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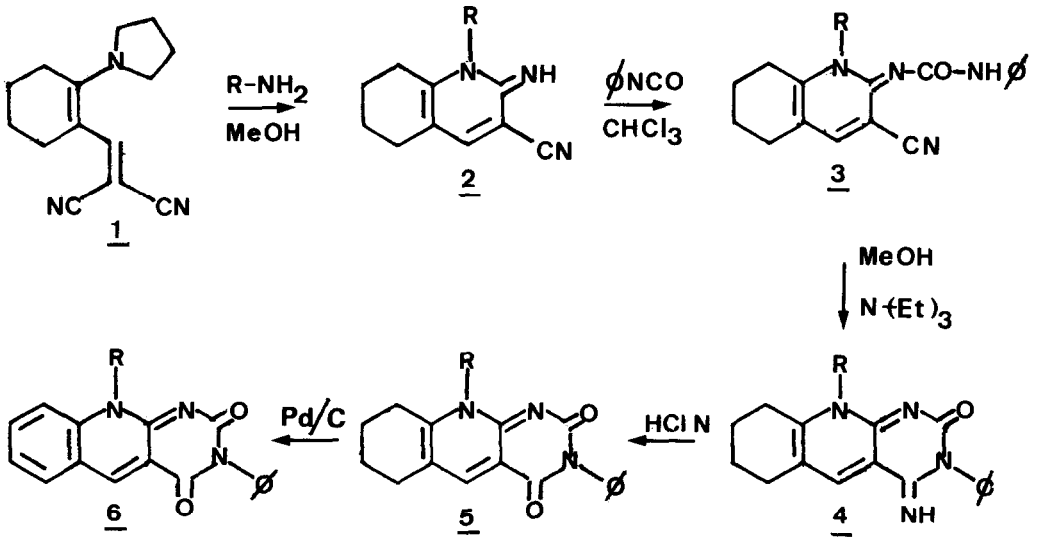
A NEW SYNTHESIS OF 5-DEAZAFLAVINS

Alain LACROIX and Jean-Pierre FLEURY
Laboratoire de Chimie Organique Générale
Ecole Nationale Supérieure de Chimie 68093 MULHOUSE Cédex F.

In recent years deazaflavins have been extensively studied because of their biochemical properties and their use as flavin model compounds[1]. We have recently described a new synthesis of flavins using methyl 1-alkyl-2-amino-1,5,6,7-tetrahydro-3-quinoxaline carboxylates as key intermediates[2]. We now wish to report a new synthetic approach to 5-deazaflavin using 1-alkyl-3-cyano-5,6,7,8-tetrahydro-2-quinolone-imines 2. These compounds have been obtained in good yields by reaction, in boiling methanol, of primary amines with the dienamine 1, itself synthesised according to the method of Kurihara and Mishima[3] by reacting the pyrrolidine enamine of cyclohexanone with methoxymethylenemalononitrile.



Reaction of the pyridone-imine 2 with one and a half molar equivalents of phenylisocyanate gave an excellent yield of N-acylated derivative 3, which upon treatment with triethylamine cyclized to the imino derivative of 3-phenyl-6,7,8,9-tetrahydro-5 -deazaisoalloxazine 4.

Hydrolyzis of the imine was achieved in boiling hydrochloric acid and the resulting 3-phenyl-6,7,8,9-tetrahydro-5-deazaisoalloxazine 5 was dehydrogenated with Pd/C in refluxing decalin.

Table : Physical properties and U.V. absorptions of compounds 2 to 6.

	mp (°C)	Yields (%)	Recrystallisation	U.V. in EtOH 96° ; λmax (nm), 10^{-3} ε
2a	81	90	CH_3OH	398 (3,8) ; 346 (3,5) ; 256 (7,8) ; 220 (9,5)
2b	68	72	CH_3OH, H_2O	399 (5,9) ; 258 (9,4) ; 223 (10,0)
3a	191	96	CH_3OH	384 (8,0) ; 294 (19,8) ; 235 (14,0)
3b	168	95	CH_3OH	385 (8,7) ; 294 (19,3) ; 236 (15,0)
4a	> 330	89	CH_3OH	387 (10,8) ; 280 (10,2) ; 214 (19,1)
4b	> 300	96	CH_3OH	387 (11,5) ; 281 (11,0) ; 213 (20,8)
5a	253	95	CH_3OH	377 (10,5) ; 274 (11,5) ; 214 (18,7)
5b	236	94	CH_3OH	380 (10,6) ; 277 (11,3) ; 210 (21,0)
6a	345	91	CH_3OH	397 (9,4) ; 321 (7,2) ; 265 (32,5) ; 220 (29,5)
6b	263	90	CH_3OH	397 (12,0) ; 323 (11,0) ; 265 (40,0) ; 222 (38,0)

a : R = $-CH_3$; b : R = $-CH_2-CH_2-OCH_3$

The 5-deazaflavins 6 thus synthesised show the expected elemental analyses and spectroscopic properties. In order to vary the substitution, reactions of various amines and isocyanates are under investigation.

References

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