

## The Reaction of Benzyne with Imines

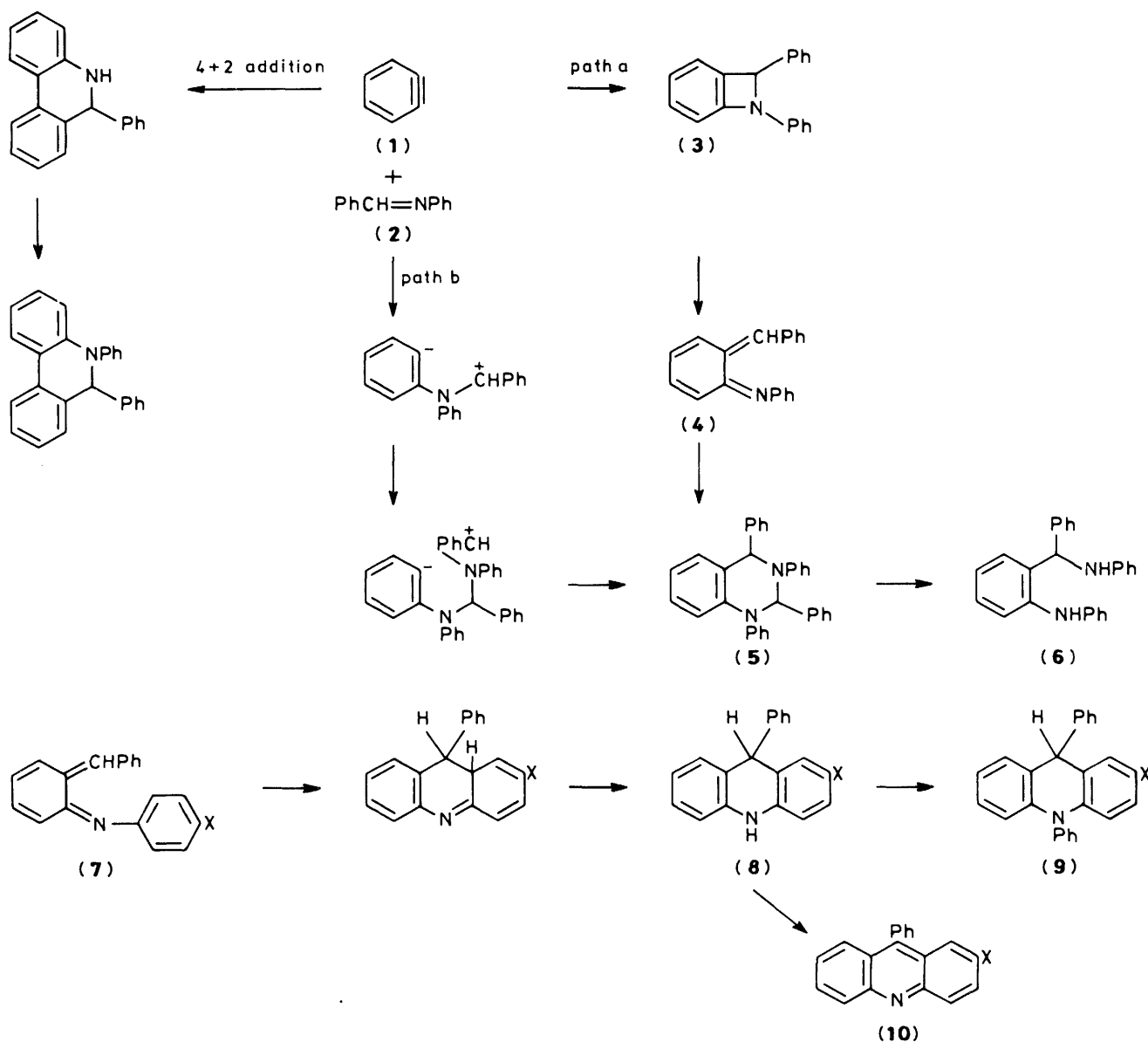
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The isolation of acridines from reaction of benzyne with the imines, *N*-benzylideneaniline and *N*-benzylidene-4-chloroaniline, and the amidines, *N,N*-dimethyl-*N'*-phenylformamidine and *N*-phenyliminomethylpyrrolidine, provides unambiguous evidence for the formation of transient benzazetidines by 2 + 2 cycloaddition.

No simple, widely applicable route to benzazetidines has yet been developed. One obvious approach is 2 + 2 cycloaddition of benzyne (1) to imines but, so far, only one claim for this reaction has appeared. Thus in 1975, Nakayama<sup>1</sup> and his co-workers isolated, *inter alia*, *N*-[ $\alpha$ -(*o*-anilinophenyl)benzyl]-aniline (6) from the thermal decomposition of benzenediazonium carboxylate in the presence of *N*-benzylideneaniline.

This was interpreted in terms of 2 + 2 addition to give diphenylbenzazetidine (3) which underwent spontaneous ring opening to an azaxylylene (4) and trapping with more *N*-benzylideneaniline to give the tetrahydroquinazoline derivative (5). This suffered hydrolysis to the observed diamine during chromatographic work-up (path a). Whilst this explanation is plausible, isolation of the diamine (6) does not constitute

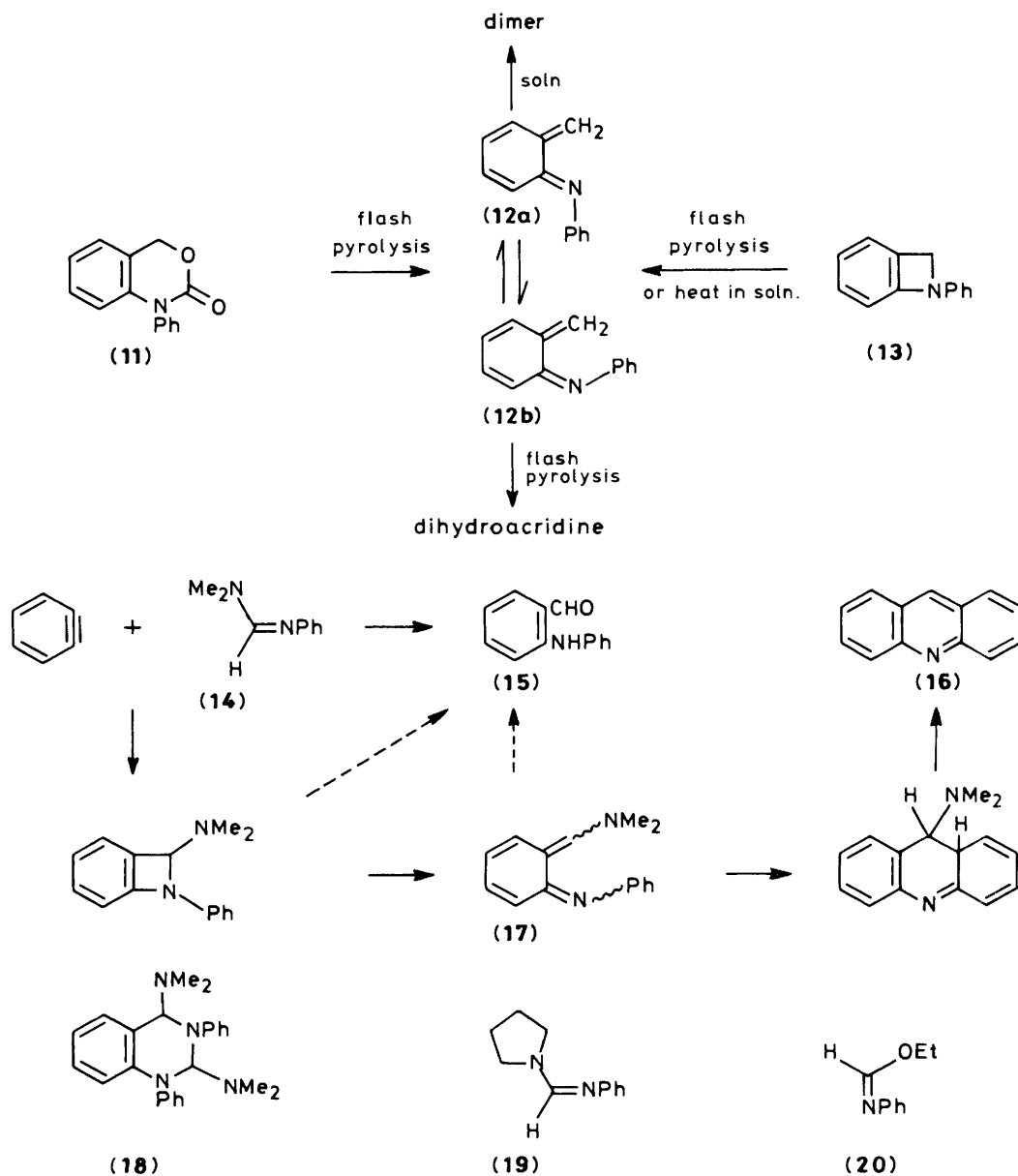


unambiguous evidence for the intervention of a benzazetidone since the proposed tetrahydroquinazoline could also, reasonably, arise by a stepwise 2 + 2 + 2 addition of the imine to benzyne (path b). Furthermore, our experience with *N*- and *C*-phenyl substituted azaxylenes led us to expect that the claimed intermediate (4) would also undergo electrocyclicisation to give dihydroacridine derivatives.<sup>2,3</sup> We now report that this is indeed the case and present other evidence which unambiguously establishes the 2 + 2 addition of benzyne to imines.

Decomposition of benzenediazonium carboxylate (10 mmol) in boiling dichloroethane (100 ml) in the presence of benzylideneaniline (5 mmol) gave a complex mixture which on chromatography on alumina gave, in addition to the diamine (6) and diphenyldihydrophenanthridine reported by Nakayama *et al.*,<sup>1</sup> 5,10-diphenyldihydroacridine (9; X = H) (5%). This last product can be explained by electrocyclicisation involving the *N*-phenyl group in the azaxylene (7; X = H) followed by H-tautomerism and phenylation with benzyne. This mechanism for formation of the acridine, rather than interception of the azaxylene with benzyne, was confirmed by the isolation of

2-chloro-5,10-diphenyldihydroacridine (9; X = Cl) (1%) and 2-chloro-10-phenylacridine (10; X = Cl) (3%) in the similar reaction of *N*-benzylidene-4-chloroaniline with benzyne. These arise from the intermediate dihydroacridine (8; X = Cl) by phenylation and dehydrogenation respectively; 2-chloro-5,6-dihydro-5,6-diphenylphenanthridine (9%) was also isolated from this reaction.

In the formation of dihydroacridines *via* azaxylenes (7), electrocyclicisation involves the *N*-phenyl rather than the *C*-phenyl substituent indicating that this more readily adopts the required 'inside' configuration (only the *Z* imine can cyclise). This *N*-phenyl cyclization occurs in high yield when the azaxylene (12) is generated flash pyrolytically from the oxazinone<sup>2</sup> (11) or benzazetidone (13). However when the benzazetidone (13) is heated in solution (up to 200 °C) no dihydroacridine is observed, only azaxylene dimer being formed. Presumably, in solution there is insufficient thermal energy to give enough *Z* imine (12b) to allow electrocyclicisation to compete with dimerization. In the gas phase at low pressure, dimerisation is suppressed and ample energy is available for



*E-Z* (12a $\rightleftharpoons$ 12b) isomerisation. In these benzyne additions conversion of the initial diarylbenzazetidines (3) into dihydroacridines in solution at 80 °C indicates that a conjugating (or see below, electron releasing) group on carbon facilitates the *E-Z* configurational changes required to convert the sterically more favoured *E* imine into the *Z* isomer.

Generation of benzyne in the presence of *N*-benzylideneethylamine gave *N,N*-diphenylethylamine (13%) as the only characterisable product, there being no evidence for formation of a benzazetidine. Because traces of water are inevitably present in the generation of benzyne from the diazonium carboxylate this amine possibly arises by phenylation of ethylamine produced by hydrolysis of the imine. Alternatively *N*-phenylation of the imine would give an immonium cation which would be especially susceptible to hydrolysis leading to phenylethylamine which could then undergo further phenylation.

The reaction of benzyne with the amidine (14) was investigated in anticipation of a more efficient addition with this relatively electron-rich imine. Chromatography of the reaction mixture over silica gel gave *N*-phenylanthranaldehyde (15) (8%) and acridine (16) (17%). The latter clearly provides further evidence for 2 + 2 addition to give a benzazetidine which again undergoes spontaneous ring opening to a transient azaxylylene followed by electrocyclisation and aromatisation of the resulting dimethylaminodihydroacridine. The amino aldehyde (15) could have arisen by hydrolysis of the benzazetidine or the azaxylylene, or indirectly by hydrolysis of the tetrahydroquinazoline (18) which, in turn, could be formed by addition of azaxylylene (17) to amidine or by 2 + 2 + 2 addition of amidine to benzyne. When the generation of benzyne was carried out at 55 °C, the ratio of amino aldehyde (15) (16%) to acridine (16) (10%) was increased possibly suggesting that at this lower temperature more benzazetidine survives to suffer ultimate hydrolysis to the amino aldehyde on work-up. Acridine (16) (15%) and amino aldehyde (15) (6%) were similarly obtained from the amidine (19). The imidate (20) also gave acridine in low yield (3%).

Although these experiments establish that 2 + 2 addition of benzyne to imines does occur, no benzazetidines can be isolated and the maximum combined yield of benzazetidine-derived products (ca. 30%) indicates that the reaction is inefficient. Generation of benzyne by oxidation of 1-aminobenzotriazole<sup>4</sup> in the presence of imines, even at -80 °C failed to give any recognisable products and the highly reactive 3-nitrobenzyne,<sup>5</sup> also produced from the 1-aminotriazole did not add to the amidine (14). Control experiments show that the amidine did not react with the aminobenzotriazoles or the lead tetra-acetate under the reaction conditions. 3,6-Dimethoxybenzyne generated from dimethoxybenzenediazonium carboxylate hydrochloride,<sup>6</sup> similarly gave no detectable benzazetidine-derived products in contrast with the exceptionally high yields of 2 + 2 adducts of this benzyne with olefins.<sup>7</sup>

## Experimental

*General Procedure for Reaction of Benzyne with Imines.*—Benzenediazonium carboxylate prepared from anthranilic acid<sup>8</sup> (10 mmol) was added slowly to a boiling solution of the

imine (5 mmol) in dichloroethane (100 ml) in an open beaker. The mixture was heated for 5 min, cooled, and filtered. The resulting brown solution was concentrated and the residue subjected to chromatography on alumina. The separated components were further purified by preparative t.l.c.

(a) *N*-Benzylideneaniline (2) gave 5,10-diphenyl-5,10-dihydroacridine (9) (5%), m.p. 172–173 °C (lit.,<sup>9</sup> m.p. 175 °C), 5,6-diphenyl-5,6-dihydrophenanthridine (6%), m.p. 139–140 °C (lit.,<sup>1</sup> m.p. 138–140 °C) and *N*-[ $\alpha$ -(*o*-anilinophenyl)-benzyl]aniline (6) (16%), m.p. 134–135 °C (lit.,<sup>10</sup> m.p. 134–135 °C).

(b) *N*-Benzylidene-4-chloroaniline gave 2-chloro-5,10-diphenyl-5,10-dihydroacridine (9; X = Cl) (1%), m.p. 195–196 °C (lit.,<sup>9</sup> m.p. 197 °C), 2-chloro-10-phenylacridine (10; X = Cl) (3%), m.p. 149–150 °C (lit.,<sup>11</sup> m.p. 150–151.5 °C) and 2-chloro-5,6-diphenyl-5,6-dihydrophenanthridine (9%), m.p. 134–135 °C from light petroleum (Found: C, 81.3; H, 4.95; N, 3.7. C<sub>25</sub>H<sub>18</sub>ClN requires C, 81.6; H, 4.9; N, 3.8%);  $\delta$ (CDCl<sub>3</sub>) 5.88 (1 H, s), 6.92–7.43 (15 H, m), and 7.62–7.78 (2 H, m); *m/z* 369 and 367.

(c) *N*-Benzylidene-ethylamine<sup>12</sup> gave *N,N*-diphenylethylamine (13%) as a colourless oil, b.p. 78 °C/ca. 1 mmHg (lit.,<sup>13</sup> 149.5–150 °C/10 mmHg).

(d) *N,N*-Dimethyl-*N'*-phenylformamidine (14)<sup>14</sup> gave *o*-anilino benzaldehyde (15) (8%), m.p. 71–72 °C (lit.,<sup>15</sup> m.p. 72.5 °C) and acridine (16) (17%), m.p. 110–111 °C (lit.,<sup>16</sup> m.p. 111 °C).

(e) *N*-Phenyliminomethylpyrrolidine (19)<sup>17</sup> gave 2-*N*-phenylaminobenzaldehyde (15) (6%), diphenylamine (2%), and acridine (15%).

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