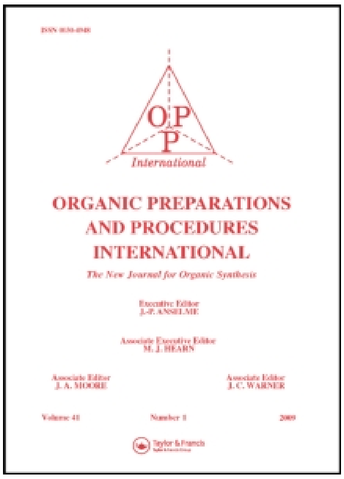

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PREPARATION OF 1,2,3-TRIAZOLO[4,5-f]QUINOLINE N-OXIDES FROM 6-NITRO-5,8-DIMETHOXYQUINALDINE

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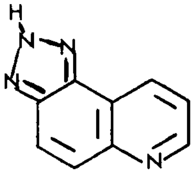
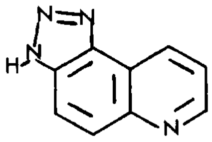
The preparation of the 2H- and 3H-1,2,3-triazolo[4,5-f] quinoline ring systems (I and II, respectively) has been accomplished *via* Skraup[1-5] or Conrad-Limpach[6] cyclization of amino-1,2,3-benzotriazoles and via oxidation of 5-arylazo-6-aminoquinolines.[7-9] Treatment of 5-amino-6-(2,4-dinitroanilino)quinoline with nitrous acid has also been reported[7] to yield a triazoloquinoline.



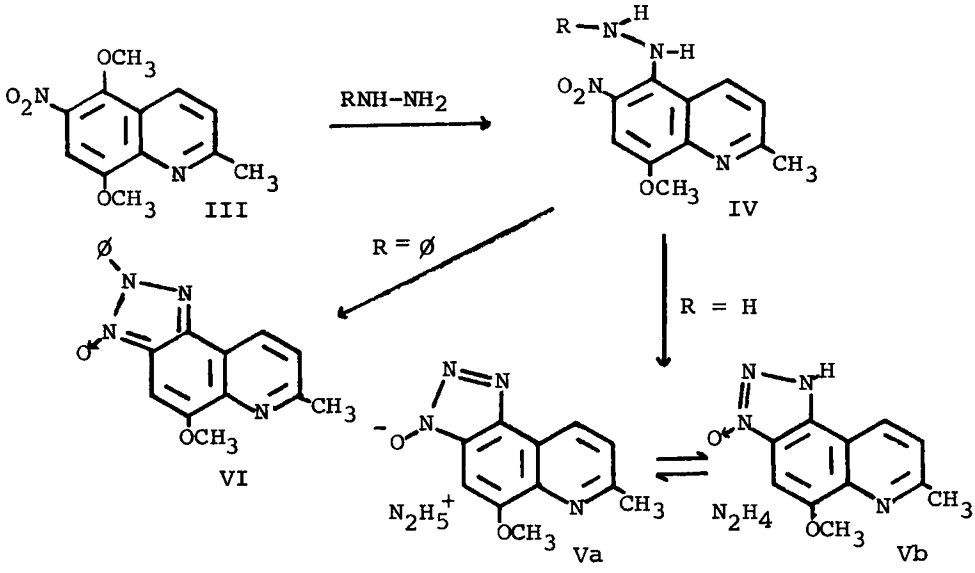
I



II

In a synthetic study on new quinoline antimalarials, it was desired to obtain 3-oxide derivatives of this triazolo[4,5-f]quinoline system. This previously unreported class of compounds, we have found, can be obtained in one step by the hydrazinolysis of the corresponding nitromethoxyquinaldine (Scheme 1), a reaction which parallels the well-known base-catalyzed cyclization of *o*-nitrophenylhydrazines to benzotriazole N-oxides.[10]

Treatment of (III) with excess hydrazine hydrate gave the tautomeric 3-N-oxide of the triazoloquinaldine (Va,b) (in 71% yield) as its hydrazinium salt. Similarly, from (III) and phenylhydrazine a 71% yield of the non-tautomeric 2-phenyl-3-N-oxide (VI) was obtained.



Scheme 1

The formation of both of these products can be envisioned as occurring *via* nucleophilic displacement on the activated 5-methoxy moiety of (III) by hydrazine or phenylhydrazine resulting in the intermediate (IV). Further nucleophilic cyclization onto the adjacent nitro group with subsequent dehydration would yield the N-oxide products. These observations should, of course, caution researchers from attempting the classic hydrazine/palladium reduction of aromatic nitro functions[11] if they are located adjacent to a group which can undergo displacement.

EXPERIMENTAL

Hydrazinium Salt of the 3-N-oxide of 5-methoxy-1,2,3-triazolo[4,5-f] quinaldine (Va,b). A mixture of 0.50 g (2.01 mmol) of (III)[12] and 2.06 g (2.0 ml, 41.1 mmol) of hydrazine hydrate in 50 ml of ethanol was stirred and heated at reflux under N_2 for 1 hr. Removal of the solvent under reduced pressure left an orange residue which crystallized upon standing. Filtration yielded 0.40 g (71%) of the triazole salt (V); mp 135°-decomposition with gas evolution. Recrystallization from 95% ethanol raised the mp of the orange crystals to 141°-dec., ir (KBr), 3240 (NH), 1627 (triazole C=N), 1572 (quinoline C=N), 1251 (N-O), 1108 (C-O-C), and 840 cm^{-1} (aromatic).

Anal. Calcd. for $C_{11}H_{14}N_6O_2 \cdot H_2O$: C, 47.13; H, 5.75; N, 29.99.
Found : C, 47.39; H, 5.91; N, 30.15.

5-Methoxy-2-phenyl-1,2,3-triazolo[4,5-f]quinaldine 3-oxide (VI). A mixture of 0.75 g (3.02 mmol) of (III) and 0.36 g (3.23 mmol) of 97% anhydrous phenylhydrazine in 20 ml of ethanol was stirred and heated at reflux under nitrogen for 22 hr. Upon cooling, a light tan precipitate formed in the dark red solution. Filtration yielded 0.70 g (71%) of the phenyl triazole (VI), mp 265°-dec. Recrystallization from benzene gave white needles of mp 270°-dec., ir (KBr), 1630 (triazole C=N), 1581 (quinoline C=N), 1250 (N-O), 1117 (C-O-C), and 799 cm^{-1} (aromatic).

Anal. Calcd. for $C_{17}H_{14}N_4O_2$: C, 66.65; H, 4.61; N, 18.30.
Found: C, 66.88; H, 4.89; N, 18.58.

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