

THE REACTIONS OF SOME INDOLES WITH IODINE AZIDE:
SYNTHESES OF 3-AZIDOINDOLENINES, 2-AZIDOMETHYLINDOLES, AND
3a-AZIDO-FURO- AND PYRROLO-[2,3-b]INDOLES

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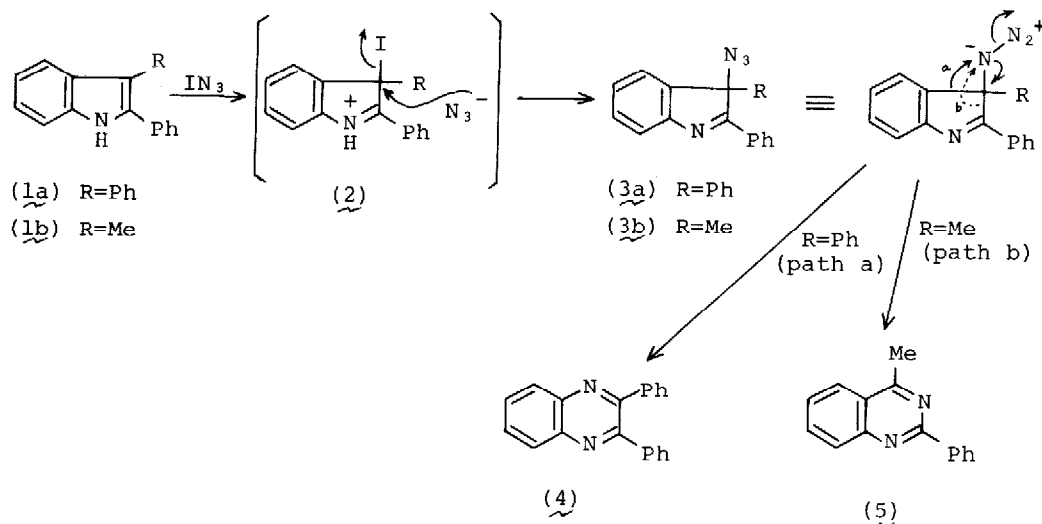
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The reactions of iodine azide (IN_3) with a wide variety of olefins have been a subject of numerous studies in recent years.¹ In a previous paper,² we reported that 1-acylindoles anomalously react with IN_3 to give 1-acyl-*cis*- and *trans*-2,3-diazidoindolines. We have now found that some indoles, on reacting with IN_3 afford different kinds of products; i.e., 3-azidoindolenines, 2-azido-methylindoles, and 3a-azido-furo- and pyrrolo-[2,3-b]indoles, depending upon the position and nature of the substituents. Some chemical transformation reactions of these new indole derivatives are also described.

The reactions were carried out by a slight modification of the procedure of Hassner.³ A solution of the indole (5 mmole) in dry acetonitrile (10 ml) was added dropwise to a stirred solution of IN_3 [prepared *in situ* from iodine monochloride (10 mmole) and sodium azide (15 mmole)] in dry acetonitrile (10 ml) at $-10\sim 0^\circ$ (for 1) or at $-20\sim -30^\circ$ (for 6 and 12). After the reaction mixture was stirred at the same temperature for 3 hr and then at room temperature overnight, the mixture was diluted with water and extracted with ether. The extract was washed with an aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution and water, dried, and concentrated to give a crude product, which was purified either by crystallization or column chromatography on alumina.

Synthesis of 3-Azidoindolenines

When 2,3-diphenylindole (1a) was treated with IN_3 , there was obtained quantitative yield of 3-azido-2,3-diphenylindolenine (3a), mp $106\text{--}107^\circ$, whose structure was assigned on the basis of the spectral and chemical evidence; its



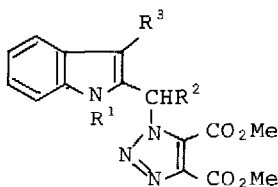
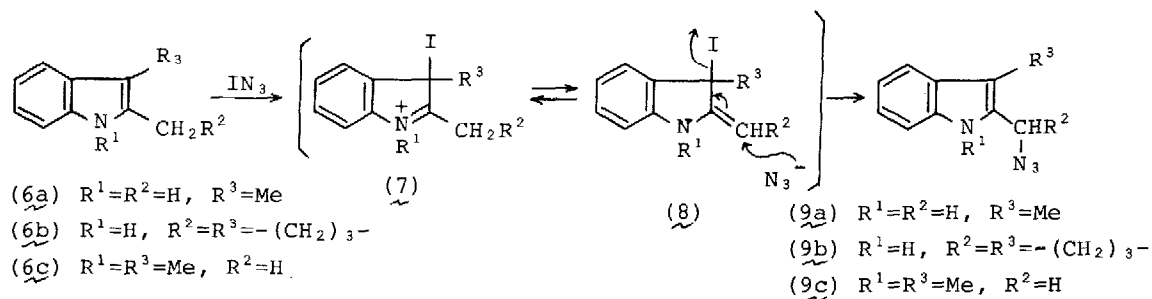
Scheme 1

ir spectrum (CHCl_3) shows a strong azide band at 2070 cm^{-1} and the uv spectrum [λ_{max} (EtOH) 220 ($\log \epsilon$ 4.19), 249 (4.13), and 318 (4.05) nm] resembles that of 2-phenyl-3,3-dimethylindolenine. Refluxing 3a in dimethylformamide gave 2,3-diphenylquinoxaline (4), mp $123\text{--}124^\circ$ (lit.⁴ 124°), in 72% yield, presumably via a concerted mechanism as shown in Scheme 1.⁵ Reduction of 3a either by catalytic hydrogenation over Pd-C or with sodium borohydride in ethanol gave only 1a in high yields.

Similarly, 2-phenyl-3-methylindole (1b) gave 3-azido-2-phenyl-3-methylindolenine (3b), oil [ν_{max} (CHCl_3) $2080\text{ (N}_3\text{) cm}^{-1}$; δ (CDCl_3) 1.60 (s, 3- CH_3)], in quantitative yield, which upon refluxing in dimethylformamide, produced 4-methyl-2-phenylquinazoline (5),⁵ mp $86.5\text{--}87^\circ$ (lit.⁶ 90°), in 81% yield.

Synthesis of 2-Azidomethylindoles

In contrast to the cases of 2-phenyl-substituted indoles 1, treatment of 2,3-dimethylindole (6a) with IN_3 afforded 2-azidomethyl-3-methylindole (9a), mp $83\text{--}84^\circ$, in 94% yield, which exhibits strong ir absorption (KCl) at 3350 (NH) and $2080\text{ (N}_3\text{) cm}^{-1}$ and uv absorption (EtOH) at 225 nm ($\log \epsilon$ 4.38), 280 (3.79), 284 (3.80), and 292 (3.73). The nmr spectrum (CDCl_3) reveals the presence of 3-methyl group at δ 2.28 and 2-methylene group at δ 4.37. Compound 9a readily underwent cycloaddition reaction with dimethyl acetylenedicarboxylate in boiling toluene to afford 1:1 cycloadduct 10a, mp $160\text{--}161^\circ$, in 63% yield. Reduction of 9a with lithium aluminum hydride in ether again reverted to the starting indole 6a in quantitative yield.



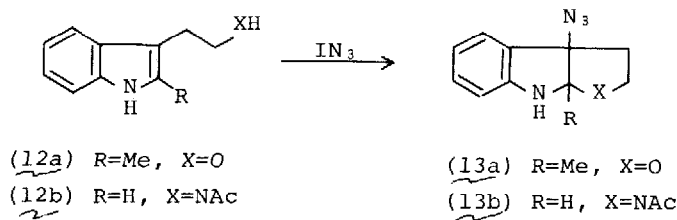
- (10a) $R^1=R^2=H, R^3=Me$
 (10b) $R^1=H, R^2=R^3=-(CH_2)_3-$
 (10c) $R^1=R^3=Me, R^2=H$

Scheme 2

Similar treatment of 1,2,3,4-tetrahydrocarbazole (6b) and 1,2,3-trimethylindole (6c) gave 1-azido-1,2,3,4-tetrahydrocarbazole (9b), mp 53-54.5° [ν_{\max} (CHCl₃) 3430 (NH), 2070 (N₃) cm⁻¹] and 2-azidomethyl-1,3-dimethylindole (9c), oil [ν_{\max} (CHCl₃) 2100 (N₃); δ (CDCl₃) 2.20 (s, 3-CH₃), 3.38 (s, 1-CH₃), 4.16 (s, 2-CH₂N₃)], in 89 and 78% yields, respectively. Both compounds (9b) and (9c) also reacted with dimethyl acetylenedicarboxylate to give the corresponding 1:1 cycloadducts (10b), mp 191-192°, and (10c), mp 127.5-128.5°, respectively.

Synthesis of 3a-Azido-furo- and pyrrolo-[2,3-b]indoles

Application of these reactions to tryptophol (12a) and tryptamine (12b) derivatives gave 3a-azido-furo- and pyrrolo-[2,3-b]indoles (13a) and (13b) in 84 and 43% yields, respectively. The structures of the cyclization products were assigned on the basis of spectral evidence [(13a), mp 37-40°, ν_{\max} (CHCl₃) 3400 (NH), 2090 (N₃) cm⁻¹; δ (CDCl₃) 1.58 (s, 1a-CH₃), 2.1-2.45 (m, 3-CH₂), 3.3-4.1 (m, 2-CH₂), 4.60 (b, NH); λ_{\max} (EtOH) 247 (log ϵ 3.88), 307 (3.24) nm; (13b), oil, ν_{\max} (CHCl₃) 3400 (NH), 2100 (N₃), 1640 (C=O) cm⁻¹; δ (CDCl₃) 2.00 (s, COCH₃), 2.1-2.6 (m, 3-CH₂), 2.9-3.8 (m, 2-CH₂), 5.4 (b, NH), 5.42 (s, CH)]. Reduction of 13a with lithium aluminum hydride gave only 12a in high yield.



Scheme 3

The most likely mechanistic interpretation of these reactions would appear to involve indolenine intermediates (e.g., 2 or 7), analogous to the usual course of halogenation of indoles.⁷ Direct nucleophilic displacement reaction at the 3-position of 2 by azide ion may lead to 3-azidoindolenines 3 (Scheme 1), and tautomerization of 7 to 8 followed by allylic displacement reaction⁸ by azide ion may account for the formation of 2-azidomethylindoles 9 (Scheme 2). The formation of 13 can be considered to be the result of intramolecular trapping of the initially formed indolenine intermediates.

References and Footnote

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