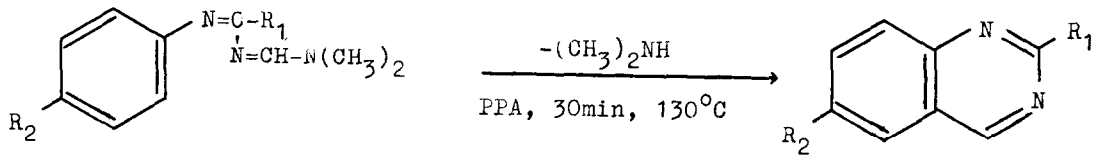
Tetrahedron Letters,Vol.24,No.40,pp 4351-4354,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

NEW SYNTHESIS OF QUINAZOLINE AND BENZOQUINAZOLINE DERIVATIVES

Stefan K. Robev
Department of Pharmacology, Faculty of Medicine
Sofia 1431, Bulgaria

Summary: The synthesis of 2-substituted quinazolines II from 1,3-diazabutadienes I and of benzoquinazolines IV and VI from N-naphthylsubstituted amidines III and V the yields being up to 90% is reported.

1-Arylated 4-dimethylamino-1,3-diazabutadienes I are easy available from the corresponding N-arylamidines and dimethylformamide diethylacetal (DMFA)[1]. In the present work we use I as starting material for the synthesis of substituted quinazolines II. We have found that on heating with polyphosphoric acid (PPA) at 130-150°C I underwent cyclization to II with liberation of dimethyl - amine according to the following scheme

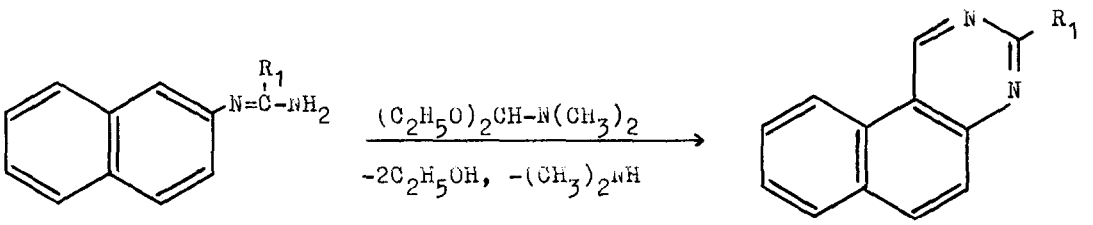


Ia-c IIa-c

R_1	R_2	I	mp C°	II	mp C°	Yield %
C_6H_5	H	a	99[1]	a	103	72
4-FC_6H_4	CH_3	b	89	b	151	69
4-ClC_6H_4	CH_3	c	85	c	176	75

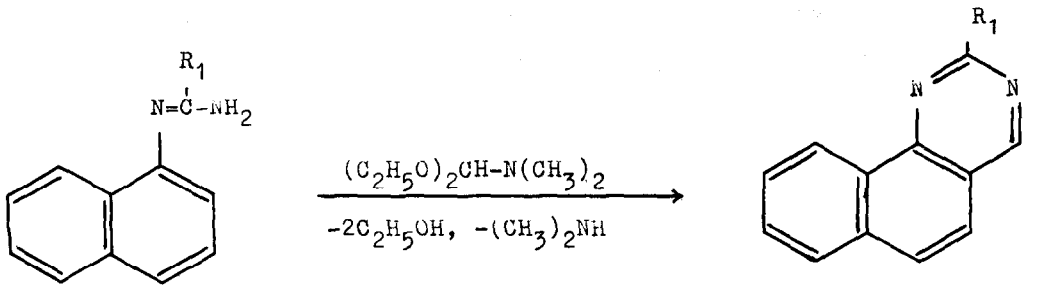
When we tried the reaction with 1-(4-nitrophenyl)-2-phenyl-4-dimethylamino-1,3-diazabutadiene no amounts of the expected 2-phenyl-6-nitroquinazoline were obtained the main product being nonreacted 1,3-diazabutadiene.

Our further experiments showed that the scope of the newly found quinazoline synthesis can be successfully extended to the benzoquinazoline series. In this case there was no need of preliminary preparation of the corresponding 1-naphthyl-4-dimethylamino-1,3-diazabutadienes and the benzoquinazoline derivatives were directly obtained simply by refluxing the N-naphthylsubstituted amidines with DMFA. 3-substituted benzo/f/quinazolines IV were synthesised in high yields from N-(2-naphthyl)-amidines III



IIIa-c IVa-c

N-(1-naphthyl)-amidines V and DMFA gave 2-substituted benzo/h/quinazolines VI whose formation, as could be concluded from general considerations, proceeded more smoothly than the formation of IV.

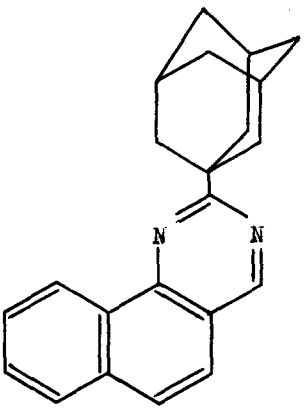


Va-c VIa-c

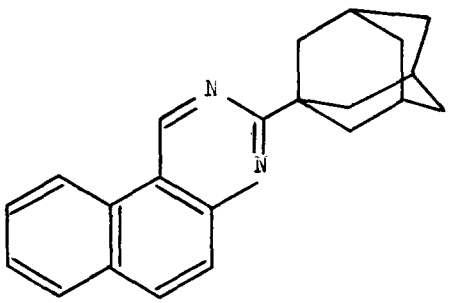
It is worth mentioning that in all cases when N-(2-naphthyl)-amidines III were reacted with DMFA only one of the two possible isomers was isolated, namely the benzo/f/quinazoline derivative. We were not able to detect any amounts of the corresponding benzo/g/quinazoline.

R_1	IV	mp C°	yield %	VI	mp C°	yield %
C_6H_5	a	135[3]	73	a	143	90
$4\text{-}ClC_6H_4$	b	210	65	b	149	86
$4\text{-}CH_3C_6H_4$	c	170	62	c	138	80

The cyclization of N-naphthylsubstituted amidines to benzoquinazolines by means of DMFA went successfully even with such comparatively bulky substituent as the adamantyl residue. Starting from the corresponding N-naphthylamidines of the adamantane-1-carboxylic acid [4] we synthesised 2-(1-adamantyl)-benzo/h/quinazoline VII[5] and 3-(1-adamantyl)-benzo/f/quinazoline VIII[6].



VII



VIII

Our attempts to prepare the quinazoline derivatives II,IV and VI from the amidines using formamide instead of DMFA gave positive results only in the case of V which yielded VI when boiled with formamide for 10 min.

The structures of the reported compounds were assigned on the basis of elemental microanalysis and spectral data or by comparison with authentical specimens.

2-(4-Fluorophenyl)-6-methylquinazoline IIb. 2,83g (10 mmole) Ib were heated with 10g PPA for 30 min. at 130-140°C. After cooling the reaction mixture was treated with 50 ml of water, made alkaline with 15% KOH and filtered. The obtained white substance was recrystallised from benzene/n-heptane and melted at 150-151°C. The yield of IIb was 1,64g (69%). $C_{15}H_{11}FN_2$, M^+ 238; UV(ethanol)λ max (log e)nm 263(4,59), 286sh(4,11), 330(3,53), 342sh(3,39).

2-Phenylbenzo/h/quinazoline VIa. 2,46g (10 mmole) Va were refluxed for one hour with 10 ml of DMFA, the solution was cooled and after addition of 10 ml ethanol the separated yellowish crystals were filtered and washed with ethanol. Mp 141-142°C (benzene/n-heptane). The yield of VIa was 2,30g (90%). $C_{18}H_{12}N_2$, M^+ 256; UV(ethanol)λ max(log e)nm 237(4,47), 266(4,48), 312(4,22),344 (3,58), 364(3,53).

R E F E R E N C E S & N O T E S

1. M.Nishi, S.Tanimoto, M.Okano, R.Oda, Yuki Gosei Kagaku Kyokai Shi, 27,/7/, (1969)754; Chem.Abstr.,71(1969)101438v.
2. M.L.Tamayo, R.Madronero, G.G.Munoz, J.M.Marzal, M.Stud, Chem.Ber.,94(1961), 199.
3. M.A.Mikhaleva, G.N.Tchernikova, V.P.Mamaev, Khimiya Gheterotz.Soedinenii , (1978)1265; Chem.Abstr., 90(1979)38858g.
4. N-(1-Naphthyl)-amidine of the adamantane-1-carboxylic acid: $C_{21}H_{24}N_2$ M^+ 304 mp 238-240°C;IR(nujol) 3455, 3355(NH), 1645(C=N) cm^{-1}. N-(2-Naphthyl)-amidine of the adamantane-1-carboxylic acid: $C_{21}H_{24}N_2$, M^+ 304; mp 217-218° C; IR(nujol) 3450, 3350(NH), 1650(C=N) cm^{-1}.
5. VIi: $C_{22}H_{22}N_2$, M^+ 314; mp 144-145°C; yield 78%; UV(ethanol)λ max(log e) nm 219(4,40), 238sh(4,42), 255(4,57), 294(3,99), 321(3,38), 336(3,51),352(3,51)
6. VIII: $C_{22}H_{22}N_2$, M^+ 314; mp 149-152°C; yield 80%; UV(ethanol)λmax(log e) nm 227(4,55), 256sh(4,33), 263(4,34), 295sh(3,77), 327(3,30), 343(3,29).

(Received in UK 19 May 1983)