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A CONVENIENT PRECURSOR TO 3,4-DIDEHYDROPYRIDINE

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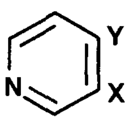
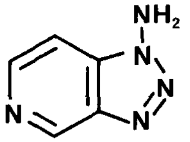
Summary: The preparation of 3-(3,3-dimethyltriazen-1-yl)pyridine-4-carboxylic acid (**5**), a convenient shelf-stable precursor to 3,4-didehydropyridine, is described.

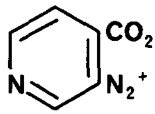
3,4-Didehydropyridine (3,4-pyridyne) is the best described of the hetarynes, the heterocyclic analogues of benzyne,[1] and a few methods are available for its generation. The most extensively studied of these are the elimination of hydrogen halide from 3- and 4-halopyridines with base.[2] Other methods involve the generation of the aryne by treatment of 3-bromo-4-chloropyridine (**1**) with lithium amalgam,[3] of 3-chloro-4-iodopyridine (**2**) with *n*-butyllithium,[4] and of 1-aminotriazolo[4,5-*c*]pyridine (**3**) with lead tetraacetate.[5] In connection with other work on the synthesis of the anti-tumour pyridocarbazole alkaloid ellipticine,[6] we required a thermal "reagent-free" source of 3,4-didehydropyridine. However, the only such precursor available is pyridine-3-diazonium-4-carboxylate (**4**),[7] but this material is difficult to prepare and somewhat unstable. We now report the preparation of 3-(3,3-dimethyltriazen-1-yl)pyridine-4-carboxylic acid (**5**), a convenient new source of 3,4-didehydropyridine.



(1) X = Br, Y = Cl
(2) X = Cl, Y = I



(3)



(4)

The choice of the dimethyltriazenyl moiety as a masked diazonium group was based on the fact that 2-(3,3-dimethyltriazen-1-yl)benzoic acid eliminates carbon dioxide, nitrogen and dimethylamine on heating in chlorobenzene to generate benzyne.[8] This benzyne precursor is relatively little used, despite the fact that it is commercially available, presumably because the preparation of benzenediazonium-2-carboxylate is so well described and easy to carry out. The pyridyl triazene (**5**) is readily prepared by diazotisation of 3-aminopyridine-4-carboxylic acid, obtained from commercially available pyridine-3,4-dicarboxylic acid by the literature method,[9] followed by treatment with alkaline dimethylamine. The details are given below.

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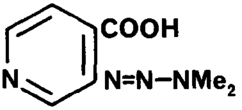
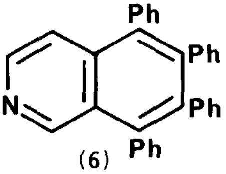
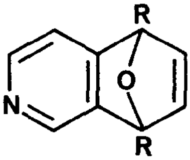


(5)



(6)



(7) R = H
(8) R = Me

The triazene (**5**) is a shelf-stable crystalline solid. However, it is decomposed by boilir acetonitrile, the decomposition being accelerated by the addition of trifluoroacetic The 3,4-didehydropyridine so generated can be intercepted in Diels-Alder reactions tetracyclone, furan and 2,5-dimethylfuran. The adducts (**6**), (**7**), and (**8**) were isolated ir 40, and 45% yields respectively, the reactions with the volatile furans being carried out sealed vessel at 120°C. No Diels-Alder adducts were obtained when the aryne was gene from the triazene (**5**) in the presence of anthracene or cyclopentadiene. This is in line earlier findings,[1,2] and confirms the view that 3,4-didehydropyridine is less predictab its dienophilic properties than 1,2-didehydrobenzene.

3-(3,3-Dimethyltriazen-1-yl)pyridine-4-carboxylic acid (5).- 3-Aminopyridine-4-carbo acid (1.36 g, 9.85 mmol) was suspended in ethanol (20 ml) and concentrated hydrochloric (2.5 ml) was added. The mixture was cooled in ice, and treated dropwise with an ice solution of sodium nitrite (1.77 g, 25 mmol) in water (25 ml). After the addition mixture was stirred at 0°C for a further 20 min. The cold diazotisation solution was added dropwise to an ice cold mixture of sodium carbonate (3.44 g, 32 mmol), and dimethyl (26% aqueous solution; 1.73 g, 10 mmol) in water (20 ml). The resulting mixture was st for a further 30 min at 0°C, acidified to pH 4-5 with concentrated hydrochloric acid extracted with chloroform (5 x 25 ml). The chloroform extracts were combined, dried (Na and evaporated to give the title compound as a pale yellow solid (1.40 g, 73%), m.p. (Found: C, 49.15; H, 5.1; N, 28.5. $C_8H_{10}N_4O_2$ requires C, 49.5; H, 5.2; N, 28.85%) δ (C 3.4 (3H, s), 3.8 (3H, s), 7.95 (1H, d), 8.50 (1H, d), and 8.95 (1H, s).

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