Organolithium Chemistry of *N*-Heterocycles. Part IV.[1] Formation of 1,2,4,5-Tetrahydro-4,4-diphenyl-2,5-methano-3,1-benzoxazepines from Quinolines

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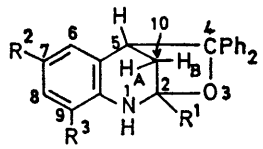
Certain quinolines react with the anion $(Ph_2COLi)^-$ derived from benzophenone and excess of lithium to give high yields of 1,2,4,5-tetrahydro-4,4-diphenyl-2,5-methano-3,1-benzoxazepines (I). These may be smoothly converted by 70% sulphuric acid into 4-(diphenylmethyl)quinolines (VIII).

DURING our studies of a lithium analogue of the Emmert reaction,[2] in which heterocyclic bases were treated with benzophenone and lithium in ether, the expected carbinol from quinoline (diphenyl-2-quinolylmethanol) was accompanied by an unexpected product subsequently shown to be 1,2,4,5-tetrahydro-4,4-diphenyl-2,5-methano-3,1-benzoxazepine (Ia), formed by attack of the anion $(Ph_2COLi)^-$ (II). We now describe experiments

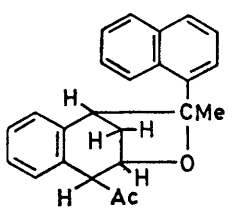


(I)

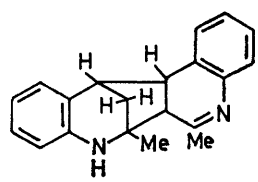
	R^1	R^2	R^3
a;	H	H	H
b;	Me	H	H
c;	Me	Me	H
d;	Ph	H	H
e;	Ph	Me	H
f;	Ph	H	Me

with substituted quinolines which led to a series of analogous compounds, present evidence for their structure, and suggest a mechanism for their formation. In all cases except for that of quinoline itself there was a substituent at position 2; position 4 was always free.

Although this tetrahydromethanobenzoxazepine system appears to be new, analogies may be recognised in certain dimeric reduction products of 1-acetylnaphthalene (III) [3] and of 2-methylquinoline (IV).[1] Data for the



(III)



(IV)

new compounds are recorded in Tables 1—4. Rast determinations of molecular weights gave unsatisfactory results, probably because of thermal decompositions; also the molecular ion peaks in the mass spectra were small.

Treatment of benzophenone with excess of sodium [4] gives first the ketyl and then the salt $(Ph_2CONa)^-Na^+$. In the corresponding benzophenone–lithium system the blue solution first formed with a 1 : 1 ratio rapidly lost its colour, slowly depositing a white precipitate, but on treatment with a further 1 equiv. of lithium the colour changed to deep red and the mixture yielded diphenylmethanol (*ca.* 80%) on hydrolysis. Treatment of the white precipitate with water gave comparable yields of tetraphenylethylene glycol. These results may be interpreted as shown (Scheme 1).

TABLE 1

Yields, m.p.s, and analytical data

	Yield (%)	M.p. (°C)	Formula	Reqd. (%) C	H	N	Found (%) C	H	N
(I)a	12·9	195	$C_{22}H_{19}NO$	84·4	6·1	4·5	84·1	6·0	4·5
b	76·2	185	$C_{23}H_{21}NO$	84·4	6·4	4·3	84·4	6·5	4·5
c	58·9	187	$C_{24}H_{23}NO$	84·4	6·7	4·1	84·2	6·7	4·1
d	52·0	153	$C_{28}H_{23}NO$	86·4	5·9	3·6	85·6	6·1	3·5
e	81·7	143	$C_{29}H_{25}NO$	86·4	6·2	3·5	86·3	6·3	3·4
f	38·6	160	$C_{29}H_{25}NO$	86·4	6·2	3·5	86·4	6·3	3·5

TABLE 2

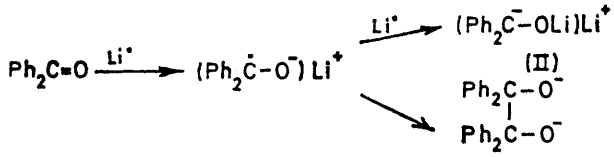
U.v. and i.r. data

	Solvent	$\lambda_{max.}$/nm (ε)	$\lambda_{min.}$/nm (ε)	$\nu_{max.}$/cm^{-1} (Nujol)
(I)a	EtOH	295 (2371), 251 (6497)	276 (1470)	3350, 1620, 1595, 1040
b	Et_2O	297 (2770), 250 (7108)	277 (1277)	3480, 1620, 1600, 1050
c	Et_2O	304 (3042), 252 (9591)	280 (1178)	3350, 1620, 1600, 1085
d	EtOH	295 (2723), 252 (7623)	283 (2489)	3450, 1620, 1592, 1040
e	Et_2O	306 (3611), 252 (13,180)	288 (3275)	3410, 1610, 1600, 1040
f	Et_2O	291 (2317), 252 (7857)	281 (2015)	3400, 1603, 1585, 1040

Since our own experiments involved a 1 : 2 ratio the effective reagent was likely to be the anion (II). This is highly reactive and reverted at once to the ketyl on addition of benzophenone. Similar single-electron transfers from such anions have been reported for such acceptors as diaryl ketones, nitroaromatic compounds, azobenzene, and some aza-aromatic compounds.[5] These facts, together with our observation that the ketyl alone cannot cause reaction, imply that the first step is

[1] Part III, A. M. Jones, C. A. Russell, and O. Meth-Cohn, *J. Chem. Soc.* (*C*), 1971, 2453.
[2] Preliminary communication, C. E. Crawforth, C. A. Russell, and O. Meth-Cohn, *Chem. Comm.*, 1970, 1406.
[3] J. Grimshaw and E. H. F. Rea, *J. Chem. Soc.* (*C*), 1967, 2628.
[4] (*a*) E. Beckman and T. Paul, *Annalen*, 1891, **266**, 1; (*b*) N. Hirota and S. J. Weissman, *J. Amer. Chem. Soc.*, 1964, **86**, 2738.
[5] G. A. Russell, E. G. Janzen, and E. T. Strom, *J. Amer. Chem. Soc.*, 1964, **86**, 1307.

transfer of one electron to yield the ketyl (V) and the quinoline radical-anion (VI). Rapid coupling would then be expected, and this would be most likely to occur at the 4-position of the heterocycle. E.s.r. observations on monosodioquinoline [6] have shown the most stable radical-anion to be (VI; $R^1 = R^2 = R^3 = H$), in accord with theoretical predictions.[7] Although such radical-anions may exist as monomers in extremely polar solvents [4b,8] it is probable that in ether dimerisation would be very rapid. Indeed, the absence of symmetrical dimers (as tetraphenylethylene glycol or biquinolyl derivatives) suggests that coupling occurs immediately



SCHEME 1

after electron transfer and before the two new radical-anions can separate. A subsequent cyclisation is likely to occur in some such manner as that indicated (Scheme 2), with nucleophilic attack on position 2. It is also consistent with the mechanisms proposed for the formation of compounds (III) [3] and (IV).[1] Protonation of the dianion (VII) has not been established but appears probable as a precondition for the internal cyclisation. That complete protonation to form compound (I) takes place before hydrolysis is shown by the lack of deuterium incorporation when hydrolysis is carried out with deuteriated water. Possibly the solvent is involved.

TABLE 3

N.m.r. spectra ($CDCl_3$ solutions)

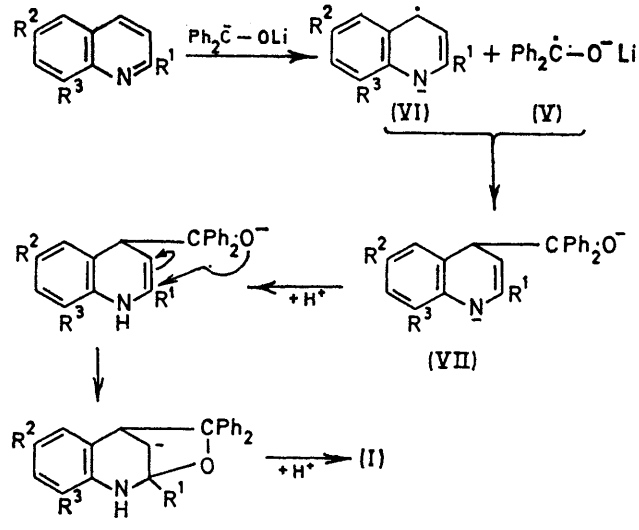
	τ Values						J/Hz
	H-1	H-2	H-10	H-5	Me	Aromatic	
(I)a	5·18(s)	4·7br(s)	7·17(q)	6·17(t)		2·35—3·82m	$J_{5,10}$ 2·5, $J_{2,10}$10 4·0
b	5·45(s)		7·77(d)	6·15(t)	8·38(s)	2·35—3·72m	$J_{5,10}$ 2·5
c	5·55(s)		7·78(d)	6·2(t)	8·04(s) (7) 8·38(s) (2)	2·30—3·78m	$J_{5,10}$ 2·5
d	5·18(s)		7·43(m)	5·95(q)		2·30—3·70m	$J_{5,10A}$ 3·5, $J_{5,10B}$ 1·2, $J_{A,B}$ 11·0
e	5·35(s)		7·47(m)	6·05(q)	8·05(s)	2·25—3·75m	$J_{5,10A}$ 3·5, $J_{5,10B}$ 1·2, $J_{A,B}$ 11·0
f	5·48(s)		7·46(m)	5·97(q)	7·98(s)	2·23—3·76m	$J_{5,10A}$ 3·5, $J_{5,10B}$ 1·2, $J_{A,B}$ 11·0

TABLE 4

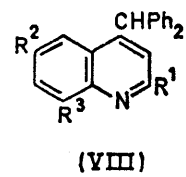
Mass spectra

	m*	m/e (%)
(I)a	54·8, 56·6, 81·7	313 (7), 182 (3), 165 (6), 131 (80), 130 (100), 129 (100), 105 (9), 91 (3), 77 (5), 51 (5)
b	56·5, 64·2	327 (7), 206 (3), 182 (7), 165 (7), 145 (87), 144 (94), 143 (16), 130 (100), 105 (18), 91 (6), 77 (17), 51 (6)
c	56·6, 74·2	341 (9), 220 (2), 182 (4), 165 (5), 159 (59), 158 (73), 157 (13), 144 (100), 105 (12), 91 (35), 77 (11), 51 (3), 28 (6)
d	56·5	389 (4), 283 (3), 207 (86), 206 (100), 205 (37), 204 (28), 182 (23), 165 (3), 130 (35), 105 (46), 77 (30), 51 (10), 28 (7)
e	56·5	403 (4), 298 (3), 283 (2), 222 (17), 221 (73), 220 (100), 219 (45), 182 (17), 165 (7), 144 (7), 142 (16), 115 (19), 105 (98), 91 (11), 77 (84), 51 (31), 28 (17)
f	56·5	403 (1), 298 (2), 283 (1), 222 (17), 221 (63), 220 (89), 219 (75), 182 (28), 165 (7), 144 (50), 142 (13), 115 (17), 105 (100), 91 (9), 77 (85), 51 (35), 28 (19)

All the tetrahydromethanobenzoxazepines were white crystalline solids, soluble in ether and insoluble in water and resistant to hydrolysis by acid or base. However, treatment with 70% sulphuric acid caused nearly quantitative conversion into the corresponding 4-(diphenylmethyl)quinolines (VIII) (Tables 5—8). The u.v.



SCHEME 2



	R¹	R²	R³
a;	H	H	H
b;	Me	H	H
c;	Me	Me	H
d;	Ph	H	H
e;	Ph	Me	H
f;	Ph	H	Me

(VIII)

spectra decisively imply the presence of a quinoline nucleus and the analytical, mass spectral, and n.m.r. data are all consistent with the structures proposed.

[6] L. Lunazzi, *J. Chem. Soc.* (*B*), 1970, 163.
[7] R. D. Brown and R. D. Harcourt, *J. Chem. Soc.*, 1959, 3451; *Tetrahedron*, 1960, **8**, 23.
[8] J. Chandhuri, S. Kume, J. Jagur-Grodzinski, and M. Szwarc, *J. Amer. Chem. Soc.*, 1968, **90**, 6421.

TABLE 5

M.p.s and analytical data

	M.p. (°C)	Formula	Reqd. (%) C	H	N	Found (%) C	H	N
(VIII)a	153	$C_{22}H_{17}N$	89·5	5·8	4·8	89·6	5·6	4·8
b	174	$C_{23}H_{19}N$	89·4	6·1	4·5	89·4	6·1	4·5
c	202	$C_{24}H_{21}N$	89·2	6·5	4·3	89·1	6·5	4·1
d	159	$C_{28}H_{21}N$	90·5	5·7	3·8	90·4	5·8	3·8
e	231	$C_{29}H_{23}N$	90·4	6·0	3·6	90·5	6·0	3·6
f	216	$C_{29}H_{23}N$	90·4	6·0	3·6	90·3	5·8	3·8

TABLE 6

U.v. and i.r. spectra

	Solvent	$\lambda_{max.}$/nm (ε)	$\nu_{max.}$ (Nujol) cm^{-1}
(VIII)a	EtOH	316 (3280), 303 (4480), 290 (6280), 285 (6280), 272 (5740)	1603, 1580
b	EtOH	319 (4120), 305 (4050), 281 (5890), 271 (6990)	1607, 1580
c	Et_2O	325 (3890), 312 (3010), 277 (5140), 271 (5140)	1603, 1580
d	EtOH	291 (9090) *	1603, 1580
e	Et_2O	342 (6144), 328 (7335)	1595, 1580
f	Et_2O	313 (9477)	1600, 1580

* Inflections at 341 (2710), 331 (6120), 324 (7320), 317 (7600), and 310 nm (8070).

TABLE 7

Mass spectra

	m/e (%)
(VIII)a	296 (23), 295 (100), 294 (26), 218 (22), 217 (27), 216 (18), 167 (23), 165 (18), 28 (36)
b	310 (25), 309 (100), 308 (17), 294 (13), 232 (19), 231 (17), 230 (13), 167 (24), 165 (15), 28 (29)
c	324 (27), 323 (100), 322 (12), 308 (17), 246 (11), 245 (6), 244 (6), 231 (9), 230 (15), 167 (23), 165 (14), 28 (17)
d	372 (31), 371 (100), 370 (49), 294 (14), 293 (10), 292 (6), 167 (8), 165 (8), 28 (27)
e	386 (31), 385 (100), 384 (37), 370 (6), 308 (11), 307 (9), 306 (5), 293 (6), 292 (8), 167 (14), 165 (13), 28 (20)
f	386 (32), 385 (100), 384 (8), 370 (3), 308 (7), 307 (8) 306 (7), 293 (6), 292 (7), 167 (9), 165 (10), 28 (20)

TABLE 8

N.m.r. spectra ($CDCl_3$ solutions)

τ Values

	H-3	Ph_2CH	Me	Aromatic
(VIII)a *	3·12(d)	3·76(s)		1·76—3·02(m)
b	3·30(s)	3·83(s)	7·42(s)	1·88—3·10(m)
c	3·30(s)	3·82(s)	7·41(s) (2) 7·63(s) (6)	2·00—3·05(m)
d	†	3·72(s)		1·70—2·95(m)
e	3·00(s)	3·79(s)	7·60(s)	1·85—2·95(m)
f	2·93(s)	3·77(s)	7·10(s)	1·70—2·90(m)

* Also τ 1·2 (d, $J_{2,3}$ 4·5 Hz, H-2). † Obscured by aromatic signals.

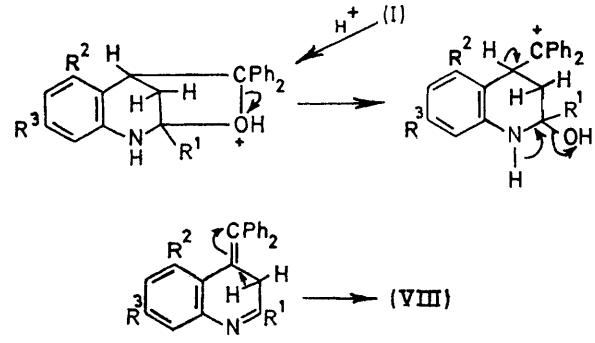
The effect of protonation is that predicted for a carbinolamine-type structure and may be represented as in Scheme 3.

EXPERIMENTAL

Benzophenone and all heterocyclic bases were distilled prior to use; ether was dried over sodium wire and redistilled; lithium was extruded through a 1 mm die.

Instruments used were Unicam SP 800 (u.v. spectra), Unicam SP 200 and Perkin-Elmer 237 (i.r. spectra), Varian A60A and HA 100 (n.m.r. spectra), and Perkin-Elmer–Hitachi RMU 6E (ionizing beam 70 eV) (mass spectra).

Action of Lithium on Benzophenone in Ether.—(a) 1 : 1 *Ratio.* Lithium wire (0·69 g, 0·1 g atom) and benzophenone (18·2 g, 0·1 mol) were heated under reflux in ether (200 ml) under dry nitrogen for 2 days, during which time the colour of the suspension changed from green to deep blue to white and all the lithium disappeared. The mixture was cooled and hydrolysed with water (10 ml). The non-aqueous layer



SCHEME 3

after drying, removal of solvent, and digestion in hot light petroleum (b.p. 40—60°) yielded tetraphenylethylene glycol (12·35 g, 67·5%) as an insoluble residue, and, from the petroleum solution, benzophenone (3·5 g, 18·9%) and a residue (1·9 g).

(b) 2 : 1 *Ratio.* Lithium wire (1·39 g, 0·2 g atom) and benzophenone (18·2 g, 0·1 mol) were heated under reflux in ether (200 ml) under dry nitrogen for 3 days. Hydrolysis of the deep red suspension, and work-up as before, yielded diphenylmethanol (14·1 g, 77·4%), benzophenone (3·1 g, 16·8%), and a residue (1·4 g).

1,2,4,5-*Tetrahydro*-4,4-*diphenyl*-2,5-*methano*-3,1-*benzoxazepines* (I).—(a) *From quinoline.* Lithium wire (1·38 g, 0·2 g atom) was suspended in boiling ether (150 ml) under nitrogen. Benzophenone (18·2 g, 0·1 mol) was dissolved in ether (50 ml) and approximately half the solution was added to the lithium suspension, which was heated and stirred until a red colouration was just visible (1 h). The rest of the solution was slowly added (2 h) and stirring was continued until reappearance of the red colour; quinoline (12·9 g, 0·1 mol) was then added rapidly and heating was continued for a further 2 h. After cooling and addition of water (50 ml) the ethereal layer was extracted with 6N-hydrochloric acid (200 ml) to give a red tar, which on successive treatments with hot ethanol and N-sodium hydroxide yielded *compound* (Ia) (2·95 g, 9·43%), which gave pale yellow needles (from aqueous acetone). Basification (NH_4OH) of the acid extract gave quinoline (10·0 g, 77·5%) and a tar (2·0 g) from which digestion with ethanol gave diphenyl-(2-quinolyl)methanol (1·9 g, 6·1%).

(b) *From other quinolines.* The example of 2-methylquinoline is typical of all the remaining cases. Yields are in Table 1. Lithium wire (1·38 g, 0·2 g atom) and benzophenone (18·2 g, 0·1 mol) were heated together for 3 days in ether. 2-Methylquinoline (14·3 g, 0·1 mol) was then added and heating was continued for 2 more days. Addition of water (50 ml) gave 1,2,4,5-*tetrahydro*-2-*methyl*-2,5-*methano*-3,1-*benzoxazepine* (Ib) as a solid (at the interface) (24·9 g, 76·2%). Recrystallisation from aqueous acetone gave white needles. Extraction of the ethereal solution with

acid yielded only 2-methylquinoline (4·0 g, 28%). The neutral residue showed the intense purple fluorescence characteristic of diphenylmethanol but was not further examined.

4-(*Diphenylmethyl*)*quinolines* (VIII).—All were prepared by similar procedures. For example, 1,2,4,5-tetrahydro-4,4-diphenyl-2,5-methano-3,1-benzoxazepine (Ia) (1·0 g, 0·0032 mol) was suspended in 70% sulphuric acid (12 ml) and maintained at 75° during 12 h. The resultant yellow tar was cooled, digested with water (50 ml), and stirred with 2N-ammonia (100 ml) to yield a cream solid, which gave white needles of 4-(*diphenylmethyl*)*quinoline* (1·0 g, 100%) (from aqueous acetone).

One of us (C. E. C.) thanks the Chemical Society for a research grant.

[1/1849 *Received*, 11*th October*, 1971