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Phosphoramides. XIII.* Phosphorus Pentaoxide–Amine Hydrochloride Mixtures as Reagents in the Synthesis of 4(3*H*)-Quinazolinones and 4-Quinazolinamines

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4(3*H*)-Quinazolinones *3a–r* have been prepared by heating methyl *N*-acylanthranilates *1a–c* and the hydrochlorides of primary aliphatic and aromatic amines with phosphorus pentaoxide and *N,N*-dimethylcyclohexylamine at 180 °C. 4-Quinazolinamines *4* and the amidine *7* were isolated as by-products. The carboxamides *5* and *6* were believed to be reaction intermediates. By raising the temperature to 250 °C *4* was obtained in a preparative yield.

Since the first report that some 4(3*H*)-quinazolinone derivatives exhibited a potent hypnotic action in animals, much attention has been focussed on these compounds.[1,2] 2-Methyl-3-(*o*-tolyl)-4(3*H*)-quinazolinone (methaqualone)[3] and 2-methyl-3-(*o*-chlorophenyl)-4(3*H*)-quinazolinone (meclaqualone)[3] have been used as hypnotic drugs. Recently, 3-methyl-4(3*H*)-quinazolinone[4] has been prepared from methyl *N*-formylanthranilate by heating with phenyl *N,N'*-dimethylphosphorodiamidate. It was therefore of interest to find whether that procedure could be extended to other phosphoramide reagents.

In this paper a new method to prepare 4-quinazolinamines is also described. Like the quinazolinones, the 4-quinazolinamines are of general interest in terms of their biological and pharmacological activities.[5–8] A 4-quinazolinamine derivative, prazosin, has been used as an antihypertensive drug.[9]

RESULTS AND DISCUSSION

Heating of methyl 2-acylaminobenzoates with primary amine hydrochlorides in a molar ratio from 1:3 to 1:5 in a mixture of phosphorus pentaoxide (P_2O_5) and *N,N*-dimethylcyclohexylamine at 180 °C gave quinazolinones *3* in 35–92 % yield. In the reactions with amine hydrochlorides, $H(CH_2)_nNH_3Cl$, where $n=0$, 1, 2, 3, an exothermic reaction was observed, starting in the temperature interval from 70 to 150 °C. For hydrazine hydrochloride a vigorous reaction started at room temperature. Compounds *3* with $R^1=CH_3$ were obtained in high yields, except for $R^2=NH_2$ or *t*-Bu. The only product isolated for $R^2=t$-Bu was the corresponding benzonitrile *10*. The relatively low yields of *3h* and *3q* indicate formation of a more complex phosphoramide in the phosphorus pentaoxide–hydrazine mixture. A benzotriazepin-5-one *2* might be expected as a by-product, but was not observed. However, benzotriazepines are extremely labile to an alkoxide-induced ring contraction producing *3h* and *3q* (Scheme 3) which may occur under the alkaline conditions during the working up.[15] The 4-quinazolinamine *4g* was isolated from the crude *3g*, but 4-quinazolinamines *4* were not found as by-product in other 2-methylquinazolinone preparations.

Methyl *N*-acetylanthranilate *1a* disappeared from the reaction mixture with the same rate as the corresponding benzoyl derivative *1b* (the reactions were followed by TLC or analytical liquid column chromatography) and no dependence of pK_A values of the reacting amines was observed. The *N*-acylanthranilamide *5* and the amidine *9* can both

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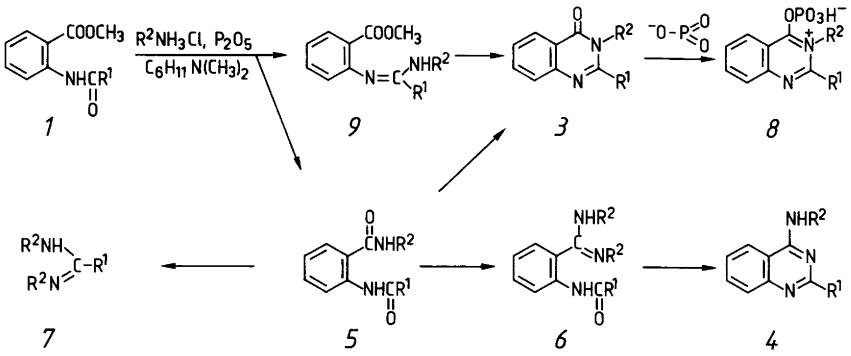
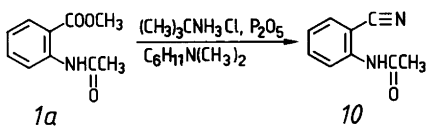
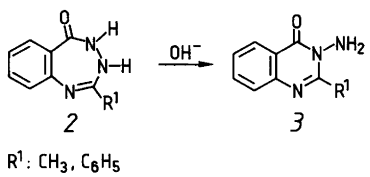


	R^1	R^2		R^1	R^2
3a	CH_3	H	*3j*	CH_3	$(CH_2)_7CH_3$
3b	CH_3	CH_3	*3k*	C_6H_5	H
3c	CH_3	CH_2CH_3	*3l*	C_6H_5	CH_3
3d	CH_3	$CH_2CH_2CH_3$	*3m*	C_6H_5	$CH_2CH_2CH_3$
3e	CH_3	$CH_2CH_2CH_2CH_3$	*3n*	C_6H_5	$CH_2CH(CH_3)_2$
3f	CH_3	$CH_2CH(CH_3)_2$	*3o*	C_6H_5	$CH(CH_3)CH_2CH_3$
3g	CH_3	$CH(CH_3)CH_2CH_3$	*3p*	C_6H_5	$CH_2CH_2CH_2N(CH_3)_2$
3h	CH_3	NH_2	*3q*	C_6H_5	NH_2
3i	CH_3	2-MeC_6H_5	*3r*	$CH_2CH_2CH_3$	CH_3

Scheme 1.



Scheme 2.



Scheme 3.

be postulated as intermediates for formation of *3*. Quinazolinones *3* have already been isolated in low yields in the synthesis of *5* from 2-phenyl-4*H*-3,1-benzoxazin-4-one by reaction with primary amines.[16] However, in similar reactions of 2-methyl-4*H*-3,1-benzoxazin-4-one the carboxylic acid corresponding to the amidine *9* (CH_3 replaced by H) was postulated as an intermediate for *3* which was the main product.[10] The intermediacy of *9* is also possible, because the reagent used in this investigation has previously been used for the synthesis of amidines from secondary carboxamides.[17] The identity of *7* was shown by an independent synthesis of *7m* from *N*-propylbenzamide by reaction with a mixture of phosphorus pentaoxide, propylamine hydrochloride, and *N*,*N*-dimethylcyclohexylamine.

In the preparation of 2-phenylquinazolinones, 4-quinazolinamines *4* were often isolated as by-products.

The 4-quinazolinamines *4* were easily detected in the NMR spectra. By treating the crude product with D_2O the N−H signal disappeared and the coupling between N−H and alkyl protons disappeared. *4* may be formed as suggested in Scheme 1: (i) *via 8* and subsequent amination at the 4-position and dealkylation at the 3-position, (ii) ring closure of *6* followed by dealkylation. In fact the amidine *6* (R^1, C_6H_5; R^2, Pr and *sec*-Bu) was isolated and in the MS spectrum of *6* a metastable decomposition product ($M^+ - C_6H_5CONH$)

Table 1. 4(3*H*)-Quinazolinones *3* and 4-quinazolinamines *4*.

R^1	R^2	Products (%)	Reaction conditions	
			Time/h	Temp./°C
CH_3	H	*3a* (33), *4*a (35)	1.5	250
CH_3	CH_3	*3b* (13), *4b* (65)	18	250
CH_3	$CH_2CH_2CH_3$	*3d* (33), *4d* (32)	20	240
CH_3	$CH(CH_3)CH_2CH_3$	*3g* (71), *4g* (11)	0.75	180
C_6H_5	H	*3k* (35), *4k* (33)	0.75	180
C_6H_5	CH_3	*4l* (89)	17	240
C_6H_5	$CH_2CH_2CH_3$	*3m* (53), *4m* (9)	0.75	180
C_6H_5	$CH_2CH(CH_3)_2$	*3n* (55), *4n* (8)	0.75	180
C_6H_5	$CH_2CH_2CH_2CH_3$	*4s* (62)	20	240

appeared from M^+. Route (i) implies that prolonged reaction times should increase the yields of *4*. As seen from Table 1, good yields of *4* were actually found when the reaction mixture was heated for 17–20 h. Under the severe reaction conditions a significant amount of the 4-methylaminoquinazolines *4b* and *4l* was observed in the NMR spectrum of the raw materials of *4d* and *4s*, respectively, indicating *N*,*N*-dimethylcyclohexylamine as a reaction partner. These by-products were not observed in the reactions at 180 °C. One experiment was made in which P_2S_5 was used instead of P_2O_5 trying to introduce a labile leaving group in the 4-position of *3*, but the yield of *4* was low.

In summary, P_2O_5-amine hydrochloride was found to be a versatile reagent in ring closure reactions of *N*-acylanthranilates, as exemplified by the commercial hypnotic methaqualone *3i* which was synthesized in 84 % yield. The ability of that reagent to effect direct transformations of oxy groups into amino groups constitutes a novel and useful method for preparation of 4-quinazolinamines.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a JEOL JWM-PMX 60 spectrometer. Mass spectra were obtained on a Varian MAT 311A and a Varian MAT CA 7A. The microanalyses were performed by Microanalytical Laboratory, University of Copenhagen.

Methyl 2-benzoylaminobenzoate 1b, m.p. 100–101 °C (EtOH) was prepared by treating the corresponding amine with benzoyl chloride in benzene and triethylamine. *Methyl 2-butyrylaminobenzoate 1c*, m.p. 71 °C, was prepared by heating the corresponding amine in butanoic anhydride and benzene.

Amine hydrochlorides were prepared by adding the amine dropwise to 2 equivalents of cooled 4 M HCl with stirring. The dry amine hydrochloride was obtained by stripping off the excess HCl.

4(3H)-Quinazolinones 3. General procedure. A mixture of methyl 2-acylaminobenzoate *1* (0.05 mol), amine hydrochloride (0.2 mol), P_2O_5 (0.21 mol) and *N*,*N*-dimethylcyclohexylamine (0.2 mol) was heated with stirring on a silicone-oil bath at 180 °C for 45 min. The mixture was allowed to cool to 100 °C and 2 M NaOH was poured into the reaction mixture until alkaline reaction (pH 8–9). Stirring was continued for 1 h. The water phase was extracted with CH_2Cl_2 (3 × 100 ml). CH_2Cl_2 was evaporated off and *N*,*N*-dimethylcyclohexylamine was distilled off at 10 mmHg. The residue was then recrystallized.

The following 4(3*H*)-quinazolinones were prepared (R^1, R^2; yield/%, m.p./°C, recrystn. solvent, lit. m.p.): *3c*, CH_3, CH_2CH_3, 85, 78–79, diisopropyl ether, 79–80;[10] *3d*, CH_3, $CH_2CH_2CH_3$, 78, 81–83, diisopropyl ether, 81–82;[11] *3e*, CH_3 $CH_2CH_2CH_2CH_3$, 92, 217–219 (m.p. of hydrochloride), –, 220–222[11] (m.p. of hydrochloride); *3f*, CH_3, $CH_2CH(CH_3)_2$, 92, 72–73, light petroleum, 71–72;[10] *3h*, CH_3, NH_2, 40, 150–151, –, 149.5;[12] *3i*, CH_3, *o*-tolyl, 84, 113–114, EtOH, 112.2–112.9;[13] *3l*, C_6H_5, CH_3, 41, 128–130, EtOH, 134–135;[4] *3q*, C_6H_5, NH_2, 41, 180, –, 182.5;[12] *3r*, $CH_2CH_2CH_3$, CH_3, 71, 76–77, EtOH, 77–78.[11]

The following 4(3*H*)-quinazolinones were prepared according to the general procedure, except that the reaction mixture was heated at 150 °C for 20 min (R^1, R^2, yield/%, m.p./°C, recrystn. solvent, lit. m.p.): *3a*, CH_3, H, 82, 240–242

(EtOH), 240–242;[10] *3b*, CH_3, CH_3, 65, 109, diisopropyl ether, 108–109.[11]

2-Methyl-4(3H)-quinazolinone 3a *and 2-methyl-4-quinazolinamine* 4a. Methyl *N*-acetylanthranilate *1a* (20 g) and ammonium chloride (21.2 g) were heated with P_2O_5 (50 g) and *N,N*-dimethylcyclohexylamine (46 g) for 1.5 h on a silicone-oil bath (250 °C) with stirring. The mixture was allowed to cool to 100 °C and 2 M NaOH was poured into the reaction mixture until alkaline reaction (p*H* 11) and stirring was continued for 1 h. The water phase was extracted with CH_2Cl_2 (3 × 100 ml). CH_2Cl_2 was evaporated and *N,N*-dimethylcyclohexylamine was distilled off at 10 mmHg and *4a* was obtained; m.p. 225–226 °C (MeOH), lit.[18] m.p. 230 °C. After extraction of *4a* the p*H* of the water phase was adjusted to 7 and extracted as above. The quinazolinone *3a* was obtained and recrystallized.

2-Methyl-3-(1-methylpropyl)-4(3H)-quinazolinone 3g and *2-methyl-N-(1'-methylpropyl)-4-quinazolinamine 4g* were prepared according to the general procedure except that 1-methylpropylamine hydrochloride (0.25 mol) was used. The residue obtained was distilled to give two fractions: 105–120 °C/0.1 mmHg (6.45 g) and 135–170 °C/0.1 mmHg (2.45 g). 2 g of the low boiling fraction yielded by preparative silica gel TLC, using CH_2Cl_2 for elution 1.6 g (71 %) *3g*; b.p. 106 °C/0.1 mmHg, n^{19} 1.5792; ^{1}H NMR, $\delta(CDCl_3)$: 0.90 (3H,t, J = 7.5 Hz), 1.65 (3H,d, J = 9.0 Hz), 2.14 (2H, sext, J = 9 Hz), 2.65 (3H,s), 4.34 (1H,m), 7.28–7.80 (3H,m), 8.20 (1H,d, J = 7.6 Hz): IR, (KBr) cm^{-1}: 1690 (C=O). UV (96 % EtOH) λ_{max} (log ε): 207 (4.33), 226 (4.42), 268 (3.95), 297 (3.48), 306 (3.56), 318 (3.45). Found: C 71.45; H 7.37; N 12.82. Calc. for $C_{13}H_{16}N_2O$: C 72.19; H 7.46; N 12.95.

4g precipitated from the high boiling fraction. The crystals were washed with light petroleum; m.p. 166–168 °C (disipropyl ether); ^{1}H NMR, (DMSO d_6): 0.95 (3H,t, J = 7 Hz), 1.25 (3H,d, J = 7 Hz), 1.64 (2H,q, J = 6 Hz), 2.52 (3H,s), 4.49 (1H,quint, J = 7.5 Hz), 7.3–7.8 (4H,m), 8.4 (1H,d, J = 7.5 Hz) MS *m/s* (%): 215 (M^+, 25), 159 (100); IR, (KBr) cm^{-1}: 3240, 3435; UV (96 % EtOH) λ_{max} (log ε): 211 (4.23), 238 (sh, 4.02), 289 (3.84), 318 (3.85). Found: C 72.10; H 7.90; N 19.23. Calc. for $C_{13}H_{17}N_3$: C 72.52; H 7.96; N 19.52.

2-Methyl-3-octyl-4(3H)-quinazolinone 3j was prepared from methyl *N*-acetylanthranilate *1a* (20 g, 0.1 mol), octylamine hydrochloride (46 g, 0.3 mol) P_2O_5 (60 g), and *N,N*-dimethylcyclohexylamine (50 ml), according to the general procedure in 88 % yield, m.p. 75 °C (cyclohexane). ^{1}H NMR; $\delta(CDCl_3)$: 0.88 (3H,t, J = 6 Hz), 1.33–1.60 (12H,m), 2.65 (3H,s), 4.10 (2H,t, J = 8 Hz), 7.27–7.80 (3H,m) 8.3 (1H,d, J = 7.5 Hz); IR, (KBr) cm^{-1}: 1680 (C=O). Anal. $C_{17}H_{24}N_2O$: C, H, N.

2-Phenyl-4(3H)-quinazolinone 3k and *2-Phenyl-4-quinazolinamine* 4k were prepared from *1b* (12.75 g, 0.05 mol), ammonium chloride (13 g, 0.25 mol), P_2O_5 (30 g), and *N,N*-dimethylcyclohexylamine (35 ml) by heating on an oil bath (180 °C) for 40 min with stirring. The mixture was allowed to cool to 100 °C. Water (400 ml) was poured into the reaction mixture and stirred for 90 min. The precipitate was filtered off, dried, suspended in 2 M NaOH and extracted with CH_2Cl_2 (3 × 50 ml). CH_2Cl_2 was evaporated and *4k* was obtained; m.p. 146–147 °C (EtOH), lit.[19] m.p. 145.5–146.5 °C. After extraction of *4k* the pH of the water phase was adjusted to 8. Extraction and evaporation as above yielded *3k*, m.p. 241–242 °C (EtOH), lit.[14] m.p. 239.

2-Phenyl-3-propyl-4(3H)-quinazolinone 3m, *2-phenyl-N-propyl-4-quinazolinamine 4m*, *N,N'-dipropylbenzamidine 7m*, and *2-benzoylamino-N,N'-dipropylbenzamidine 6m* were prepared from *1b* (0.1 mol, 25.5 g), propylamine hydrochloride (0.3 mol, 28.5 g), P_2O_5 (60 g), and *N,N*-dimethylcyclohexylamine (50 ml) according to the general procedure. The quinazolinone *3m* (53 %) crystallized from the residue by addition of light petroleum, m.p. 88–91 °C (toluene); ^{1}H NMR, $\delta(CDCl_3)$: 0.76 (3H,t, J = 7.4 Hz), 1.66 (2H, sext; J = 7.6 Hz), 3.97 (2H,t, J = 8.4 Hz), 7.35–7.85 (3H,m) 7.60 (5H,s), 8.36 (1H,d, J = 8 Hz; IR (KBr) cm^{-1}: 1677 (C=O); UV (96 % EtOH) λ_{max} (log ε): 208 (4.54), 227 (4.46), 303 (3.99), 327 (3.73), 340 (sh 3.60); Anal. $C_{17}H_{16}N_2O$: C, H, N. The light petroleum phase was distilled into two fractions: (i) 85–110 °C/0.1 mmHg to give *7m* (2 %). MS: Found: *m/e*, M^+ = 204.1626. Calc. for $C_{13}H_{20}N_2$: *m/e* 204.1626. *7m* was also prepared from *N*-propylbenzamide as shown below. (ii) 185–220 °C/0.1 mmHg. This fraction was subjected to silica gel preparative TLC using CH_2Cl_2 for elution and *4m* and *6m* were obtained. *4m* (9 %): m.p. 104–106 (ligroin 80–100 °C); ^{1}H NMR; $\delta(CDCl_3)$: 1.03 (3H,t, J = 7 Hz), 1.74 (2H,sext, J = 7 Hz), 3.72 (2H,q; J = 6.7 Hz), 5.80 (1H, N–H), 7.20–8.0 (7H,m), 8.50–8.70 (2H,m); MS; *m/e* (%): 263 (M^+, 40), 221 (100); IR; (KBr) cm^{-1} 3440, 3320; UV (96 % EtOH) λ_{max} (log ε): 207 (4.57), 256 (4.49), 322 (4.08). Anal. $C_{17}H_{17}N_3$: C, H, N. *6m* (5 %); ^{1}H NMR, $\delta(CDCl_3)$: 0.89 (6H,t, J = 7.5 Hz), 1.6 (4H,m), 3.13 (4H,t, J = 7 Hz), 7.0–8.6 (10H,m). MS; *m/e* (%): 323 (M^+, 4) 235 (100). Found: M^+, 323.1952. Calc. for $C_{20}H_{25}N_3O$: *m/e* 323.1997.

N,N'-Dipropylbenzamidine 7m was prepared from *N*-propylbenzamide (8.15 g, 0.05 mol) and propylamine hydrochloride (24 g, 0.25 mol), P_2O_5 (30 g), and *N,N*-dimethylcyclohexylamine (35 ml) by heating on a silicone-oil bath at 240 °C for 90 min with stirring. The mixture was then worked up as in the general procedure for *3*. Distillation

82 °C/0.15 mmHg afforded 9 g (88 %) of *7m:* m.p. 30 °C ^{1}H NMR $\delta(CDCl_3)$: 0.90 (6H,t, $J=7$ Hz), 1.56 (4H,sext, $J=6.5$ Hz), 3.13 (4H,t, $J=7$ Hz), 7.33 (5H,s). MS, *m/e* (%) 204 (M^+, 24), 203 (39), 175 (14), 161 (23), 146 (13), 120 (22), 118 (56), 104 (100), 77 (24); Anal. $C_{13}H_{20}N_2$: C, H, N.

2-Phenyl-3-(2-methylpropyl)-4(3H)-quinazolinone 3n, N,N'-*bis(2-methylpropyl)benzamidine 7n*, and *2-phenyl*-N-*(2-methylpropyl)-4-quinazolinamine 4n* were prepared according to the general procedure. The residue obtained was distilled into three fractions. (i) 110 °C/0.2 mmHg *7n* (0.8 g); ^{1}H NMR, $\delta(CDCl_3)$: 0.89 (12H,d, $J=6.7$ Hz), 1.77 (2H,m), 3.0 (4H,d, $J=7$ Hz), 7.32 (5H,s); IR; (KBr) cm^{-1}: 1635; MS, *m/e* (%) 232.1919 (M^+, 17). Calc. for $C_{15}H_{24}N_2$: *m/e* 232.1939.

(ii) 180 °C/0.1 mmHg. The fraction was subjected to silica gel preparative TLC using CH_2Cl_2 for elution and *3n* (55 %) was obtained, m.p. 58 – 60 °C; ^{1}H NMR $\delta(CDCl_3)$: 0.7 (6H,d, $J=6.5$ Hz), 1.9 (1H,sext, $J=7.2$ Hz), 4.0 (2H,d, $J=7.2$ Hz) 7.49 (5H,s) 7.1 – 7.95 (3H,m), 8.3 (1H,d, $J=7.6$ Hz); IR, (KBr) cm^{-1} 1670 (C=O). Found: C 76.96; H 6.42; N 9.59. Calc. for $C_{18}H_{18}N_2O$: C 77.67; H 6.52; N 10.07.

(iii) 200 °C/0.1 mmHg. The fraction was subjected to silica gel column chromatography, using CH_2Cl_2 for elution and *4n* (8 %) was obtained; m.p. 95 – 97 °C; ^{1}H NMR, $\delta(CDCl_3)$: 1.03 (6H,d, $J=6.8$ Hz), 2.03 (1H,sext, $J=7$ Hz), 3.56 (2H,t, $J=6.5$ Hz), 6.15 (1H, N – H), 7.3 – 9.5 (7H,m), 8.50 – 8.75 (2H,m); MS; *m/e* (%): 277 (M^+, 20), 221 (100); IR; (KBr) cm^{-1}: 3440, 3300. Anal. $C_{18}H_{19}N_3$: C, N, H.

2-Phenyl-3-(1-methylpropyl)-4(3H)-quinazolinone 3o and *2-benzoylamino*-N,N'-*bis(1-methylpropyl)-benzamidine 6o* were prepared according to the general procedure, except that 0.25 mol *sec*-butylamine hydrochloride was used. The residue was distilled. (i) 155 – 160 °C/0.1 mmHg yielded *3o* (61 %); ^{1}H NMR, $\delta(CDCl_3)$: 0.70 (3H,t, $J=7.2$ Hz), 1.63 (3H,d, $J=7.2$ Hz), 2.32 (2H,sext, $J=7.2$ Hz), 4.88 (1H,sext, $J=7.2$ Hz), 7.25 – 7.90 (8H,m), 8.35 (1H,d, $J=7$ Hz). IR; (KBr) cm^{-1} 1670 (C=O). Anal: $C_{18}H_{18}N_2O$: C, H, N. (ii) 190 – 240 °C/0.1 mmHg (1 g). From this fraction *6o* (5 %) precipitated. The crystals were washed with light petroleum; m.p. 109 – 112 °C; ^{1}H NMR, $\delta(CDCl_3)$: 0.83 (6H,t, $J=7$ Hz), 1.10 (6H,d, $J=6.5$ Hz), 1.37 (4H,q, $J=7.2$ Hz), 8.83 (1H,d, $J=7.7$ Hz); MS, *m/e* (%) 351 (M^+, 14), 277 (14), 231 (26), 152,0(231^2/351), 223 (83), 162 (12), 145 (21), 119 (24), 104 (100), 77 (69), 72 (33). MS: *m/e* 351.2296. Calc. for $C_{22}H_{29}N_3O$: *m/e* 351.2310. UV (96 % EtOH) λ_{max} (log ε): 215 (4.37), 230 (sh,4.31), 260 (sh,4.05).

3-(3-Dimethylaminopropyl)-2-phenyl-4(3H)-quinazolinone 3p was prepared from *1b* (10 g 0.04 mol), according to the general procedure. The residue obtained was distilled 180 – 225 °C/0.1 mmHg to give *3p*, (68 %), m.p. 85 – 87 °C (ether).

^{1}H NMR, $\delta(CDCl_3)$: 1.5 – 2.3 (4H,m), 2.5 (6H,s), 4.7 (2H,t, $J=6.8$ Hz), 7.33 – 7.6 (9H,m), 8.34 (1H,d, $J=7$ Hz). IR; (KBr) cm^{-1}: 1673 (C=O). Anal: $C_{19}H_{21}N_3O$: C, H, N.

2,N-*Dimethyl-4-quinazolinamine* 4b. The general procedure for preparation of *3* was followed, except that the mixture was heated for 18 h at 250 °C. The residue was distilled 125 – 155 °C/0.1 mmHg; m.p. 155 – 157 °C (diisopropyl ether); pK_A 7.3, lit.[20] pK_A 7.4. MS: *m/e* (%) 173 (M^+, 100), 103 (43), lit.[21] MS: *m/e* (%) 173 (M^+, 100), 103 (64).

2-Methyl-N-*propyl-4-quinazolinamine* 4d. The general procedure for preparation of *3* was followed, except that propylamine hydrochloride (0.25 mol) was used and the mixture was heated for 20 h at 240 °C. The ^{1}H NMR spectrum showed a considerable amount of *3d* and *4b* in the raw product. By preparative silica gel TLC with ether for elution *4d* was purified: m.p. 171 – 173 °C (ligroin 100 – 140 °C); ^{1}H NMR, $\delta(CDCl_3)$: 1.02 (3H,t, $J=7$ Hz), 1.75 (2H,sext, $J=7.5$ Hz), 2.66 (3H,s), 3.64 (2H,q, $J=6.5$ Hz), 6.06 (1H,NH), 7.3 – 7.8 (4H,m). MS, *m/e* (%) 201 (M^+, 34), 159 (100). IR (KBr) cm^{-1}: 3222, 3420. Found: C 70.79; H 7.31; N 20.65. Calc. for $C_{12}H_{15}N_3$: C 71.61; H 7.51; N 20.88.

N-*Methyl-2-phenyl-4-quinazolinamine* 4l. The general procedure for preparation of *3* was followed, except that methylamine hydrochloride (0.25 mol) was used and the mixture was heated for 17 h at 240 °C. The residue was distilled 225 °C/0.08 mmHg and *4l* was obtained; m.p. 126 – 127 °C (toluene/diisopropyl ether) ^{1}H NMR, $\delta(CDCl_3)$: 3.23 (3H,d, $J=5.3$ Hz), 5.82 (1H,N – H), 7.18 – 8.0 (7H,m), 8.53 – 8.70 (2H,m); IR; (KBr) cm^{-1}: 3445, 3300. Anal. $C_{15}H_{13}N_3$: C, N, H.

N-*Butyl-2-phenyl-4-quinazolinamine* 4s. The general procedure for preparation of *3* was followed, except that butylamine hydrochloride (0.3 mol) was used and the mixture was heated for 20 h at 240 °C. The residue was distilled 190 – 205 °C/0.1 mmHg to give *4s*; m.p. 100 – 103 °C (ligroin 80 – 100 °C); ^{1}H NMR, $\delta(CDCl_3)$: 0.97 (3H,t, $J=6$ Hz), 1.17 – 1.90 (4H,m), 3.73 (2H,q, $J=6$ Hz), 5.76 (1H,N – H), 7.3 – 8.0 (7H,m), 8.53 – 8.70 (2H,m); IR (KBr) cm^{-1}: 3335, 3440. Anal. $C_{18}H_{19}N_3$: C, H, N.

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