COMMUNICATIONS

- New or improved synthetic methods
- Key intermediates
- with full experimental and analytical data

Synthesis of 1,4-Ethano-3,4-dihydro-2*H*-1,5-naphthyridines

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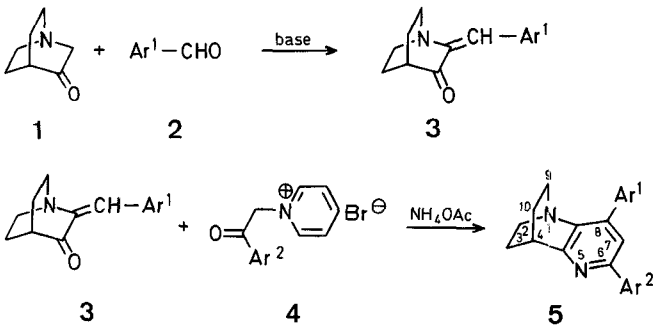
The importance of the quinuclidine moiety in various potential drug compounds cannot be underestimated[1]. We have been interested in developing nitrogen heterocycles incorporating a quinuclidine nucleus. These condensed heterocycles, i.e. with a quinuclidine nucleus fused to a pyridine ring, represent a new ring system.

The 3-quinuclidinone **(1)** was converted into 2-benzylidene derivatives **3** by the base-catalysed condensation of aromatic aldehydes **2**[2]. The benzylidene compounds of the type **3** are synthetically useful as a variety of heterocycles can be prepared therefrom using appropriate condensing agents. Earlier, we described condensation of 4-benzylidene derivatives of 1-substituted 2,3-dioxopyrrolidines with the reactive phenacylpyridinium bromides **4** to give a new route to 5*H*-pyrrolo[3,4-*b*]pyridine derivatives[3]. A similar approach was used to react the bright yellow coloured arylidene derivatives of 3-quinuclidinone with phenacyl bromide. The reaction was conducted in a mixture of acetic acid/ethanol containing ammonium acetate, producing good yields of desired products, i.e. the 6,8-disubstituted-1,4-ethano-3,4-dihydro-2*H*-1,5-naphthyridines **5**, a new class of compounds.



1 2 3 3 4 5

The compounds **5c–e** were converted into the corresponding hydrochlorides to achieve water solubility. These hydrochlorides were tested for antibacterial activity with *Staph. aureus*, *E. coli*, and *Pseudomonas aeroginosa* and were found to be inactive.

6,8-Diaryl-1,4-ethano-3,4-dihydro-2*H*-1,5-naphthyridines 5a–e; General Procedure:

The 2-arylidene-3-quinuclidinone **3** (0.005 mol), phenacylpyridinium bromide **4** (0.005 mol), and ammonium acetate (1.0 g) are refluxed in ethanol/acetic acid (20 ml/1 ml) for 2–3 h. The reaction mixture is poured into ice-cold water (300 ml), when a crystalline solid product precipitates. The solid is filtered, washed with water (200 ml) and crystallized from dimethylformamide/ethanol (Table).

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Table. 6,8-Diaryl-1,4-ethano-3,4-dihydro-2*H*-1,5-naphthyridines **5a–e**

Product No.	Ar^1	Ar^2	Yield [%]	m.p. [°C]	Molecular formula[a]	I.R. (nujol) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3/CF_3COOH$) δ [ppm]
5a	C_6H_5	C_6H_5	69	280–282°	$C_{22}H_{20}N_2$	1618	2.1 (m, 4H); 2.85 (q, 1H); 3.2 (m, 4H); 6.80 (s, 1H); 7.3–7.9 (m, 10H)
5b	4-H_3CO—C_6H_4	C_6H_5	62	230–233°	$C_{23}H_{22}N_2O$ (342.2)	1616	2.15 (m, 4H); 2.96 (q, 1H); 3.2 (m, 4H); 3.80 (s, 3H); 6.95 (s, 1H); 7.4–8.1 (m, 9H)
5c	4-Cl—C_6H_4	C_6H_5	58	>285°	$C_{22}H_{19}ClN_2$ (346.6)	1613	2.1 (m, 4H); 2.78 (q, 1H); 3.15 (m, 4H); 6.90 (s, 1H); 7.45–8.1 (m, 9H)
5d	C_6H_5	4-Br—C_6H_4	61	220–222°	$C_{22}H_{19}BrN_2$ (391.1)	1610	2.2 (m, 4H); 2.69 (q, 1H; 3.15 (m, 4H); 6.95 (s, 1H); 7.3–7.95 (m, 9H)
5e	4-H_3CO—C_6H_4	4-Br—C_6H_4	57	>290°	$C_{23}H_{21}BrN_2O$ (421.1)	1615	2.1 (m, 4H); 2.90 (q, 1H); 3.2 (m, 4H); 3.72 (s, 3H); 6.85 (s, 1H); 7.4–7.9 (m, 8H)

[a] Satisfactory microanalyses obtained: C ±0.31, H ±0.34, N ±0.29.

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