1660; 3360, 3080	1.12 (6H, s, $2CH_3$); 2.33 (2H, s, CH_2 in R); 2.62 (2H, s, CH_2 in R); 2.77-3.19 (4H, m, $2CH_2$); 3.61 (1H, J = 5.5, OH); 4.18 (4H, m, $2CH_2$ in R); 7.52 (3H, m, H_{arom}); 8.55 (2H, m, H_{arom}); 8.77 (1H, d, J = 13.0, =CH–); 9.30 (1H, s, H-4); 12.66 (1H, d, J = 13.0, NH)

* The spectra were recorded in DMSO-d_6.

TABLE 2. Characteristics of Compounds **3a-v**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield,%
		C	H	N		
3a	$C_{20}H_{19}N_5O$	69.39 / 69.54	5.40 / 5.54	20.11 / 20.28	215-216	73
3b	$C_{25}H_{22}N_4O$	75.88 / 76.12	5.47 / 5.62	14.02 / 14.20	110-111	71
3c	$C_{21}H_{20}N_5O$	70.20 / 70.37	5.45 / 5.62	19.39 / 19.54	128-130	89
3d	$C_{22}H_{26}N_4O_2$	69.65 / 69.81	6.90 / 6.93	14.66 / 14.80	108-109	55
3e	$C_{26}H_{28}N_4O$	75.53 / 75.70	6.88 / 6.84	13.44 / 13.58	82-83	57
3f	$C_{27}H_{24}N_4O$	77.18 / 77.12	5.63 / 5.75	13.25 / 13.32	150-151	48
3g	$C_{21}H_{18}N_4O$	73.50 / 73.66	5.19 / 5.30	16.23 / 16.36	150-151	56
3h*	$C_{22}H_{18}ClN_3O$	70.11 / 70.30	4.69 / 4.83	11.11 / 11.18	181-182	72
3i	$C_{17}H_{17}N_3O_2$	69.01 / 69.13	5.68 / 5.80	14.14 / 14.23	132-133	82
3j	$C_{25}H_{27}N_3O$	77.72 / 77.89	6.95 / 7.06	10.77 / 10.90	160-161	65
3k	$C_{27}H_{31}N_3O$	78.27 / 78.41	7.41 / 7.56	10.00 / 10.16	183-185	70
3l	$C_{23}H_{23}N_3O_3$	70.70 / 70.93	5.77 / 5.95	10.61 / 10.79	308-309	46
3m	$C_{21}H_{17}N_3O$	76.83 / 77.04	5.18 / 5.24	12.66 / 12.84	196-197	82
3n	$C_{22}H_{16}FN_3O$	66.98 / 66.83	4.00 / 4.08	10.51 / 10.63	143-145	55
3o	$C_{26}H_{23}N_5O_2$	71.25 / 71.38	5.18 / 5.30	15.88 / 16.01	247-248	66
3p	$C_{22}H_{17}N_5O$	72.05 / 71.92	4.60 / 4.67	18.88 / 19.06	259-260	60
3q*[2]	$C_{23}H_{18}N_4OS$	69.10 / 69.32	4.54 / 4.55	13.92 / 14.06	267-268	42
3r	$C_{25}H_{19}N_3O_3$	73.11 / 73.34	4.71 / 4.68	10.15 / 10.26	272-273	56
3s	$C_{20}H_{23}N_5O$	68.50 / 68.74	6.50 / 6.64	19.90 / 20.04	211-212	51
3t	$C_{28}H_{21}N_5O$	75.63 / 75.82	4.66 / 4.77	15.61 / 15.79	233-235	43
3u	$C_{30}H_{27}N_5O_2$	73.41 / 73.60	5.40 / 5.56	14.40 / 14.31	254-255	41
3v	$C_{26}H_{27}N_5O_3$	68.08 / 68.25	5.90 / 5.95	15.40 / 15.31	198-200	26

* Found, %: Cl 9.30. Calculated, %: Cl 9.43.

*[2] Found, %: S 7.80. Calculated, %: S 8.05.

EXPERIMENTAL

The IR spectra were obtained on a Specord IR-75 spectrometer for the substances in nujol mulls (1800-1500 cm^{-1}) and hexachlorobutadiene mulls (3600-2000 cm^{-1}). The frequencies of the stretching vibrations of the C–H bonds in the 3050-2800 cm^{-1} region are not given. The ^1H NMR spectra were recorded on a Bruker WH 90/DS spectrometer (90 MHz) and a Varian Mercury BBC spectrometer (200 MHz) in $CDCl_3$ and DMSO-d_6 solutions, internal standard TMS.

We give the general synthesis procedures. The physicochemical characteristics are given in Table 2.

6-[2-(4-Imidazolyl)ethylaminomethylene]- (3a), 6-[3-(3-Indolyl)propylaminomethylene]- (3b) and 6-[2-(1-Naphthylamino)ethylaminomethylene]- (3f), 6-(1-Adamantylaminomethylene)- (3j), 6-[1-(1-Adamantyl)ethylaminomethylene]-5-oxo-2-phenyl-5,6,7,8-tetrahydroquinazoline (3k). Hydrochloride of amine **2a,b,f,j,k** (2.0 mmol) and quinazoline **1** or **2** (2.0 mmol) were boiled in pyridine (20 ml) for 3 h. The pyridine was driven off to dryness under vacuum, and the residue was recrystallized from 2-propanol (**3a,b,j**), ethanol (**3f**), and pyridine (**3k**). In all cases, activated carbon was added during crystallization.

6-(5,5-Dimethyl-1,3-dioxocyclohex-2-ylaminomethylene)-5-oxo-2-phenyl-5,6,7,8-tetrahydroquinazoline (3l). Hydrochloride of 2-aminodimedone **2l** (2.0 mmol) and quinazoline **1** (2.0 mmol) were boiled in ethanol (20 ml) in the presence of an equimolar amount of piperidine for 3 h. After the usual treatment, compound **3l** was recrystallized from 2-propanol with addition of DMF.

6-[3-(1-Imidazolyl)propylaminomethylene]- (3c), 6-[3-(4-Morpholyl)propylaminomethylene]- (3d), 6-(1-Benzyl-4-piperidylaminomethylene)- (3e), 6-(2-Pyridylmethylaminomethylene)- (3g), 6-(4-Chlorobenzylaminomethylene)- (3h), and 6-(2-Hydroxyethylaminomethylene)- (3i) 5-oxo-2-phenyl-5,6,7,8-tetrahydroquinazolines. Quinazoline **1** (2.0 mmol) and an equimolar amount of the corresponding amine **2** were boiled in methanol (20 ml) for 3 h. The methanol was driven off to dryness; the residue was recrystallized from 2-propanol (**3c,d,e,i**) and ethanol (**3g,h**) with addition of activated carbon.

6-Phenylaminomethylene- (3m), 6-(3-Trifluoromethylphenylaminomethylene)- (3n), 6-(4-Methyl-1-piperazinylaminomethylene)-5-oxo-2-phenyl-5,6,7,8-tetrahydroquinazoline (3s). Amine **2m,n,s** (2.0 mmol) and quinazoline **1** (2.0 mmol) were boiled in ethanol (20 ml) for 3 h. The ethanol was driven off completely under vacuum; the residue was recrystallized twice, with addition of activated carbon, from 2-propanol (compounds **3m,n)** and pyridine (**3s**).

6-(2-Benzimidazolylaminomethylene)- (3p), 6-(5-Methyl-2-benzothiazolylaminomethylene)- (3q), 6-(1,5-Dimethyl-3-oxo-2-phenylpyrazol-4-ylaminomethylene)- (3o), 6-[2-(2-Hydroxyethyl)-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydro-3-indazolylaminomethylene]- (3v) 5-oxo-2-phenyl-5,6,7,8-tetrahydroquinazoline. Amine **2o,p,q,v** (2.0 mmol) and quinazoline **1** (2.0 mmol) were boiled in butanol (20 ml) for 5 h. After the usual treatment, compound **3z** was recrystallized from DMF, **3q** and **3o** were recrystallized from pyridine, and **3p** was recrystallized from 2-propanol.

6-[2-(2-Benzimidazolyl)phenylaminomethylene]- (3t), 6-[4-(2-Cyano-5,5-dimethyl-3-oxocyclohex-1-en-1-ylamino)phenylaminomethylene]- (3u), 6-(4-Methyl-7-coumarinylaminomethylene)- (3r) 5-Oxo-2-phenyl-5,6,7,8-tetrahydroquinazoline. Amine **2t,u,r** (2.0 mmol) and quinazoline **1** (2.0 mmol) were boiled in pyridine (20 ml) for 3 h. The reaction mixture was treated as described above. Compounds **3t** and **3u** were recrystallized from 2-propanol; **3r** was recrystallized from pyridine.

REFERENCES

1. N. N. Tonkikh, A. Strakovs, and M. V. Petrova, *Khim. Geterotsikl. Soedin.*, 212 (2000).
2. A. Ya. Strakovs, N. N. Tonkikh, M. V. Petrova, K. V. Rizhanova, and E. L. Palitis, *Khim. Geterotsikl. Soedin.*, 515 (2002).
3. R. N. Atkinsons and S. B. King, *Bioorg. Med. Chem. Lett.*, **9**, 2953 (1999).
4. H. Miyachi, H. Kiyoto, and M. Segawa, *Bioorg. Med. Chem. Lett.*, **9**, 2953 (1999).
5. M. J. Torez, I. M. Buck, T. Cooke, S. B. Kalindjian, I. M. McDonald, M. J. Pether, and K. I. M. Steel, *Bioorg. Med. Chem. Lett.*, **9**, 3103 (1999).
6. A. B. Zhivich, E. Nordlander, and G. I. Koldobskii, *Zh. Org. Khim.*, **35**, 332 (1999).
7. Y. Takeuchi, H. Abe, and T. Harayama, *Chem. Pharm. Bull.*, **47**, 905 (1999).
8. N. J. Liverton, D. J. Armstrong, D. A. Claremon, D. C. Remy, J. J. Baldwin, R. J. Lynch, G. Thang, and R. J. Gould, *Bioorg. Med. Chem. Lett.*, **8**, 483 (1998).

9. J. K. Padia, M. Field, J. Hinton, K. Meecham, J. Pablo, R. Pinnock, B. D. Roth, L. Singh, N. Suman-Chauhan, B. K. Trivedi, and L. Webdale, *J. Med. Chem.*, **41**, 1042 (1998).
10. J. W. Chern, P.-L. Tao, K.-C. Wang, A. Gutcait, S. W. Lih, M.-H. Yem, S.-L. Cien, and J.-K. Rong, *J. Med. Chem.*, **41**, 3128 (1998).
11. S. Uesato, Y. Kuroda, M. Kato, Y. Fujiwara, Y. Hase, and T. Fujita, *Chem. Pharm. Bull.*, **46**, 1 (1998).
12. J.-W. Chern, H.-T. Chen, N.-Y. Lai, K.-R. Wu, and Y.-Chern, *Chem. Pharm. Bull.*, **46**, 928 (1998).
13. B. S. Holla, M. T. Padmaja, M. K. Shivananda, and P. M. Akbarali, *Indian J. Chem.*, **37B**, 715 (1998).
14. M. S. Amine, A. M. F. Eissa, A. F. Shaaban, A. El-Sanyed, and R. El-Sayed, *Indian J. Chem.*, **37B**, 1153 (1998).
15. M. S. Amine, A. M. F. Eissa, A. F. Shaaban, A. El-Sawy, and R. El-Sayed, *Indian J. Heterocycl. Chem.*, **7**, No. 3, 169 (1998).
16. J. K. Padia, H. Chilvers, P. Daum, R. Pinnock, N. Suman-Chauhan, L. Webdale, and B. K. Trivedi, *Bioorg. Med. Chem. Lett.*, **7**, 805 (1997).
17. K. Terashima, H. Shimamura, A. Kuwase, Y. Tanaka, T. Tanimura, T. Kamisaki, Y. Ishizuka, and M. Sato, *Chem. Pharm. Bull.*, **43**, 2021 (1995).