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STUDIES ON TRIAZOLO- AND IMIDAZO-[4.5-*f*]QUINOLINES

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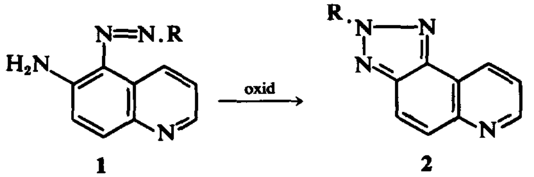
Abstract—Oxidation of 5-arylazo-6-aminoquinoline with copper sulphate in pyridine gives the corresponding 2-aryltriazolo[4.5-*f*]quinolines. Condensation of halogenated nitrobenzenes with triazolo-[4.5-*f*]quinoline yields the corresponding 2- and 3-derivatives. Imidazo[4.5-*f*]quinoline behaves similarly and furnishes the 3-derivative. NMR, IR and UV spectra of several of the products are discussed.

In continuation of previous investigations dealing with the condensation of benzotriazoles[1–3] and naphthotriazoles[4] with halogenated nitrobenzenes, the present work reports the condensation of triazolo- and imidazo-[4.5-*f*]quinolines with halogenated nitrobenzenes and a spectral study of the products obtained.

A new series of 2-aryltriazolo[4.5-*f*]quinolines [(2a–i) were synthesised by the oxidation[5] of the corresponding 5-arylazo-6-aminoquinolines (1a–i), respectively.



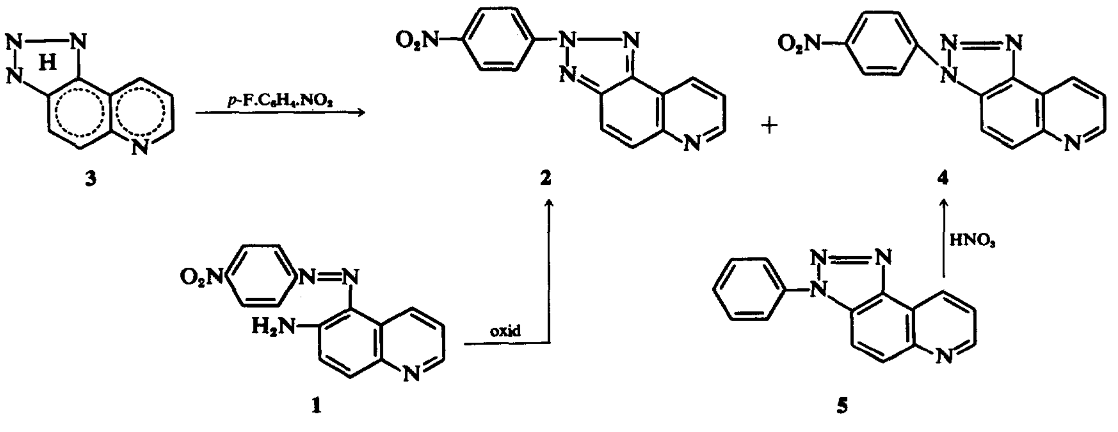
	R		R
1a, 2a	Ph	**1f, 2f**	1,2-dimethyl-5-benzimidazolyl
1b, 2b	*p*-NO_2—C_6H_4		
1c, 2c	*p*-Me—C_6H_4	**1g, 2g**	1-methyl-5-benzotriazolyl
1d, 2d	2,4-$(NO_2)_2$.C_6H_3	**1h, 2h**	5-benzothiophenyl
1e, 2e	5-indazolyl	**1i, 2i**	6-quinolinyl

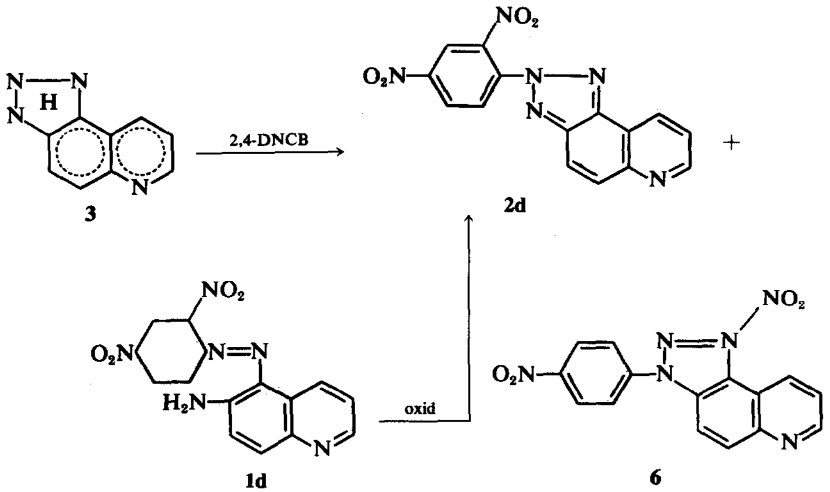
Triazolo[4.5*f*]quinoline (**3**) on condensation with *p*-nitrofluorobenzene yielded only two substances, one having m.p. 258–59° and the other melting at 305° in the ratio 1:1·5, respectively.

The first product was assigned formula **2b** since it is identical with the product obtained by the oxidation of **1b**. The other, was given formula **4**, since it was found identical with the compound obtained from the nitration of **5**. The structure of this nitration product is based on: (i) elemental analysis and (ii) NMR spectrum (TFA), which indicates the presence of an A_2B_2 pattern at δ_A 8·25; δ_B 8·82 suggesting a *para* substituted ring.

Condensation of triazolo[4.5-*f*]quinoline (**3**) with 2,4-dinitrochlorobenzene proceeds along similar lines and affords a mixture of (**2d**) and (**6**) in the ratio 1·5:1, respectively. These results are in conformity with the fact that position 1 in naphtho-[1.2-*d*]triazole is inactive,[4] probably due to steric factors.

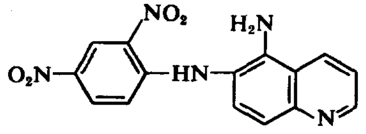
5,6-Diaminoquinoline dihydrochloride condenses with 2,4-dinitrochlorobenzene to give 5-amino-6-(2,4-dinitroanilino)quinoline (**7**), since it yields on





3 2d 1d 6

cyclisation with nitrous acid compound **6**, mentioned above. It also reacts with formic acid and with acetic anhydride to yield the benzimidazole derivatives (**8a** and **b**), respectively.



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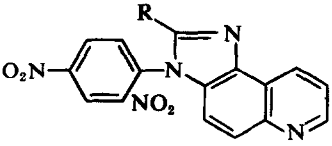
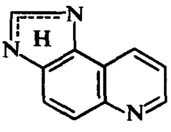


8a, R = H
b, R = Me



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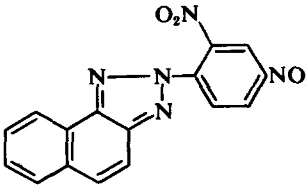
Recently, Simonov *et al.*[6] studied the methylation of imidazo[4.5-*f*]quinoline and concluded that position 3 in the imidazole ring is by far the most reactive as compared with position 1. In confirmation with this conclusion it is now found that imidazo[4.5-*f*]quinoline (**9**) on fusion with 2,4-dinitrochlorobenzene affords only one product which was found to be identical with compound (**8a**). This is in agreement with the result reported with triazolo-[4.5-*f*]-quinoline that position 1 is inactive.

Attempts to nitrate the parent triazoloquinoline (**3**) failed, probably due to the deactivating action of the strong electrophilic quinolinium centre formed in the nitration mixture on position 8 of the quinoline ring.

The NMR spectra of compounds **2d**, **6**, **7** and **8a** were measured in DMSO solution, the results obtained are in favour of the proposed structures for these compounds. The spectral assignments are in Table 1. The resonances were assigned to specific protons on their multiplicity, expected chemical shift and correlation of position in the series of compounds. The chemical shift of the proton is assigned on a first order spectral analysis, i.e. as the centre of the multiplet.

The UV spectra of the above synthesised triazolo- and imidazo- quinolines were taken in 95% ethanolic solutions and the data are listed in Table 2.

Examination of the spectral data shows that: There is always a bathochromic shift specially in the bands corresponding to π-π^* excitation of the phenyl group and this shift is greater in the 2-substituted triazole derivatives as compared to the 3-isomer, due to the extensive conjugation of the molecule when the triazole ring exists in the quinonoid form. Support for the quinonoid structure was obtained by comparing the IR spectra of the monoazo compound **1i** with that of the corresponding cyclised derivative **2i**. This conclusion is in agreement with the results reported recently[4] from the analysis of the UV spectra of the naphtho[1,2-*d*] triazole derivatives, e.g. **10** and **11**.



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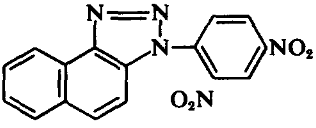

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Table 1. NMR shifts in ppm

Compound	Proton	Chemical shift (δ)	Compound	Chemical shift (δ)
	2	9·04		9·12
	3	7·76		7·90
2d	4	8·82	**6**	9·06
	7[a]	8·16		8·26[a]
	8[a]	7·96		8·16[a]
	3′[b]	9·03		9·10
	5′[b]	8·76		8·90
	6′[b]	8·56		8·48
	2	8·82		8·90
	3	7·40		7·65
	4	8·76		8·90
7	5[c]	9·60	**8a**	—
	6[d]	6·10		—
	7	6·59		7·68[a]
	8	7·43		7·90[a]
	9[e]	—		8·70
	3′[b]	8·90		9·06
	5′[b]	8·13		8·78
	6′[b]	7·26		8·24

[a] Proton assignment could be reversed.

[b] 3′, 5′, 6′ refer to the 3, 5, 6 protons in the 2,4-dinitrophenyl residue.

[c] NH_2

[d] NH

[e] The position 9 refers to the proton in the imidazole ring.

EXPERIMENTAL

All m.ps are uncorrected. NMR spectra were measured on a Varian HA-100 spectrometer. UV spectra were recorded with a Carl Zeiss PMQII and Beckmann DK-2A spectrophotometers and IR spectra with Perkin-Elmer Model 137 B Infracord using KBr discs.

Coupling of 6-aminoquinoline with diazonium salts. General method: 6-Aminoquinoline[7] (1·44 g, 0·01 mol) was dissolved in EtOH (20 ml) and cooled to 0–5°. A solution of the corresponding diazotised amine (0·01 mol) was added slowly with constant stirring. The pH of the mixture was adjusted to 6 by careful addition of NaOAc aq. The precipitated azo dye was collected and crystallised from the appropriate solvent. The yields are almost quantitative, and the dyes obtained are in Table 3.

Oxidation of the o-Amino azo compounds (**1a–i**) *to the corresponding triazoloquinoline derivatives.*[5] General method: The azo dye (1 g) was dissolved in pyridine (15 ml) by gentle warming. A solution of $CuSO_4$ (2 g in 15 ml water) was added and the mixture refluxed for 3 hr. Then the mixture was poured onto ice and the precipitated material collected and crystallised from the appropriate solvent. The results are in Table 4.

Table 2

Compound	λ$_{max}$ nm (log ε)	Compound	λ$_{max}$ nm (log ε)
3	253·5 (4·59)	**2e**	225 (4·45)
			275 (4·55)
2a	225 (4·39)		340 (4·37)
	285 (4·58)		
	326 (4·20)	**2f**	224 (4·38)
	336 (4·175)		254 (4·45)
			290 (4·45)
5	238 (4·58)		337 (4·37)
	253·5 (4·56)		
	286 sh (4·04)	**2g**	225 (4·455)
	312 (3·69)		270 (4·545)
	328 (3·66)		294 (4·51)
			335 (4·37)
2c	295 (4·41)		
	330 (4·25)	**2h**	235 (4·36)
			275 (4·62)
2b	262 sh (4·04)		295 (4·54)
	294 (4·40)		340 (4·48)
	300 (4·39)		
	343 (4·44)	**2i**	225 (4·72)
			270 (4·825)
4	253·5*		295 (4·68)
	300		340 (4·61)
	333		
2d	255 (4·25)	**9**	250 (4·38)
	295 (4·36)		253·5 (4·41)
	345 (4·31)		
		8a	250 (4·79)
6	250 (4·87)		300 (4·02)
	294 sh (4·33)		328 (3·93)
	330 (4·27)		

*Compound exhibits low solubility in EtOH, saturated solution is used, thus the evaluation of ε could not be carried out.

5-Amino-1-phenylbenzotriazole. To a suspension of 5-nitro-1-phenylbenzotriazole[10] (5 g) and Raney nickel (0·5 g) in warm absolute EtOH (50 ml), hydrazine hydrate (99–100%) (3 ml) was added dropwise. After addition was complete, the mixture was refluxed for 45 min, filtered and concentrated to small volume. The amine crystallised from benzene as yellowish-brown plates, m.p. 158°. (lit.[10,11] 158–59°).

3-(4-Nitrophenyl)triazolo[4.5-f]quinoline (**4**). 3-Phenyltriazolo[4.5-*f*]quinoline[12](**5**) (1 g) was heated with a mixture of conc. H_2SO_4 (10 ml) and fuming HNO_3 (14 ml) on a water-bath for 3 h. The mixture was poured on ice and the product that separated, was collected and crystallised from AcOH to give 0·99 g of **4** as pale yellow crystals, m.p. 305°. (Calc. for $C_{15}H_9N_5O_2$: C, 61·85; H,

Table 3. Azo Dyes **1a–i**

Compound	Colour	m.p. c° (Solvent of cryst.)	Formula	Analysis % Calc. C	H	N	Found C	H	N
1a*	—	—	—		—			—	
1b	Reddish-orange	245 (AcOH)	$C_{15}H_{11}N_5O_2$	64·84	3·75	23·90	64·61	3·51	23·58
1c†	—	—	—		—			—	
1d	Red	270 (AcOH)	$C_{15}H_{10}N_6O_4$	53·26	2·96	24·85	53·54	2·75	24·63
1e	Orange	225 (EtOH)	$C_{16}H_{12}N_6$	66·60	4·17	29·16	66·32	4·30	29·52
1f	Orange	307 (EtOH)	$C_{18}N_{16}N_6$	68·35	5·06	26·58	68·41	5·30	26·73
1g	Orange	224 (C_6H_6)	$C_{16}H_{13}N_7$			32·40			32·28
1h	Orange	155 (EtOH)	$C_{17}H_{12}N_4S$			18·42			18·12
						S: 10·53	10·32		
1i	Orange	223 (EtOH)	$C_{18}H_{13}N_5$	72·24	4·35	23·40	72·30	4·40	23·00

*Lit. 8: m.p. 144–46°
†Lit. 9 m.p. 245° (decomp.)

Table 4. Triazoloquinoline derivatives (**2a–i**)

Compound	Yield %	m.p. c° (Solvent of cryst.)	Formula	Analysis % Calc. C	H	N	Found C	H	N
2a	84	167 (EtOH)	$C_{15}H_{10}N_4$	73·17	4·06	22·76	73·20	4·10	23·10
2b	90	258–59 (AcOH)	$C_{15}H_9N_5O_2$	61·85	3·11	24·04	61·90	3·05	24·16
2c	80	185 (AcOH)	$C_{16}H_{12}N_4$	73·85	4·61	21·54	73·50	4·70	21·80
2d	85	215–16 (AcOH)	$C_{15}H_8N_6O_4$	53·57	2·38	25·00	53·60	2·30	24·90
2e	85	216–17 (AcOH)	$C_{16}H_{10}N_6$	67·13	3·50	29·37	66·70	3·50	29·20
2f	75	272 (EtOH)	$C_{18}H_{14}N_7$	68·79	4·46	26·75	68·60	4·60	26·60
2g	75	245 (EtOH)	$C_{16}H_{11}N_7$	63·90	3·65	32·56	63·51	3·64	32·30
2h	70	199–200 (AcOH)	$C_{17}H_{10}N_4S$	67·55	3·31	18·54	67·50	3·30	18·40
						S: 10·60	10·10		
2i	85	319–20 (AcOH)	$C_{18}H_{11}N_5$	72·72	3·70	23·57	72·60	3·60	23·40

3·11; N, 24·04. Found: C, 61·70; H, 3·40; N, 24·20%).

Condensation of triazolo[4.5-*f*]*quinoline with* p-*fluoronitrobenzene*. Triazolo[4.5-*f*]quinoline[13] 3 (1·7 g, 0·01 mol), *p*-fluoronitrobenzene (1·41 g, 0·01 mol) and anhyd NaOAc (0·6 g) was fused at 150–60° for 2 hr, the temp was then raised to 190–95° and maintained for 2 hr. The mixture was cooled, water washed, and extracted several times with boiling EtOH. Concentration of the alcoholic solution afforded 2(4-nitrophenyl)triazolo[4.5-*f*]quinoline (0·4 g, 14%) (from AcOH) as pale yellow needles, m.p. 258–59°, identical with 2b prepared as before.

The alcoholic insoluble portion of the reaction product was crystallised twice from AcOH to give 3-(4-nitrophenyl)triazolo-[4.5-*f*]quinoline (0·6 g 20·7%) as pale yellow crystals, m.p. 305° no m.m.p. depression with 4 obtained above.

Condensation of triazolo[4.5-*f*]*quinoline with* 2,4-*dinitrochlorobenzene*. Triazolo[4.5-*f*]quinoline (1·7 g, 0·01 mol), 2,4-dinitrochlorobenzene (2·02 g, 0·01 mol) and anhyd NaOAc (0·6 g) were refluxed in EtOH (100 ml) for 8 hr and the crystalline product (2·3 g) that separated was collected and water washed. Crystallisation from AcOH gave **2d** (1·2 g, 35%) as pale yellow needles, m.p. 215–16°, no m.m.p. depression **2d** is partially soluble in EtOH, soluble in hot AcOH, but insoluble in benzene, $CHCl_3$, ether and petroleum ether.

The AcOH mother liquor was diluted with water and the solid obtained collected and crystallised from dilute

AcOH to give **6** (0·8 g, 23·8%) as pale yellow plates, m.p. 239°. (Calc. for $C_{15}H_8N_6O_4$: C, 53·57; H, 2·38; N, 25·00. Found: C, 53·76; H, 2·37; N, 25·02%).

5-*Amino-6-(2,4-dinitroanilino)quinoline* (**7**). A mixture of 5,6-diaminoquinoline dihydrochloride[14] (2·31 g, 0·01 mol), 2,4-dinitrochlorobenzene (2·02 g, 0·01 mol) and anhyd NaOAc (1 g) in EtOH (150 ml) was refluxed for 5 hr then cooled. The precipitated product was filtered, water washed and crystallised from EtOH as reddish-orange crystals, m.p. 210–12°. (Calc. for $C_{15}H_{11}N_5O_4$: C, 55·39; H, 3·41; N, 21·53. Found: C, 55·69; H, 3·23; N, 21·30%).

3-(2,4-*Dinitrophenyl)triazolo*[4.5-*f*]*quinoline* (**6**). 5-Amino-6(2,4-dinitroanilino)quinoline (1·5 g) in conc. HCl (10 ml) and water (30 ml) at 0°, was treated with $NaNO_2$ aq (0·7 g in 5 ml water) and allowed to stand overnight on ice, then neutralised with Na_2CO_3 aq. The product was collected and crystallised from dilute AcOH as pale yellow plates, m.p. 239°, not depressed on admisture with **6** obtained before.

3-(2,4-*Dinitrophenyl)imidazo*[4.5-*f*]*quinoline* (**8a**). The aminoanilinoquinoline **7** (1·5 g), formic acid (15 ml) and few drops of conc. HCl were refluxed for 5 h. The mixture was neutralised with Na_2CO_3 aq and **8a** was obtained as orange needles (from EtOH), m.p. 232°. (Calc. for $C_{16}H_9N_5O_4$: C, 57·32; H, 2·71; N, 20·89. Found: C, 57·00; H, 2·70; N, 20·70%).

3-(2,4-*Dinitrophenyl)-2-methylimidazo*[4.5-*f*]*quinoline* (**8b**). When 5-amino-6-(2,4-dinitroanilino)quinoline **7** (1·5 g), AcOH (15 ml), Ac_2O (10 ml) and few drops of conc HCl were refluxed for 5 hr and the mixture worked up as above. The imidazole **8b** was obtained as golden yellow needles from AcOH, m.p. 319°. (Calc. for $C_{17}H_{11}N_5O_2.H_2O$: C, 55·60; H, 3·50; N, 19·10. Found: C, 55·90; H, 3·80; N, 18·70%).

Condensation of imidazo[4.5-*f*]*quinoline with 2,4-dinitrochlorobenzene.* Imidazo[4.5-*f*]quinoline[14] **9** (1·69 g, 0·01 mol) was fused with 2,4-dinitrochlorobenzene (2·03 g, 0·01 mol) and NaOAc (0·6 g) at 120–30° for 3 hr. The melt was cooled and dissolved in EtOH. Concentration of the alcoholic solution gave 3-(2,4-dinitrophenyl)imidazo[4.5-*f*]quinoline **8a** (1·8 g), m.p. 232°, not depressed on admixing with an authentic sample prepared as before.

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