Synthesis, Alkylation and Ring Opening of Two Differently Fused Pyridoquinazolones

Géza Timári, György Hajós and András Messmer*

Central Research Institute for Chemistry,
H-1525 Budapest, P. O. Box 17, Hungary

Received March 26, 1990

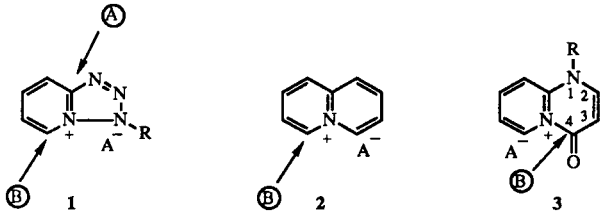
Alkylation of two differently (linearly and angularly) fused pyridoquinazolones **7** and **10** have been investigated. The linear **7** afforded exclusively *N*-alkyl derivatives **4**, whereas the angular **10** gave both *N*- and *O*-alkyl products **5** and **11**, respectively depending on the type of the reagent used. Reaction of the new alkylated salts **4**, **5**, and **11** with nucleophiles was found strongly dependent on the fusion type of the substrates: the reaction of the linear salt **4** led to opening of the pyrimidine moiety, and the angularly fused salts **5**, **11** reacted at the pyridine site to give quinazolyldieneamines **17**, **19**. Regioselectivities of the observed conversions were interpreted on FMO basis.

J. Heterocyclic Chem., **27**, 2005 (1990).

Some of our recent results indicated [1,2] that treatment of pyridine-fused azolium salts (*i.e.* 5-membered hetaryl systems; *e.g.* **1**) with nucleophiles can conveniently be applied for preparation of azolyldiene derivatives. These activated olefins formed through a retroelectrocyclic ring opening of the pyridine ring are of push-pull type compounds and proved to be excellent precursors for several ring closure reactions [3,4,5].

As a continuation of these studies we decided to make an effort to extend these reactions for fused azinium (*i.e.* 6-membered) systems. Synthesis and nucleophilic reaction of the simplest bridge-head containing azinium system: quinolizinium cation (**2**) has been investigated by different research groups [6,7]. An additional fused azinium salt: the oxo derivative of the pyrido[1,2-*a*]pyrimidinium system **3** has also been studied in this respect [8,9].

Scheme 1

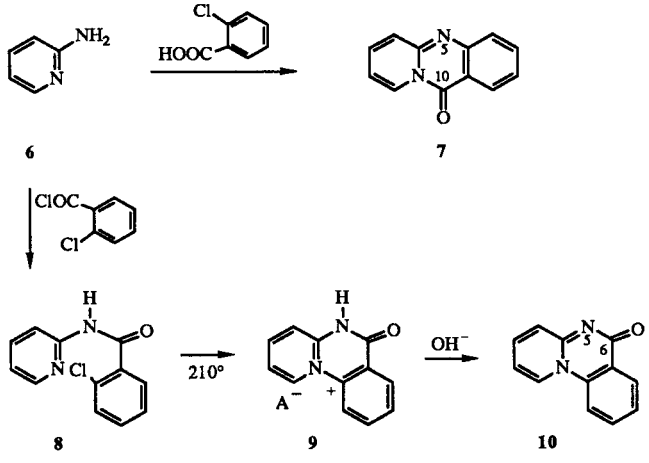


While azolium salt **1** was found to be attacked by nucleophiles mostly or exclusively at two sites (A and B) [2], studies on azinium salt **2** revealed [7] that attack type B is predominant and thus the pyridine ring opened up to a diene substituted by the group deriving from the reagent. Studies on fused pyrimidinium system **3** where the two "B-type" carbon atoms (*i.e.* C-4 and C-6) are located in two different hetero rings, showed that position 4 activated by the oxo group is superior to 6, and therefore opening of rather the pyrimidine than the pyridine ring took place providing thereby products different from dienes.

Scheme 2

Since we sought for extension of the diene formation reaction of new fused azinium salts, we decided now to prepare two differently annelated benzologues of ring system of **3**: oxo substituted fused quinazolium salts **4** and **5**. In the angularly fused **5**, C-10a deriving from C-4 of the pyrimidine ring is a bridge-head atom and therefore the ring opening of the pyrimidine moiety observed with **3** can not take place. Linearly fused benzologue **4**, however, still implies the reactive carbon atom similarly to bicycle **3**, and its study seemed therefore also as a comparison of interest.

Scheme 3



A feasible route to both selected model compounds seemed to be the synthesis of the parent neutral quinazolones **7** and **10** and their subsequent alkylation. The

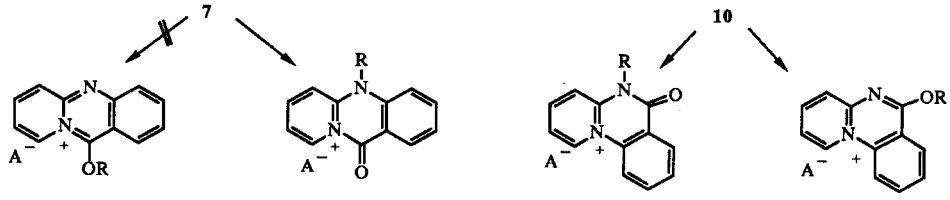
linearly fused pyracridone **7** was prepared according to an early literature procedure starting from 2-aminopyridine [10]. The analogous angularly fused isomer **10** known earlier only in polysubstituted form was synthesized [12] as follows: 2-aminopyridine (**6**) was acylated first with *o*-chlorobenzoyl chloride and the resulting amide was refluxed at elevated temperature to give the hydrochloride salt of the ring closed compound **9**; the free base was then simply obtained upon neutralization.

Alkylation experiments with the two differently fused pyridoquinazolones **7** and **10** were carried out by using three different reagents of hard and soft character [13]. The two ring systems showed, interestingly, entirely different behaviour.

While linear compound **7**, regardless of the nature of the reagent, gave the desired *N*-alkyl compounds **4** only (*i.e.* **12** was not formed), the angularly fused **10** afforded both *N*-alkyl and *O*-alkyl salts **5** and **11**, respectively depending on the type of the alkylating agent used. Thus, the soft methyl iodide gave pure *N*-alkyl product **5**, and *O*-alkyl derivative **11** was obtained predominantly with the typically hard oxonium reagent.

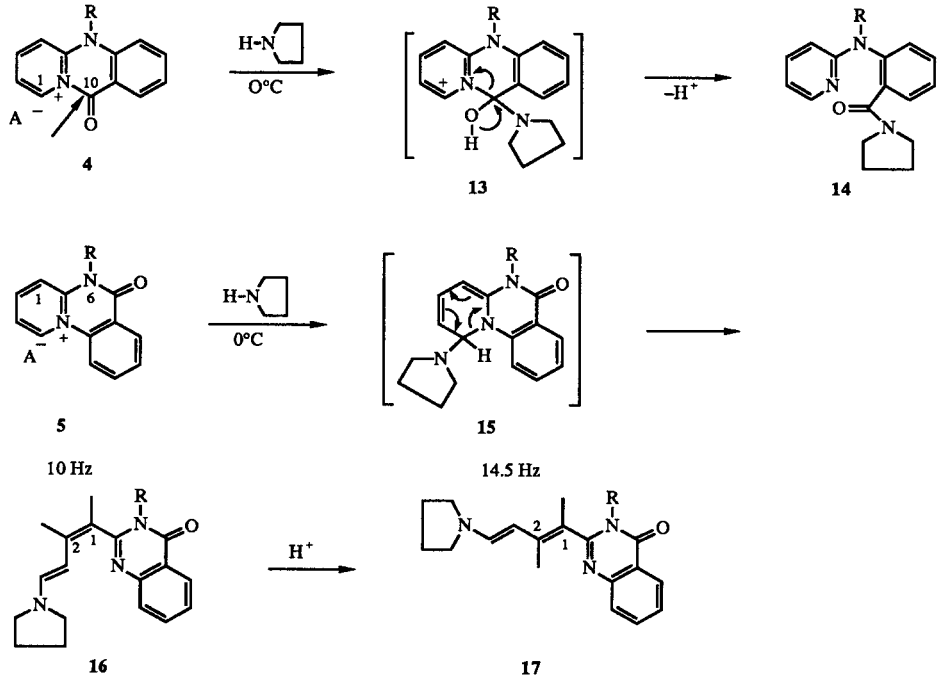
Reactivities of the linearly and angularly fused *N*-alkyl oxopyridoquinazolinium salts **4** and **5** towards nucleophiles were found to be different in accordance with our expectation. The linear *N*-methylpyridoquinazolonium salt (**4**) reacted with the carbonyl carbon atom (*i.e.* with C-10) and - probably through intermediate **13** - gave rise to

Scheme 4



12	4	reagent	5	11
–	–	CH_3I	100	0
0	100	Me_2SO_4	75	25
0	100	$Et_3O^+BF_4^-$	16	84

Scheme 5



amide derivative **14**. This reaction is reminiscent of that of the bicyclic analogue **3** cited above. Compound **5**, on the other hand, implying the corresponding carbon atom as a bridge-head atom, reacted at the other carbon atom adjacent to the positive nitrogen. In this reaction, intermediate **15** was possibly formed first which underwent a retro-electrocyclization to yield quinazolyldieneamine **16** as revealed by its ^{1}H-nmr spectrum. Similarly to earlier observations [1,7a], the 1-*cis*-3-*trans* isomer **16** was detected as the primary product undergoing a slow isomerization to the all-*trans* diene **17** when standing at room temperature for a longer period or when treated with protic solvents (even with deuteriochloroform due to the traces of proton). The isomerization of **16** to **17** was unambiguously showed by the change of $J_{1,2}$ coupling constant from 10 Hz to 14.5 Hz [7b].

As the alkylation experiments revealed, alkoxy derivative **11** could also be prepared by the choice of the appropriate reagent. Reactivity of this angularly fused compound **11** having heteroaromatic electronic structure unlike **4** and **5** towards nucleophiles seemed also of interest. Ethoxy salt **11a** was found undergo nucleophilic substitution readily and thus the methoxy **11b** and pyrrolidino **18** salts could be obtained under mild conditions in good yield. Use of an excess of the amine reagent and raise of the reaction temperature to 25°, however, gave rise to an additional reaction in which the substitution was followed by ring opening to yield all-*trans* quinazolyldieneamine **19** in good yield.

Comparison of the behaviour of the linear and angular systems concerning both the synthesis and the reactivity of the azinium salts towards nucleophiles reveals that in most cases selective reactions take place. For rationalization of these selectivities, we carried out semiquantitative calculations (AM1) [14] for the model compounds and applied the FMO theory.

Scheme 6

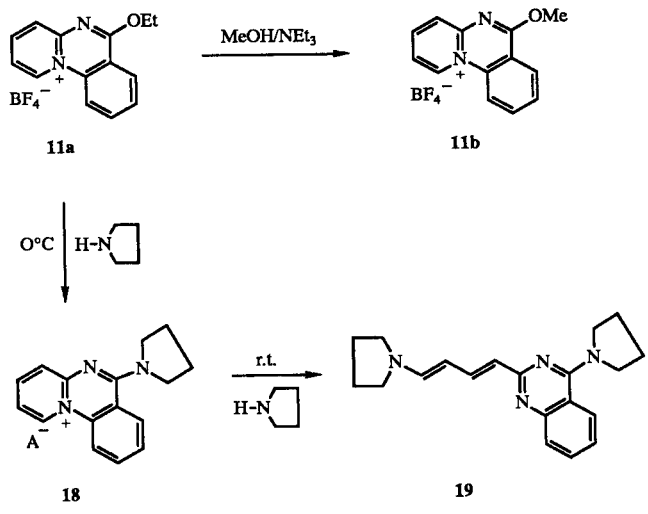


Table 1

Compound	atom	q_{NET}	c_n-HOMO's c_s	c_{px}	c_{py}	Σc^2
7	N	-0.21	0.33	0.36	0.51	0.50
	O	-0.34	0	0.06	0.08	0.01
10	N	-0.27	0.16	0.51	0.20	0.33
	O	-0.30	0	0.53	0.25	0.34

q_{NET} and Σc^2 values of nitrogen an oxygen atoms available for alkylating reagents in fused quinazolones in **7** and **10** calculated by AMI [14] method, Geometry was optimized, 150 SCF iterations were carried out in both cases.

In Table 1, we collected the q_{NET} charges of the two target atoms of the alkylation (*N* and *O*) and the coefficients of the highest occupied orbital that has a non negligible density only in the plane of the hetero ring (called as $c_{n\text{-HOMO}}$'s). Recently we have found that these values can be better correlated with the preference of the electrophilic attack than the c_{HOMO}'s having a π type symmetry, because the electrophilic attacks proceed in the plane of the ring [15]. Comparison of the c^2 values calculated for the linearly fused **7** and angularly fused **10** cases shows that the attack of the oxygen atom is very improbable in the linear case **7** because of the very low c values, and attack of the nitrogen atom with considerably high coefficient can be expected. The situation is entirely different with the angularly fused compound **10**: here both q_{NET} and c^2 values are almost the same and therefore a dependency on the nature of the reagent can be anticipated. The experimental findings seem to be in satisfactory correlation with these predictions: *O* alkylation of **7** failed totlally whereas both heteroatoms (*N* and *O*) of **10** underwent alkylation yielding *N*-and *O*-alkyl products in different ratio depending on the hard or soft character of the reagent.

Table 2

Compound	pyridyl carbon c_{LUMO}	pyridyl carbon q_{NET}	carbonyl carbon c_{LUMO}	carbonyl carbon q_{NET}
4b	0.34	+0.17	0.10	+0.32
5b	0.46	+0.14	0.02	+0.35

AMI calculations [14] for fused oxoquinazolium salts **4b** and **5b**: c_{LUMO} coefficients and q_{NET} charges of the pyridyl carbon atoms (C-1) and carbonyl carbon atoms (C-10 and C-6, respectively). Geometry was optimized, 150 iterations were carried out in both cases.

As the experiments showed, significant difference between behaviour of the linear and angular oxopyridoquinazolium salts **4** and **5** toward nucleophiles was found and selectively two different types of ring openings were observed in the two cases. A possible rationalization of this finding can be obtained by inspection of the figures listed in Table 2: we compared here the c_{LUMO} coefficients and q_{NET} charges of the two types of carbon atoms at which the

observed reactions took place. We can conclude from these data that, concerning the positive net charge, the carbonyl carbon atom is superior to the pyridine-carbon atom in both cases. Interestingly enough, however, the c_{LUMO} coefficient for the carbonyl carbon atom vanishes in the angular case and is still reasonably high for the pyridine carbon atom. This may be accounted for the fact that the pyridyl carbon atom is attacked selectively to yield diene **16** as final product.

The authors feel that these results and interpretation provide a novel contribution to understanding the "heteroaromatic annelation effect" [16].

EXPERIMENTAL

Melting points were determined on a Büchi apparatus and are uncorrected. The ir spectra were recorded with a Specord 75 IR apparatus. The nmr spectra were registered on a Varian XL-400 equipment (TMS as internal standard). The quantum chemical calculations were carried out by PC AT computer.

2-*o*-Chlorobenzoylaminopyridine (**8**).

2-Chlorobenzoyl chloride (10 g, 57 mmoles) was added dropwise to a stirred solution of 2-aminopyridine (5.4 g; 57 mmoles) in dry pyridine (30 ml) at 10°. The mixture was stirred for 1 hour and was then poured into ice water (150 ml). The precipitated crystals were filtered off and recrystallized from ethanol to give **8** (11 g, 83%) as colorless prisms, mp 160-161°; ir (potassium bromide): 1665, 1575, 1525, 1430, 1310 cm^{-1}; ^{1}H-nmr (TFA): δ 8.8-8.4 (2H, m), 7.9-7.4 (6H, m).

Anal. Calcd. for $C_{12}H_9ClN_2O$ (232.64): C, 61.94; H, 3.89; N, 12.03. Found: C, 61.95; H, 3.97; N, 12.00.

Pyrido[1,2-*a*]quinazolin-11-ium-6(5*H*)-one Chloride (**9**).

A solution of *o*-chlorobenzoylaminopyridine **8** (8 g, 34 mmoles) in tetraline (40 ml) was stirred at reflux temperature for 12 hours. The separated solid was collected by filtration and washed with benzene to give 7.6 g of product (95%) as colorless crystals, mp >350°; ir (potassium bromide): 1695, 1615, 1455, 1330 cm^{-1}; ^{1}H-nmr (TFA): δ 9.6 (1H, d), 8.9-8.0 (7H, m).

Anal. Calcd. for $C_{12}H_9ClN_2O$ (232.64): C, 61.94; H, 3.89; N, 12.03. Found: C, 61.86; H, 3.90; N, 11.89.

Pyrido[1,2-*a*]quinazolin-6(11*H*)-one (**10**).

Pyrido[1,2-*a*]quinazolin-11-ium-6(5*H*)-one chloride (**9**, 3.75 g, 12.8 mmoles) was dissolved in 1*N* aqueous sodium hydroxide solution (12.8 ml, 12.8 mmoles), and the resulting solution was extracted with dichloromethane (75 ml). The residue obtained by evaporation was recrystallized from a mixture of benzene-petroleum ether (1:1) to give **10** (2.8 g, 88%) as colorless crystals, mp 255-256°; ir (potassium bromide): 1600, 1505, 1440, 1325 cm^{-1}.

Anal. Calcd. for $C_{12}H_8N_2O$ (196.19): C, 73.46; H, 4.10; N, 14.27. Found: C, 73.28; H, 3.95; N, 14.15.

General Procedure for Alkylation of Fused Quinazolones **7** and **10**.

Method A. Methylation with Methyl Iodide.

A solution of the appropriate oxo compound (2 mmoles) in absolute acetonitrile (5 ml) was refluxed with methyl iodide (2 ml) for 4 hours. The precipitated crystals were filtered off and washed with ether to give crude iodide salt.

Method B. Methylation with Dimethyl Sulfate.

A solution of the appropriate oxo compound (2 mmoles) in dimethyl sulfate (5 ml) was stirred at 120° for 6 hours. The reaction mixture was evaporated, the residue was dissolved in water (5 ml) and this solution was mixed with 70% perchloric acid. The resulting crude perchlorate salt precipitated in the form of colorless crystals.

Method C. Alkylation with Triethyloxonium Tetrafluoborate.

A solution of the appropriate oxo compound (2 mmoles) in absolute dichloromethane (5 ml) was stirred at 20° with 0.6 g (3.3 mmoles) of triethyloxonium tetrafluoborate for 20 hours. The reaction mixture was treated with ether (10 ml), and the resulting precipitate was filtered off.

5-Ethylpyrido[2,1-*b*]quinazolin-10(5*H*)-one-11-ium Tetrafluoborate (**4a**).

The crude product obtained from piracridone **7** by using method C was recrystallized from ethanol to give product **4a** (73%) as pale yellow needles, mp 278-279°; ir (potassium bromide): 1730, 1620, 1600, 1515, 1475, 1130; ^{1}H-nmr (perdeuterioacetonitrile): δ ppm 9.35 (1H, d), 8.8-7.7 (7H, m), 4.7 (2H, q), 1.6 (3H, t).

Anal. Calcd. for $C_{14}H_{13}BF_4N_2O$ (312.04): C, 53.89; H, 4.19; N, 8.97. Found: C, 53.75; H, 4.10; N, 8.99.

5-Methylpyrido[2,1-*b*]quinazolin-10(5*H*)-one-11-ium Perchlorate (**4b**).

The crude product obtained from piracridone **7** by using method B was recrystallized from ethanol to give **4b** (66%) as colorless needles, mp 300° dec; ir (potassium bromide): 1720, 1620, 1600, 1510, 1480, 1080 cm^{-1}; ^{1}H-nmr (TFA): δ 9.5 (1H, d), 8.8-7.6 (7H, m), 4.3 (3H, s).

Anal. Calcd. for $C_{13}H_{11}ClN_2O_5$ (310.67): C, 50.24; H, 3.56; N, 9.01. Found: C, 50.47; H, 3.77; N, 9.08.

5-Methylpyrido[1,2-*a*]quinazolin-6(5*H*)-one-11-ium Iodide (**5b**).

The crude product obtained from pyrido[1,2-*a*]quinazolin-6(11*H*)-one (**10**) by using method A was recrystallized from ethanol to give **5b** (97%) as yellow crystals, mp 274-275°; ir (potassium bromide): 1695, 1625, 1505, 1450, 1350, 1325 cm^{-1}; ^{1}H-nmr (TFA): δ 9.6 (1H, d), 8.8-7.9 (7H, m), 4.05 (3H, s).

Since this compound did not prove to be suitable for elementary analysis, it was converted to its perchlorate analogue as follows: a solution of **5b** in acetonitrile was treated with 70 per cent perchloric acid and the resulting precipitate was filtered off and recyrstallized from ethanol; mp: 298-299°.

Anal. Calcd. for $C_{13}H_{11}ClN_2O_5$ (310.67): C, 50.24; H, 3.56; N, 9.01. Found: C, 50.60; H, 3.23; N, 9.11.

6-Ethoxypyrido[1,2-*a*]quinazolium Tetrafluoroborate (**11a**).

The crude product obtained from pyrido[1,2-*a*]quinazolin-6(11*H*)-one (**10**) by using method C was recrystallized three times from ethanol to give compound **11** (R = C_2H_5) in 62% yield as colorless needles, mp 229-230°; ir (potassium bromide): 1550, 1505, 1440, 1320, 1050 cm^{-1}; ^{1}H-nmr (perdeuterioacetonitrile): δ 9.7 (1H, d), 8.8-7.8 (7H, m), 4.9 (2H, q), 1.6 (3H, t).

Anal. Calcd. for $C_{14}H_{13}BF_4N_2O$ (312.04): C, 53.89; H, 4.19; N, 8.97. Found: C, 53.79; H, 4.16; N, 9.08.

6-Methoxypyrido[1,2-*a*]quinazolium Tetrafluoroborate (**11b**).

Triethylamine (0.5 g, 5 mmoles) was added to a stirred solution of 6-ethoxypyrido[1,2-*a*]quinazolium tetrafluoroborate (**11a**, 0.31 g, 1 mmole) in dry methanol (10 ml). The reaction mixture was stirred at 20° for 1 hour and the solid residue obtained by evaporation of the solvent was recrystallized from methanol to give 0.24 g of product (83%), mp 214-215°; ^{1}H-nmr (perdeuterioacetonitrile): δ 9.6 (1H, d), 8.8-7.8 (7H, m), 4.55 (3H, s).

Anal. Calcd. for $C_{13}H_{11}BF_4N_2O$ (298.02): C, 52.38; H, 3.72; N, 9.39. Found: C, 52.07; H, 3.58; N, 9.22.

N-(2'-Pyrrolidinocarbonylphenyl)-*N*-methyl-2-aminopyridine (**14**).

Pyrrolidine (10 ml) was added to a stirred solution of **4b** (0.4 g, 1.3 mmoles) in acetonitrile (10 ml) at 20°. The reaction mixture was allowed to stand overnight and the solvent was then removed under reduced pressure. The residue was purified by column chromatography on aluminium oxide using benzene as eluent to give 0.15 g of product (42%) as a yellow oil; ms: (m/e, %) 281 (M^+, 11), 212 (26), 211 (44), 183 (100), 181 (10), 168 (11), 140.5 (M^{++}, 3); ^{1}H-nmr (deuteriochloroform): δ 8.05 (1H, d), 7.4-7.1 (5H, m), 6.6-6.35 (2H, m), 3.4 (3H, s), 3.35-3.1 (4H, m), 1.75-1.5 (4H, m).

Anal. Calcd. for $C_{17}H_{19}N_3O$ (281.34): C, 72.57; H, 6.80; N, 14.93. Found: C, 72.28; H, 6.91; N, 15.07.

1-*cis*-3-*trans*-1-(3-Methylquinazol-4(3*H*)-one-2-yl)-4-pyrrolidino-1,3-butadiene (**16**).

Compound **5b** was reacted with an excess of pyrrolidine in hexadeuteriodimethyl sulfoxide at 25° in an nmr tube, and the reaction was monitored by measuring the ^{1}H-nmr spectrum in regular intervals until no further change was observed. The spectrum recorded within a few hours after completion of the reaction showed the presence of the 1-*cis*-3-*trans* isomer **16** as the only component which subsequently began to isomerize slowly into its all- *trans* isomer **17**; ^{1}H-nmr (DMSO-d_6): δ 8.0 (1H, d); 7.8-7.2 (4H, m), 7.0 (1H, m), 6.6 (1H, t), 5.6 (1H, d), $J_{1,2}$ = 10.5 Hz, $J_{2,3}$ = 11.5 Hz, $J_{3,4}$ = 12.5 Hz.

1-*trans*-3-*trans*-1-(3-Methylquinazol-4(3*H*)-one-2-yl)-4-pyrrolidino-1,3-butadiene (**17**).

Pyrrolidine (2 ml) was added to a solution of 5-methylpyridio-[1,2-*a*]quinazolin-6(5*H*)-one-11-ium iodide (**5b**, 0.6 g, 1.7 mmoles) in acetonitrile at 20°. The reaction mixture was stored at room temperature for overnight and was then poured into ice-water. The separated solid was collected by filtration and was recrystallized from ethanol to give 0.4 g of product (81%) as yellow crystals, mp 134-135°; ^{1}H-nmr (deuteriochloroform): δ 8.2 (1H, d), 7.8 (1H, dd), 7.65-7.2 (3H, m), 7.0 (1H, d), 6.1 (1H, d), 5.3 (1H, dd), 3.7 (3H, s), 3.4-3.2 (4H, m), 2.0-1.8 (4H, m), $J_{1,2}$ = 14.5 Hz, $J_{2,3}$ = 11.6 Hz, $J_{3,4}$ = 12.5 Hz.

Anal. Calcd. for $C_{17}H_{19}N_3O$ (281.34): C, 72.57; H, 6.80; N, 14.93. Found: C, 72.68; H, 6.92; N, 15.05.

6-Pyrrolidinopyrido[1,2-*a*]quinazolium Tetrafluoroborate (**18**).

Pyrrolidine (0.11 ml, 1.6 mmoles) was added to a stirred solution of ethoxy compound **11a** (0.5 g, 1.6 mmoles) in dry acetonitrile (10 ml) at 0°. The mixture was stirred for 1 hour. The solid residue obtained by evaporation of the solvent was recrystallized from ethanol to give 0.43 g of product (80%) as colorless needles, mp 228-229°; ^{1}H-nmr (perdeuterioacetonitrile): δ 9.1 (1H, d), 8.8-7.3 (7H, m), 4.3-3.8 (4H, m), 2.3-1.8 (4H, m).

Anal. Calcd. for $C_{16}H_{16}BF_4N_3$ (337.11): C, 57.00; H, 4.78; N, 12.46. Found: C, 56.88; H, 4.85; N, 12.50.

1-(4-Pyrrolidinoquinazolyl-2)-4-pyrrolidinobutadiene (**19**).

Pyrrolidine (1 ml) was added to a stirred solution of 6-methoxypyrido[1,2-*a*]quinazolium tetrafluoroborate (**11a**, 0.4 g, 1.3 mmoles) or 6-pyrrolidinopyrido[1,2-*a*]quinazolium tetrafluoroborate (**18**, 0.44 g, 1.3 mmoles) in dry acetonitrile (10 ml) at 20°. The reaction mixture was stirred for 24 hours and was then poured onto ice-water. A solid separated which was filtered and recrystallized from ethanol to give **19** (0.26 g, 68%) as deep yellow crystals, mp 189-190°; ^{1}H-nmr (deuteriochloroform): δ 8.15-6.95 (5H, m), 6.75 (1H, d), 6.15 (1H, d), 5.15 (1H, t), 4.05-3.75 (4H, m), 3.4-3.0 (4H, m), 2.05-1.6 (8H, m), $J_{1,2}$ = 16 Hz, $J_{2,3}$ = 12 Hz, $J_{3,4}$ = 13 Hz.

Anal. Calcd. for $C_{20}H_{24}N_4$ (320.42): C, 74.96; H, 7.55; N, 17.48. Found: C, 75.10; H, 7.72; N, 17.29.

Acknowledgement.

Thanks are due to Dr. Gy. Tasi (József Attila University, Department of Applied Chemistry, Szeged, Hungary) for kindly providing an AM1 calculation program adapted for PC AT.

REFERENCES AND NOTES

[1] A. Messmer, Gy. Hajós and A. Gelléri, *Tetrahedron*, **42**, 4827 (1986).

[2] Gy. Hajós and A. Messmer, *J. Heterocyclic Chem.*, **21**, 809 (1984).

[3] A. Messmer, Gy. Hajós and G. Timári, *Monats. Chem.*, **119**, 1113 (1988).

[4] G. Timári, Gy. Hajós and A. Messmer, *Monats. Chem.*, **119**, 1037 (1988).

[5] A. Messmer, G. Timári and Gy. Hajós, *Monats. Chem.*, **119**, 1121 (1988).

[6] D. Morler and F. Krohnke, *Liebigs Ann. Chem.*, **744**, 65 (1971).

[7a] G. M. Sanders, M. van Dijk and H. C. van der Plas, *J. Heterocyclic Chem.*, **19**, 797 (1982); [b] F. Krebs and H. Maas, *Synthesis*, 735 (1989).

[8a] S. Tamura and M. Ono, *Chem. Pharm. Bull.*, **26**, 3167 (1978); [b] I. Hermecz and Z. Meszáros, Advances in Heterocyclic Chemistry, Vol **33**, A. R. Katritzky ed, Academic Press, New York, 1983, p 242.

[9] J. K. Landquist, *J. Chem. Soc.(C)*, 2735 (1971).

[10a] O. Seide, *Liebigs Ann. Chem.*, **440**, 311 (1924); [b] For a recent application of this procedure see: M. Davis, R. J. Hook and W. Y. Wu, *J. Heterocyclic Chem.*, **21**, 369 (1984).

[11] P. J. Abbott, M. Acheson, M. Y. Kornilov and J. K. Stubbs, *J. Chem. Soc., Perkin Trans. I*, 2322 (1975).

[12] Similar synthetic route has been published for an aza-analogue of **10**, A. Kamal, M. W. Rao and P. B. Sattur, *Heterocycles*, **24**, 3075 (1976).

[13] T.-L. Ho, Hard and Soft Acids and Bases Principle in Organic Chemistry, Academic Press, New York, NY, 1977.

[14] M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, J. J. P. Stewart, *J. Am. Chem. Soc.*, **107**, 3902 (1985).

[15] The concept of the in-the-plane approach of the electrophile was originally supposed for cases of ring nitrogens having lone pairs in the aromatic plane only, and now, for simplicity, a similar approach is supposed for the exo oxygen atoms, too. A more detailed study concerning the possible contribution of the π-type electrons to the nucleophilicity of the carbonyl bond is in progress.

[16] A. Messmer, Gy. Hajós, Zs. Juhász-Riedl and P. Sohár, *J. Org. Chem.*, **53**, 973 (1988).