Metal–Halogen Exchange Reactions of Mono- and Poly-halogenoimidazoles [1]

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4(5)-Bromoimidazole gave a mixture of 4- and 5-bromo-1-methylimidazole on treatment with 1 or 2 mol equiv. of n-butyl-lithium in ether or THF under various reaction conditions followed by addition of dimethyl sulphate. 5-Iodo- and 2,4,5-tribromo-1-methylimidazole were prepared similarly. Attempts to exchange the bromine atoms for lithium in 5-bromo- or 2,4,5-tribromo-1-methylimidazole with n-butyl-lithium failed. 2,4,5-Tribromo-1-ethoxymethylimidazole was prepared by N-1-alkylation of tribromoimidazole with chloromethyl ethyl ether in benzene in the presence of triethylamine. Corresponding alkylation of 2,4,5-tri-iodoimidazole required the use of sodium methoxide in dioxan and gave mainly 1-ethoxymethyl-4,5-di-iodoimidazole. Successive treatment of 2,4,5-tribromo-1-ethoxymethylimidazole with n-butyl-lithium and diphenyl disulphide gave 4,5-dibromo-1-ethoxymethyl-2-phenylthioimidazole which, on further reaction with n-butyl-lithium followed by addition of dimethyl disulphide, gave 4-bromo-1-ethoxymethyl-5-methylthio-2-phenylthioimidazole. 1-Ethoxymethyl-4,5-di-iodoimidazole reacted successively with n-butyl-lithium and diphenyl disulphide to give a mixture of 1-ethoxymethyl-4-iodo-2-phenylthioimidazole (major product) and 1-ethoxymethyl-4-iodo-2,5-bisphenylthioimidazole.

Stensiö *et al.*[2] converted 2,4,5-tribromoimidazole into 4(5)-bromoimidazole by successively treating it with 4 mol equiv. of n-butyl-lithium and acid, and prepared 4(5)-deuterioimidazole by successive treatment of the monobromo-compound with almost 5 mol equiv. of n-butyl-lithium, deuteriomethanol, and acid. Later, in 1978, Breslow's group [3] reported that attempts to make organometallic reagents from N-1-protected 5-halogenoimidazoles failed, leading either to reduction or C-2 metallation. At the beginning of our work these were the only reports of metal–halogen exchange reactions of mono- or poly-halogenoimidazoles. Indeed the synthesis of 4-(or 5)-mono- or 4,5-di-substituted imidazoles *via* organometallic derivatives, whether by metal–halogen exchange or direct metallation, had otherwise not been exploited previously.[4,5] In 1979, a Russian group [6] treated 4-iodo-1-methylimidazole with 3 mol equiv. of n-butyl-ithium and, after addition of iodine, isolated from a mixture of products a 40% yield of 2,4-di-iodoimidazole. They considered that 1-methylimidazol-4-yl-lithium, 4-iodo-1-methylimidazol-2-yl-lithium, and 2,4-dilithio-1-methylimidazole were present prior to quenching. In an earlier paper, we reported the first synthesis of an imidazol-4-yl-lithium compound (1) by a bromine–lithium exchange between the corresponding bromoimidazole and n-butyl-lithium.[7] We now report further studies on reactions of this type.†

As expected, when we treated an ethereal solution of 4(5)-bromoimidazole [2] at −70 °C successively with 1 mol equiv. of n-butyl-lithium and dimethyl sulphate, a mixture (ratio 1 : 2 by integration of the 1-Me signals in the ^{1}H n.m.r. spectrum) (60% yield) of 4- (2) and 5-bromo-1-methylimidazole (3) was obtained. The use of 2 mol equiv. of n-butyl-lithium gave a similar result, as did changing the solvent from ether to tetrahydrofuran (THF). In the Table we have summarised the results of several reactions. For comparison purposes an authentic sample of 5-bromo-1-methylimidazole (3) was prepared by methylation of 4(5)-bromoimidazole with neat dimethyl sulphate.[8]

To our surprise, however, successive treatment of an ethereal solution of 5-bromo-1-methylimidazole (3) at −70 °C with 1 mol equiv. of n-butyl-lithium and dimethyl sulphate gave mainly starting material. In order to test the hypothesis that the equilibrium lies well over to the left in this metal–halogen exchange reaction, we repeated the reaction using t-butyl-lithium instead of n-butyl-lithium.[9] This also gave mainly starting material contaminated by two other products which we believe, from an examination of the ^{1}H n.m.r. spectrum of the mixture, to be 1,5- and 1,4-dimethylimidazole (product ratio 11 : 5 : 1, respectively).

In contrast to 4(5)-bromoimidazole, with 1 mol equiv. of n-butyl-lithium at −70 °C followed by addition of dimethyl sulphate, an ethereal solution of 4(5)-iodoimidazole gave mainly starting material containing only traces of 4- (4) and 5-iodo-1-methylimidazole (5) (ratio 18 : 1 : 1). Under the same conditions 2 mol equiv. of n-butyl-lithium gave only 5-iodo-1-methylimidazole (5). For comparison purposes an authentic sample of this material was prepared by methylation of 4(5)-iodoimidazole with neat dimethyl sulphate (*cf.* ref. 6). We found the method of Brunings [10] extremely tedious for the preparation of large quantities of 2,4,5-tri-iodoimidazole because of the relative insolubility of iodine in hexane and

Table. Metallation of 4(5)-bromoimidazole

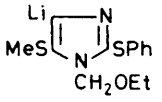
Bu^{n}Li (mol equiv.)	Solvent	Reaction time (min)	Reaction temp. (°C)	Ratio (2) : (3)	Yield (%)
1	Ether	30 [a]	−70 [c]	1 : 2	60
		40 [b]	−70 [d]		
2	Ether	30	−70	1 : 3	63
		40	−70		
1	Ether	60	−70	2 : 5	58
		60	−70		
1	THF	60	−70	1 : 1	46
		60	−70		
1	THF	30	−70	1 : 1	53
		60	Room temp.		

[a] Time after addition of Bu^{n}Li. [b] Time after addition of Me_2SO_4. [c] Temperature at which Bu^{n}Li was added. [d] Temperature at which Me_2SO_4 was added.

† Note added in proof: see p. 738.

the heterogeneous nature of the reaction. Instead, we iodinated imidazole in up to 75% yield with iodine and potassium iodide in aqueous sodium hydroxide (*cf.* ref. 11). 2,4,5-Triiodoimidazole was converted into 4(5)-iodoimidazole with sodium sulphite.[12,13]

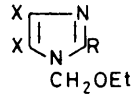
With 1 mol equiv. of n-butyl-lithium in ether at −70 °C followed by addition of dimethyl sulphate at the same temperature, 2,4,5-tribromoimidazole[2] gave its 1-methyl derivative in 83% yield. Balaban and Pyman[8] obtained this compound in only 15% yield by bromination of 1-methylimidazole, whilst treatment of *N,N'*-dimethyloxamide with a mixture of phosphorus pentabromide and phosphorus oxychloride gives a mixture of 5-bromo-, 4,5-dibromo-, and 2,4,5-tribromo-1-methylimidazole.[14] Methylation of 2,4,5-tribromoimidazole with methyl iodide gives the 1-methyl derivative in only 20% yield.[15] Further treatment of the tribromo-compound with 2 mol equiv. of n-butyl-lithium, in this case in THF at 0 °C, followed by addition of dimethyl sulphate gave a complex mixture (by t.l.c., g.l.c., *etc.*) which was not examined further.



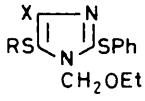
(1)

(2) X = Br
(4) X = I

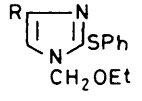
(3) X = Br
(5) X = I



(6) R = X = Br
(7) R = SPh, X = Br
(10) R = X = I
(11) R = H, X = I



(8) R = Me, X = Br
(13) R = Ph, X = I

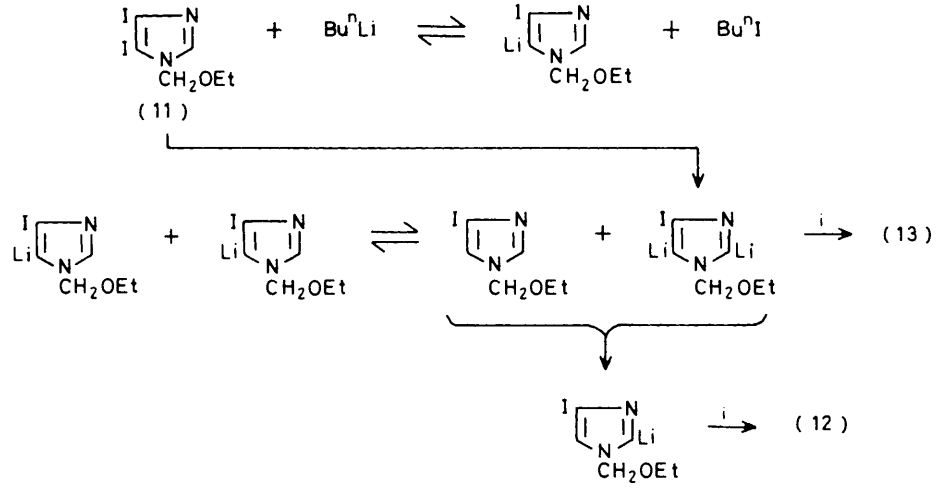


(9) R = SMe
(12) R = I

Further work is necessary to explain the difficulties so far encountered with metal–halogen exchange reactions of mono- and poly-halogenoimidazoles. Compared with benzophenone,[5] dimethyl sulphate may be an inferior trapping reagent for some lithiated imidazoles because of its ability to quaternise pyridine-like nitrogen atoms. On the other hand, it is possible that n-butyl-lithium co-ordinates with the pyridine-like nitrogen atom in imidazoles. Therefore, we decided to investigate the use of an N-1-protecting group which is able both to co-ordinate with the reagent and direct its position of attack.[3]

2,4,5-Tribromo-1-ethoxymethylimidazole (6) was prepared in quantitative yield by alkylation of 2,4,5-tribromoimidazole with chloromethyl ethyl ether in benzene in the presence of triethylamine, and treated successively with 1 mol equiv. of n-butyl-lithium and diphenyl disulphide in ether at −70 °C to give 4,5-dibromo-1-ethoxymethyl-2-phenylthioimidazole (7) (67%). This compound was synthesised unambiguously by bromination of 1-ethoxymethyl-2-phenylthioimidazole[3,7] in order to confirm the position of entry of the phenylthio-group. Further treatment of compound (7) with 1 mol equiv. of n-butyl-lithium followed by addition of dimethyl disulphide, all carried out in ether at −78 °C, gave 4-bromo-1-ethoxymethyl-5-methylthio-2-phenylthioimidazole[7] (8) (63%) together with a small amount (6%) of 1-ethoxymethyl-4-methylthio-2-phenylthioimidazole (9). We are not sure how the latter compound is formed at this stage of our investigations. However, there is no doubt about its structure since its physical properties are different from those of the 5-methylthio-isomer which we have reported previously.[7]

An attempt to prepare 1-ethoxymethyl-2,4,5-tri-iodoimidazole (10) by reaction of 2,4,5-tri-iodoimidazole with chloromethyl ethyl ether in benzene in the presence of triethylamine failed. However, replacement of the triethylamine with sodium methoxide and the solvent by dioxan allowed the reaction to proceed at ambient temperature, but the major product (63%) was 1-ethoxymethyl-4,5-di-iodoimidazole (11). Only a small amount (3%) of the tri-iodo-compound (10) was formed. This is not surprising in view of the ease with which iodine is lost from the 2-position of polyiodoimidazoles.[6] Reaction of the di-iodo-compound (11) with 1 mol equiv. of n-butyl-lithium in THF at −70 °C followed by addition of diphenyl disulphide gave a mixture of two compounds which we believe to be 1-ethoxymethyl-4-iodo-2-phenylthioimidazole (12) (74%) and 1-ethoxymethyl-4-iodo-2,5-bisphenylthioimidazole (13) (16%) on the basis that it is the 5-halogen



Scheme. *Reagents:* i, Ph_2S_2

atom in 1,2-disubstituted 4,5-dihalogenoimidazoles which normally undergoes metal–halogen exchange, particularly when a suitable N-1-directing group is present. A possible mechanism which accounts for the formation of these products is shown in the Scheme.

Experimental

The instruments used to record i.r., mass, and ^1H and ^{13}C n.m.r. spectra and the general experimental conditions were the same as those described in a previous paper.[5]

The following compounds were prepared by literature procedures: 2,4,5-tribromoimidazole[2] (68%), m.p. 225—226 °C (lit.,[2] 71% and m.p. 221—222 °C); 4(5)-bromoimidazole[2] (77%), m.p. 129—130 °C (lit.,[2] 62% and m.p. 130 °C); 4(5)-iodoimidazole[12] (67%), m.p. 133—134 °C (lit.,[12] m.p. 137—138 °C and[13] 50% and m.p. 135—136 °C); and 5-bromo-1-methylimidazole[8] (62%), b.p. 120 °C at 15.0 mmHg, m.p. 40—41 °C (lit.,[8] b.p. 128 °C at 15.0 mmHg, m.p. 45—46 °C); δ($CDCl_3$) 3.60s (3 H, 1-Me), 7.02s (1 H, 4-H), and 7.52s (1 H, 2-H). 5-Iodo-1-methylimidazole (67%), m.p. 102—103 °C [from light petroleum (b.p. 60—80 °C)] (lit.,[6] m.p. 106—107 °C); δ($CDCl_3$) 3.60s (3 H, 1-Me), 7.14s (1 H, 4-H), and 7.62s (1 H, 2-H), was prepared by methylation of 4(5)-iodoimidazole with neat dimethyl sulphate using a procedure identical with that used to methylate 4(5)-bromoimidazole.[8]

2,4,5-*Tri-iodoimidazole*.—A solution of iodine (45.0 g, 0.18 mol) in 20% aqueous potassium iodide (300 ml) was added dropwise to a stirred solution of imidazole (6.8 g, 0.1 mol) in 2M-sodium hydroxide (600 ml) at ambient temperature, and the resulting mixture was stirred overnight. Addition of acetic acid until the mixture was neutral gave a white precipitate which was filtered off, washed with water, and air dried, to give the crude product (21.7—33.3 g, 49—75%), m.p. 180—183 °C, 190—191 °C (from ethanol) (lit.,[10] m.p. 190—192 °C).

4- (2) *and* 5-*Bromo*-1-*methylimidazole* (3).—1.84M-n-Butyl-lithium in hexane (5.5 ml, 10.0 mmol) was added dropwise to 4(5)-bromoimidazole (1.47 g, 10.0 mmol) in ether (20 ml) at −70 °C. Stirring was continued for 0.5 h, and a solution of dimethyl sulphate (1.1 ml, 1.46 g, 11.6 mmol) in ether (5 ml) was then added dropwise. After 40 min at −70 °C, the reaction mixture was allowed to warm up to ambient temperature. Water (10 ml) was added, followed by concentrated aqueous ammonia (*d* 0.880) (10 ml). The ethereal layer was collected and the aqueous layer was extracted several times with ether. The combined ethereal extracts were dried ($MgSO_4$) and the solvent evaporated to give an orange oil. On distillation under reduced pressure (6×10^{-4} mmHg at 95 °C) a clear colourless oil was obtained (0.93 g, 60%), the ^1H n.m.r. spectrum of which showed that it was a mixture of 4- (2) and 5-bromo-1-methylimidazole (3) (ratio 1 : 2, respectively): 4-bromo-1-methylimidazole, δ($CDCl_3$) 3.59s (3 H, 1-Me), 6.84s (1 H, 5-H), and 7.29s (1 H, 2-H); 5-bromo-1-methylimidazole, δ($CDCl_3$) 3.65s (3 H, 1-Me), 6.99s (1 H, 4-H), and 7.50s (1 H, 2-H) (*cf.* values given in ref. 15). Results from the metallation of 4(5)-bromoimidazole using varying reaction conditions are summarised in the Table.

5-Bromo-1-methylimidazole (3) (1.0 g, 6.2 mmol) was treated similarly with t-butyl-lithium and work-up in the same way gave a yellow oil (0.4 g) which was shown by ^1H n.m.r. spectroscopy to be mainly starting material, possibly containing 1,5- and 1,4-dimethylimidazole (ratio 11 : 5 : 1, respectively).

Reactions of 4(5)-*Iodoimidazole with n-Butyl-lithium*.—(*a*) 1.93M-n-Butyl-lithium in hexane (2.7 ml, 5.16 mmol) was added dropwise to a stirred suspension of 4(5)-iodoimidazole (1.0 g, 5.16 mmol) in ether (20 ml) at −70 °C followed, after 1.5 h, by dropwise addition of dimethyl sulphate (1.0 ml, 1.33 g, 10.6 mmol) in ether (5 ml). Then water (5.0 ml) was added, followed by concentrated aqueous ammonium hydroxide (*d* 0.880) (5 ml), and the mixture was allowed to warm up slowly to ambient temperature. The aqueous layer was separated and extracted with ether. The ethereal extracts and ethereal layer were combined, dried ($MgSO_4$), and the solvent distilled to give a white solid (0.66 g), shown by ^1H n.m.r. spectroscopy to be mainly starting material containing traces of 4- (4) and 5-iodo-1-methylimidazole (5) (ratio 18 : 1 : 1, respectively).

(*b*) The reaction described in (*a*) was repeated using twice the quantity of n-butyl-lithium, and work-up in the same way gave 5-iodo-1-methylimidazole (5) (0.6 g, 56%), m.p. 103—104 °C [from light petroleum (b.p. 60—80 °C)], identical (i.r. and ^1H n.m.r. spectra) with the sample prepared as described before.

2,4,5-*Tribromo*-1-*methylimidazole*.—2,4,5-Tribromoimidazole (3.0 g, 9.8 mmol) in ether (40 ml) was cooled to −70 °C and 1.84M-n-butyl-lithium in hexane (5.5 ml, 10.0 mmol) was added dropwise with stirring. The resulting mixture was stirred at −70 °C for a further 0.5 h, then dimethyl sulphate (1.2 ml, 1.60 g, 12.7 mmol) in ether (5.0 ml) was added dropwise. After 40 min, the mixture was allowed to warm up to ambient temperature, water (5.0 ml) was added followed by concentrated aqueous ammonium hydroxide (*d* 0.880) (25.0 ml), and work-up in the usual way gave the product (2.6 g, 83%), m.p. 93—94 °C (from 50% aqueous ethanol) (lit.,[8] m.p. 93—94.5 °C).

Reaction of 2,4,5-*Tribromo*-1-*methylimidazole with n-Butyl-lithium*.—1.5M-n-Butyl-lithium in hexane (14.0 ml, 21.0 mmol) was added dropwise to 2,4,5-tribromo-1-methylimidazole (3.2 g, 10.0 mmol) in THF (35.0 ml) at 0 °C and the mixture was stirred for 1.25 h, then cooled to −70 °C. Dimethyl sulphate (3.5 ml, 4.66 g, 37.0 mmol) in THF (10.0 ml) was added dropwise and the mixture was stirred at −70 °C for a further 1 h, then allowed to warm up slowly to ambient temperature. Water (10.0 ml) was added followed by concentrated aqueous ammonium hydroxide (*d* 0.880) (15 ml), and extraction with ether gave a viscous brown oil shown by g.l.c., t.l.c. (on silica using ethyl acetate), and ^1H n.m.r. spectroscopy to be a complex multicomponent mixture which was not examined further.

2,4,5-*Tribromo*-1-*ethoxymethylimidazole* (6).—Chloromethyl ethyl ether (0.31 g, 3.23 mmol) in benzene (10.0 ml) was added to a stirred solution of 2,4,5-tribromoimidazole (1.0 g, 3.28 mmol) in benzene (50 ml) containing triethylamine (0.47 ml, 0.34 g, 3.4 mmol) at ambient temperature and the mixture was stirred for a further 2 h. The solvent was distilled off and water (30 ml) added to the residue. Extraction with chloroform gave a yellow viscous oil which was chromatographed on alumina. Light petroleum–chloroform eluted the product (1.19 g, 100%), a colourless oil (lit.,[16] b.p. 120—121 °C at 0.02 mmHg), $\nu_{max.}$ 1 000—1 180 cm^{-1} (OEt); δ($CDCl_3$) 1.20t (3 H, Me), 3.65q (2 H, OCH_2), and 5.40s (2 H, NCH_2); δ(^{13}C) ($CDCl_3$) 118.77s (C-2), 117.29s (C-4), 105.39s (C-5), 75.90t (NCH_2), 64.77t (OCH_2), and 14.53q p.p.m. (Me).

4,5-*Dibromo*-1-*ethoxymethyl*-2-*phenylthioimidazole* (7).—(*a*) 1.0M-n-Butyl-lithium in hexane (1.38 ml, 1.38 mmol) was

added dropwise to a stirred solution of 2,4,5-tribromo-1-ethoxymethylimidazole (0.5 g, 1.38 mmol) in ether (45 ml) at −70 °C followed, after 1 h, by addition of diphenyl disulphide (0.3 g, 1.38 mmol) in small quantities. The reaction mixture was allowed to warm up slowly to ambient temperature and work-up in the usual way gave an oil which was chromatographed on alumina. Light petroleum-chloroform eluted 4,5-*dibromo*-1-*ethoxymethyl*-2-*phenylthioimidazole* (7) (0.36 g, 67%), a pale yellow oil; $\nu_{max.}$ 1 580 cm^{-1} (Ph); δ($CDCl_3$) 1.09t (3 H, Me), 3.44q (2 H, OCH_2), 5.43s (2 H, NCH_2), and 7.30m (5 H, SPh); δ(^{13}C) ($CDCl_3$) 140.11s (C-2), 132.94s (C-1 of SPh), 129.25d (C-2, C-6, and C-4 of SPh), 127.53d (C-3 and C-5 of SPh), 118.51s (C-4), 106.79s (C-5), 75.32t (NCH_2), 64.56t (OCH_2), and 14.51q (Me) (Found: C, 36.9; H, 3.1; N, 7.0%; M^+, 390. $C_{12}H_{12}Br_2N_2OS$ requires C, 36.8; H, 3.1; N, 7.1%; *M*, 390).

(*b*) Bromine (1.09 g, 6.84 mmol) in acetic acid (2.0 ml) was added dropwise to a stirred mixture of 1-ethoxymethyl-2-phenylthioimidazole[3,7] (0.8 g, 3.42 mmol) and anhydrous sodium acetate (0.75 g) in acetic acid (10.0 ml). After 1 h, when t.l.c. indicated that the reaction was complete, the acetic acid was distilled off and water (25 ml) was added to the residue. Extraction with chloroform (3 × 30 ml) gave a brown oil which was chromatographed on alumina. Light petroleum–chloroform eluted 4,5-dibromo-1-ethoxymethyl-2-phenylthioimidazole (0.38 g, 28%) as an oil, identical (t.l.c. and i.r. and ^1H and ^{13}C n.m.r. spectroscopy) with the sample prepared as described in (*a*).

Reaction of 4,5-*Dibromo*-1-*ethoxymethyl*-2-*phenylthioimidazole* (7) *with n-Butyl-lithium*.—1.12M-n-Butyl-lithium in hexane (1.16 ml, 1.3 mmol) was added dropwise to a stirred solution of 4,5-dibromo-1-ethoxymethyl-2-phenylthioimidazole (7) (0.5 g, 1.28 mmol) in ether (40 ml) at −78 °C followed, after 1 h, by addition of dimethyl disulphide (0.12 g, 1.3 mmol), and the mixture was then allowed to warm up slowly to ambient temperature and was stirred at this temperature for a further 1 h. Work-up in the usual way gave a yellow oil (0.4 g) which was chromatographed on a silica-gel column under medium pressure. Light petroleum–ethyl acetate eluted the following: (i) unchanged dimethyl disulphide (trace); (ii) 4-bromo-1-ethoxymethyl-5-methylthio-2-phenylthioimidazole (8) (0.29 g, 63%), m.p. 56—57 °C (from light petroleum) (lit.,[7] m.p. 56—57 °C), identical in other respects (t.l.c. and i.r. and ^1H n.m.r. spectra) with the sample prepared previously;[7] and (iii) 1-ethoxymethyl-4-methylthio-2-phenylthioimidazole (9) (0.02 g, 6%) (see Discussion section), an oil, $\nu_{max.}$ 1 580 cm^{-1} (Ph); δ($CDCl_3$) 1.09t (3 H, Me), 2.50s (3 H, SMe), 3.32q (2 H, OCH_2), 5.32s (2 H, NCH_2), 7.20s (1 H, 5-H), and 7.30s (5 H, SPh) (Found: M^+, 280. $C_{13}H_{16}N_2OS_2$ requires *M*, 280).

Reaction of 2,4,5-*Tri-iodoimidazole with Chloromethyl Ethyl Ether*.—2,4,5-Tri-iodoimidazole (5.6 g, 12.5 mmol) was added in portions to a solution of sodium methoxide (0.68 g, 12.5 mmol) in methanol (100 ml) and the solution was stirred for 0.5 h at ambient temperature. The methanol was distilled off and replaced by anhydrous dioxan (100 ml). To this rapidly stirred suspension was added dropwise chloromethyl ethyl ether (1.18 ml, 1.13 g, 12.5 mmol), then the mixture was stirred overnight at ambient temperature. Water (20 ml) was added, the aqueous layer was extracted with chloroform and the combined organic layer and extracts yielded a viscous orange oil which was chromatographed on alumina. Light petroleum–ethyl acetate eluted the following: (i) 1-*ethoxymethyl*-2,4,5-*tri-iodoimidazole* (10) (0.2 g, 3%) as a yellow oil which solidified, m.p. 94—95 °C, $\nu_{max.}$ 1 000—1 120 cm^{-1} (OEt); δ($CDCl_3$) 1.20t (3 H, Me), 3.55q (2 H, OCH_2), and 5.37s (2 H, NCH_2) (Found: C, 14.4; H, 1.4; N, 5.5%; M^+, 504. $C_6H_7I_3N_2O$ requires C, 14.3; H, 1.4; N, 5.6%; *M*, 504); and (ii) 1-*ethoxymethyl*-4,5-*di-iodoimidazole* (11) (3.0 g, 63%), m.p. 108 °C (from light petroleum–carbon tetrachloride); δ($CDCl_3$) 1.19t (3 H, Me), 3.50q (2 H, OCH_2), 5.31s (2 H, NCH_2), and 7.73s (1 H, 2-H); δ(^{13}C) ($CDCl_3$) 141.37d (C-2), 96.85s (C-4), 81.65s (C-5), 77.75t (NCH_2), 64.44t (OCH_2), and 14.52q p.p.m. (Me) (Found: C, 19.1; H, 2.15; N, 7.4%; M^+, 378. $C_6H_8I_2N_2O$ requires C, 19.1; H, 2.1; N, 7.4%; *M*, 378).

Reaction of 1-*Ethoxymethyl*-4,5-*di-iodoimidazole* (11) *with n-Butyl-lithium*.—1.12M-n-Butyl-lithium in hexane (1.18 ml, 1.32 mmol) was added dropwise to a stirred solution of 1-ethoxymethyl-4,5-di-iodoimidazole (0.5 g, 1.32 mmol) in THF (45 ml) at −70 °C followed, after 1 h, by addition in one portion of diphenyl disulphide (0.29 g, 1.32 mmol). The resulting mixture was stirred at −70 °C for a further 20 min, then warmed up slowly to ambient temperature. 20% Aqueous ammonium chloride (10 ml) was added and work-up in the usual way gave a yellow oil which was chromatographed on a silica-gel column under medium pressure. Light petroleum–ethyl acetate eluted: (i) a mixture of diphenyl disulphide and butyl phenyl sulphide (0.22 g); (ii) 1-*ethoxymethyl*-4-*iodo*-2,5-*bisphenylthioimidazole* (13) (0.1 g, 16%), $\nu_{max.}$ 1 580 cm^{-1} (Ph); δ($CDCl_3$) 0.90t (3 H, Me), 3.32q (2 H, OCH_2), 5.45s (2 H, NCH_2), 7.20s (5 H, 5-SPh), and 7.32s (5 H, 2-SPh); δ(^{13}C) ($CDCl_3$) 129.63, 129.12, 127.54, 127.07, and 126.54 (as a complex multiplet assigned to C-2, C-5 and other aromatic C's), 100.34s (C-4), 74.64t (NCH_2), 64.34t (OCH_2), and 14.42q p.p.m. (Me) (Found: C, 46.2; H, 3.7; N, 6.0%; M^+, 468. $C_{18}H_{17}IN_2O_2S_2$ requires C, 46.2; H, 3.7; N, 6.0%; *M*, 468); and (iii) 1-*ethoxymethyl*-4-*iodo*-2-*phenylthioimidazole* (12) (0.35 g, 74%), an oil, $\nu_{max.}$ 1 580 cm^{-1} (Ph); δ($CDCl_3$) 1.09t (3 H, Me), 3.39q (2 H, OCH_2), 5.32s (2 H, NCH_2), 7.25m (5 H, SPh), and 7.35s (1 H, 5-H); δ(^{13}C) ($CDCl_3$) 139.90s (C-2), 133.69s (C-1 of SPh), 129.04d (C-5), 128.55d (C-2 and C-6 of SPh), 127.95d (C-4 of SPh), 126.96d (C-3 and C-5 of SPh), 82.71s (C-4), 75.50t (NCH_2), 64.47t (OCH_2), and 14.42q p.p.m. (Me) (Found: C, 40.0; H, 3.7; N, 7.9%; M^+, 360. $C_{12}H_{13}IN_2OS$ requires C, 40.0; H, 3.6; N, 7.8%; *M*, 360).

Note added in proof: Recently Tertov's group have reported that bromine in 4(5)-bromoimidazole can be exchanged for lithium with lithium naphthalenide [B. A. Tertov, Yu. V. Koshchienko, and V. V. Bessonov, *Khim. Geterotsikl. Soedin.*, 1982, 1279 and USSR Patent SU 891,664/1981 (*Chem. Abstr.*, 1982, **96**, 199690)] whilst another group have exchanged bromine for lithium in 2-bromo-4,5-dichloroimidazole using n-butyl-lithium (J. P. Dirlam, R. B. James, and E. V. Shoop, *J. Org. Chem.*, 1982, **47**, 2196).

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