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Direct Arylation of Tetrazolo[1,5—*a*]pyridine and Its Benzenologues[1]

Short Communication

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Diphenyliodonium fluoroborate proved to be a suitable reagent for direct arylation of bridge head nitrogen containing fused heteroaromatic systems. By this one step method, 1-aryl-tetrazolo[1,5—*a*]pyridinium salt (**3**) can be obtained. Arylation of related benzenologues gave not only 1-aryl but also 2-aryltetrazolium salts.

(Keywords: Arylation; Fused tetrazolium salts; Heterocyclic synthesis)

Direkte Arylierung von Teterazolo[1,5—a]pyridin und dessen Benzologen (Kurze Mitteilung)

Kondensierte Heteroaromaten mit Brückenkopf-Stickstoff können direkt mit Diphenyl-Jodonium Fluoroborat aryliert werden. In dieser Weise wird 1-Aryltetrazolo[1,5—*a*]pyridinium Salz (**3**) in einer Reaktionsstufe synthetisiert. Arylierung der verwandten Benzologen führten nicht nur zu 1-Aryl, sondern auch zu 2-Aryltetrazolium Salzen.

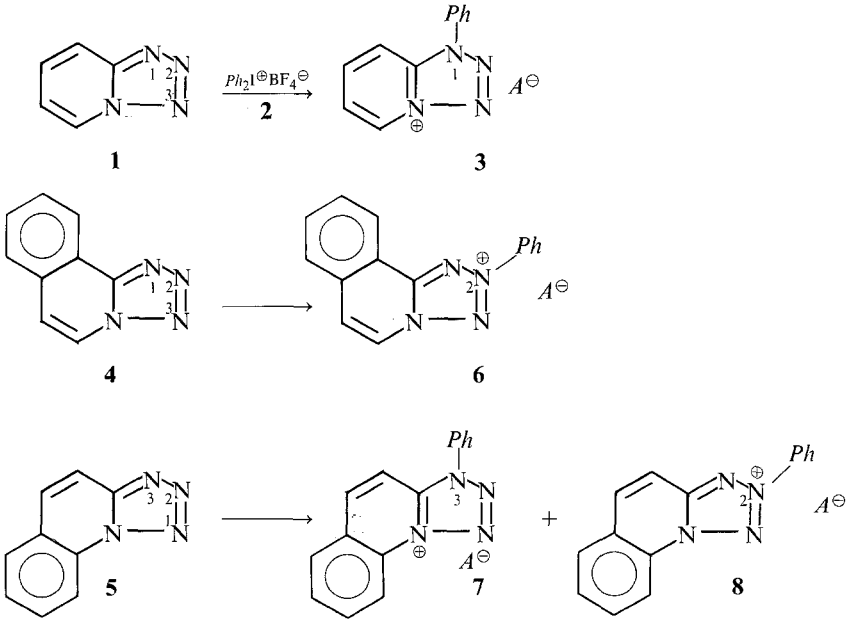
In the course of our studies on nucleophilic reactivity of bridge head nitrogen containing azolium salts[1—3] a direct ring closure to 3-aryltetrazolo[1,5—*a*]pyridinium salts and to its benzenologues has been elaborated earlier. In order to investigate the positional effect of the aryl substituent on reactivity of the fused azolium salts, we wished to synthesize the analogous 1-aryl compounds. Only one example has been known for such derivatives: *Glover* et al.[4] published the formation of 1-phenyltetrazolo[1,5—*a*]pyridinium bromide (**3**, A = Br) in a poor overall yield (less than 1%) calculated for 2-bromopyridine as starting com-

pound. Elaboration of a simple and more economic way to 1-aryl derivatives seemed to be desirable.

We describe now the direct arylation of tetrazolo[1,5—*a*]pyridine (**1**) with diphenyliodonium fluoroborate (**2**). Diaryl iodonium salts proved to be excellent N-arylating agents for several anionic[6] and a couple of neutral[7] compounds, whereas arylation of bridge head nitrogen containing fused heteroaromatics has not yet been reported.

While treatment of tetrazolo[1,5—*a*]pyridine (**1**) with diphenyliodonium chloride results only in decomposition products, in the case of fluoroborate salt **2** prepared by us by a simplified procedure, arylation takes place at 180 °C and 1-phenyltetrazolo[1,5—*a*]pyridinium fluoroborate (**3**) is formed. The position of the aryl group was supported by preparation of the perchlorate salt (**3**, $A = ClO_4$) which proved to be identical with that obtained by the method cited above[4].

This successful arylation prompted us to extend the reaction to benzenologous of **1**. Thus, we found that both angular benzenologous (**4** and **5**) undergo arylation under similar conditions. Interestingly, however, selective formation of one single arylated product was found in the case of the tetrazolo[5,1—*a*]isoquinoline system (**4**), while a mixture of two isomers (**7** and **8**; in about 3 : 1 ratio shown by NMR) was obtained with tetrazolo[1,5—*a*]quinoline compound **5**. By comparison of these products with 3-phenyltetrazolo[5,1—*a*]isoquinolinium and 1-



phenyltetrazolo[1,5—*a*]quinolinium salts prepared by us earlier[8,9], formation of the latter isomers could be excluded[11].

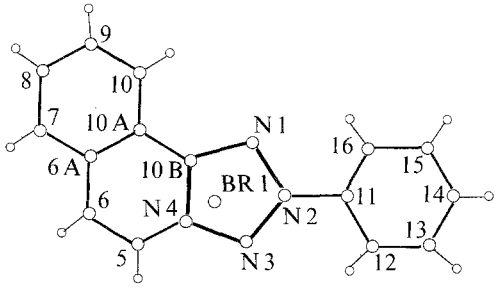
X-ray proved to be a suitable method for the determination of the position of the aryl substituent and supported the formation of the 2-phenyl compound **6** in case of the isoquinoline system. The structure was solved by a combined direct method—*Fourier* techniques and refined to an *R* value of 0.125 for 2 368 observed reflexions. One of the molecules in the asymmetric unit has the structure and conformation as depicted in Fig. 1. The other molecule has its phenyl group slightly rotated with respect to the one displayed.

The isomeric mixture of 3-phenyl- and 2-phenyltetrazolo[1,5—*a*]-quinolines could, unfortunately, not be separated. Earlier literature data[12], however, show that 1-arylation is more probable with this ring system and, for this reason, we propose structure **7** for the major product of the arylation reaction of tetrazolo[1,5—*a*]quinoline (**5**).

The regiospecific 2-arylation of **4**—similarly to methylation of related systems[13]—can be interpreted by a steric obstruction of the annelating benzene ring. The case of the quinoline system **5** also supports this suggestion: because of the sterically more favourable annelation in **5**, attack of reagent **2** at position 3 (corresponding to position 1 in **3** and **6**) may become predominant.

An attempt to arylate the linearly fused benzenologue failed because of the violent decomposition of the reaction mixture observed at 170 °C. As reported earlier[10] this tetrazole compound, contrary to the angularly fused benzenologues (**4** and **5**), exists as an equilibrium of tetrazole and azide forms and, at elevated temperatures, the ring opened azide isomer is the major component.

As a conclusion it can be stated that arylation occurred never at the adjacent but at the most distant nitrogen atom from the bridge head nitrogen of fused tetrazoles. If this far one is sterically hindered its neighbour is preferred. Further studies on extension of direct arylation of fused heteroaromatics are in progress.



Experimental

All melting points are uncorrected and were determined by a Büchi apparatus. IR spectra were performed on a Specord 75 IR equipment, ^{1}H-NMR spectra were recorded on a Varian XL-100 spectrometer. An Enraf-Nonius CAD-4 diffractometer was used for X-ray determination, 3134 independent reflexions were collected from a single crystal [$a = 31.446$ (9), $b = 6.314$ (2), $c = 15.907$ (7) Å, $\beta = 104.47$ (3)°, space group P 2_1/n, $Z = 8$]. Elementary analysis (C, H and N were in good agreement with the calculated values.

Diphenyliodonium fluoroborate (**2**)

The procedure for preparation of the chloride salt described by *Beringer* et al.[14] was applied with the following modification: the reaction mixture obtained from 80 g of potassium iodate was treated with ammonium fluoroborate. The precipitated crude product was filtered, and recrystallized from acetonitrile-ether to give 60 g (41%) of fluoroborate salt, m.p. 133–135 °C (Lit.[5], m.p. 136 °C).

1-Phenyltetrazolo[1,5—a]pyridinium fluoroborate (**3**)

A mixture of diphenyliodonium fluoroborate (**2**) (5.0 g, 13.7 mmol) and tetrazolo[1,5—*a*]pyridine (1.5 g, 1.25 mmol) was stirred at 180 °C for one hour, then addition two portions of reagent **2** (2.0 g, 5.5 mmol) was added to the mixture in 1 hour intervals. After a period of alltogether 3 h, the viscous brown mixture was treated with ethanol (10 ml), the dark crystalline mass was filtered and recrystallized from methanol to give 0.75 g (22%) of fluoroborate salt, m.p. 224–227 °C. IR (KBr): 3120, 3060 (CH), 1630, 1520 (C=C, C=N) and 1060 cm^{-1} (BF_4^-).

^{1}H-NMR (*DMSO-d*$_6$): 7.85 (s, 1 H, H-aryl), 8.15 (q, 1 H, H-7), 8.48 (m, 1 H, H-5), 8.65 (m, 1 H, H-6) and 9.82 ppm (d, 1 H, H-4).

2-Phenyltetrazolo[5,1—a]isoquinolinium fluoroborate (**6**, $A = BF_4$)

A mixture of reagent **2** (2.0 g, 5.5 mmol) and tetrazole **4** (0.75 g, 4.4 mmol) was stirred at 180 °C for one hour. To the mixture 1.0 g of reagent **2** was added 3 times in 1 hour intervals, and stirring was finally continued for additional 6 h. The mixture was then cooled, treated with 10 ml of ethanol, and the precipitated crystals were filtered and recrystallized from methanol to give 0.44 g (30%) of product, m.p. 248–250 °C. IR (KBr): 3050 (CH), 1630, 1550, 1530 (C=C, C=N) and 1070 cm^{-1} (BF_4^-). ^{1}H-NMR (CH_3CN): 9.02 (d, 1 H, H-5), 8.31 (d, 1 H, H-6), and 8.9–7.8 ppm (m, 9 H). $J_{5,6} = 7.5$ Hz. The bromide salt (**6**, $A = Br$) was obtained by treatment of **6**, $A = BF_4$ with tetrabutyl ammonium bromide in acetonitrile, and was recrystallized from acetic acid, m.p. 291–292 °C.

Arylation of tetrazolo[1,5—a]quinoline (**5**)

Tetrazole **5** (0.75 g, 4.4 mmol) was treated with iodonium salt **2** as above. The same work up yielded 0.59 g (51%) of the mixture of **7** and **8**, m.p. 198–204 °C (ethanol). $C_{15}H_{11}N_4BF_4$ (324.11): Calcd. C 53.92; H 3.32; N 16.77. Found C 54.02; H 3.78; N 16.81. ^{1}H-NMR (CD_3CN): 8.95 and 8.73 (two doublets corresponding to H-9 in compounds **6** and **7** with an integral ratio 3:1, $J = 10$ Hz); 9.0–7.8 ppm (m, 10 H, H-aryl).

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