A Lithium Analogue of the Emmert Reaction

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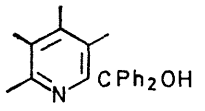
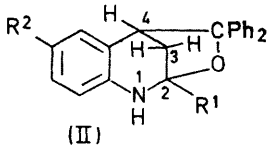
Summary Treatment of pyridines and benzopyridines with benzophenone and lithium in ether affords a convenient route to the alcohols (I) and (with some quinolines) leads to the formation of the 4,4-diphenyl-1,2,4,5-tetrahydro-2,5-methano-3,1-benzoxazepines (II).

THE Emmert reaction for the production of heterocyclic alcohols[1] is usually performed with the heterocycle, a ketone, and either magnesium or aluminium amalgam. We now report that the use of benzophenone and lithium wire in a 1 : 2 ratio offers in some cases a more convenient route to the compounds (I), most of which are new. With the quinolines the cyclised product (II) is formed in some cases. All the reactions were carried out in boiling ether, under nitrogen, over a period of several hours.



(I)



(II)

When a benzophenone : lithium ratio of 1 : 1 was used the chief product was the pinacol $Ph_2C(OH)\cdot C(OH)Ph_2$, presumably formed from dimerisation of the corresponding ketyl.[2] Insertion of the alcohol group occurs exclusively at the α-position. These facts are consistent with the intermediacy of the cyclic intermediate (III), analogous to that recently suggested for the Emmert reaction,[3] and imply initial attack by the anion $(Ph_2C\cdot OLi)^-$ (see Scheme 1).

TABLE 1

Products from the reaction between heterocyclic bases, benzophenone and lithium wire (ratio 1 : 1 : 2)

Heterocycle	Yield of (I) (%)	Yield of (II) (%)
4-Methylpyridine	47·0	—
Quinoline	31·8	19·6
Isoquinoline	20·1	—
4-Methylquinoline	53·4	—
2-Methylquinoline	—	76·0
2,6-Dimethylquinoline	—	59·0
2-Phenylquinoline	—	52·0

TABLE 2

4,4-Diphenyl-1,2,4,5-tetrahydro-2,5-methano-3,1-benzoxazepines (II)

R¹	R²	M.p. (°)	U.v. λ_{max} (nm)	I.r. ν_{max} (cm^{-1}) (Nujol)	M.p. of derived 4-(diphenylmethyl)quinolines
H	H	195	251, 295 (EtOH)	3350, 1620, 1595, 1040	158°
Me	H	185	250, 297 (Et_2O)	3480, 1620, 1600, 1050	174°
Me	Me	187	252, 304 (Et_2O)	3350, 1620, 1600, 1085	201°
Ph	H	153	252, 295 (EtOH)	3450, 1620, 1592, 1040	159°

		N.m.r. τ-Values (Me_4Si = 7·00)						Coupling constants Hz				
R¹	R²	1-H	2-H	3-H	4-H	Aromatic H	Methyl H	$J_{2,3}$	$J_{2,3'}$	$J_{3,4}$	$J_{3',4}$	$J_{3,3'}$
H	H	5·18(s)	4·70(s)	7·17(q)	6·17(t)	2·35—3·82(m)	—	4·0	0·0	2·5	0·0	0·0
Me	H	5·45(s)	—	7·77(d)	6·15(t)	2·35—3·72(m)	8·38(s)	—	—	2·5	0·0	0·0
Me	Me	5·55(s)	—	7·78(d)	6·20(t)	2·30—3·78(m)	8·04(s); 8·38(s)	—	—	2·5	0·0	0·0
Ph	H	5·30(s)	—	7·41(m); 7·60(m)	6·03(d)	2·20—3·82(m)	—	—	—	3·5	0·5	12·0

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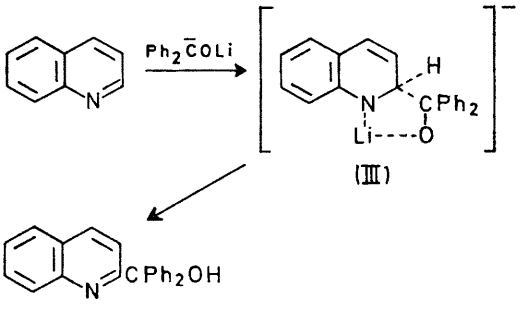
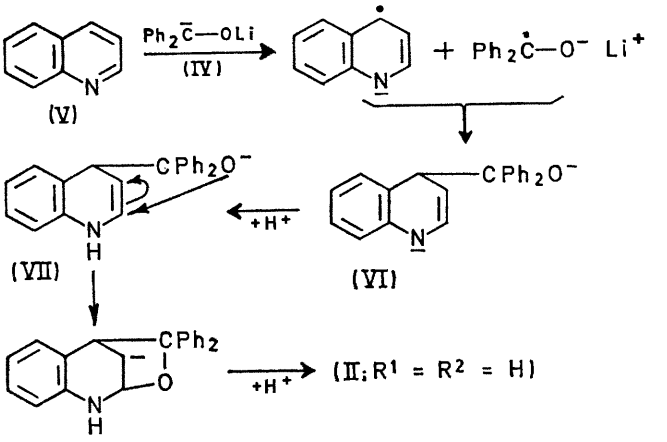
The alternative reaction, leading to (II), (see Scheme 2) may be rationalised in terms of a single electron transfer from the anion (IV) to the heterocycle (V), followed by a



SCHEME 1

radical coupling to give (VI). The subsequent internal Michael reaction appears to be most probable for the monoprotonated anion (VII) which may acquire its proton from solvent or unchanged heterocyclic base. It is noteworthy that a rather similar mechanism has been suggested for the formation of one of the electrolytic reduction products of 1-acetylnaphthalene.[4]

The structures of the cyclised products (II) follow principally from the spectroscopic data recorded in Table 2. When R = H and Me, the aliphatic protons appear as an AB_2 system, but when R = Ph an ABX spectrum is evident for the aliphatic protons 3-H and 4-H; the small couplings of 3-H and 3'-H with 4-H are consistent with the known behaviour of the tetrahydromethanobenzoxepine from 1-acetylnaphthalene.[4]



SCHEME 2

Each of the tetrahydromethanobenzoxazepines yields a 4-(diphenylmethyl)quinoline with concentrated sulphuric acid. They, and the alcohols (I), have all been characterised by spectral and elemental analysis.

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