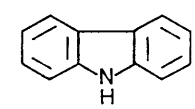
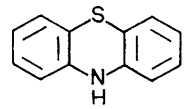
Reactions of Condensed *N*-Heteroaromatic Molecules. Part I. Alkylation by Thallium(I) Ethoxide

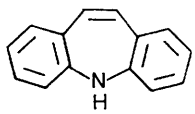
By L. J. Kricka and A. Ledwith,* Donnan Laboratories, University of Liverpool, Liverpool

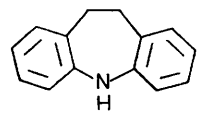
Thallium(I) derivatives of carbazole, phenothiazine, and (to a lesser extent) dibenz[*b,f*]azepine (iminostilbene) may be readily alkylated by reactions with n-alkyl iodides and bromides under extremely mild conditions. 10,11-Dihydrodibenz[*b,f*]azepine (iminobibenzyl) is essentially unreactive and this, together with the complete inactivity of secondary alkyl halides, is indicative of serious steric constraints on the transition states for the alkylations *via* thallium(I) derivatives. The method is particularly valuable for alkylation of carbazoles having base-sensitive carbonyl and vinyl ring substituents.

THALLIUM(I) salts of β-dicarbonyl compounds,[1] cyclic amides,[2] and pyrroles [3] may be conveniently alkylated with an excess of an alkyl iodide, bromide, or, in exceptional circumstances, a chloride.[3] We now report that this procedure applied to carbazole (I), phenothiazine (II), and (to a lesser extent) dibenz[*b,f*]azepine (III),


(I)


(II)

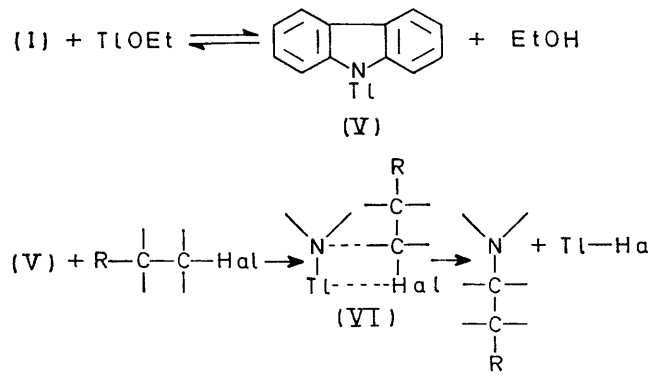

(III)


(IV)

affords under mild conditions high yields of *N*-alkylated products, required as part of a continuing interest in cation radical intermediates.[4] Previously alkylation of these heterocycles has usually been accomplished *via* a sodium or potassium salt under relatively forcing conditions.[5] In a typical alkylation the heterocycle and a slight excess of thallium(I) ethoxide dissolved in dimethylformamide–ether were stirred together at room temperature, and treated with an excess of an alkyl iodide or bromide; the mixture was warmed briefly on a water-bath and worked-up in the usual manner. The results are summarised in the Table.

Particular features of this alkylation procedure are that methylation may be accomplished at room temperature, and that carbazoles having reactive ring substituents (*e.g.* acetyl, vinyl) are efficiently alkylated whereas corresponding reactions using potassium metal as a base give low yields (<10%) of alkylated product. The thallium alkylation procedure, unlike those employing alkali metals and alkali metal amides, is restricted to primary alkyl halides. The failure of carbazole to react with branched chain alkyl halides (*e.g.* Pr^{i}I, Bu^{i}I, and cyclopropyl and cyclohexyl bromides) suggests that alkylation with thallium(I) ethoxide as a base proceeds *via* a mechanism different from that employing an alkali metal or alkali metal amides.

A possible mechanism, which accommodates the observed steric limitations, involves reaction *via* a four-centre transition state such as (VI). Branching at the


(V)

α- or β-carbon atom of the alkali halide would hinder close approach to the carbazole thallium salt (V), and thus preclude reaction, as indicated. For the non-planar [6] dibenz[*b,f*]azepine molecule (III) the etheno-bridge sterically restricts reaction with all but the smallest primary alkyl iodides (*e.g.* Me, Et, and Pr^{n}), whilst the ring puckering effect of the ethano-bridge of 10,11-dihydrodibenz[*b,f*]azepine [iminobibenzyl (IV)] precludes reaction with even methyl iodide and methyl bromide, although the *N*-methylated compound was identified by mass spectrometry as a contaminant of recovered starting material.

Alkylation of these heterocyclic molecules may be achieved by reactions of branched alkyl halides with sodium and especially potassium derivatives. Although potassium and thallium are comparable in size, the former gives rise to bonds to nitrogen having considerably more charge separation (ionic character), possibly accounting for the higher reactivity towards branched alkyl halides. Molecular models indicate clearly the normal S_N2 substitution of the alkyl halide by free heterocyclic anion (or appropriate solvent-separated ion pairs) would not be so critically affected by the steric

[1] E. C. Taylor, G. H. Hawks, and A. McKillop, *J. Amer. Chem. Soc.*, 1968, **90**, 2421.
[2] E. C. Taylor in ' Reagents for Organic Synthesis,' vol. II, eds. M. Fieser and L. F. Fieser, Wiley-Interscience, New York, 1969, p. 410; A. G. Lee, ' The Chemistry of Thallium,' Elsevier, London, 1971; E. C. Taylor and A. McKillop, *Accounts Chem. Res.*, 1970, **3**, 338.
[3] C. F. Candy and R. A. Jones, *J. Org. Chem.*, 1971, **36**, 3993.
[4] A. Ledwith, *Accounts Chem. Res.*, 1972, **5**, 133.
[5] S. H. Tucker and T. S. Stevens, *J. Chem. Soc.*, 1923, **123**, 2140.
[6] R. Huisgen, E. Laschtuvka, and F. Bayerlein, *Chem. Ber.*, 1960, **93**, 392.

restrictions imposed by (III) and (IV) on a four-centre transition state. These observations are supported by the results of Candy and Jones,[3] who found that the thallium derivatives of the comparatively sterically unhindered, but related, molecule pyrrole, could be readily alkylated by branched alkyl halides.

Thallium(I) ethoxide induced *N*-alkylation of condensed heterocycles

Substrate	Alkyl halide	Product	Yield* (%)	M.p. (°C)
Carbazole	MeI	9-Me	78	87—88 [a]
	EtI	9-Et	85	65—66 [b]
	Pr^nI	9-Pr^n	72	49—50 [c]
	Bu^nI	9-Bu^n	71	57—58 [d]
	Bu^nBr	9-Bu^n	62	57—58
	$PhCH_2Br$	9-$PhCH_2$	97	119—120 [e]
	$CH_2{:}CH{\cdot}CH_2Br$	9-$CH_2{:}CH{\cdot}CH_2$	67	55—56 [f]
	$I[CH_2]_3I$	9,9′-$[CH_2]_3$	50	184—185 [g]
	$Br[CH_2]_4Br$	9,9′-$[CH_2]_4$	69	208—209 [h]
	$Br[CH_2]_6Br$	9,9′-$[CH_2]_6$	30	125—127 [i]
2-Acetylcarbazole	EtI	2-Ac-9-Et	62	94—96
2-Vinylcarbazole †	EtI	9-Et-2-$CH_2{:}CH$	61	89—90
Dibenz[*b*,*f*]azepine	MeI	5-Me	74	141—143 [j]
	EtI	5-Et	61	102—103
	Pr^nI	5-Pr^n	29	85—87
Phenothiazine	MeI	5-Me	80	100—101 [k]
	EtI	5-Et	97	100—102 [l]
	Pr^nI	5-Pr^n	66	48—49 [m]

[a] Lit.,[7] m.p. 88°. [b] Lit.,[7] m.p. 68—70°. [c] Lit.,[8] m.p. 50°. [d] Lit.,[8] m.p. 58°. [e] Lit.,[9] m.p. 118—120°. [f] Lit.,[8] m.p. 56°. [g] Lit.,[10] m.p. 186°. [h] Lit.,[10] m.p. 208°. [i] Lit.,[10] m.p. 128°. [j] Lit.,[6] m.p. 143—144·5°. [k] Lit.,[11] m.p. 100—102°. [l] Lit.,[12] m.p. 102·5—103°. [m] Lit.,[13] m.p. 49—50°.

* Of isolated product.

† P. Hyde, L. J. Kricka, and A. Ledwith, *Polymer*, 1972, in the press.

The largely or completely inactive behaviour of alkyl chlorides, including benzyl chloride, in alkylation *via* thallium compounds remains enigmatic.

EXPERIMENTAL

I.r. spectra were recorded for Nujol mulls. ^1H N.m.r. spectra were measured at 60 MHz for solutions in deuteriochloroform with tetramethylsilane as internal standard. Mass spectra were measured by the Physico-Chemical Measurements Unit, Harwell.

2-Acetylcarbazole, m.p. 229—230° (lit.,[14] 230—231°) was obtained as reported.[14] Dibenz[*b*,*f*]azepine was purified by chromatography on a column of neutral alumina (Brockmann Grade I; B.D.H.).

General Procedure for N-*Alkylation of Carbazole.*—Thallium(I) ethoxide (2·6 g) was added to a solution of carbazole (1·7 g) in dimethylformamide–ether (2 : 1 v/v; 30 ml), and the mixture was stirred at room temperature for 0·5 h. An excess of the alkyl halide was added and stirring was continued for a further 0·25 h at room temperature, and then at 50—60° until precipitation of the thallium halide was complete (*ca.* 0·25 h). Precipitated thallium halide was filtered off, and the filtrate was poured into water (*ca.* 30 ml). The aqueous layer was repeatedly extracted with chloroform and the combined extracts were washed with water and dried ($MgSO_4$). Evaporation afforded the *N*-alkylated carbazole, which was recrystallised from alcohol.

The following new compounds were prepared.

2-*Acetyl*-N-*ethylcarbazole* (62%) as needles, m.p. 94—96° [from petroleum (b.p. 60—80°)] (Found: C, 81·3; H, 6·3; N, 6·0. $C_{16}H_{15}NO$ requires C, 81·0; H, 6·4; N, 5·9%), $\nu_{max.}$ 1680 (C=O), 1630, 1480br, 1355, 1340, 1260, 925, 915, 825, 815, 750, and 730 cm^{-1}, τ 1·9—3·0 (7H, m, ArH), 5·69 (2H, q, N·CH_2), 7·31 (3H, s, OMe), and 8·62 (3H, t, $CH_3{\cdot}CH_2$), *m/e* 237 (M^+, 57%), 238 (11), 223 (8), 222 (100, M — Me), 194 (16, M — COMe), 180 (7), 179 (18), 178 (6), 167 (4), and 165 (4), *m** 208 (237 ⟶ 222), and 170 (222 ⟶ 194).

N-*Ethyl*-2-*vinylcarbazole* (61%) as needles, m.p. 89—90° (from ethanol) (Found: C, 86·7; H, 6·7; N, 6·4. $C_{16}H_{15}N$ requires C, 86·8; H, 6·8; N, 6·4%), $\nu_{max.}$ 1630 ($CH{=}CH_2$), 1340br, 1235, 1155, 995, and 805 ($CH{=}CH_2$), 860, 830, 750, and 730 cm^{-1}, τ 1·9—3·4 (8H, m, ArH and an olefinic proton), 4·07 and 4·35 (1H, two d, J_{gem} 2 Hz, *trans*,*gem* olefinic proton), 4·67 and 4·86 (1H, two d, *cis*,*gem* olefinic proton), 4·71 (2H, q, N·CH_2), and 8·63 (3H, t, $CH_2{\cdot}CH_3$), *m/e* 221 (M^+, 61%) 222 (12), 208 (8), 207 (17), 206 (100, M — Me), 204 (12), 192 (8, M — Et), 191 (9), 180 (18), 178 (11), 152 (7), 85 (12), and 83 (19), *m** 192 (221 ⟶ 206).

N-*Ethyldibenz*[b,f]*azepine* (61%) as yellow needles, m.p. 102—103° (from ethanol) (Found: C, 86·8; H, 6·8; N, 6·4. $C_{16}H_{15}N$ requires C, 86·8; H, 6·8; N, 6·4%), $\nu_{max.}$ 1595w, 1585w, 1490, 1315, 1230, 1120, 1105, 1040, 900, 800, and 760 cm^{-1}, τ 2·7—3·2 (8H, m, ArH), 3·32 (2H, s, CH=CH), 4·26 (2H, q, N·CH_2), and 8·82 (3H, t, $CH_2{\cdot}CH_3$), *m/e* 221 (M^+, 55%), 208 (19), 206 (M — Me, 100), 194 (19), 193 (72), 192 (M — Et, 100), 191 (46), 190 (25), 180 (21), 179 (32), 178 (23), 165 (35), 139 (15), 91 (36), 85 (36), and 83 (63), *m** 192 (221 ⟶ 206).

N-*n*-*Propyldibenz*[b,f]*azepine* (29%) as yellow needles, m.p. 85—87° (from ethanol) (Found: C, 86·6; H, 7·4; N, 5·9. $C_{17}H_{17}N$ requires C, 86·8; H, 7·3; N, 5·9%), $\nu_{max.}$ 1595, 1570, 1320, 1240, 1120, 1110, 1040, 1000, 900, 795, and 760 cm^{-1}, τ 2·8—3·5 (8H, m, ArH), 3·45 (2H, s, CH=CH), 6·40 (2H, t, N·CH_2), 8·45 (2H, m, $CH_2{\cdot}CH_3$), and 9·10 (3H, t, $CH_2{\cdot}CH_3$), *m/e* 235 (M^+, 27%), 207 (17), 206 (M — Et, 100), 192 (M — C_3H_7, 14), 191 (10), and 178 (10).

We thank the S.R.C. for a Research Assistantship (to L. J. K.).

[2/1110 *Received*, 17*th May*, 1972]

[7] S. H. Tucker and F. R. Storrie, *J. Chem. Soc.*, 1931, 2255.
[8] B. Levy, *Monatsh.*, 1912, **33**, 177.
[9] L. Cassella and Co., Ger.P. 224,951/1910; *cf. Chem. Zentr.*, 1910, II, 699.
[10] E. Hannig and B. Schobess, *Pharm. Zentralhalle*, 1963, **102**, 500.
[11] K. Fujii, *J. Pharm. Soc.* (*Japan*), 1957, **77**, 3.
[12] H. Gilman, R. D. Nelson, and J. F. Champaigne, *J. Amer. Chem. Soc.*, 1952, **74**, 4205.
[13] H. Gilman, R. K. Ingham, J. F. Champaigne, J. W. Diehl, and R. O. Ranck, *J. Org. Chem.*, 1954, **19**, 560.
[14] R. H. F. Manske and M. Kulka, *Canad. J. Res.*, 1950, **28***B*, 443.