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Selective Ring Opening of Linearly and Angularly Fused Triazolium Salts°

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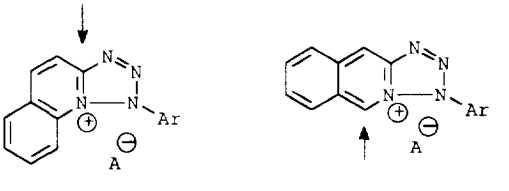
Abstract: Angularly and linearly fused, 1,2-, and 1,3-disubstituted [1,2,4]triazolium salts were synthesised and reacted with nucleophiles. The sites of attack were found to depend both on the type of annelation and substitution pattern: the linearly fused derivative reacted at the pyridine moiety, whereas the angularly condensed salts were attacked at one of the carbon atoms of the triazole ring, and subsequent ring openings occurred in both cases. For the experienced ambident reactivity a general mechanistic scheme was proposed and the annelation-dependent regioselectivity was rationalised on the basis of an MO approach.

INTRODUCTION

In the course of our earlier studies we found[1] that some tricyclic azolium salts, *e.g.* the angularly (**1**) and linearly fused tetrazolium salts (**2**) react with nucleophiles (*e.g.* with tetramethylammonium hydroxide) in two different regioselective ways as shown by the arrows in Scheme 1. These results aroused our interest in transformations of related tricyclic triazolium salts.

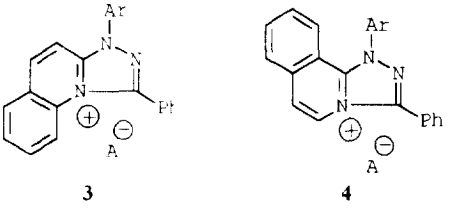


1 2

Scheme 1

SYNTHESIS OF THE MODEL TRICYCLIC TRIAZOLIUM SALTS

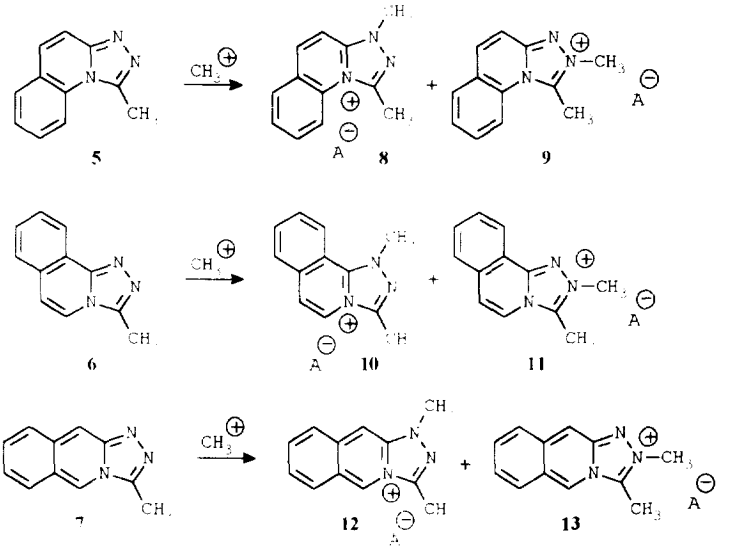
Although the synthesis of some angularly fused 1,3-diaryltriazolium salts (*e.g.* **3** and **4**) by direct ring closure was earlier published by our group[2], more recent studies suggested[3] that direct alkylation of neutral fused triazoles might provide a more general and easy access to the target compounds.



3 **4**

Scheme 2

To this end we decided first to investigate the alkylation reactions of the angularly fused 1-methyl-[1,2,4]triazolo[4,3-a]quinoline[4] (**5**), 3-methyl-[1,2,4]triazolo[3,4-a]isoquinoline[5] (**6**) and the linearly fused 3-methyl-[1,2,4]triazolo[4,3-b]isoquinoline[6] (**7**) with dimethyl sulphate.



Product ratio:

70 : 30

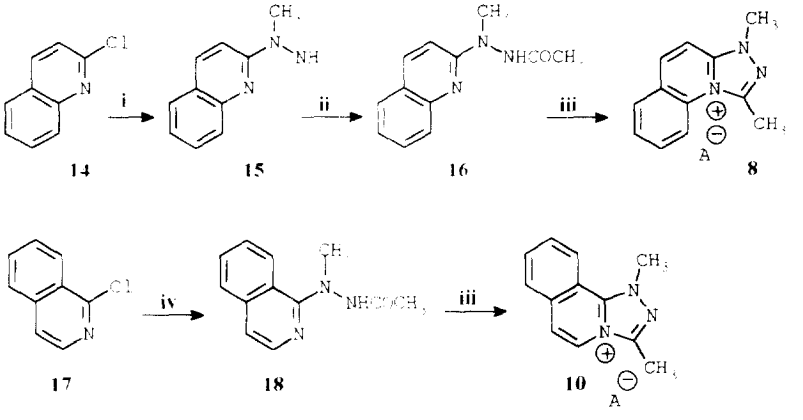
80 : 20

95 : 5

Scheme 3

As Scheme 3 shows, in all the three cases mixtures of the two possible alkylation products have been obtained. Unfortunately, in the alkylation reactions of the angularly fused ring systems **5** and **6** the observed selectivity was rather poor and, thus, these conversions could not be utilised even for the synthesis of the main

products. In the case of the linearly fused compound 7, however, the methylated salt **12** was obtained in a fairly high excess and could be isolated in pure form after a single recrystallisation.



i: CH_3NHNH_2, ii: Ac_2O/Py, iii: $POCl_3$, iv: $CH_3CONHNHCH_3$

Scheme 4

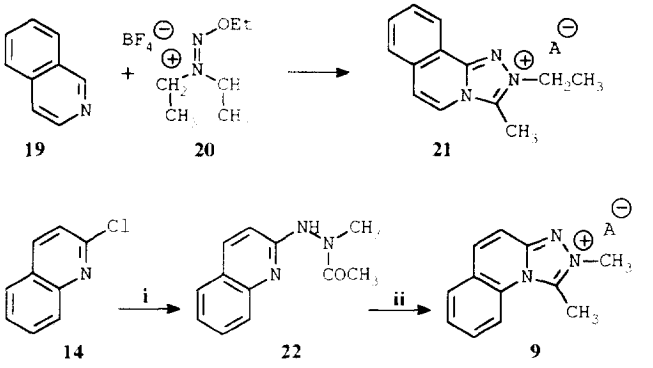
The lack of selectivity in the above alkylation reactions prompted us to elaborate preparative routes leading selectively to the desired model compounds. As Scheme 4 shows a synthetic path starting from 2-chloroquinoline (**14**) has been performed reaction with methylhydrazine at room temperature, in agreement with an analogous case[7], afforded 2-(1-methylhydrazino)-quinoline (**15**) which was acylated to 2-(2'-acetyl--1'-methylhydrazino)-quinoline (**16**) and subsequently ring closed to **8** by using phosphorus oxychloride. The analogous transformation of 1-chloro-isoquinoline (**17**) could also be accomplished with the difference[8] that 2-acetyl-1-methylhydrazine was used as a reagent to afford **18** which upon ring closure gave the 1,3-disubstituted salt **10**.

Besides the 1,3-disubstituted alkylation products **8** and **10**, selective procedures to the 1,2-disubstituted isomers **9** and **11** (*i.e.* to the minor products of the alkylation reactions shown in Scheme 3) seemed also of interest. Thus, a closely related derivative of **11** was synthesised according to the procedure of Eicher et al.[9]: reaction of isoquinoline (**19**) with 1,1-diethyl-2-ethoxy-diazenium fluoroborate (**20**) afforded 2-ethyl-3-methyl-[1,2,4]triazolo[3,4-a]isoquinolinium fluoroborate (**21**) in 50% yield. As quinoline, unfortunately, failed to give the same reaction the analogous triazoloquinolinium salt (**9**) was synthesised in a different way: 2-(2'-acetyl-2'-methyl-hydrazino)-quinoline (**22**), obtained from the reaction of 2-chloroquinoline (**14**) with 1-acetyl-1-methylhydrazine, was ring closed in boiling $POCl_3$ to give the desired product: 1,2-dimethyl-[1,2,4]triazolo[4,3-a]quinolinium fluoroborate (**9**) in high yield.

As a result of the above syntheses we had tricyclic triazolium salts of three types:

- type a. the angularly fused 1,2-dialkyl-[1,2,4]triazolo[4,3-a]quinolinium salt (**9**) and the analogous isoquinolinium salts (**21**);

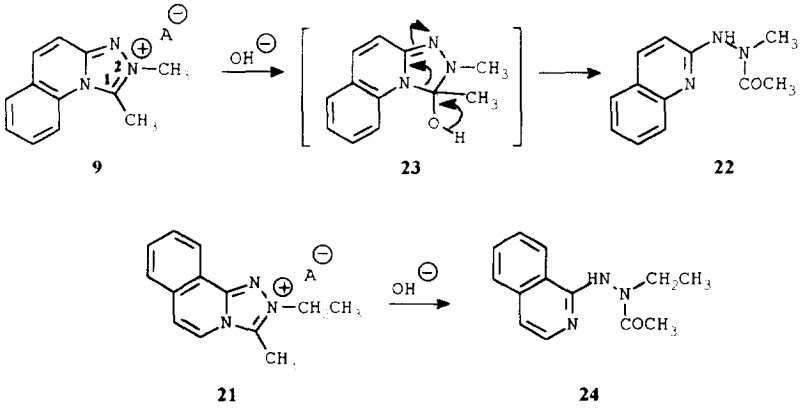
- type b: the linearly fused 1,3-dimethyl-[1,2,4]triazolo[4,3-b]isoquinolinium salt (**13**).
- type c: the angularly fused 1,3-dimethyl-[1,2,4]triazolo[4,3-a]quinolinium salt (**8**) and the analogous isoquinolinium salt (**10**) as well as the corresponding diaryl substituted compounds **3** and **4**.



Scheme 5

RING OPENING REACTIONS

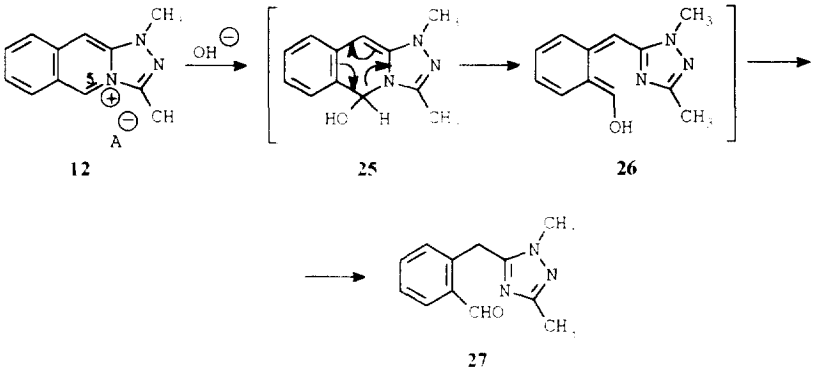
These new triazolium salts reacted with tetramethylammonium hydroxide smoothly as expected, and yielded one single product in each case. Interestingly, however, all the three types (a, b, and c) showed different reactivities.



Scheme 6

1. Type a: Compound **9** reacted selectively at the triazole ring-carbon atom next to the formulated positive charge, *i.e.* at C-1, followed by ring opening of the triazole moiety to give the acylhydrazinoquinoline compound **22**[10]. This ring opening obviously proceeds via intermediate **23** which undergoes the electron shifts

shown by the arrows. Also, the related 1,2-dialkylisoquinolinium salt **21** reacted analogously and the product **24** was obtained.



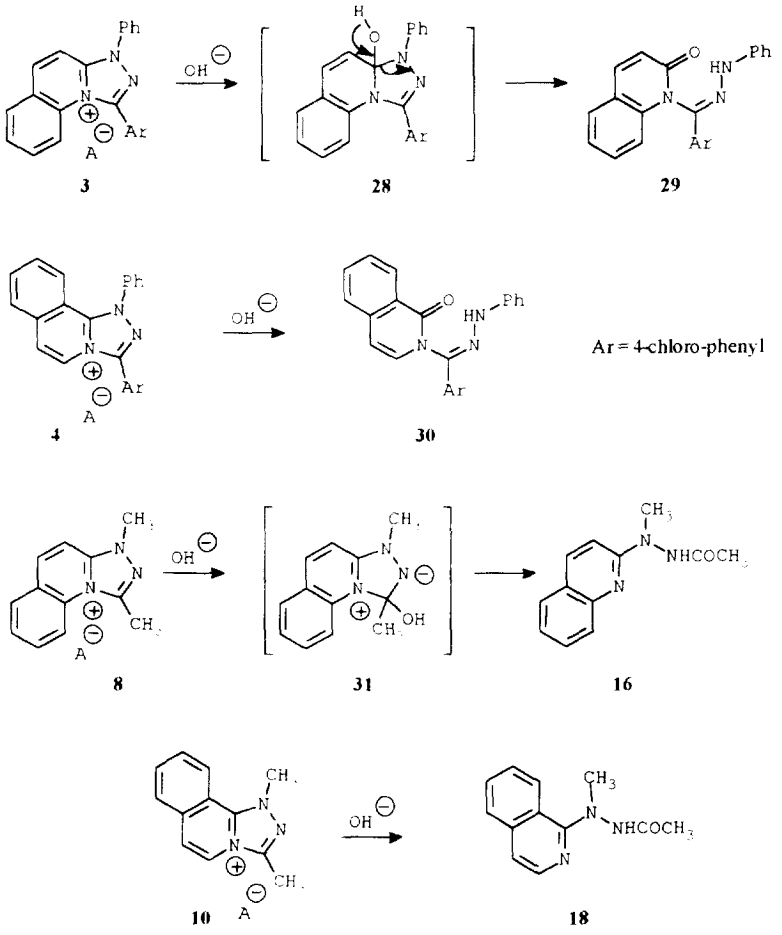
Scheme 7

Type b: In contrast to the above results, the 1,3-dimethyl substituted linearly fused triazolium salt **12** reacted entirely differently and product **27** was isolated. In this case the nucleophile attacked the C-5 carbon atom in the isoquinoline ring (*n.b.* this carbon is also adjacent to the bridgehead nitrogen) to lead to the pseudo base **25**. This intermediate easily undergoes retroelectrocyclic ring opening to **26** which is stablized by tautomerism to the isolated dimethyltriazolyl-tolualdehyde compound **27**.

Type c: Interesting and unexpected results have been obtained with transformations of the angularly fused 1,3-diaryl (**3** and **4**) and 1,3-dimethyl (**8** and **10**) triazolium salts. Reaction of **3** with tetramethyl-ammonium hydroxide resulted in the opening of the triazole ring the amidrazone **29** was isolated in good yield which suggests the attack of the hydroxide ion at the bridgehead carbon atom. Such an attack should afford the pseudo base **28** which upon heterolytic bond cleavage and proton transfer leads to the product **29**. The related triazoloisoquinolinium salt (**4**) showed similar reactivity and gave rise to the amidrazone **30**.

Reactions of the corresponding 1,3-dialkyltriazolium salts **8** and **10** with hydroxide ion also gave single products in both cases, but in contrast to the aryl substituted cases (**3** and **4** leading to amidrazones), acylhydrazines **16** and **18** were obtained in good yield. Formation of these products can be interpreted by the attack of the nucleophile at the carbon atom of the triazole ring bearing the methyl group which necessarily results in a zwitterionic intermediate (*e.g.* **8** should lead to **31**) which can be stabilised by ring opening to the final neutral product (*e.g.* **16**).

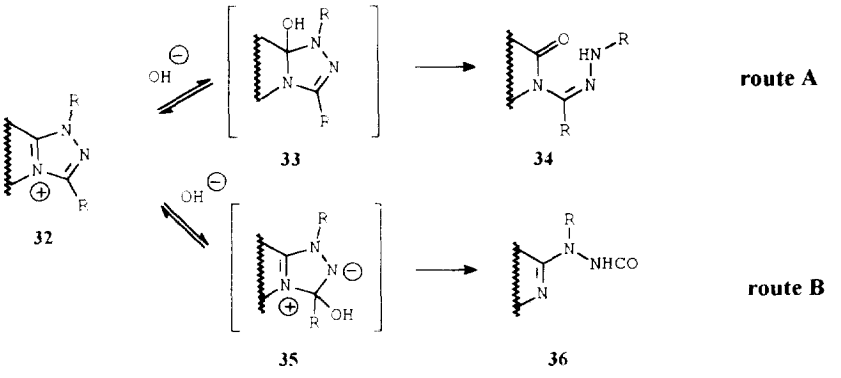
A rationalisation of this dramatic difference between the experienced reactivity of the diaryl (**3** and **4**) and dimethyl (**8** and **10**) salts is shown in Scheme 9. This scheme clearly demonstrates that the nucleophilic reagent can attack two positions adjacent to the positively charged bridgehead nitrogen atom of the triazolium salt (**32**): either the bridgehead carbon atom to yield the pseudo base of type **33** (**route A**) or the triazole-carbon atom to give rise to the zwitterionic species **35** (**route B**). Qualitative considerations (*i.e.* the obviously higher stability of the neutral species **33** compared to the zwitterion **35**) as well as quantum chemical calculations (see below)



Scheme 8

suggest that **route A** leading to **33** is superior to the alternative **route B**. The fate of this intermediate (**33**) depends, then, on how easily the heterolytic bond cleavage leading to **34** can take place. As this cleavage involves the shift of the sigma bond onto the nitrogen atom, any substituent - such as an aryl group - stabilising the negative charge by conjugation should facilitate this step. Our experiments showed, indeed, that the diaryl compounds **3** and **4** afforded the products **29** and **30** corresponding to the general structure **34**.

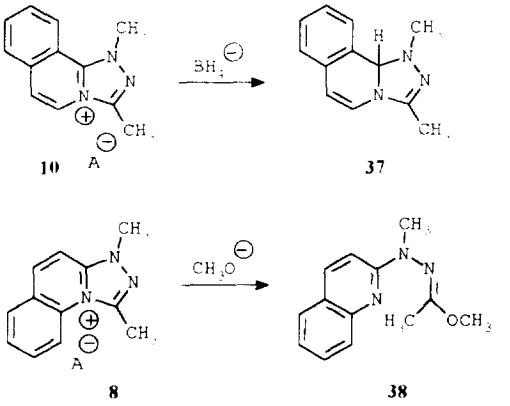
With substituents, in turn, that can not stabilise the negative charge, the heterolytic cleavage to **34** is rather hindered and is therefore so slow that the formation of **35** through the equilibria **33**→**32** and **32**→**35** can be established. The unstable zwitterion **35** can be, however, easily stabilised by ring opening to the neutral product **36**. This is the case of the dialkyl compounds **8** and **10** which gave the products **16** and **18** corresponding to the general structure **36**.



32 33 34 35 36

Scheme 9

This mechanistic picture is based, thus, on the supposition that the primary attack of the nucleophile should occur in each case - independent of the nature of the substituents - at the bridgehead carbon atom of the triazole ring (*i.e.* pseudo base of type **33** should be formed first) and the final outcome of the reaction (*i.e.* ring opening to the amidrazone **34** or establishment of consecutive equilibria to **35** and subsequent ring opening to **36**) depends on the electron stabilising ability of the group R



10 37 8 38

Scheme 10

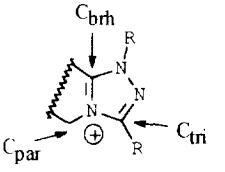
Experimental support of the above mechanism was provided by the reaction of the dimethyl substituted salt **10** with sodium borohydride. This reagent can be considered as a hydride anion equivalent that reacts irreversibly, to afford thereby necessarily the product of the primary attack. We found that a single product was formed in this reaction which was identified as **37.** In contrast, when the dimethyl substituted salt **8** was reacted with sodium methoxide - a nucleophile highly suitable for elimination, (*i.e.* formation of **35** from the primary

product **33** is possible) the product **38** was isolated in good yield. These results demonstrate that in the reaction of the 1,3-disubstituted salts with nucleophiles the primary attack takes always place on the bridgehead carbon atom of the triazole ring and the outcome of the reaction will be determined by the transformation of the intermediate of ambident reactivity.

MO INTERPRETATION

All the experimental results obtained with the selected three types of the model compounds (*i.e.* type a, b, and c) show that the primary attack of the nucleophile is different in each case and depends on the substitution pattern or type of annelation. In order to rationalise this finding we carried out semiempirical calculations and correlated the calculated c_{LUMO} coefficients and q_{NET} charges for all the three carbon atoms adjacent to the bridgehead nitrogen atom with the experimental findings. The results are summarised in Table 1.

Table 1. Calculated c_{LUMO} Densities and q_{NET} Charges of the Three Carbon Atoms Adjacent to the Bridgehead Nitrogen in the Ring Systems 9,21,8,10 and 12.



Ring system	C_{brh}, $c_{LUMO}(q_{NET})$	C_{tri}, $c_{LUMO}(q_{NET})$	C_{par}, $c_{LUMO}(q_{NET})$
9	0.124 (0.04)	0.627 (0.07)*	0.231 (-0.04)
21	0.129 (0.05)	0.614 (0.07)*	0.235 (-0.08)
8[a]	0.471 (0.12)*	0.070 (0.01)	0.063 (-0.03)
10	0.560 (0.13)*	0.110 (0.02)	0.098 (-0.08)
12	0.083 (0.07)	0.104 (-0.03)	0.565 (0.06)*

(C_{brh}-bridgehead triazole carbon, C_{tri}-triazole ring carbon, C_{par}-parent heterocycle carbon next to the bridgehead nitrogen) (MOPAC 6.0, AM1). The experimentally found sites of primary attacks are marked by asterisks.

[a] supposed (and in the case of the related diaryl compound **3** - analogous to **8** - also experimentally proved) site of attack.

This table convincingly shows that the positions having outstanding LUMO coefficients proved to be the target sites of the observed reactions in accordance with the kinetically controlled nature of the nucleophilic attacks. The authors feel that these results present a novel manifestation of the heteroaromatic annelation effect[11] and provide relatively facile access to some new quinolone and isoquinolone derivatives.

ACKNOWLEDGEMENT

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EXPERIMENTAL

Mps were determined by a Büchi apparatus and are uncorrected

1,3-Dimethyl-[1,2,4]triazolo[4,3-b]isoquinolinium fluoroborate (12)

A mixture of dimethyl sulphate (0.500 ml) and a solution of 3-methyl-[1,2,4]triazolo[4,3-b]isoquinoline (**7**) (0.18 g, 1 mmol) in acetonitrile (3 ml) was refluxed for 1 hour. After cooling ether was added to the yellow solution, the resulting white precipitate was filtered and washed with ether to give pure product, 0.240 g (84%), mp: 254-256 °C, UV (EtOH) λ 238 nm, IR (KBr) ν 3439, 3091, 1645, 1621, 1586 cm^{-1}; ^1H -NMR (CD_3CN+DMSO-d_6, 400 MHz) δ ppm 9.98 (s,1H), 8.82 (s,1H), 8.26 (d,1H), 8.11 (d,1H), 7.86 (t,1H), 7.65 (t,1H), 4.31 (s,3H), 3.01 (s,3H); Anal. Calcd for $C_{12}H_{12}N_3BF_4$: C, 50.56; H, 4.24; N, 14.74. Found C, 50.77; H, 4.29; N 14.89.

2-(Methylhydrazino)-quinoline (15)

A solution of 2-chloroquinoline (**14**) (1.08 g 6.6 mmol) and methylhydrazine (1 ml) in ethanol (5 ml) was allowed to stand at room temperature and the reaction was monitored by TLC. After disappearance of the starting compound water was added and the product was extracted with dichloromethane. The yellow oily residue was taken up in toluene, petroleum ether was added whereupon the product precipitated as colourless crystals: 0.84 g (74%), mp 62-64 °C; UV (EtOH) λ 248, 348 nm; IR (KBr) ν 3395, 3306, 3202, 1642, 1617, 1604, 1555 cm^{-1}; ^1H-NMR ($CDCl_3$, 400 MHz) δ ppm: 7.86 (d,1H), 7.72 (d,1H), 7.59 (d,1H), 7.53 (t,1H), 7.27 (d,1H), 7.22 (t,1H), 4.28 (brs,2H), 3.38 (s,3H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ ppm: 159.20, 147.47, 137.10, 129.43, 127.30, 126.32, 123.02, 122.23, 110.05, 40.78, Anal. Calcd for $C_{10}H_{11}N_3$: C, 69.34; H, 6.40; N 24.26 Found C, 69.43; H, 6.51, N 24.14

2-(2'-Acetyl-1'-methylhydrazino)-quinoline (16)

A mixture of 2-(methylhydrazino)-quinoline (**15**) (0.173 g , 1 mmol), acetic anhydride (0.105 ml, 1.1 mmol) and abs. pyridine (1 ml) was allowed to stand at room temperature for 2 hours. After removal of the solvent the residue was crystallised from ethanol-water to give 0.155 g (72%) of product, mp: 121-123 °C; UV (EtOH) λ 242, 336 nm, IR (KBr) ν 3504, 3278, 1669, 1620, 1607, 1566 cm^{-1}; ^1H -NMR ($CDCl_3$, 400 MHz) a 65:35 mixture of amide-rotational isomers. Major component: δ ppm: 8.35 (brs,1H), 7.81 (d,1H), 7.79(d,1H), 7.72 (d,1H), 7.51 (t,1H), 7.25 (t,1H), 6.88 (d,1H), 3.41 (s,3H), 2.03 (s,3H). Minor component: δ ppm: 8.35 (brs,1H), 7.92 (d,1H), 7.78 (d,1H), 7.66 (d,1H), 7.58(t,1H), 7.32 (t,1H), 7.01 (d,1H), 3.44 (s,3H), 2.04 (s,3H); ^{13}C -NMR ($CDCl_3$, 100 MHz) Major component: δ ppm: 169.56, 157.54, 147.04, 137.86, 129.64, 127.32, 126.80, 123.63, 123.12, 109.18, 38.52, 21.00. Minor component: δ ppm: 176.34, 157.74, 147.22, 138.37, 129.97, 127.44, 127.16, 123.85, 123.67, 108.66, 39.29, 19.13; Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found C, 66.99; H, 6.26; N 19.67

General procedure for the reaction of the chloro heterocycles with acetyl hydrazines.

A solution of the starting chloro compound (10 mmol) and the appropriate acetyl-methyl-hydrazine (20 mmol) in dimethylformamide (5 ml) was refluxed and the reaction was monitored by TLC. After disappearance of the starting chloro compound (in 4 hours, approximately) ether was added, the resulting precipitate was filtered off, the filtrate was treated with water extracted with cyclohexane. Extraction of the aqueous phase gave oily crude products which were crystallised from toluene/hexane.

1-(2'-Acetyl-1'-methylhydrazino)-isoquinoline (18)

This compound was obtained from 1-chloroisoquinoline and 2-acetyl-1-methylhydrazine; 1.376 g (64%). mp: 112-114 °C; UV (EtOH) λ 212, 292, 326 nm; IR (KBr) ν 3447, 3279, 1663, 1565 cm^{-1}; ^1H -NMR ($CDCl_3$, 400 MHz) a 70:30 mixture of amide-rotational isomers. Major component: δ ppm: 8.40 (brs,1H), 8.31 (d,1H), 8.13 (d,1H), 7.77 (d,1H), 7.65 (t,1H), 7.55 (t,1H), 7.37 (d,1H), 3.28 (s,3H), 2.03 (s,3H). Minor component δ ppm: 8.23 (d,1H), 8.21 (d,1H), 8.02 (brs,1H), 7.83 (d,1H), 7.70 (t,1H), 7.62 (t,1H), 7.45 (d,1H), 3.18 (s,3H), 2.20 (s,3H); Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.96, H, 6.09; N, 19.52. Found C, 66.98; H, 5.99; N 19.69.

2-(2'-Acetyl-2'-methyl-hydrazino)-quinoline (22)

This compound was obtained from 2-chloroquinoline and 2-acetyl-2-methylhydrazine; 1.29 g (60%). mp: 138-140 °C; UV (EtOH) λ 238, 328 nm; IR (KBr) ν 3429, 3290, 1645, 1618, 1609, 1534 cm^{-1}; ^1H-NMR ($CDCl_3$, 400 MHz) δ ppm: 8.11 (d,1H), 7.73 (d,1H), 7.71 (d,1H), 7.64 (t,1H), 7.38 (t,1H), 7.19 (s, 1H, NH), 6.78 (d,1H), 3.26 (s,3H), 2.18 (s,3H); ^{13}C -NMR ($CDCl_3$, 100 MHz) δ ppm: 175.01, 156.80, 147.62, 139.82, 130.83, 128.10, 126.70, 125.16, 124.30, 107.98, 35.48, 21.10; Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found C, 66.97; H, 6.16; N 19.67.

General procedure for synthesis of triazolium salts by ring closure.

A solution of the appropriate 2-acetyl-1-hetaryl-hydrazine compound (1 mmol) was refluxed in $POCl_3$ (3 ml) for 1 hour. After removal of the solvent in *vacuo* the residue was dissolved in water and neutralised with sodium hydrogencarbonate. Sodium tetrafluoroborate was added and the solution was extracted with nitromethane to give the crude triazolium salt which was recrystallised from acetonitrile/ether.

1,3-Dimethyl-[1,2,4]triazolo[4,3-a]quinolinium fluoroborate (8)

This compound was prepared from **16**, yield: 0.197 g (69%), mp: 224-226 °C; UV(EtOH) λ 216, 296, 320 nm; IR(KBr) ν 3466, 3037, 1631, 1613, 1576, 1543 cm^{-1}; ^1H -NMR (CD_3CN, 400 MHz) δ ppm: 8.59 (d,1H), 8.43 (d,1H), 8.24 (d,1H), 8.07 (t,1H), 7.90 (t,1H), 7.83 (d,1H), 4.21 (s,3H), 3.21 (s,3H); Anal. Calcd for $C_{12}H_{12}N_3BF_4$: C, 50.56; H, 4.24, N, 14.74. Found C, 50.62,H, 4.20; N 14.56.

1,2-Dimethyl-[1,2,4]triazolo[4,3-a]quinolinium fluoroborate (9)

This compound was prepared from **22**, yield: 0.185 g (65%), mp: 261-262 °C; UV(EtOH) λ 228, 282 nm; IR(KBr) ν 3436, 3015, 1631, 1611 cm^{-1}; ^1H -NMR (CD_3CN, 400 MHz) δ ppm: 8.44 (d,1H), 8.07 (d,1H), 8.05 (d,1H), 7.90 (t,1H), 7.80 (t,1H), 7.63 (d,1H), 4.23 (s,3H), 3.26 (s,3H, slow exchange with D_2O); Anal. Calcd for $C_{12}H_{12}N_3BF_4$: C, 50.56; H, 4.24, N, 14.74. Found C, 50.64; H, 4.26; N 14.92.

1,3-Dimethyl-[1,2,4]triazolo[3,4-a]isoquinolinium fluoroborate (10)

This compound was prepared from **18**, yield 0.185 g (65%); mp: 178-180 °C; UV(EtOH) λ 246, 272, 326 nm; IR(KBr) ν 3411, 3025, 1646, 1585, 1558, 1533, 1440, 1400, 1364, 1171, 1035, 804 cm^{-1}; ^{1}H-NMR (CD_3CN, 400 MHz) δ ppm: 8.74 (d,1H), 8.22 (d,1H), 8.21 (d,1H), 8.11 (t,1H), 8.04 (t,1H), 7.81 (d,1H), 4.58 (s,3H), 2.84 (s,3H). Anal. Calcd for $C_{12}H_{12}N_3BF_4$: C, 50.56; H, 4.24; N, 14.74. Found C, 50.62;H, 4.20; N 14.56.

2-(2'-Acetyl-2'-methyl-hydrazino)-quinoline (22)

To a solution of (**9**) (1 mmol) in acetonitrile (3 ml) 10% aqueous tetramethylammonium hydroxide (1 ml, 1.1 mmol) was added and the solution was allowed to stand at room temperature, and the reaction was followed by TLC. After disappearance of the starting compound the solvent was removed, the residue was triturated with ethyl acetate. This mixture was filtered, the filtrate was evaporated, and the solid residue was recrystallised from toluene/hexane yield 0.125 g (58%) of product, which proved to be identical (mp, ^{1}H-NMR) with that obtained from 2-chloroquinoline with 2-acetyl-2-methylhydrazine (see above).

1-(2'-Acetyl-2-ethyl-hydrazino)-isoquinoline (24)

To a solution of (**21**) (1 mmol) in acetonitrile (3 ml) 10% aqueous tetramethylammonium hydroxide (1 ml, 1.1 mmol) was added and the solution was allowed to stand at room temperature. The procedure described for the synthesis of **22** yielded 0.117 g (51%) of product; mp: 124-126 °C; UV(EtOH): λ 210, 296, 326 nm; IR(KBr) ν 3433, 3282, 1648, 1592,1569, 1533 cm^{-1}, ^{1}H -NMR ($CDCl_3$, 400 MHz) δ ppm: 8.11 (d, 1H), 7.91 (d, 1H), 7.78 (d, 1H), 7.68 (t, 1H), 7.56 (t, 1H), 7.26 (br s, 1H), 7.15 (d, 1H), 3.66 (q, 2H), 2.13 (s, 3H), 1.14 (t, 3H). , Anal. Calcd for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33; Found C, 67.96; H, 6.81; N 18.26.

α-(1,3-dimethyl-1H-[1,2,4]triazol-5-yl)-o-tolualdehyde (27)

To a solution of (**12**) (1 mmol) in acetonitrile (3 ml) 10% aqueous tetramethylammonium hydroxide (1 ml, 1.1 mmol) was added and the solution was allowed to stand at room temperature. The procedure described for the synthesis of **22** yielded 0.082 g (38%) of **27** mp: 98-100 °C; UV(EtOH) λ 216, 230 nm; IR(KBr) ν 1665, 1594, 1503 cm^{-1}, ^{1}H -NMR ($CDCl_3$, 400 MHz) δ ppm: 10.13 (s,1H), 7.82 (d,1H), 7.57 (t,1H), 7.51 (t,1H), 7.28 (d,1H), 4.51 (s,2H), 3.79 (s,3H), 2.31 (s,3H). Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52 Found C, 67.08; H, 6.15; N 19.44.

1-[(Phenylhydrazono)-4-chloro-benzoyl]-quinoline-2(1H)-one (29)

To a solution of **3** (A = BF_4^-, 1 mmol) in acetonitrile (3 ml) 10% aqueous tetramethylammonium hydroxide (1 ml, 1.1 mmol) was added and the mixture was stirred for 2 hours. The resulting precipitate was filtered off and recrystallised from toluene to give 0.284 g (76%) of **29**. mp: 224-227 °C; MS ***m/e*** 373 (M+,18), 228 (63), 91 (100); UV(EtOH) λ 230, 284, 342 nm; IR(KBr) ν 3421, 3247, 1662, 1596 cm^{-1}; ^{1}H - NMR ($CDCl_3$, 400 MHz) δ ppm: 7.85 (d, 1H), 7.64 (d, 1H), 7.61 (br s, 1H), 7.44 (d, 1H), 7.38 (t,1H), 7.28-7.20 (m, 6H), 7.09 (d, 2H), 6.96 (d, 1H), 6.89 (t, 1H), 6.76 (d, 1H), ^{13}C - NMR ($CDCl_3$, 100 MHz) δ ppm: 160.46, 143.23, 141.32, 136.88, 134.52, 131.62, 129.10, 128.91, 126.26, 123.75, 121.83, 121.30, 120.45, 114.90, 113.65, 113.61. Anal. Calcd for $C_{22}H_{16}ClN_3O$: C, 70.68; H, 4.31; N, 11.24. Found C, 70.58; H, 4.15; N 11.44

2-[(Phenylhydrazono)-4-chloro-benzoyl]-isoquinoline-1(2H)-one (30)

By the above procedure described for **29**, compound **4** (A = BF_4^-, 1 mmol) afforded 0.30 g (81%) of **30**; mp: 194-196 °C; MS *m/e* 373 (M+,23), 228 (49), 91 (100); UV(EtOH) 238, 286, 342 nm; IR(KBr) 3430, 3305, 1652 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 8.45 (d, 1H), 7.76 (t, 1H), 7.71 (br s, 1H), 7.62 (d, 1H), 7.56 (t,1H), 7.48 (d, 2H), 7.29 (d, 2H), 7.24 (d, 2H), 7.14 (d, 2H), 6.92 (t, 1H), 6.87 (d, 1H), 6.69 (d, 1H); Anal. Calcd for $C_{22}H_{16}ClN_3O$: C, 70.68; H, 4.31; N, 11.24. Found C, 70.72; H, 4.35; N 11.18.

1,10b-Dihydro-1,3-dimethyl-[1,2,4]triazolo[3,4-a]isoquinoline (37)

To a solution of **10** (0.2 mmol) in acetonitrile (0.500 ml) sodium borohydride (0.8 mmol) was added and the resulting suspension was stirred for 6 hours. After filtration and the evaporation of the filtrate the crude product was purified by column chromatography (alumina/hexane-ethyl acetate) to yield 0.026 g (65%) of **37**. MS *m/e* 199 (M+,44), 183 (100); ^{1}H - NMR ($CDCl_3$, 400 MHz) δ ppm: 7.31 (d, 1H), 7.25-7.22 (m, 2H), 7.06 (d, 1H), 6.47 (d, 1H), 5.82 (d, 1H), 5.11 (s, 1H), 3.07 (s, 3H), 2.03 (s, 3H)

Methyl-[2-methyl-2-(quinolin-2'-yl)-hydrazono]-acetate (38)

To a suspension of **8** (0.2 mmol) in methanol (0.5 ml) 1.0 M methanolic sodium methoxide solution (0.2 ml, 0.2 mmol) was added at 0 °C and the mixture was stirred for 30 minutes. After evaporation of the solvent the crude product was purified by column chromatography (alumina/hexane-ethyl acetate) to yield 0.033 g (72%) of **38** as a yellow oil. MS *m/e* 229 (M+,34), 151 (100); ^{1}H - NMR ($CDCl_3$, 400 MHz) δ ppm: 7.85 (d, 1H), 7.76 (d, 1H), 7.61 (d, 1H), 7.54 (t, 1H), 7.22 (t, 1H), 6.94 (d, 1H), 3.92 (s, 3H), 3.48 (s, 3H), 2.06 (s, 3H).

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