# Generation and Trapping of Benzyl Radicals from Benzyl Iodides by Cobaloxime-mediated Iodine Atom Abstractions

**Trevor M. Brown,*[a] Christopher J. Cooksey,[b] David Crich,[c] Alan T. Dronsfield*[a] and Robert Ellis[a]**

[a] *Chemistry Department, University of Derby, Kedleston Road, Derby DE22 1GB, UK*
[b] *Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ, UK*
[c] *Department of Chemistry (M/C 111), University of Illinois at Chicago, 801 W. Taylor Street, Rm. 4500, Chicago, IL 60607-7061, USA*

Ethylcobaloxime has been demonstrated to function as a convenient source of ethyl radicals on white light photolysis in ethanol. The ethyl radicals so generated take part in iodine abstractions with benzyl iodides giving benzyl radicals which may be trapped with 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO) or lepidinium camphor-10-sulfonate.

The use of free radical reactions in organic synthesis is currently an extremely active field whose origins can be traced back to the initial studies of Kuivila on the reaction of organotin hydrides with alkyl halides.[1,2] This method of radical generation, together with its close cousin the Barton–McCombie reaction,[3] is still by far the most widely applied in the field of organic synthesis. The reasons for the great success of the 'tin hydride method' are to be found in its ease of operation, the availability of starting materials and reagents, its compatibility with many common functional groups, the mildness of the reaction conditions and, most importantly, the ability to generate a low but reasonably constant flux of radicals (under the correct experimental conditions) enabling the use of complex chain sequences. Other significant milestones in the elevation of radical chemistry to its present prominence include the original Julia cyclizations,[4] the extremely important quantifications mainly from the Ingold, Beckwith and Giese groups,[5] the Beckwith transition state hypothesis for the hex-5-enyl radical cyclization,[6] the development of the organomercury hydride method by the Giese group,[7] the Stork-type vinyl radical cyclizations and the recognition of the mechanism by which they give the *endo*-mode products,[8] the Barton decarboxylation reaction,[9] the Keck allylstannane chemistry,[10] the Curran demonstration of tandem cyclizations,[11] the Porter macrocyclizations,[12] the exploitation of organocobalt complexes as radical precursors by various groups,[13] and the Curran iodine atom-transfer chemistry.[14] The recent, beautifully simple, but elegant work of the Porter, Giese and Curran groups on the design of highly diastereoselective acyclic radical reactions is also of major significance in so far as it demonstrates that radical reactions may be equally, if not more, diastereoselective than their two electron and pericyclic counterparts.[15]

Undoubtedly one of the most important goals in the application of radical reactions to organic synthesis at the present time is the replacement of the tin hydride type system by equally powerful yet simple methods which facilitate purification, are environmentally acceptable, and in which hydrogen atom transfer is not an obligatory propagation step. To this end we have recently described the acyl aryl tellurides as convenient photolytic sources of acyl radicals.[16] We describe here our attempts at the design of a further such system based on the cobaloximes as convenient stable sources of alkyl radicals in conjunction with an iodine atom-transfer step.

We were attracted to the idea of halogen abstraction from an alkyl iodide by another higher energy alkyl radical (Scheme 1) as a means of generating alkyl radicals.

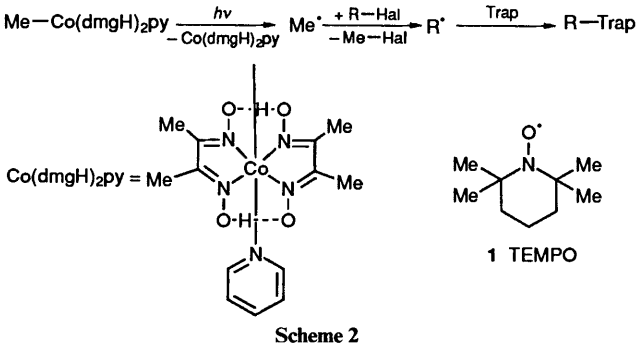
The obvious choice for the radical R$^{\bullet}$ is the methyl radical

$$R^{\bullet} + R'—I \longrightarrow R—I + R'^{\bullet}$$

**Scheme 1**

with rate constants for the abstraction of iodine from simple aliphatic iodides typically greater than $10^6$ dm$^3$ mol$^{-1}$ s$^{-1}$.[17] Minisci has explored this concept for aqueous solutions, using a number of different systems for the generation of the iodine-abstracting methyl radical, with some success.[18] Very recently the Italian group has also reported the use of phenyl radicals, generated from dibenzoyl peroxide, in conjunction with thiocarbonyl esters as sources of alkyl radicals under non-reductive conditions.[19] We sought a convenient source of methyl radicals that could be used as a shelf reagent and activated by simple photolysis or thermolysis in organic solvents. The use of organocobaloximes and the related salens and salophens in synthesis has been exploited by a number of groups, but most notably those of Pattenden, Baldwin, Branchaud and Johnson.[20] Methyl radicals generated from methylcobaloxime have been used by Tada to effect radical substitution on sulfur of the thioester group to produce thioesters of the type MeSAr.[21] Catalytic cycles seemingly involving organocobalt derivatives have been developed by Scheffold.[22]

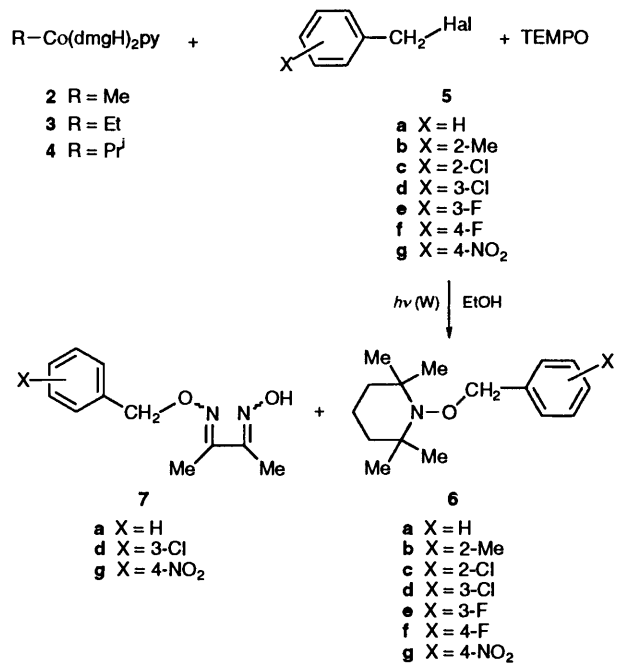
The fundamental idea underlying this study, outlined in Scheme 2, is that methylcobaloxime [Me–Co(dmgH)$_2$py]




**Scheme 2**

would function as a source of methyl radicals which would abstract iodine from alkyl iodides giving alkyl radicals which would, in turn, be trapped by any compatible radical trap.

In the first instance we elected to use the commercial 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO, **1**) as a convenient trap. Rate constants for the quenching of alkyl radicals by TEMPO have been measured: trapping of benzyl radicals in isooctane at




Scheme 3

**Table 1** Photolysis of benzyl bromides and iodides with methylcobaloxime and TEMPO

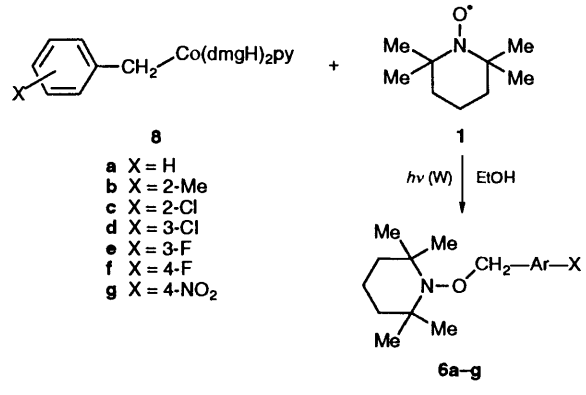
| Entry | Benzyl halide | Products (% yield) |
|---|---|---|
| 1 | **5a** (Iodide) | **6a** (37) |
| 2 | **5d** (Iodide) | **6d** (44) |
| 3 | **5g** (Iodide) | **6g** (40) |
| 4 | **5a** (Bromide) | **6a** (7) + **7a** (7) |
| 5 | **5d** (Bromide) | **6d** (12) + **7d** (13) |
| 6 | **5g** (Bromide) | **6g** (20) + **7g** (11) |

**Table 2** Photolysis of 4-nitrobenzyl iodide **5g** with alternative radical sources and TEMPO

| Radical source | Product (% yield) |
|---|---|
| **2** Me–Co(dmgH)$_2$py | **6g** (40) |
| **3** Et–Co(dmgH)$_2$py | **6g** (69) |
| **4** Pr$^i$–Co(dmgH)$_2$py | **6g** (68) |
| **9** Me–salophen | **6g** (68) |

room temperature occurs with a rate constant of $4.9 \times 10^8$ s$^{-1}$, whilst the corresponding values for the nonyl and *tert*-butyl radicals are $1.2 \times 10^9$ and $7.6 \times 10^8$ s$^{-1}$ respectively.[23] In order to facilitate the iodine atom-abstraction, and so limit diversion of the methyl radicals by reaction with TEMPO, benzyl iodides were chosen as substrate in this study.[24] Very recently Breslow has described a closely related process in which a cobalamine-derived cyclodextrin radical abstracts iodine from benzyl iodides in aqueous solution.[25] In the event, white light photolysis of three benzyl iodides **5** with methylcobaloxime **2**, conducted in ethanol at reflux under an inert atmosphere, gave moderate yields of the expected *N*-benzyloxy-2,2,6,6-tetramethylpiperidines **6** (Table 1, entries 1–3, Scheme 3, R = Me). A control experiment, in which benzyl iodide was photolysed in the presence of TEMPO resulting in the formation of only 2% of the *N*-benzyloxypiperidine, indicated that the observed results were not due to 'homosolvolysis' as described by Tedder.[26] A second control experiment in which benzyl iodide was photolysed in ethanol alone afforded only benzyl ethyl ether. This presumably arises from nucleophilic attack of the solvent on the benzyl iodide. Careful GC–MS of the product mixture revealed no trace of bibenzyl, suggesting that (in the absence of cobaloxime mediation) radical processes were not implicated in this conversion. In the reactions described here which involve the production of free radicals either directly from cobaloxime photolysis or by cobaloxime mediation (Schemes 3–5) no aryl ethyl ethers were detected, suggesting that radical quenching is a more rapid process than nucleophilic attack of the solvent. Not too surprisingly, attempts to use the corresponding benzyl bromides rather than the iodides in Scheme 3 as substrate led to much reduced yields of *N*-benzyloxypiperidines (Table 1, entries 4–6) and the unexpected formation of the mono-*O*-benzyl-1,2-dimethylglyoximes **7** as by-products.

The moderate yields in the above reactions are attributable, at least in part, to inefficient cleavage of the Co–Me bond. Indeed, even after prolonged photolysis, examination of the reaction mixtures by TLC analysis revealed the presence of substantial amounts of residual cobaloxime. This suggested that improved yields might be obtained with a more readily cleavable Co–alkyl bond. The Co–C bond dissociation energy for isopropylcobaloxime is estimated to be 89 kJ mol$^{-1}$ as opposed to 138 kJ mol$^{-1}$ in methylcobaloxime[27] and whilst that for ethylcobaloxime is apparently unknown it can reasonably be assumed to have an intermediate value. Both ethyl- and isopropyl-cobaloxime were prepared and photolysed with nitrobenzyl iodide and TEMPO resulting in significant increases in yield of the *N*-benzyloxypiperidines **6** (Table 2, Scheme 3, R = Me and Pr$^i$) over that obtained with methylcobaloxime. In a similar vein, the alkylsalophens are believed to have lower Co–alkyl bond energies than the alkylcobaloximes,[28] and so **9**, an example, was prepared and used in place of methylcobaloxime in the nitrobenzyl iodide–TEMPO reaction, again with a significant increase in yield (Table 2). Of the three improved alkyl radical sources we selected ethylcobaloxime for further development on the grounds that, unlike the salophen, it was easy to prepare and store, and also that the ethyl radical would provide greater scope for the ensuing chemistry than the isopropyl radical. A number of benzyl iodides were photolysed with ethylcobaloxime and TEMPO and the isolated yields of *N*-benzyloxypiperidines are recorded in Table 3 (Scheme 3; R = Et). These yields compared well with those obtained by photolysis of the appropriate benzylcobaloximes **8** in the presence of TEMPO (Table 3, Scheme 4) and with one exception are in the moderate to good range.




Scheme 4

It would appear that the reaction of the benzylic radical with TEMPO is faster than its reaction with the cobalt(II) radical produced by homolytic cleavage of the alkyl cobaloxime, otherwise some benzyl cobaloximes would be expected as intermediates or by-products. These were not encountered as reaction products from Schemes 3 and 5. Further confirmation

**Table 3** Photolysis of benzyl iodides with ethylcobaloxime and TEMPO

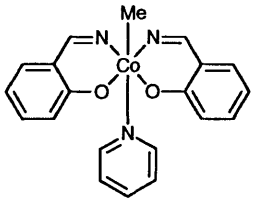
| Entry | Iodide | Product (% yield) | Authentic sample **6** (% yield)[a] |
|---|---|---|---|
| 1 | **5a** | **6a** (50) | **6a** (53) |
| 2 | **5b** | **6b** (25) | **6b** (35) |
| 3 | **5c** | **6c** (54) | **6c** (33) |
| 4 | **5d** | **6d** (54) | **6d** (57) |
| 5 | **5e** | **6e** (52) | **6e** (55) |
| 6 | **5f** | **6f** (66) | **6f** (48) |
| 7 | **5g** | **6g** (69) | **6g** (72) |

[a] Yield of authentic sample of **6a–g** prepared by photolysis of cobaloximes **8a–g** with TEMPO

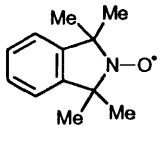
of the 'non-intermediacy' of benzyl cobaloximes in Scheme 3 was obtained simply by photolysing ethyl cobaloxime with benzyl iodide in the absence of TEMPO. No benzyl cobaloxime was obtained, the sole cobaloxime product being identified as iodocobaloxime. The major isolated product from this control experiment was *O*-benzyl-1,2-dimethylglyoxime, obtained in 58% yield.

Examination of the $^1H$ and $^{13}C$ NMR spectra of the *N*-benzyloxypiperidines **6a–g** revealed, in each case, the presence of two pairs of non-equivalent methyl groups suggesting either slow nitrogen inversion or restricted rotation about the N–O bond.[29] Similar effects have been observed by Beckwith in his studies on the calibration of the rate of trapping by the closely related tetramethylisoindoxyl radical **10**,[30] and Solomon[31] has measured coalescence temperatures for alkyl radical adducts of **10** but was unable to differentiate satisfactorily between nitrogen inversion and restricted rotation about the N–O bond as the slow step. We simply report the coalescence temperature (348 ± 5 K) for **6f** and note that it is somewhat higher than the corresponding value measured for the benzyl adduct of **10** by Solomon.

Having established the validity of the iodine atom abstraction process, at least for benzyl iodides, we turned our attention to the formation of carbon–carbon bonds. Protonated heteroatomic bases have been reported by several groups to be good traps of alkyl and benzyl radicals generated by a variety of methods.[32] Indeed, Branchaud has reported that photolysis of alkylcobaloximes in the presence of a 2–10 fold excess of protonated heteroaromatic base does enable formation of alkylated bases in moderate to good yields (40–90%).[20] We chose to employ lepidine (4-methylquinoline) as base as it possesses a single favoured site for attack by nucleophilic radicals and so should not give rise to isomeric mixtures. Thus, tungsten photolysis of various benzyl iodides with 1 mol equiv. each of ethylcobaloxime and lepidinium camphor-10-sulfonate in ethanol under nitrogen resulted in rapid consumption of the cobaloxime (< 3 h, TLC control) and isolation of moderate yields of the expected 2-benzyl-4-methylquinolines (Table 4, Scheme 5). Perhaps not too surprisingly, no addition product was obtained for the 4-nitrobenzyl radical in view of its much reduced nucleophilicity (Table 4, entry 8). It is noteworthy in all of these experiments that the 2-benzyl-4-methylquinolines are formed as the free base and may be obtained from the reaction




**9**



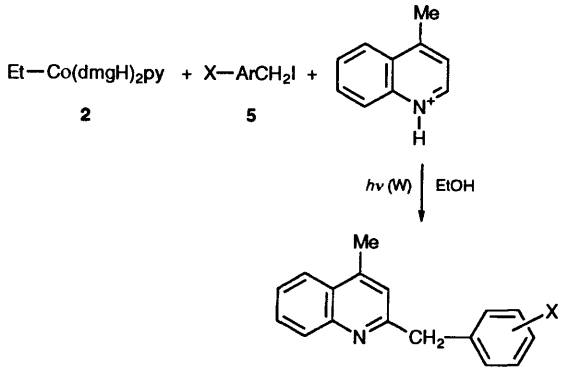

**10**

**Table 4** Photolysis of benzyl iodides with ethylcobaloxime and lepidinium camphor-10-sulfonate

| Entry | Iodide | Product (% yield) |
|---|---|---|
| 1 | **5a** | **11a** (10) |
| 2 | **5b** | **11b** (12) |
| 3 | **5c** | **11c** (36) |
| 4 | **5d** | **11d** (30) |
| 5 | **5d** | **11d** (53)[a] |
| 6 | **5e** | **11e** (31) |
| 7 | **5f** | **11f** (34) |
| 8 | **5g** | **11g** (0) |
| 9[b] | $Pr^iI$ | **12** (5)[c] + **13** (trace) |
| 10[d] | $Pr^iI$ | **13** (22) |

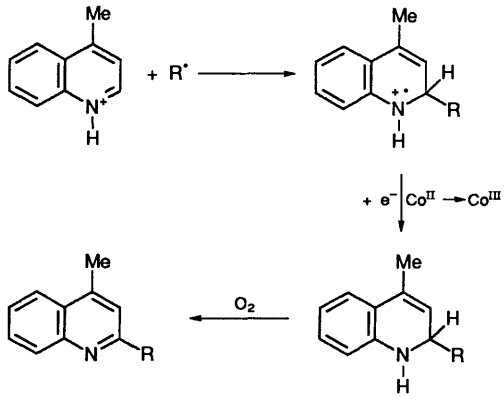
[a] 2 Mol equiv. of lepidinium salt were employed. [b] The mol ratio of $EtCo(dmgH)_2py$:$Pr^iI$:base was 1:1:10. [c] The low yield probably reflects difficulties in isolation from excess lepidine. [d] The mol ratio of $EtCo(dmgH)_2py$:$Pr^iI$:base was 1:10:10.

mixture by simple dilution with water and diethyl ether extraction, without prior basification. This is to be contrasted to the work of Branchaud wherein basification was apparently necessary to liberate the products from their salts.[20] A plausible rationalization, possibly also operating unnoticed in the Branchaud chemistry, is the reduction of the aminium radical cation formed on addition of the benzyl radical to the lepidinium




**11**
**a** X = H
**b** X = 2-Me
**c** X = 2-Cl
**d** X = 3-Cl
**e** X = 3-F
**f** X = 4-F
**g** X = 4-$NO_2$

**Scheme 5**




**12** R = Et
**13** R = $Pr^i$

**Scheme 6**

ion by the cobaloxime radical giving a dihydroquinoline species which then suffers oxidation on work-up (Scheme 6).

Finally, addition of isopropyl radicals generated from isopropyl iodide, by photolysis in the presence of ethylcobaloxime, to the lepidinium salt was attempted. With a 1:1 ratio of isopropyl iodide and ethylcobaloxime the only addition product observed was 2-ethyl-4-methylquinoline[33] **12** (Table 4, entry 9), however when isopropyl iodide was used in 10-fold excess the known[34] 2-isopropyl-4-methylquinoline **13** was indeed isolated in 22% yield (Table 4, entry 10). The poor yields of isolated products in these latter two experiments reflect to some extent the difficulties observed in isolation of **12** and **13** from the excess of lepidinium camphorsulfonate employed as trap. Work in progress involves the development of cobaloximes of greater photolytic fragility for the more effective production of a wide range of radicals from their corresponding iodo substrates. The intention is to evaluate this procedure as a general synthetic approach to carbon–carbon bond formation.

## Experimental

$^1$H NMR spectra were recorded on Jeol PMX-60, Varian T-60, Varian VXR-400, Bruker WP-200, Bruker ACP-300 and Bruker AM-400 spectrometers. $CDCl_3$ was used as solvent with $Me_4Si$ as internal standard. Coupling constants ($J$) are given in Hz. Melting points are uncorrected. Column chromatography was performed with Merck silica gel 100 (70–230 mesh). Flash column chromatography was carried out using Sorbsil flash silica gel C60 (mean pore diameter 60 Å). Solvents were standard grade Aldrich chemicals and were distilled before use. Allyl bromides and benzyl bromides were converted into the iodides by a standard Finkelstein procedure.[35] Cobaloximes were prepared according to literature methods[36] and purified by crystallisation from MeOH or column chromatography (ethyl acetate as eluent) immediately before use.

GC–MS was performed using a Hewlett Packard GC 5890 Series II chromatograph in conjunction with mass spectrometer MS5971. Separations were achieved on a 12 m silicone gum capillary column and products identified using a Wiley 138 library, where appropriate.

*Preparation of Authentic Samples of* N-*Benzyloxypiperidines* **6** *by Photolysis of Benzylcobaloximes with TEMPO.*—N-*Benzyloxy*-2,2,6,6-*tetramethylpiperidine* **6a**. Benzylcobaloxime (1.38 g, 3.00 mmol) and TEMPO (0.47 g, 3.00 mmol) were dissolved in a 1:2 mixture of $CH_2Cl_2$ and $CCl_4$ (90 cm$^3$). (Note that $CH_2Cl_2$–$CCl_4$ was found to be a more effective solvent system than ethanol for benzylic systems. The use of $CH_2Cl_2$ alone resulted in much longer reaction times. No quenching of the benzyl radicals by $Cl^\bullet$ or $Cl_3C^\bullet$ was observed. A feature of this solvent system is that the cobalt(II) radical is trapped as soluble chlorocobaloxime and no precipitation occurs). The stirred solution was degassed using nitrogen prior to irradiation with two 200 W tungsten filament lamps. The reaction was stopped when the TEMPO had been consumed (TLC analysis). Chromatography using $CH_2Cl_2$ as eluent yielded an opaque oil (lit.[20a]). Distillation (Kugelrohr) gave the title compound **6a** as a mobile colourless oil (0.39 g, 53%), $\delta_H$(400 MHz) 1.15 (6 H, s), 1.25 (6 H, s), 1.3–1.6 (6 H, m), 4.82 (2 H, s) and 7.37–7.34 (5 H, m); $\delta_C$(100 MHz) 17.11, 20.30, 33.09, 39.70, 60.00, 78.70, 127.29, 127.45, 128.22 and 138.29 (Found: C, 77.6; H, 9.9; N, 5.6. $C_{16}H_{25}NO$ requires C, 77.65; H, 10.18; N, 5.66%).

2,2,6,6-*Tetramethyl*-N-(2-*methylbenzyloxy*)*piperidine* **6b**. The title compound was prepared by the standard procedure from **8b** (1.42 g, 3.00 mmol). Chromatography using $CH_2Cl_2$ as eluent followed by distillation (Kugelrohr) gave **6b** as a colourless solid (0.27 g, 35%), m.p. 51–52 °C; $\delta_H$(400 MHz) 1.15 (6 H, s), 1.26 (6 H, s), 1.3–1.7 (6 H, m), 2.31 (3 H, s), 4.83 (2 H, s), 7.14–7.19 (3 H, m) and 7.43–7.47 (1 H, m); $\delta_C$(100 MHz) 17.12, 20.30, 33.05, 39.72, 59.90, 76.81, 125.67, 127.09, 127.71, 129.82, 135.66 and 136.67 (Found: C, 78.15; H, 10.2; N, 5.3. $C_{17}H_{27}NO$ requires C, 78.11; N, 10.41; N, 5.35%).

N-(2-*Chlorobenzyloxy*)-2,2,6,6-*tetramethylpiperidine* **6c**. The title compound was prepared by the standard procedure from **8c** (1.48 g, 3.00 mmol). Chromatography using $CH_2Cl_2$ as eluent followed by distillation (Kugelrohr) gave **6c** as a colourless solid (0.28 g, 33%), m.p. 49.5–51 °C; $\delta_H$(400 MHz) 1.20 (6 H, s), 1.27 (6 H, s), 1.3–1.7 (6 H, m), 4.94 (2 H, s), 7.22 (1 H, t), 7.29 (1 H, t), 7.36 (1 H, d, $J$ 7.9) and 7.60 (1 H, d); $\delta_C$(100 MHz), 17.09, 20.33, 32.92, 39.69, 60.00, 75.49, 126.58, 128.04, 128.53, 129.01, 132.18 and 136.29 (Found: C, 68.1; H, 8.4; N, 4.9. $C_{16}H_{24}ClNO$ requires C, 68.19; H, 8.58; N, 4.97%).

N-(3-*Chlorobenzyloxy*)-2,2,6,6-*tetramethylpiperidine* **6d**. The title compound was prepared by the standard procedure from **8d** (1.48 g, 3.00 mmol). Chromatography using $CH_2Cl_2$ as eluent followed by distillation (Kugelrohr) gave **6d** as a clear mobile oil (0.48 g, 57%), $\delta_H$(400 MHz) 1.17 (6 H, s), 1.24 (6 H, s), 1.3–1.7 (6 H, m), 4.80 (2 H, s) and 7.2–7.5 (4 H, m); $\delta_C$(100 MHz) 17.06, 20.29, 33.03, 39.66, 60.03, 77.86, 125.32, 127.32, 127.34, 129.48, 134.05 and 140.29 (Found: C, 67.7; H, 8.4; N, 4.9. $C_{16}H_{24}ClNO$ requires C, 68.18; H, 8.58; N, 4.96%).

N-(3-*Fluorobenzyloxy*)-2,2,6,6-*tetramethylpiperidine* **6e**. The title compound was prepared by the standard procedure from **8e** (1.43 g, 3.00 mmol). Chromatography using $CH_2Cl_2$ as eluent followed by distillation (Kugelrohr) gave **6e** as a clear mobile oil (0.44 g, 55%), $\delta_H$(400 MHz), 1.18 (6 H, s), 1.25 (6 H, s), 1.3–1.7 (6 H, m), 4.80 (2 H, s), 6.97 (1 H, dddd, $J$ 8.95, 8.90, 2.67 and 0.67), 7.10 (2 H, m) and 7.30 (1 H, td, $J$ 8.26 and 6.30); $\delta_C$(100 MHz) 17.07, 20.28, 33.02, 39.67, 60.03, 77.90, 113.90 ($J$ 46), 114.11 ($J$ 49), 122.62, 129.64 ($J$ 77), 146.89 ($J$ 74) and 162.83 ($J$ 244) (Found: C, 72.0; H, 8.85; 5.2. $C_{16}H_{24}FNO$ requires C, 72.41; H, 9.11; N, 5.27%).

N-(4-*Fluorobenzyloxy*)-2,2,6,6-*tetramethylpiperidine* **6f**. The title compound was prepared by the standard procedure from **8f** (1.43 g, 3.00 mmol). Chromatography using $CH_2Cl_2$ as eluent followed by distillation (Kugelrohr) gave **6f** as a clear mobile oil (0.38 g, 48%), $\delta_H$(400 MHz) 1.16 (6 H, s), 1.27 (6 H, s), 1.3–1.7 (6 H, m), 4.75 (2 H, s), 7.04 (2 H, dd, $J$ 8.8 and 8.8) and 7.34 (2 H, dd, $J$ 8.2 and 5.50); $\delta_C$(100 MHz) 17.07, 20.25, 33.07, 39.66, 59.97, 77.99, 115.02 ($J$ 21), 115.02 ($J$ 21), 129.15 ($J$ 7.8), 129.15 ($J$ 7.8), 133.94 ($J$ 3.1), 162.10 ($J$ 244) (Found: C, 72.0; H, 8.85; N, 5.2. $C_{16}H_{24}FNO$ requires C, 72.41; H, 9.11; N, 5.27%).

2,2,6,6-*Tetramethyl*-N-(4-*nitrobenzyloxy*)*piperidine* **6g**. The title compound was prepared by the standard procedure from **8g** (1.51 g, 3.00 mmol). Chromatography using $CH_2Cl_2$ as eluent followed by distillation (Kugelrohr) gave **6g** as an opaque solid (0.63 g, 72%), m.p. 62.5–64.5 °C; $\delta_H$(400 MHz) 1.17 (6 H, s), 1.21 (6 H, s), 1.3–1.7 (6 H, m), 4.39 (2 H, s), 7.51 (2 H, d, $J$ 8.8) and 8.21 (2 H, d, $J$ 8.8); $\delta_C$(100 MHz) 17.00, 20.26, 32.95, 39.61, 60.10, 77.48, 123.50, 127.31, 145.93 and 146.99 (Found: C, 66.0; H, 8.3; N, 9.6. $C_{16}H_{24}N_2O_3$ requires C, 65.72; H, 8.27; N, 9.58%).

*Solvolysis of Benzyl Iodide with Ethanol.*—Benzyl iodide (0.40 g, 1.83 mmol) was dissolved in ethanol (100 cm$^3$) and the solution degassed with nitrogen (20 min). It was then irradiated in a nitrogen atmosphere for 17 h (2 × 200 W lamps) to give a straw-coloured solution which was shown by GC–MS to contain only one volatile product, benzyl ethyl ether. The excess of ethanol was removed by rotary evaporation to give a brown oil which was shown by NMR spectroscopy to contain the ether and ethanol. The latter was removed by re-evacuation from $CCl_4$ solution to give the pure benzyl ethyl ether (0.23 g, 92%).

*Standard Protocol for the Photolysis of Methylcobaloxime, Benzyl Iodides or Bromides and TEMPO: Formation of N-Benzyloxypiperidines and Benzyl-1,2-dimethylglyoximes.*—*O-Benzyl-1,2-dimethyglyoxime* **7a**. Methylcobaloxime (1.15 g, 3.00 mmol), TEMPO (0.47 g, 3.00 mmol) and benzyl bromide (0.36 $cm^3$, 3.00 mmol) were dissolved in ethanol (100 $cm^3$). The stirred solution was degassed using nitrogen prior to irradiation with two 200 W tungsten filament lamps and the reaction was stopped after 18 h. Column chromatography using $CH_2Cl_2$ as eluent gave an oil containing compound **6a**, the title compound **7a** and benzyl bromide. Flash column chromatography using $CH_2Cl_2$ as eluent gave the piperidine **6a** as a colourless oil (0.07 g, 10%) and *O*-benzyl-1,2-dimethylglyoxime **7a** as long white needles (0.04 g, 7%), m.p. 104–105 °C (lit.,[37] 90–92 °C); $\delta_H$(60 MHz) 2.06 (6 H, d), 5.15 (2 H, s), 7.30 (5 H, s) and 8.66 (1 H, s) (Found: C, 63.95; H, 6.9; N, 13.5. $C_{11}H_{14}N_2O_2$ requires C, 64.06; H, 6.84; N, 13.58%).

O-(3-*Chlorobenzyl*)-1,2-*dimethylglyoxime* **7d**. The standard procedure with 3-chlorobenzyl bromide (0.39 $cm^3$, 3.00 mmol) gave the title compound **7d** as white needles (0.10 g, 13%), m.p. 118–120 °C; $\delta_H$(60 MHz) 2.23 (6 H, s), 5.10 (2 H, s), 7.83 (4 H, m) and 8.83 (1 H, s) (Found: C, 54.9; H, 5.4; N, 11.7. $C_{11}H_{13}ClN_2O_2$ requires C, 54.89; H, 5.44; N, 11.64%).

O-(4-*Nitrobenzyl*)-1,2-*dimethylglyoxime* **7g**. The standard procedure with 4-nitrobenzyl bromide gave the title compound **7g** as white needles (0.08 g, 11%), m.p. 141.2 °C (lit.,[37] 99 °C); $\delta_H$(60 MHz) 2.00 (6 H, d), 5.23 (2 H, s), 7.43 (2 H, d), 8.40 (2 H, d) and 8.76 (1 H, s) (Found: C, 52.8; H, 5.1; N, 16.2. $C_{11}H_{13}N_3O_4$ requires C, 52.58; H, 5.21; N, 16.72%).

*Photolysis of* 4-*Nitrobenzyl Iodide with Isopropylcobaloxime and TEMPO.*—4-Nitrobenzyl iodide (0.158 g, 0.60 mmol), isopropylcobaloxime (0.248 g, 0.60 mmol) and TEMPO (0.094 g, 0.60 mmol) were added to ethanol (20 $cm^3$). The stirred solution was purged with nitrogen for 20 min and then irradiated with a 300 W tungsten filament lamp at a distance of 5 cm. After 3 h the TEMPO and the nitrobenzyl iodide were completely consumed. The solvent was evaporated under reduced pressure to give a residue which after column chromatography (silica, $CH_2Cl_2$ as eluent) gave the pure product **6g** as an opaque oil (0.118 g, 68%) which slowly crystallised to give a solid, identical (m.p. and NMR spectroscopy) to the authentic sample previously prepared.

*Photolysis of* 4-*Nitrobenzyl Iodide with Methyl Salophen and TEMPO.*—4-Nitrobenzyl iodide (0.158 g, 0.60 mmol), methyl salophen (0.280 g, 0.60 mmol) and TEMPO (0.094 g, 0.60 mmol) were photolysed in ethanol as described above for isopropylcobaloxime mediation. A similar isolation procedure gave pure product **6g** as an opaque oil (0.118 g, 68%) the identity of which was confirmed as before.

*Standard Protocol for Photolysis of Benzyl Iodides with Ethylcobaloxime and TEMPO.*—The benzyl iodide (1.5 mmol), ethylcobaloxime (0.60 g, 1.5 mmol) and TEMPO (0.23 g, 1.5 mmol) were added to ethanol (50 $cm^3$). The solution was purged with nitrogen prior to irradiation with a 300 W tungsten filament lamp at a distance of 5 cm. After 3 h, TEMPO and the benzyl iodide were completely consumed. The solvent was evaporated under reduced pressure to give a residue which was purified by column chromatography (silica, $CH_2Cl_2$ as eluent) to give the pure product as a mobile oil, the identity of which was confirmed by comparison of its $^1H$ NMR spectrum with that of an authentic sample previously prepared. The yields of **6a–e** are given in Table 3.

*Photolysis of Benzyl Iodide with TEMPO in the Absence of Cobaloximes.*—Benzyl iodide (0.654 g, 3.0 mmol) and TEMPO (0.468 g, 3.0 mmol) were added to ethanol (100 $cm^3$) and the solution was purged with nitrogen for 20 min prior to irradiation with 2 × 200 W tungsten filament lamps at distances of 5 cm. The reaction was stopped after 18 h. Column chromatography using cyclohexane–ethyl acetate (9:1) as eluent gave unchanged TEMPO (0.257 g, 55% recovery) and an oil (0.277 g) which was shown by GC–MS to consist of unchanged benzyl iodide (0.125 g, 19% recovery), benzyl ethyl ether (0.140 g, 34%) and the piperidine **6a** (0.014 g, 2%).

*Photolysis of Ethyl Cobaloxime with Benzyl Iodide in the Absence of a Substrate.*—Ethyl cobaloxime (0.197 g, 0.50 mmol) and benzyl iodide (0.109 g, 0.50 mmol) were dissolved in ethanol (70 $cm^3$) and the solution degassed with nitrogen for 20 min. The stirred solution was irradiated (2 × 200 W tungsten filament lamps, at distances of 5 cm). The reaction was stopped after 17 h. The solvent was removed by rotary evaporation to give a brown solid which was purified by column chromatography (ethyl acetate as eluent) to give iodocobaloxime (0.085 g, 34%) confirmed by TLC and comparison of its IR spectrum with that of an authentic sample together with *O*-benzyl-1,2-dimethylglyoxime **7a** (0.060 g, 58%), confirmed by mass spectroscopy and comparison of its $^1H$ NMR spectrum with that of an authentic sample. GC–MS Examination of the product mixture before rotary evaporation indicated the presence of trace amounts of the following materials: pyridine, benzyl ethyl ether and unchanged benzyl iodide.

2-*Benzyl*-4-*methylquinolines* **11**: *Standard Protocol for the Photolysis of Benzyl Iodides with Ethylcobaloxime and Lepidinium Camphor*-10-*sulfonate.*—The benzyl iodide **5a–f** (1.5 mmol), ethylcobaloxime (0.60 g, 1.5 mmol) and lepidinium camphor-10-sulfonate (5.63 g, 15 mmol) were dissolved in ethanol (50 $cm^3$). The stirred solution was degassed using nitrogen prior to irradiation with a 300 W tungsten filament lamp and the reaction monitored by TLC. The reaction was judged to be complete after 3 h. Solvent was removed from the cooled solution under reduced pressure. The residue was extracted twice with diethyl ether, washed with saturated brine and dried ($MgSO_4$). The solvent was evaporated under reduced pressure to give a brown oil, column chromatography of which using $CH_2Cl_2$ as eluent yielded a brown viscous oil. Distillation (Kugelrohr) of this gave the following products as viscous brown oils which crystallised with time. In a few cases, where the amount of material was limited, some compounds could not be obtained in an analytically pure condition, but gave satisfactory MS and NMR data.

2-*Benzyl*-4-*methylquinoline* **11a**. This is a known compound[38] and was identified by $^1H$ NMR spectroscopy.

4-*Methyl*-2-(2-*methylbenzyl*)*quinoline* **11b**. M.p. 67.2–69.2 °C; $\delta_H$(400 MHz) 2.30 (3 H, s), 2.57 (3 H, s), 4.31 (2 H, s), 6.94 (1 H, s), 7.15–7.21 (4 H, m), 7.51 (1 H, t, *J* 6.95), 7.68 (1 H, t, *J* 6.91), 7.93 (1 H, d, *J* 8.37) and 8.07 (1 H, d, *J* 8.45) (Found: C, 85.5; H, 7.0; N, 5.5%; $M^+$, 247.1365. $C_{18}H_{17}N$ requires C, 87.41; H, 6.93; N, 5.66%; *M*, 247.1361).

2-(2-*Chlorobenzyl*)-4-*methylquinoline* **11c**. M.p. 83.6–84.1 °C; $\delta_H$(400 MHz) 2.62 (3 H, s), 4.45 (2 H, s), 7.05 (1 H, s), 7.19 (2 H, m), 7.27 (1 H, m), 7.41 (1 H, m), 7.52 (1 H, t, *J* 6.99), 7.69 (1 H, t, *J* 6.93), 7.95 (1 H, d, *J* 8.32) and 8.07 (1 H, d, *J* 8.42) [Found: C, 75.3; H, 5.2; N, 5.1%; ($M^+$ − H), 266.0730. $C_{17}H_{14}ClN$ requires C, 76.26; H, 5.27; N, 5.23%; ($M^+$ − H), 266.0737].

2-(3-*Chlorobenzyl*)-4-*methylquinoline* **11d**. M.p. 66.5–66.8 °C; $\delta_H$(400 MHz) 2.63 (3 H, s), 4.26 (2 H, s), 7.05 (1 H, s), 7.21 (3 H, m), 7.31 (1 H, m), 7.53 (1 H, t, *J* 7.61), 7.70 (1 H, t, *J* 7.66), 7.95 (1 H, d, *J* 8.29) and 8.08 (1 H, d, *J* 8.45) [Found: C, 76.1; H,

5.4; N, 5.0%; ($M^+$ − H), 266.0736. $C_{17}H_{14}ClN$ requires C, 76.26; H, 5.27; N, 5.23%; ($M^+$ − H), 266.0737].

2-(3-*Fluorobenzyl*)-4-*methylquinoline* **11e**. M.p. 64.9 °C; $\delta_H$ (400 MHz) 2.63 (3 H, s), 4.28 (2 H, s), 6.91 (1 H, t, *J* 8.52), 7.01 (1 H, d, *J* 10.44), 7.06 (1 H, s), 7.09 (1 H, d, *J* 8.36), 7.25 (1 H, m), 7.53 (1 H, t, *J* 7.62), 7.70 (1 H, t, *J* 7.66), 7.95 (1 H, d, *J* 7.78) and 8.08 (1 H, d, *J* 8.45) [Found: C, 81.1; H, 5.6; N, 5.5; ($M^+$ − H), 250.1039. $C_{17}H_{14}FN$ requires C, 81.27; H, 5.62; N, 5.58%; ($M^+$ − H), 250.1032].

2-(4-*Fluorobenzyl*)-4-*methylquinoline* **11f**. Oil; $\delta_H$(400 MHz) 2.62 (3 H, s), 4.25 (2 H, s), 6.98 (2 H, t, *J* 8.78), 7.04 (1 H, s), 7.27 (2 H, m), 7.52 (1 H, t, *J* 7.60), 7.69 (1 H, t, *J* 7.66), 7.94 (1 H, d, *J* 8.31) and 8.08 (1 H, d, *J* 8.45) (Found: C, 79.2; H, 6.1; N, 5.4. $C_{17}H_{14}FN$ requires C, 81.27; H, 5.62; N, 5.58%).

2-*Ethyl*-4-*methylquinoline* **12**.—Isopropyl iodide (0.102 g, 0.60 mmol), ethylcobaloxime (0.24 g, 0.60 mmol) and lepidinium camphor-10-sulfonate (2.26 g, 6.00 mmol) were added to ethanol 20 $cm^3$). The stirred solution was purged with nitrogen for 20 min and then irradiated with a tungsten filament lamp (300 W) at a distance of 10 cm. After 3 h the ethylcobaloxime had been completely consumed. The solution was evaporated under reduced pressure and the residue diluted with water (50 $cm^3$) and extracted with diethyl ether (2 × 50 $cm^3$). The combined extracts were washed with saturated brine dried ($MgSO_4$) and evaporated under reduced pressure to give a brown oil which was purified by column chromatography (silica, $CH_2Cl_2$ as eluent). The major product was identified as the title compound **12**[33] (0.003 g, 5%); $\delta_H$(200 MHz) 1.40 (3 H, t), 2.64 (3 H, s), 2.98 (2 H, q), 7.24 (1 H, s), 7.48 (1 H, s), 7.66 (1 H, t), 7.94 (1 H, d) and 8.05 (1 H, d). A trace amount of a minor product was obtained which was tentatively identified (200 MHz $^1$H NMR) as 2-*isopropyl*-4-*methylquinoline* **13** $\delta_H$(200 MHz), 1.38 (6 H, d, *J* 6.80), 2.68 (3 H, s), 3.21 (1 H, sep, *J* 6.90), 7.16 (1 H, s), 7.47 (1 H, t, *J* 7.2), 7.65 (1 H, t, *J* 7.2), 7.93 (1 H, d, *J* 8.2) and 8.04 (1 H, d, *J* 8.4).

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