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OXIDATIVE ALKYLAMINATION OF 2-METHYL-3(2H)-CINNOLINONE: UNEXPECTED DEALKYLATION OF THE ENTERING ALKYLAMINO GROUP*

O. N. Burov[1], A. V. Gulevskaya[1], and A. F. Pozharskii[1]**

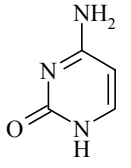
The oxidative alkylamination of 2-methyl-3(2H)-cinnolinone by secondary alkylamines in the presence of $KMnO_4$ leads to the smooth formation of the expected 4-alkylamino-2-methyl-3(2H)-cinnolinones. The analogous reaction with primary alkylamines is accompanied by the partial or complete N-dealkylation of the entering alkylamino group depending on the temperature.

Keywords: 4-alkylamino-2-methyl-3(2H)-cinnolinones, 2-methyl-3(2H)-cinnolinone, nucleophilic aromatic substitution of hydrogen, oxidative alkylamination.

Aminoazinones are an important class of biomolecules, including the nucleic acids, cytosine **1** and guanine **2**, which are nitrogen bases (Scheme 1). These compounds possess various pharmacological properties such as antiarrhythmic, hypotensive, antithrombotic effects etc [1-10].

Some aminoazinones are used in medical practice such as the antiviral drug *acyclovir* **3**, the immunomodulator *bropirimine* **4**, as well as *lamivudine* **5** and *zalcytabine* **6**, which are used in treating HIV infections [11]. The unique properties of aminoazinones, such as their tendency to form hydrogen bonds, undergo complexation, and perform self-assembly, are related to the internal amide fragment and external amino group.

Scheme 1



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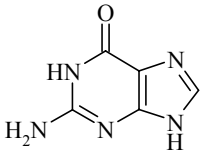

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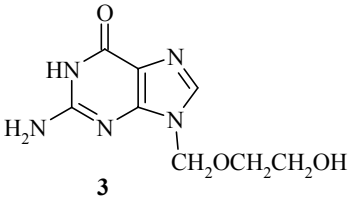

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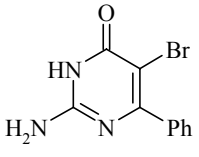

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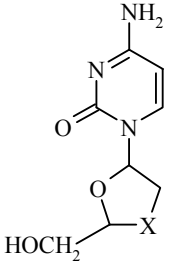

5, **6**

5 X = S, **6** X = CH_2

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** To whom correspondence should be addressed, e-mail: agulevskaya@rsu.ru.

[1]Southern Federal University, Chemistry Faculty, Rostov-on-the-Don 344090, Russia.

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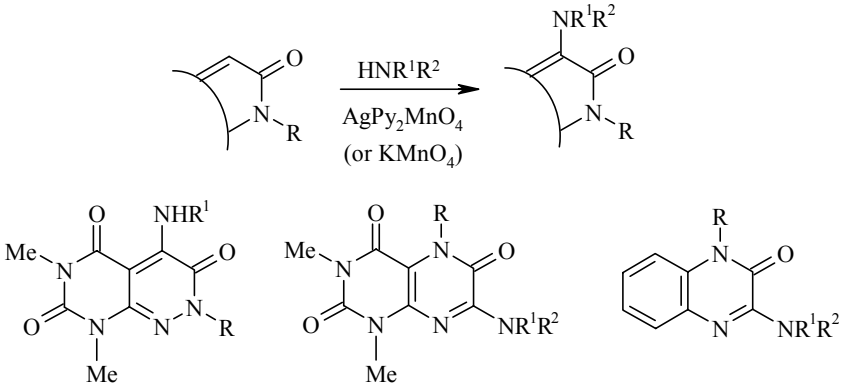
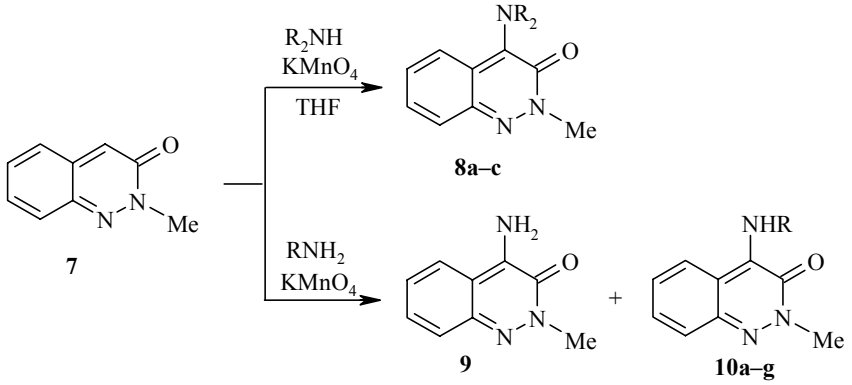
The reported methods for the preparation of aminoazinones and alkylaminoazinones are based predominantly on cyclization and nucleophilic substitution of good leaving groups (halogen, RS, CN, SCN) in the azinones. A detailed discussion of these methods is given in our previous work [12]. Many of these methods are laborious and have low selectivity. We have recently shown that oxidative alkylamination may be a good alternative in the case of condensed azinones [12]. Diazinones condensed with a uracil ring and 2(1H)-quinoxalone are readily aminated in systems containing an alkylamine and oxidizing agent in the *ortho* position to the amide carbonyl group as shown in Scheme 2. In the present work, we studied the oxidative alkylamination of 2-methyl-3(2H)-cinnolinone (**7**), which displays new aspects of this reaction.

Scheme 2



We found that 4-alkylamino derivatives **8a-c** are formed in moderate yields upon treating cinnolinone **7** with $KMnO_4$ and secondary alkylamines, such as pyrrolidine, piperidine, and morpholine, in tetrahydrofuran at 20°C over 15 h (Scheme 3, Table 1).

Scheme 3



8 a NR_2 = N , **b** NR_2 = N , **c** NR_2 = N O

10 a R = Et, **b** R = *n*-Pr, **c** = *i*-Pr, **d** R = *n*-Bu, **e** R = *cyclo*-C_6H_{11}, **f** R = $PhCH_2$, **g** R = *t*-Bu

The reaction of cinnolinone **7** with benzylamine or cyclohexylamine under the same conditions proceeds anomalously to give 4-amino-2-methyl-3(2H)-cinnolinone (**9**) as the only product in 41-59% yield. Treatment of cinnolinone **7** with excess propylamine or butylamine and $KMnO_4$ but without THF also gives amine **9** exclusively in 37-41% yield. Lowering the temperature of the oxidative alkylamination to -12°C permitted us to obtain the desired 4-alkylaminocinnolinones **10a-d** in 33-37% yield although the formation of 4-aminocinnolinone **9** in 13-16% yield could not be avoided.

TABLE 1. Reaction of 2-Methyl-3(2H)-cinnolinone **7** with Alkylamines and $KMnO_4$

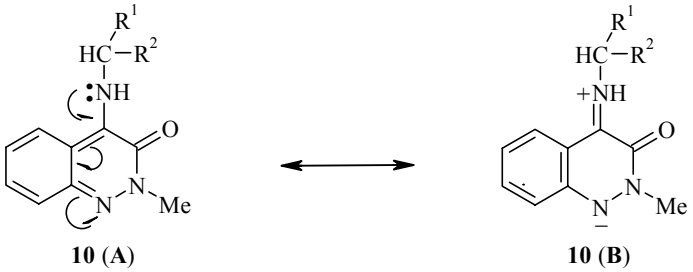
Alkylamine	Reaction products*	Yield, %	Reaction products *[2] (Yield, %)
$(CH_2)_4NH$	**8a**	17	*[3]
$(CH_2)_5NH$	**8b**	35	*[3]
	**8c**	28	*[3]
$EtNH_2$	*[3]		**10a** (34) + **9** (16)
n-$PrNH_2$	**9**	41	**10b** (33) + **9** (13)
i-$PrNH_2$	*[3]		**10c** (37) + **9** (16)
n-$BuNH_2$	**9**	37	**10d** (36) + **9** (15)
cyclo-$C_6H_{11}NH_2$	**9**	41	*[3]
$PhCH_2NH_2$	**9**	59	*[3]
t-$BuNH_2$	**10g**	6	*[3]

* 20 °C, 15 h.

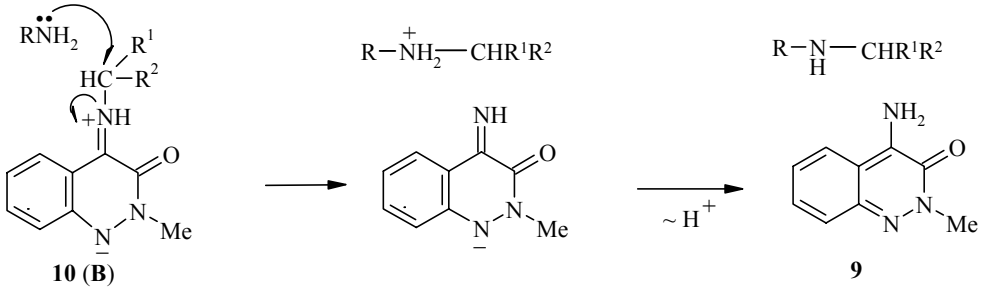
*[2] -12 °C, 6 h.

*[3] Reaction not csrried out under these conditions

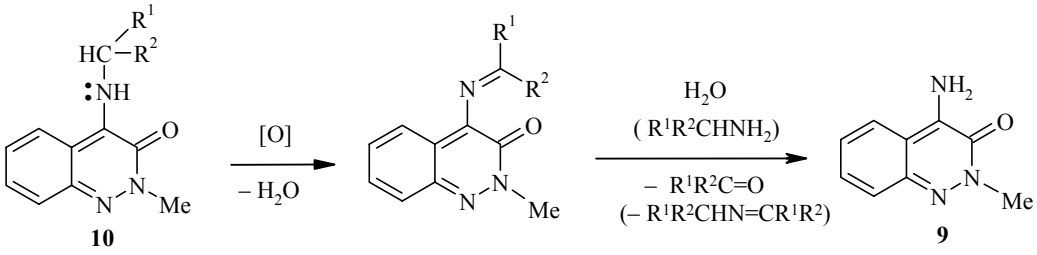
Scheme 4



Pathway ***a***



Pathway ***b***



This finding indicates that the formation of 4-aminocinnolinone **9** results from the dealkylation of 4-alkylaminocinnolinones **10**. To the best of our knowledge, such processes in the oxidative alkylamination of arenes and hetarenes have not been reported (see our recent review [13]). Three questions are fundamental for understanding the dealkylation mechanism:

1. Why is the reaction characteristic precisely for 4-alkylaminocinnolinones?
2. Why does this reaction proceed only in the case of primary alkylamines?
3. Does the oxidizing agent participate in the dealkylation reaction?

We propose that the tendency of compounds **10** to undergo dealkylation is a consequence of resonance structures **(A) ↔ (B)**, which imparts properties of quaternary ammonium salts (Scheme 4). In this case, the dealkylation may be seen as the result of nucleophilic attack on the α-carbon atom of the alkylamino group, in which 4-amino-2-methyl-3(2H)-cinnolinone **9** acts as the leaving group (Pathway ***a***). However, this hypothesis could not be confirmed: prolonged stirring of 4-ethylamino-2-methyl-3(2H)-cinnolinone **10a** in propylamine at room temperature did not lead to the formation of amino derivative **9**. An alternative mechanism involves the oxidation of 4-alkylaminocinnolinones **10** to the corresponding azomethines with subsequent hydrolysis or transamination (Pathway ***b***). This pathway finds support in the finding that the addition of an oxidizing agent to a solution of 4-ethylamino-2-methyl-3(2H)-cinnolinone **10a** in propylamine leads to complete dealkylation and formation of 4-aminocinnolinone **9**.

The oxidation of amines is known to begin with the formation of a radical-cation, which then loses a proton (Scheme 5) [14, 15]. Disproportionation or further oxidation of the radical thus formed gives an azomethine.

Scheme 5

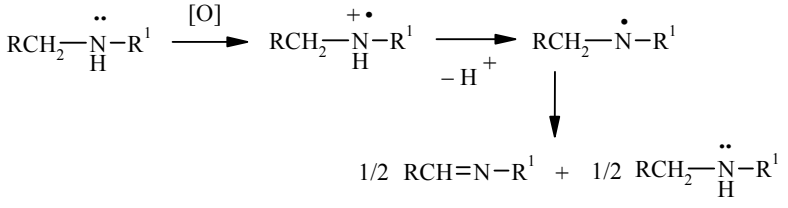


TABLE 2. Elemental Analysis Data of Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			mp, °C
		C	H	N	
8a	$C_{13}H_{15}N_3O$	67.96 / 68.10	6.43 / 6.59	18.49 / 18.33	78-80
8b	$C_{14}H_{17}N_3O$	68.92 / 69.11	6.95 / 7.04	17.41 / 17.27	89-91
8c	$C_{13}H_{15}N_3O_2$	63.78 / 63.66	6.33 / 6.16	17.04 / 17.13	106-108
9	$C_9H_9N_3O$	61.52 / 61.70	5.25 / 5.18	24.15 / 23.99	169-170
10a	$C_{11}H_{13}N_3O$	65.12 / 65.01	6.58 / 6.45	20.49 / 20.68	78-80
10b	$C_{12}H_{15}N_3O$	66.51 / 66.34	7.14 / 6.96	19.17 / 19.34	99-101
10c	$C_{12}H_{15}N_3O$	66.19 / 66.34	6.79 / 6.96	19.43 / 19.34	103-104
10d	$C_{13}H_{17}N_3O$	67.65 / 67.51	7.23 / 7.41	18.02 / 18.17	75-77
10g	$C_{13}H_{17}N_3O$	67.38 / 67.51	7.59 / 7.41	18.34 / 18.17	101-103

The **10(A) ↔ 10(B)** resonance may result in enhanced NH-acidity so that molecular **10** does not undergo the oxidation but rather the corresponding anion. This behavior would account for the observed ease of the dealkylation. Indeed, we found pK_a 11.95 for 2-methyl-4-propylamino-3(2H)-cinnolinone **10b** in 1:1 ethanol-water by titration with 0.1 N aqueous KOH at 20°C. The equilibrium concentration of the N-anion in the case of such N-acidity should be sufficient for the reaction to proceed in this direction.

TABLE 3. IR and UV Spectra of Compounds **8-10**

Compound	IR spectrum, ν, cm^{-1}		UV spectrum, λ_{max}, nm (log ε)
	C=O	N–H	
8a	1625	—	262 (3.95), 268 sh (3.39), 428 (3.64), 452 (3.60)
8b	1616	—	262 (4.05), 280 sh (3.84), 447 (3.94)
8c	1620	—	261 (4.04), 284 sh (3.81), 441 (3.88)
9	1596	3194, 3299, 3406, 3445	257 (4.47), 313 (3.02), 328 (2.88), 366 sh (3.71), 401 (3.88), 421 (3.86)
10a	1607	3258	258 (4.05), 318 (3.28), 333 (3.28), 364 sh (3.81), 401 (4.03), 422 (3.99)
10b	1603	3251	258 (4.41), 318 (3.42), 333 (3.42), 372 sh (3.88), 401 (4.15), 422 (4.12)
10c	1603	3253	262 (4.35), 318 (3.36), 333 (3.34), 372 sh (3.79), 402 (4.05), 423 (4.03)
10d	1609	3246	260 (4.37), 318 (3.37), 333 (3.35), 383 (3.88), 401 (4.09), 423 (4.06)
10g	1613	3272	270 (4.57), 325 (3.33), 405 (3.06), 425 (3.09)

TABLE 4. ^{1}H NMR Spectra of Compounds **8-10**

Compound	Chemical shifts, δ, ppm (*J*, Hz)
8a	1.93 (4H, m, $2CH_2$); 3.93 (3H, s, NCH_3); 4.14 (4H, m, $2CH_2$); 6.84 (1H, m, H-6); 7.07 (1H, m, H-7); 7.32 (1H, d, *J* = 8.8, H-8); 7.67 (1H, d, *J* = 9.2, H-5)
8b	1.60 (6H, m, $3CH_2$); 3.58 (4H, m, $2CH_2$); 3.85 (3H, s, NCH_3); 6.89 (1H, ddd, *J* = 6.3, *J* = 9.1, *J* = 1.1, H-6); 7.00 (1H, ddd, *J* = 6.3, *J* = 9.1, *J* = 1.1, H-7); 7.28 (1H, dm, *J* = 9.1, H-8); 7.36 (1H, dm, *J* = 9.1, H-5)
8c	3.66 (4H, m, $2CH_2$); 3.87 (4H, m, $2CH_2$); 4.01 (3H, s, NCH_3); 7.05 (1H, ddd, *J* = 6.5, *J* = 9.1, *J* = 1.4, H-6); 7.13 (1H, ddd, *J* = 6.5, *J* = 8.8, *J* = 1.4, H-7); 7.44 (1H, dm, *J* = 8.8, H-8); 7.49 (1H, dm, *J* = 8.8, H-5)
9	4.05 (3H, s, NCH_3); 5.70 (2H, br. s, NH_2); 7.04 (1H, ddd, *J* = 6.3, *J* = 8.8, *J* = 1.3, H-6); 7.18 (1H, ddd, *J* = 6.3, *J* = 9.2, *J* = 1.3, H-7); 7.30 (1H, dm, *J* = 8.8, H-8); 7.42 (1H, dm, *J* = 8.8, H-5)
10a	1.41 (3H, t, *J* = 7.2, $CH_2C\underline{H}_3$); 3.83 (2H, m, $C\underline{H}_2CH_3$); 3.99 (3H, s, NCH_3); 6.62 (1H, br. s, NH); 6.88 (1H, ddd, *J* = 6.4, *J* = 9.1, *J* = 1.2, H-6); 7.11 (1H, ddd, *J* = 6.4, *J* = 9.1, *J* = 1.2, H-7); 7.34 (1H, dm, *J* = 9.1, H-8); 7.76 (1H, dm, *J* = 9.1, H-5)
10b	1.06 (3H, t, *J* = 7.4, $CH_2CH_2C\underline{H}_3$); 1.81 (2H, m, $CH_2C\underline{H}_2CH_3$); 3.76 (2H, m, $C\underline{H}_2CH_2CH_3$): 4.01 (3H, s, NCH_3); 6.70 (1H, br. s, NH); 6.89 (1H, ddd, *J* = 6.4, *J* = 9.1, *J* = 1.1, H-6); 7.12 (1H, ddd, *J* = 6.4, *J* = 9.1, *J* = 1.1, H-7); 7.36 (1H, dm, *J* = 9.1, H-8); 7.78 (1H, dm, *J* = 9.1, H-5)
10c	1.39 (6H, d, *J* = 6.1, $CH(C\underline{H}_3)_2$); 4.00 (3H, s, NCH_3); 4.36 (2H, m, $C\underline{H}(CH_3)_2$); 6.65 (1H, br. s, NH); 6.92 (1H, m, H-6); 7.14 (1H, m, H-7); 7.36 (1H, d, *J* = 9.0, H-8); 7.68 (1H, d, *J* = 9.4, H-5)
10d	0.97 (3H, t, *J* = 7.3, $(CH_2)_3C\underline{H}_3$); 1.50 (2H, m, $(CH_2)_2C\underline{H}_2CH_3$); 1.77 (2H, m, $CH_2C\underline{H}_2CH_2CH_3$); 3.79 (2H, m, $C\underline{H}_2(CH_2)_2CH_3$); 4.02 (3H, s, NCH_3); 6.72 (1H, br. s, NH); 6.91 (1H, ddd, *J* = 6.4, *J* = 9.1, *J* = 1.1, H-6); 7.14 (1H, ddd, *J* = 6.4, *J* = 9.0, *J* = 1.1, H-7); 7.37 (1H, d, *J* = 8.9, H-8); 7.79 (1H, d, *J* = 9.0, H-5)
10g	1.52 (9H, s, $C(CH_3)_3$); 4.01 (3H, s, NCH_3); 6.76 (1H, br. s, NH); 6.95 (1H, ddd, *J* = 6.4, *J* = 9.1, *J* = 1.2, H-6); 7.11 (1H, ddd, *J* = 6.4, *J* = 9.1, *J* = 1.1, H-7); 7.35 (1H, d, *J* = 9.1, H-8); 7.72 (1H, d, *J* = 9.1, H-5)

Support for an oxidative mechanism of the dealkylation is found in the exclusive formation of 4-*tert*-butylaminocinnolinone **10g** in 6% yield when the reaction of 2-methyl-3(2H)-cinnolinone **7** with *tert*-butylamine and $KMnO_4$ is carried out at room temperature. Cinnolinone **10g** cannot form azomethine in oxidation reaction and, thus, undergoes dealkylation. The reason for the low yield of amine **10g** is the low solubility of $KMnO_4$ in *tert*-butylamine. The use of $AgMnO_4$, which has good solubility in amines, permits us to obtain 4-*tert*-butylamino-2-methyl-3(2H)-cinnolinone **10g** in 62% yield without any trace of 4-aminocinnolinone **9**. The reaction of 3-methyl-3(2H)-cinnolinone **7** with butylamine and $AgMnO_4$ at 20°C gives a mixture of amino derivatives **10d** (45% yield) and **9** (33% yield), i.e., the dealkylation product in this case is formed in somewhat higher yield than in the reaction with $KMnO_4$.

The structures of the products were supported by IR, ^{1}H NMR, and UV spectroscopy, mass spectrometry, and elemental analysis (Tables 2-5).

Aminocinnolinones **8-10** are yellow crystalline compounds with λ_{max} 421-452 nm. The IR spectra of these products show the characteristic amide carbonyl band at 1603-1625 cm^{-1}. The band at 3246-3445 cm^{-1} in the spectra of cinnolinones **10** corresponds to stretching of the N-H bond. The amino group in cinnolinone **9** gives four bands at from 3194 to 3272 cm^{-1}. The ^{1}H NMR spectra of aminocinnolinones **8-10** show signals for all the protons of the substituents at N-2 and C-4 in the cinnolinone system as well as the signals of the aromatic protons, thus providing reliable evidence for the structure of these compounds. The mass spectra of cinnolinones **8** and **10** show molecular ion peaks as well as peaks for the $[M\text{-}NR^1R^2\text{-}H]^+$ ion, corresponding to the loss of an alkylamino group.

Thus, we have discovered the first case of oxidative alkylamination accompanied by the partial or complete N-dealkylation of the entering alkylamino group. 2-Methyl-3(2H)-cinnolinone **7** in the $R_2NH/KMnO_4$ system was found to form 4-alkylamino derivatives. The reaction of cinnolinone **7** with primary amines leads to the formation of 4-alkylaminocinnolinones and/or 4-aminocinnolinone, depending on the reaction temperature.

TABLE 5. Mass Spectra of **8-10**

Com-pound	Mass-spectrum, *m*/*z* (I_{rel}, %)
8a	229 $[M]^+$ (10), 215 (5), 188 (9), 175 (18), 167 (13), 160 $[M–C_4H_7N]^+$ (28), 155 (9), 111 (5), 97 (12), 91 (5), 83 (16), 77 (6), 69 (31), 57 (58), 43 (100)
8b	243 $[M]^+$ (100), 228 (11), 215 $[M–CO]^+$ (10), 200 $[M–(CH_2)_2NH]^+$ (4), 175 (5), 160 $[M–C_5H_9N]^+$ (5), 147 (5), 132 (6), 102 (6), 89 (7), 84 (11), 76 (6), 55 (7), 41 (34)
8c	245 $[M]^+$ (39), 217 $[M–CO]^+$ (7), 202 (9), 186 (19), 174 (100), 160 $[M–C_4H_7ON]^+$ (49), 146 (33), 131 (29), 117 (25), 103 (34), 89 (48), 86 (25), 76 (26), 70 (18), 63 (26), 56 (15), 51 (20), 43 (59)
9	175 $[M]^+$ (100), 147 $[M–CO]^+$ (60), 132 (11), 128 (7), 118 (26), 104 (52), 91 (12), 77 (76), 65 (26), 63 (12), 51 (42), 43 (33), 39 (30)
10a	203 $[M]^+$ (100), 188 (85), 175 $[M–CO]^+$ (26), 160 $[M–C_2H_5N]^+$ (38), 146 (61), 132 (40), 117 (71), 103 (70), 90 (45), 76 (70), 69 (10), 63 (39), 57 (15), 50 (48), 43 (62), 39 (46)
10b	217 $[M]^+$ (80), 202 (5), 188 $[M–CH_2=NH]^+$ (100), 175 $[M–C_3H_6]^+$ (42), 160 $[M–C_3H_7N]^+$ (32), 146 (29), 132 (33), 117 (40), 103 (31), 90 (18), 76 (33), 63 (12), 50 (14), 41 (65)
10c	217 $[M]^+$ (29), 202 (16), 175 $[M–C_3H_6]^+$ (25), 147 (26), 132 (16), 117 (16), 103 (22), 90 (12), 76 (29), 63 (10), 58 (20), 50 (21), 43 (100)
10d	231 $[M]^+$ (10), 188 (16), 175 $[M\text{-}C_4H_8]^+$ (9), 160 $[M–C_4H_9N]^+$ (7), 146 (10), 132 (11), 117 (20), 103 (20), 90 (16), 83 (7), 76 (31), 69 (15), 63 (15), 57 (39), 51 (18), 41 (100)
10g	231 $[M]^+$ (21), 175 $[M–C_4H_8]^+$ (100), 147 $[M– C_4H_8–CO]^+$ (67), 132 (10), 104 (20), 57 (13), 41 (10)

EXPERIMENTAL

The IR spectra were taken on a Specord IR-71 spectrometer for vaseline mulls. The ^{1}H NMR spectra were taken on a Bruker-250 spectrophotometer at 250 MHz in $CDCl_3$ with TMS as the internal standard. The UV spectra were taken on a Specord M-40 spectrophotometer in chloroform. The mass spectra were taken on a Finnigan MAT INCOS 50 mass spectrometer. The reaction course and purity of the products were monitored by thin-layer chromatography using alumina plates (Brockmann activity III-IV) using 20:1 dichloromethane–methanol as the eluent. Commercial samples of the alkylamines obtained from Acros and Aldrich were used in this work.

2-Methyl-3(2H)-cinnolinone (7). K_2CO_3 (276 mg, 2 mmol) was added to a solution of 3(2H)-cinnolinone [16] (146 mg, 1 mmol) in acetone (15 ml) and stirred for 30 min. Then, methyl iodide (0.1 ml, 1.3 mmol) was added and the mixture was stirred for 4 h. An additional methyl iodide (0.1 ml, 1.3 mmol) was then added and the reaction mixture was left with stirring overnight. The precipitate was filtered off and washed with three 25 ml chloroform portions. The mother liquor was evaporated on a rotary evaporator. The dry residue was triturated with 4-5 g alumina and subjected to chromatography on a 2×25 cm alumina column using dichloromethane as the eluent. The first yellow fraction with R_f 0.4 was taken. Dichloromethane was removed on a rotary evaporator to give 80 mg (50%) compound **7** as yellow crystals with mp 134-136°C, in accord with the data of Alford [17].

Synthesis of 4-(Alkylamino)-2-methyl-3(2H)-cinnolinones 8a-c (General Method). $KMnO_4$ (156 mg, 1 mmol) was added with stirring to a solution of cinnolinone **7** (80 mg, 0.5 mmol) and alkylamine (morpholine, piperidine, or pyrrolidine) (2 ml) in THF (15 ml). Stirring was discontinued after 15 h and the reaction mixture was evaporated on a water bath. The dry residue was triturated with 4-5 g alumina, placed on a 2×25 cm alumina column, and subjected to column chromatography using dichloromethane as the eluent. The first yellow fraction with R_f 0.4 was taken. Dichloromethane was removed on a rotary evaporator to give 17-35% cinnolinone **8** as yellow crystals.

Reaction of 2-methyl-3(2H)-cinnolinone with Primary Alkylamines at 20°C (General Method). A. $KMnO_4$ (156 mg, 1 mmol) was added with stirring to a solution of cinnolinone **7** (80 mg, 0.5 mmol) and amine (cyclohexylamine, benzylamine) (2 ml) in THF (15 ml). Stirring was discontinued after 15 h and the reaction mixture was evaporated on a water bath. The dry residue was triturated with 4-5 g alumina, placed on a 2×25 cm alumina column, and eluted with dichloromethane. The first yellow fraction with R_f 0.1 was taken. Dichloromethane was evaporated off on a rotary evaporator. The residue was recrystallized from dioxane to give 41-59% 4-amino-2-methyl-3(2H)-cinnolinone (**9**) as light-yellow crystals.

B. $KMnO_4$ (156 mg, 1 mmol) was added with stirring to a solution of cinnolinone **7** (80 mg, 0.5 mmol) in alkylamine (propylamine, butylamine) (10 ml). Stirring was discontinued after 15 h and the reaction mixture was evaporated on a rotary evaporator. Separation and purification of the product were carried out analogously to method A to give 37-41% cinnolinone **9** as light-yellow crystals.

C. $AgMnO_4$ (227 mg, 1 mmol) was added with stirring to a solution of cinnolinone **7** (160 mg, 1 mmol) in alkylamine (*tert*-butylamine, butylamine) (20 ml). Stirring was discontinued after 15 h and the mixture was evaporated on a rotary evaporator. The dry residue was triturated with 4-5 g alumina, placed on a 2×25 cm alumina column, and eluted with dichloromethane.

In the experiment with *tert*-butylamine, the yellow fraction with R_f 0.4 was taken. Dichloromethane was evaporated off on a rotary evaporator. The residue was recrystallized from dioxane to give 143 mg (62%) 4-*tert*-butylamino-2-methyl-3(2H)-cinnolinone (**10d**) as yellow crystals.

In the experiment with butylamine, the fraction with R_f 0.4 was initially taken. Dichloromethane was removed on a rotary evaporator. The residue was recrystallized from dioxane to give 104 mg (45%) 4-butylamino-2-methyl-3(2H)-cinnolinone (**10d**) as yellow crystals. Then, 58 mg (33%) cinnolinone **9** was isolated from the next fraction with R_f 0.1 as light-yellow crystals.

The reaction of 2-methyl-3(2H)-cinnolinone with Primary Alkylamines at -12°C (General Method). $KMnO_4$ (156 mg, 1 mmol) was added with stirring to a solution of cinnolinone **7** (80 mg, 0.5 mmol) in alkylamine (ethylamine, propylamine, isopropylamine, butylamine) (10 ml) cooled to -12°C. Stirring was discontinued after 6 h and the reaction mixture was evaporated without warming in a strong air stream. The dry residue was triturated with 4-5 mg alumina, placed on a 2×25 cm alumina column, and eluted with dichloromethane. The yellow fraction with R_f 0.4 was initially taken. Dichloromethane was removed on a rotary evaporator. The residue was recrystallized from dioxane to give 33-37% corresponding 4-(alkylamino)-2-methyl-3(2H)-cinnolinone **10** as yellow crystals. Then, cinnolinone **9** was isolated in 13-16% yield from the next fraction with R_f 0.1.

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