Reactions of the alkyl radical attached to the ring nitrogen of 2-phenylthio-indole, -benzimidazole and -uracil

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Alkyl radicals have been generated on the 1-*N*-alkyl group of 2-phenylthioindole, 2-phenylthiobenzimidazole and 6-phenylthiouracil derivatives. These *N*-alkyl radicals have been generated from the corresponding *N*-alkyl bromides by the action of triphenyltin hydride–azoisobutyronitrile, triphenyltin-cobaloxime or by the photolysis of the corresponding *N*-alkylcobaloxime. Reaction modes differ little with the method of radical generation except for the substantial formation of alkyl phenyl sulfide, a radical substitution product of the alkylcobaloximes, in the photolysis of the cobaloximes. The cobaloxime(II) species, which exists in the reaction system *N*-alkyl bromide–triphenyltincobaloxime, activates the phenylthio group for the radical substitution, and the lack of the tin hydride makes it possible for the reaction to occur at a higher concentration than the reaction with the hydride reagent.

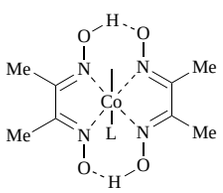
Introduction

The indole skeleton is widely formed in natural products such as the indole alkaloids,[1] some of which contain an additional carbocycle condensed at the nitrogen and the C-2 position of the pyrrole part as exemplified by vicamine.[2] Both the wide distribution of the indole system in nature and its basic character as a heterocyclic aromatic system have provided us a stage for the study of organic reactions.[3] Benzimidazole, although belonging to the same class of aromatic compounds as indole, has the ability to ligate strongly to transition metals, a property which may modify its chemical properties in the presence of transition metal ions. A 6-heteroatom substituent in uracils is important for biological activity,[4] whilst the presence of an α,β-unsaturated carbonyl moiety and its behaviour toward a radical species in these compounds is important in relation to their biochemistry and chemistry. Indole, benzimidazole and uracil, have in common a formal enamine partial structure and we have studied the cyclization of an alkyl radical attached to the ring nitrogen both in the presence and absence of the transition metal complex, bis(dimethylglyoximato)-(4-*tert*-butylpyridine)-cobalt(II), hereafter referred to as cobaloxime.

The versatility and usefulness of a radical strategy for the construction of carbocycles has been demonstrated together with a number of successful examples reported for the radical annelation of indole[5–10] and benzimidazole.[11] Caddick *et al.* showed the usefulness of the sulfur function in the radical annelation in which the intramolecular alkyl radical causes an *ipso* substitution to yield a carbocycle by the extrusion of the sulfur function.[10] The reactivity of the sulfur functions in the *ipso* substitution increases in the order of sulfide, sulfoxide and sulfone. This result is in accordance with our findings that the radical attack on sulfur functions has nucleophilic character.[12]

In a series of studies we have demonstrated that the reactivity of an alkyl radical to a sulfur function is affected by a co-existing cobalt(II) species in the reaction system[13] and that the effect is derived from coordination of the sulfur function to cobalt(II).[14] By Caddick's criteria, a sulfide has the lowest radicophilicity with respect to an alkyl radical, but we can expect this to be enhanced in the presence of cobalt(II) species.

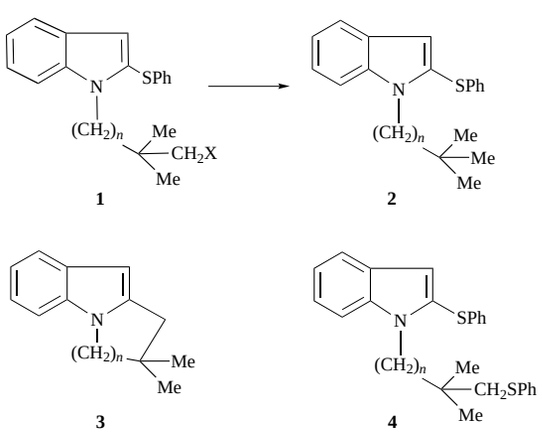
This background information prompted us to investigate radical annelation on indole, benzimidazole and uracil in the presence and absence of cobalt(II) species. To test the effect of cobalt(II) species, we generated 3-indol-1-ylpropyl **5** ($n = 1$), 4-indol-1-ylbutyl **5** ($n = 2$), 3-benzimidazol-1-ylpropyl **10** ($n = 1$), 4-benzimidazol-1-ylbutyl **10** ($n = 2$), 3-(3-methyl-6-phenylthiouracil-1-yl)propyl **11** ($n = 1$, radical instead of Br), and 4-(3-methyl-6-phenylthiouracil-1-yl)butyl radical **11** ($n = 2$, radical instead of Br) by (a) bromide–triphenyltin hydride, (b) bromide–triphenyltincobaloxime, and (c) the homolysis of ω-indol-1-yl and ω-benzimidazol-1-yl-alkylcobaloxime.



Cobaloxime [Co], L = 4-*tert*-butylpyridine

Results and discussion

Treatment of 1-(3-bromo-2,2-dimethylpropyl)-2-phenylthio-1*H*-indole **1a** with triphenyltin hydride gave a reduction product **2a** and a cyclization product **3a**. The same treatment of 4-(4-bromo-3,3-dimethylbutyl)-2-phenylthio-1*H*-indole **1b** yielded a reduction product **2b** and a cyclization product **3b**. Both reactions gave diphenyl disulfide as a by-product (Scheme 1 and Table 1). The structures of the products were



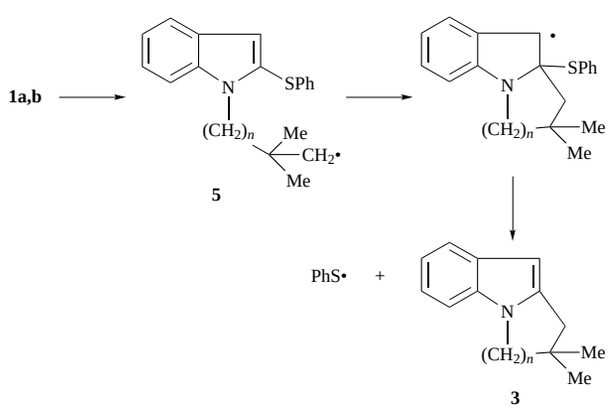
Scheme 1

Table 1 Reaction of ω-(2-phenylthioindol-1-yl)alkyl radical

Entry	Compd.	X	*n*	Conditions	Yield (%) 2	3	4	$(PhS)_2$
1	**1a**	Br	1	Ph_3SnH–AIBN[a]	22	58	—	36
2	**1b**	Br	2	Ph_3SnH–AIBN[a]	33	43	—	28
3	**1a**	Br	1	Ph_3Sn[Co]/heat[b]	3	67	—	45
4	**1b**	Br	2	Ph_3Sn[Co]/heat[c]	8	74	—	41
5	**1c**	[Co]	1	*hν*[d]	—	56	32	—
6	**1d**	[Co]	2	*hν*[d]	—	44	30	—

[a] **1a** and **1b** 2.0×10^{-3} mol dm^{-3}, Ph_3SnH 4.0×10^{-3} mol dm^{-3}. Reflux 6 h in benzene. [b] **1a** 2.0×10^{-2} mol dm^{-3}, Ph_3Sn[Co] 6.0×10^{-2} mol dm^{-3}. 130 °C, 24 h in DMF. [c] **1b** 2.0×10^{-2} mol dm^{-3}, Ph_3Sn[Co] 1.2×10^{-1} mol dm^{-3}. 130 °C, 24 h in DMF. [d] **1c** and **1d** 4.0×10^{-3} mol dm^{-3}, 350 nm, 24 h.

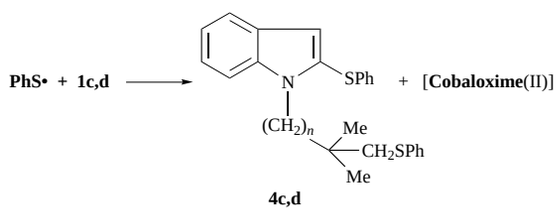
deduced from the appearance in the NMR spectrum of the *tert*-butyl group as a terminal group in **2a** and **2b** and the disappearance of the phenylthio group in **3a** and **3b**. Both the radical intermediates **5** (*n* = 1 and 2) are considered to abstract hydrogen from triphenyltin hydride at a similar rate because the steric bulkiness of the radical centres is comparable in those intermediates. Hence the increased yield of **2b** from **2a** (22–33%) and the decreased yield of **3b** from **3a** (58–43%) must be due to the lower efficiency of 6-*exo-trig* cyclization compared to 5-*exo-trig* cyclization of the intermediate radical **5**.[15,16] This is a general feature of the intramolecular radical addition of the hex-5-enyl[17] and hept-6-enyl radical.[18] The extruded phenylthio radical dimerizes to give diphenyl disulfide. The reactions of the bromides **1a** and **1b** with triphenyltincobaloxime, Ph_3Sn[Co], gave the same cyclization products **3a** and **3b** in better yields than the reaction with triphenyltin hydride, the result of the reduction products **2a** and **2b** being reduced (Scheme 2). The lack of a hydride reagent made it possible to carry out the reaction without great dilution and to use the reagent in excess, in contrast to the reaction with the tin hydride (see footnotes in Table 1).



Scheme 2

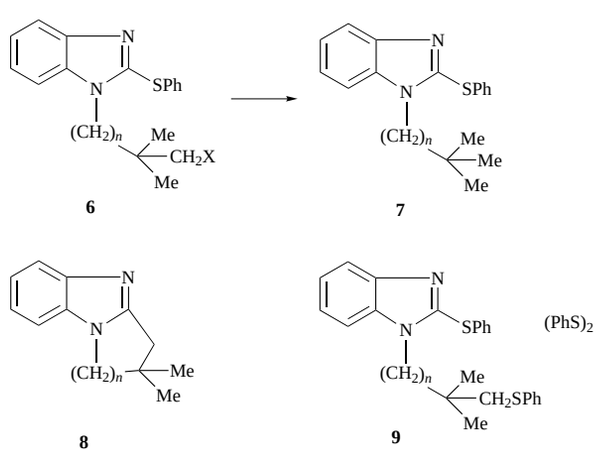
We had expected that the reactivity would be profoundly affected by the presence of cobaloxime(II) species, since it had been shown that they coordinate to sulfide. The effect of cobaloxime(II), however, was modest, an unexpected result which indicates that there is little or no coordination between the cobaloxime(II) and the sulfide moiety of the intermediate radical **5**. Nevertheless, the yields of **3a** and **3b** were improved from those of the reactions with tin hydride (**3a**, 58→67%; **3b**, 43→74%) by using an excess of triphenyltincobaloxime, whereas the use of an excess of tin hydride gave decreased yields of **3a** and **3b**. Thus, the product yield and the reaction conditions show the usefulness of triphenyltincobaloxime as a radical generator. The reaction using triphenyltincobaloxime, however, is rather slow and an excess (3–6 equiv.) of the reagent is necessary for practical synthesis.

Next, the intermediate radicals **5a** and **5b** were generated by photolyses of the corresponding organocobaloximes **1c** and **1d**. It has been established that the longest wavelength band of the UV absorption is a ligand-to-metal charge transfer (LMCT) band[19] and this excitation causes homolysis of the carbon–cobalt bond of the organocobaloxime.[13,20,21] The radical cyclization products **3a** and **3b**, however, are formed in comparable yields to the reaction with tin hydride. The phenylthiyl radical formed in the radical cyclization reacts with organocobaloxime to give the phenyl sulfides **4a** and **4b** (Scheme 3). The structure



Scheme 3

was confirmed by the appearance of signals in the ^1H NMR spectrum due to the methylene adjacent to the sulfur (δ = 3.05) and an additional phenylthio group. Thus, the phenylthiyl radical generated as a by-product of the cyclization yielded the substitution products **4c** and **4d** of the organocobaloxime **1c** and **1d** instead of the formation of diphenyl disulfide. This type of reaction producing a sulfide from a thiyl radical and an organo-cobaloxime has been reported by Huston *et al.*[22] and us.[13d]



Scheme 4

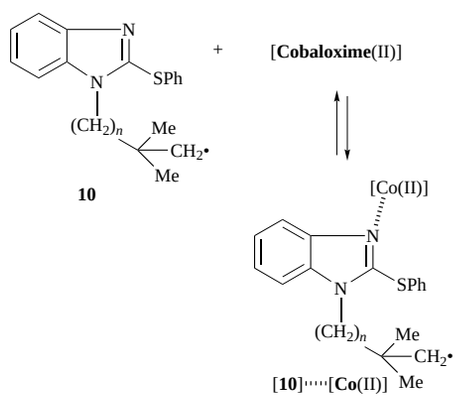
N-(ω-Bromoalkyl)benzimidazoles (**6a** and **6b**) and *N*-(ω-cobaloximatoalkyl)benzimidazoles **6c** and **6d** were subjected to the same reaction conditions as the reactions of the indole derivatives **1a** and **1b**, and the results are summarized in Table 2 and Scheme 4. Benzimidazole is a strong nitrogen ligand to cobalt(II), and the radical intermediate of benzimidazole derivative **10** can coordinate to cobaloxime(II) (Scheme 5).

In comparison with the reaction of indole derivatives, a general feature of the reaction of benzimidazole derivatives with

Table 2 Reaction of ω-(2-phenylthiobenzimidazol-1-yl)alkyl radical

Entry	Compd.	X	*n*	Conditions	Yield (%) 7	8	9	$(PhS)_2$
1	**6a**	Br	1	Ph_3SnH–AIBN[a]	50	22	—	21
2	**6b**	Br	2	Ph_3SnH–AIBN[a]	35	64	—	46
3	**6a**	Br	1	Ph_3Sn[Co]/heat[b]	23	45	—	38
4	**6b**	Br	2	Ph_3Sn[Co]/heat[c]	11	81	—	30
5	**6c**	[Co]	1	*hν*[d]	—	36	35	—
6	**6d**	[Co]	2	*hν*[d]	—	54	36	—

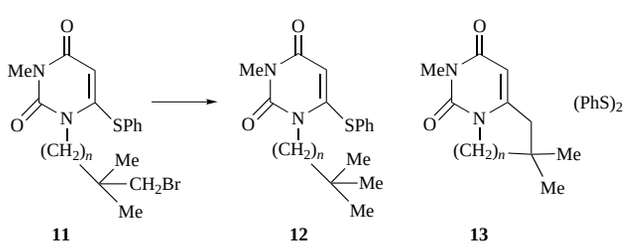
[a] **6a** and **6b** 2.0×10^{-3} mol dm^{-3}, Ph_3SnH 4.0×10^{-3} mol dm^{-3}. Reflux 6 h in benzene. [b] **6a** 2.0×10^{-2} mol dm^{-3}, Ph_3Sn[Co] 6.0×10^{-2} mol dm^{-3}. 130 °C, 24 h in DMF. [c] **6b** 2.0×10^{-2} mol dm^{-3}, Ph_3Sn[Co] 1.2×10^{-1} mol dm^{-3}. 130 °C, 24 h in DMF. [d] **6c** and **6d** 4×10^{-3} mol dm^{-3}, 350 nm, 24 h.



Scheme 5

triphenyltin hydride is the increased yields of the hydrogen abstraction products **7a** and **7b**. It is also a general trend that the 2,2-dimethylbutyl radical **10** ($n = 2$) cyclizes slightly more efficiently than the 2,2-dimethylpropyl radical **10** ($n = 1$) under the same conditions (see entries 1, 2 and entries 5, 6 in Table 2). This is a reversed trend compared to the case of the ω-indol-1-yl-2,2-dimethylalkyl radical. Contrary to our expectations, other features of the radical of the benzimidazole derivative **10** are the same as those of the radical of the indole derivative **5**, and the effect of the coordination with cobaloxime(II) is less than profound.

Next, 1-(ω-bromoalkyl)-3-methyl-6-phenylthiouracil derivatives **11a** ($n = 1$) and **11b** ($n = 2$) were allowed to react with



Scheme 6

the triphenyltin radical in the absence and presence of cobaloxime(II) and the results are summarized in Table 3 and Scheme 6. The new appearance of the *tert*-butyl group and the retention of the phenylthio group define the structures **12**. The appearance of the methylene group connected to the olefinic moiety and the disappearance of the phenylthio group define the structure **13**. The general trends are the same as those for the indole and benzimidazole derivatives, but it is noteworthy that the radical cyclization (*ipso* substitution) decreases substantially when the alkyl chain lengthens. Thus, a 6-*exo*-*trig* radical addition is much less efficient than a 5-*exo*-*trig* radical addition.

In the indole system, Caddick *et al.* reported[8] that phenylsulfonyl and phenylsulfinyl radicals were better leaving groups than a phenylthiyl radical, and hence more cyclization product was obtained from phenylsulfonyl derivatives. This difficulty,

Table 3 Reaction of ω-(6-phenylthiouracil-1-yl)alkyl radical

Entry	Compd.	*n*	Conditions	Yield (%) 12	13	$(PhS)_2$
1	**11a**	1	Ph_3SnH–AIBN[a]	28	54	*b*
2	**11b**	2	Ph_3SnH–AIBN[a]	76	5	26
3[c]	**11a**	1	Ph_3Sn[Co]/heat[d]	0	43	61
4[e]	**11b**	2	Ph_3Sn[Co]/heat[d]	21	18	45

[a] **11a** or **11b** 3.0×10^{-3} mol dm^{-3}, Ph_3SnH 9.0×10^{-3} mol dm^{-3}. Reflux 4 h in benzene. [b] Considerable amount but not determined. [c] 13% of **11a** was recovered. [d] **11a** or **11b** 2.0×10^{-2} mol dm^{-3}, Ph_3Sn[Co] 1.2×10^{-1} mol dm^{-3}. 120 °C, 24 h in DMF. [e] 38% of **11b** was recovered.

however, is overcome by using triphenyltincobaloxime as a radical generator, which also avoids the high dilution conditions used to prevent reduction. Radical cyclization using triphenyltin hydride as a radical generator must be carried out at a concentration of the order of 10^{-3} mol dm^{-3} to obtain a practical yield of the cyclization product. The cyclization using triphenyltincobaloxime, on the other hand, can be carried out more conveniently at a higher concentration of the order of 10^{-2} mol dm^{-3}. The radical cyclization using the alkylcobaloximes **1c** and **6c** is not practical because a considerable amount of the starting cobaloximes is consumed by the substitution reaction with the phenylthio radical liberated in the *ipso* substitution.

In conclusion, 2-phenylthioindole, 2-phenylthiobenzimidazole and 6-phenylthiouracil behave in a manner similar to that in the reaction with the intramolecular alkyl radical, although minor modifications are seen. The co-existence of cobaloxime(II) species in these radical reactions affects the reaction process only in minor aspects, but the use of triphenyltin cobaloxime as a radical generator is convenient and profitable for practical syntheses of indole, benzimidazole and uracil derivatives having a carbocycle containing the nitrogens of pyrrole, imidazole and uracil moieties.

Experimental

General

Benzene and DMF were purified by distillation over sodium–benzophenone and 4 Å molecular sieves, respectively. ^1H NMR spectra were recorded on JEOL JME-EX270 (270 MHz) and Hitachi R-90 (90 MHz) spectrometers in $CDCl_3$ solution using tetramethylsilane as an internal reference. Chemical shifts and coupling constants are recorded in δ values and Hz, respectively. IR spectra were recorded on a Perkin-Elmer 1640 FT-IR spectrometer in chloroform solution. Mass spectra were recorded on JEOL JMS Automass 150 and JEOL DX-300 (high resolution) spectrometers by electron impact ionization at 70 eV. Melting points are uncorrected. Chromatography was performed using flash silica (Merck 60, 230–400) under positive pressure. Preparative TLC was performed using a $20 \times 20 \times 0.2$ cm plate of silica gel (Merck 60, PF_{254}).

All the spectra and elemental analyses were performed using the facilities of the Materials Characterization Central Laboratory of Waseda University.

Starting materials

(a) Bromides. 1-(3-Bromo-2,2-dimethylpropyl)-2-phenylthio-1*H*-indole **1a**, 1-(4-bromo-3,3-dimethylbutyl)-2-phenylthio-1*H*-indole **1b**, 1-(3-bromo-2,2-dimethylpropyl)-2-phenylthiobenzimidazole **6a** and 1-(4-bromo-3,3-dimethylbutyl)-2-phenylthiobenzimidazole **6b** were prepared by alkylation of 2-phenylthioindole[23] and 2-phenylthiobenzimidazole.[24]

2-Phenylthioindole or 2-phenylthiobenzimidazole (1.0–5.0 mmol), 1,3-dibromo-2,2-dimethylpropane[25] or 1,4-dibromo-2,2-dimethylbutane[26] (3.0 equiv.), and powdered potassium hydroxide (1.2 equiv.) were mixed in 5.0–7.0 cm^3 (indole) or 10–15 cm^3 of DMF (benzimidazole). The mixture containing 1,3-dibromo-2,2-dimethylpropane was heated at 130 °C for 40–48 h, and the mixture containing 1,4-dibromo-2,2-dimethylbutane was stirred at room temperature (*ca.* 20 °C) for 16–19 h under argon. The cooled reaction mixture was treated with water and extracted with diethyl ether. The extract gave a crude product after washing with brine, drying, and concentration. The crude product thus obtained was purified by chromatography on a silica gel column using hexane–ethyl acetate (50 : 1) as eluent. The pure products **1a**, **1b**, **6a** and **6b** were obtained in 44, 77, 51 and 73% yields respectively. They are spectrometrically pure but thermally too unstable to provide correct elemental analyses.

Compound **1a**, an oil; δ_H(270 MHz) 1.09 (6H, s), 3.42 (2H, s), 4.19 (2H, s), 6.81–7.32 (8H, m), 7.50 (1H, dd, *J* 8.3 and 0.7) and 7.62 (1H, dd, *J* 8.3 and 0.7); ν_{max}/cm^{-1} 1582, 1471, 1450 and 1310; *m*/*z* 375 (M^+, 100%), 373 (M^+, 100), 238 (81), 205 (77) and 160 (16) (Found: M^+, 373.0488. $C_{19}H_{20}BrNS$ requires 373.0500).

Compound **1b**, mp 57.2–58.4 °C (hexane–ethanol) (Found: C, 61.50; H, 5.28; N, 3.33. $C_{20}H_{22}BrNS$ requires C, 61.85; H, 5.71; N, 3.61%); δ_H(270 MHz) 1.01 (6H, s), 1.05–1.14 (2H, m), 3.24 (2H, s), 4.20–4.44 (2H, m), 6.95 (1H, s), 7.13–7.32 (7H, m), 7.39 (1H, d, *J* 8.2) and 7.65 (1H, d, *J* 8.2); ν_{max}/cm^{-1} 1582, 1462, 1446 and 1313; *m*/*z* 389 (M^+, 90%), 387 (M^+, 90), 238 (79) and 205 (51).

Compound **6a**, an oil; δ_H(270 MHz) 1.16 (6H, s), 3.44 (2H, s), 4.29 (2H, s), 7.21–7.42 (7H, m), 7.45–7.51 (1H, m) and 7.67–7.77 (1H, m); ν_{max}/cm^{-1} 1582, 1480, 1448, 1369 and 1343; *m*/*z* 376 (M^+, 13%), 374 (M^+, 13), 295 (7), 239 (48), 109 (45) and 55 (100) (Found: M^+, 376.0461. $C_{18}H_{19}BrN_2S$ requires 376.0433).

Compound **6b**, an oil; δ_H(270 MHz) 1.09 (6H, s), 1.62–1.74 (2H, m), 3.29 (2H, s), 4.15–4.28 (2H, m), 7.22–7.42 (8H, m) and 7.75–7.81 (2H, m); ν_{max}/cm^{-1} 1582, 1463 and 1360; *m*/*z* 388 (M^+, 12%), 386 (M^+, 12), 309 (5), 253 (48), 225 (43) and 51 (100) (Found: M^+, 388.0600. $C_{19}H_{21}BrN_2S$ requires 388.0609).

1-(3-Bromo-2,2-dimethylpropyl)-3-methyl-6-phenylthiouracil **11a** and 1-(4-bromo-3,3-dimethyl)butyl-3-methyl-6-phenylthiouracil **11b** were prepared by essentially the same procedure as the corresponding compounds for the indole and benzimidazole derivatives but using sodium hydride as a base. A solution of 3-methyl-6-phenylthiouracil[27] (234 mg, 1.0 mmol) in DMF (5.0 cm^3) was added to sodium hydride (washed with hexane; 1.2 mmol) under argon, and the mixture was stirred for 3.0 h at room temperature (*ca.* 20 °C) to prepare the sodium salt of uracil. The sodium salt thus formed was treated with the corresponding dibromides and then heated at 120 °C (**11a**) or 70 °C (**11b**) for 2.0 h. The cooled mixture was mixed with dilute hydrochloric acid (1 mol dm^{-3}) and extracted with ethyl acetate. Concentration of the extract after washing with water and drying gave the crude product which was purified successively by silica gel column chromatography eluting with hexane–ethyl acetate (1 : 1) and on a preparative silica gel TLC plate using the same solvent. The yields of the products were poor (<10%), and solvolysis products of the bromides (alcohol instead of bromide) and the cyclic ethers (from the alcohols) were obtained in substantial yields.

Compound **11a**, an oil; δ_H(270 MHz) 1.19 (6H, s), 3.30 (3H, s), 3.59 (2H, s), 4.16 (2H, s), 5.08 (1H, s) and 7.42–7.60 (5H, m); ν_{max}/cm^{-1} 1698, 1680, 1654, 1575, 1466 and 1460; *m*/*z* 384 (M^+, 9%), 382 (M^+, 9), 303 (13), 247 (81), 123 (100) and 77 (18) (Found: M^+, 382.0329. $C_{16}H_{19}BrN_2O_2S$ requires 382.0351).

Compound **11b**, an oil; δ_H(270 MHz) 1.18 (6H, s), 1.82–1.93 (2H, m), 3.29 (3H, s), 3.36 (2H, s), 4.04–4.15 (2H, m), 5.01 (1H, s) and 7.43–7.61 (5H, m); ν_{max}/cm^{-1} 1694, 1677, 1636, 1578, 1442 and 1418; *m*/*z* 398 (M^+, 18%), 396 (M^+, 18), 261 (14), 234 (29), 201 (28), 123 (49), 83 (37) and 55 (199) (Found: M^+, 396.0536. $C_{17}H_{21}BrN_2O_2S$ requires 396.0508).

Cobaloximes

A stirred and cooled suspension of chloro(4-*tert*-butylpyridine)cobaloxime[28] (771 mg, 2.0 mmol) in methanolic sodium hydroxide (20 cm^3, 96 mg, 2.4 mmol) under argon was treated in small portions with sodium borohydride (38 mg, 1.0 mmol) over a period of 15 min. The cobaloxime(I) anion thus obtained was treated with the corresponding bromide (1.0 mmol) after which the mixture was heated at 50 °C for 4.0 h. It was then cooled, diluted with water and extracted with chloroform. Conventional work-up of the extract gave the crude product which was purified by silica gel column chromatography using chloroform–methanol (20 : 1) as eluent. Analytical grade organocobaloximes were obtained by the diffusional mixing of the dichloromethane solution with pentane. Although elemental analyses failed on occasions to give the correct values because of thermal instability, the ^1H NMR spectra showed that all the cobaloximes were essentially pure.

Compound **1c**, orange crystals, mp 164 °C (decomp.) (Found: C, 59.45; H, 6.53; N, 11.29. $C_{36}H_{47}CoN_6O_4S$ requires C, 60.16; H, 6.59; N, 11.69%); δ_H(270 MHz) 0.79 (6H, s), 1.25 (9H, s), 1.72 (2H, s), 2.03 (12H, s), 3.93 (2H, s), 6.91 (1H, s), 7.11–7.42 (9H, m), 7.62 (2H, d, *J* 6.9) and 8.36 (2H, dd, *J* 6.9 and 1.3); ν_{max}/cm^{-1} 1616, 1562, 1452 and 1370.

Compound **1d**, orange crystals, mp 152 °C (decomp.) (Found: C, 60.32; H, 6.53; N, 11.38. $C_{37}H_{49}CoN_6O_4S$ requires C, 60.64; H, 6.74; N, 11.47%); δ_H(270 MHz) 0.79 (6H, s), 1.24 (9H, s), 1.28–1.37 (2H, m), 1.61 (2H, s), 2.00 (12H, s), 4.01–4.10 (2H, m), 6.87 (1H, s), 7.03–7.38 (9H, m), 7.60 (2H, d, *J* 6.9) and 8.35 (2H, dd, *J* 6.9 and 1.3); ν_{max}/cm^{-1} 1616, 1561, 1461 and 1379.

Compound **6c**, orange crystals, mp 160 °C (decomp.) (Found: C, 58.32; H, 6.42; N, 13.16. $C_{35}H_{46}CoN_7O_4S$ requires C, 58.40; H, 6.44; N, 13.62%); δ_H(270 MHz) 0.82 (6H, s), 1.26 (9H, s), 1.71 (2H, s), 2.12 (12H, s), 4.03 (2H, s), 7.22–7.48 (9H, m), 7.63 (2H, d, *J* 6.9) and 8.38 (2H, d, *J* 6.9); ν_{max}/cm^{-1} 1616, 1561, 1461 and 1368.

Compound **6d**, orange crystals, mp 163 °C (decomp.) (Found: C, 58.23; H, 6.58; N, 13.46. $C_{36}H_{48}CoN_7O_4S$ requires C, 58.92; H, 6.59; N, 13.46%); δ_H(270 MHz) 0.84 (6H, s), 1.25 (9H, s), 1.40–1.51 (2H, m), 1.63 (2H, s), 2.03 (12H, s), 4.10–4.19 (2H, m), 7.18–7.46 (9H, m), 7.71 (2H, d, *J* 6.9) and 8.35 (2H, dd, *J* 6.9 and 1.7); ν_{max}/cm^{-1} 1616, 1562, 1463 and 1371.

Reactions of the bromide derivatives of indole (1a and 1b), benzimidazole (6a and 6b) and uracil (11a and 11b)

(a) Reaction with triphenyltin hydride. A mixture of triphenyltin hydride (40 mg, 0.4 mmol) and AIBN (33 mg, 0.2 mmol) in benzene (20 cm^3) was added over 15 min under argon to a refluxing solution of one of the bromides (**1a**, **1b**, **6a** or **6b**) (0.2 mmol) in benzene (80 cm^3). The mixture was then refluxed for 6 h, cooled and concentrated. The residue was dissolved in ethyl acetate and stirred with saturated aqueous potassium fluoride (10 cm^3). The organic layer was then separated, dried and concentrated. The residue was passed through a short

column of silica gel using hexane–ethyl acetate (10:1) as eluent to remove polar by-products, and further purified using a preparative silica-gel TLC plate and hexane–ethyl acetate (50:1) as a developing solvent. The results are summarized in the Tables.

(b) Reactions with triphenyltin(4-*tert*-butylpyridine)cobaloxime. A mixture of the cobaloxime (464 mg, 0.6 mmol for **1a**, **6a**, **11a** and **11b**; 928 mg, 1.2 mmol for **1b** and **6b**) and one of the bromides (0.2 mmol) in dry DMF (10 cm^3) was heated at 130 °C for 24 h (**1a**, **1b**, **6a** and **6b**) or 120 °C (**11a** and **11b**) under argon. The cooled mixture was diluted with ethyl acetate (filtered in the case of **11a** and **11b**), washed with saturated aqueous sodium chloride, dried and concentrated. The residue was passed through a short column of silica gel using hexane–ethyl acetate (59:1) (**1a**, **1b**, **6a** and **6b**) or ethyl acetate (**11a** and **11b**) to remove the cobaloxime and polar by-products. The eluate was subjected further to a preparative silica gel TLC plate using the same solvent as a developing solvent.

Essentially the same procedure was used for the reaction of the uracil derivatives **6a** and **6b** except for the amount of the solvent (35 cm^3 of DMF), the amount of the triphenyltincobaloxime, and the reaction time (4 h). In this case, the precipitate formed on treatment with potassium fluoride solution was filtered off, and the filtrate was subjected to the same work-up procedure as recorded above. The results are summarized in the Tables.

(c) Photoreaction of cobaloxime derivatives of indole (1c and 1d) and benzimidazole (6c and 6d). One of the cobaloxime derivatives **1c**, **1d**, **6c** or **6d** (0.06 mmol) was dissolved in benzene (15 cm^3) and the solution dipped in an ultrasonic bath and deaerated by bubbling argon through it *via* a syringe needle. The mixture was irradiated for 24 h using a Rayonet Photoreactor (RPR-100) equipped with 350 nm lamps. The residue after concentration of the reaction mixture was subjected to the same purification procedure as in the case of reactions with triphenyltincobaloxime. The results are summarized in the Tables.

Compound **2a**, an oil; δ_H(270 MHz) 1.01 (9H, s), 4.02 (2H, s), 6.88–7.26 (8H, m), 7.41 (1H, d, *J* 7.9) and 7.61 (1H, d, *J* 7.9); ν_{max}/cm^{-1} 1582, 1478, 1451 and 1366; *m/z* 295 (M^+, 85%), 238 (100), 205 (46), 160 (9), 121 (20) and 91 (42) (Found: M^+, 295.1360. $C_{19}H_{21}NS$ requires 295.1395).

Compound **3a**, mp 82.4–83.8 °C (hexane–ethanol); δ_H(270 MHz) 1.29 (6H, s), 2.81 (2H, s), 3.80 (2H, s), 6.14 (1H, d, *J* 0.7), 6.99–7.23 (3H, m) and 7.53 (1H, dd, *J* 6.9 and 1.0); ν_{max}/cm^{-1} 1614, 1554, 1479, 1456 and 1377; *m/z* 185 (M^+, 100%), 170 (48), 144 (24), 129 (66), 115 (14) and 102 (19) (Found: M^+, 185.1192. $C_{13}H_{15}N$ requires 185.1204).

Compound **4a**, an oil; δ_H(270 MHz) 1.09 (6H, s), 3.05 (2H, s), 4.19 (2H, s), 6.90–6.98 (2H, m), 7.06–7.32 (11H, m), 7.50 (1H, d, *J* 6.6) and 7.61 (1H, d, *J* 6.6); ν_{max}/cm^{-1} 1582, 1479, 1450 and 1346; *m/z* 403 (M^+, 37%), 294 (58), 238 (100), 205 (40), 165 (15) and 109 (67) (Found: M^+, 403.1413. $C_{25}H_{25}NS_2$ requires 403.1428).

Compound **2b**, mp 55.4–56.8 °C (hexane–ethanol); δ_H(270 MHz) 0.90 (9H, s), 1.38–1.46 (2H, m), 4.11–4.19 (2H, m), 6.93 (1H, d, *J* 0.7), 7.16–7.33 (7H, m), 7.50 (1H, d, *J* 7.9) and 7.64 (1H, d, *J* 7.9); ν_{max}/cm^{-1} 1582, 1460, 1447 and 1352; *m/z* 309 (M^+, 100%), 238 (49), 205 (31), 117 (16) and 91 (24) (Found: M^+, 309.1524. $C_{20}H_{23}NS$ requires 309.1551).

Compound **3b**, mp 52.2–53.4 °C (hexane–ethanol); δ_H(270 MHz) 1.01 (6H, t, *J* 6.6), 1.81 (2H, t, *J* 6.6), 2.73 (2H, s), 4.05 (2H, t, *J* 6.6), 6.17 (1H, s) and 7.03–7.62 (4H, m); ν_{max}/cm^{-1} 1610, 1547, 1460 and 1358; *m/z* 199 (M^+, 50%), 184 (6), 167 (6), 143 (100) and 130 (19); *m/z* 199 (M^+, 50%), 184 (6), 167 (6), 143 (100), 130 (19) and 115 (21) (Found: M^+, 199.1390. $C_{14}H_{17}N$ requires 199.1361).

Compound **4b**, mp 104.4–104.8 °C (hexane–ethanol); δ_H(270 MHz) 1.01 (6H, s), 1.57–1.65 (2H, m), 2.86 (2H, s), 4.15–4.23 (2H, m), 6.92 (1H, s), 7.06–7.41 (13H, m) and 7.63 (1H, d, *J* 6.6); ν_{max}/cm^{-1} 1583, 1461 and 1353; *m/z* 417 (M^+, 60%), 308 (8), 238 (38), 193 (93), 123 (100) and 91 (28) (Found: M^+, 417.1565. $C_{26}H_{27}NS_2$ requires 417.1585).

Compound **7a**, mp 98.4–100.2 °C (hexane–ethanol); δ_H(270 MHz) 1.07 (9H, s), 4.10 (2H, s), 7.18–7.44 (8H, m) and 7.67–7.76 (1H, m); ν_{max}/cm^{-1} 1611, 1582, 1460, 1369 and 1340; *m/z* 296 (M^+, 54%), 281 (15), 225 (34), 187 (13), 161 (11), 91 (87) and 76 (100) (Found: M^+, 296.1341. $C_{18}H_{20}N_2S$ requires 296.1347).

Compound **8a**, mp 57.8–58.4 °C (hexane–ethanol); δ_H(270 MHz) 1.36 (6H, s), 2.89 (2H, s), 3.84 (2H, s), 7.16–7.29 (3H, m) and 7.66–7.74 (1H, m); ν_{max}/cm^{-1} 1621, 1534, 1454, 1390 and 1312; *m/z* 186 (M^+, 95%), 171 (100), 156 (10), 145 (25), 131 (41) and 117 (10) (Found: M^+, 186.1172. $C_{12}H_{14}N_2$ requires 186.1157).

Compound **9a**, mp 68.8–69.4 °C (hexane–ethanol); δ_H(270 MHz) 1.15 (6H, s), 3.08 (2H, s), 4.28 (2H, s), 7.13–7.48 (13H, m) and 7.66–7.76 (1H, m); ν_{max}/cm^{-1} 1582, 1461, 1369 and 1342; *m/z* 404 (M^+, 7%), 295 (100), 139 (35), 109 (27) and 77 (26) (Found: M^+, 404.1382. $C_{24}H_{24}N_2S_2$ requires 404.1381).

Compound **7b**, mp 61.6–62.8 °C (hexane–ethanol); δ_H(270 MHz) 0.98 (9H, s), 1.46–1.55 (2H, m), 4.17–4.26 (2H, m), 7.20–7.36 (6H, m), 7.37–7.45 (2H, m) and 7.72–7.80 (1H, m); ν_{max}/cm^{-1} 1582, 1462, 1442 and 1359; *m/z* 310 (M^+, 63%), 253 (90), 225 (100), 109 (30) and 69 (12) (Found: M^+, 310.1489. $C_{19}H_{22}N_2S$ requires 310.1504).

Compound **8b**, a white powder; δ_H(270 MHz) 1.11 (6H, s), 1.92 (2H, t, *J* 6.3), 2.85 (2H, s), 4.08 (2H, t, *J* 6.3), 7.18–7.32 (3H, m) and 7.64–7.72 (1H, m); ν_{max}/cm^{-1} 1616, 1459 and 1371; *m/z* 200 (M^+, 50%), 144 (100), 117 (37) and 77 (43) (Found: M^+, 200.1291. $C_{13}H_{16}N_2$ requires 200.1313).

Compound **9b**, a white powder; δ_H(270 MHz) 1.09 (6H, s), 1.67–1.75 (2H, m), 2.93 (2H, s), 4.21–4.29 (2H, m), 7.16–7.21 (1H, m), 7.22–7.34 (7H, m), 7.35–7.42 (5H, m) and 7.74–7.82 (1H, m); ν_{max}/cm^{-1} 1583, 1463 and 1360; *m/z* M^+ 418 (M^+, 93%), 309 (100), 253 (58), 239 (66), 109 (58) and 77 (57) (Found: M^+, 418.1553. $C_{25}H_{26}N_2S_2$ requires 418.1537).

Compound **12a**, a yellow oil; δ_H(90 MHz) 1.08 (9H, s), 3.29 (3H, s), 4.01 (2H, s), 5.05 (1H, s) and 7.46–7.63 (5H, m); ν_{max}/cm^{-1} 1698, 1649, 1442 and 1398; *m/z* 304 (M^+, 100%), 289 (9), 248 (49), 247 (45), 234 (28), 215 (35), 195 (19), 190 (40), 123 (47), 109 (11) and 77 (7) (Found: M^+, 304.1280. $C_{16}H_{20}N_2O_2S$ requires 304.1245).

Compound **13a**, mp 86.1–89.3 °C (ethyl acetate); δ_H(90 MHz) 1.21 (6H, s), 2.70 (2H, d, *J* 1.3), 3.32 (3H, s), 3.69 (2H, s) and 5.64 (1H, t, *J* 1.3); ν_{max}/cm^{-1} 1703, 1666, 1640, 1382 and 1322; *m/z* 194 (M^+, 58%), 179 (52), 136 (14), 122 (100), 109 (22), 94 (20) and 81 (43) (Found: M^+, 194.1075. $C_{10}H_{14}N_2O_2$ requires 194.1055).

Compound **12b**, a yellow oil; δ_H(90 MHz) 1.04 (9H, s), 1.66–1.76 (2H, m), 3.29 (3H, s), 4.04–4.13 (2H, m), 4.99 (1H, s) and 7.42–7.61 (5H, m); ν_{max}/cm^{-1} 1694, 1646, 1575, 1442, 1390 and 1372; *m/z* 318 (M^+, 13%), 261 (4), 201 (13), 167 (13), 149 (41), 123 (23), 85 (27) and 69 (100) (Found: M^+, 318.1434. $C_{17}H_{22}N_2O_2S$ requires 318.1402).

Compound **13b**, mp 138.2–140.1 °C (ethyl acetate); δ_H(90 MHz) 1.05 (6H, s), 1.73 (2H, t, *J* 6.7), 2.42 (2H, br s), 3.34 (3H, s), 3.84 (2H, t, *J* 6.7) and 5.53 (1H, t, *J* 1.2); ν_{max}/cm^{-1} 1668, 1656, 1490 and 1457; *m/z* 208 (M^+, 69%), 193 (32), 180 (7), 165 (11), 152 (13), 140 (89) and 95 (100); *m/z* 208 (M^+, 69%), 193 (32), 180 (7), 165 (11), 152 (13), 140 (89) and 95 (100) (Found: M^+, 208.1259. $C_{11}H_{16}N_2O_2$ requires 208.1212).

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