The first efficient method for the intramolecular trapping of benzynes by phenols: a new approach to xanthenes

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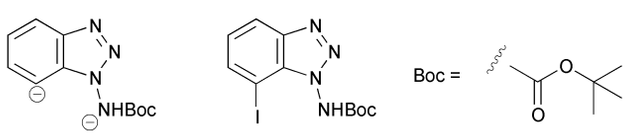
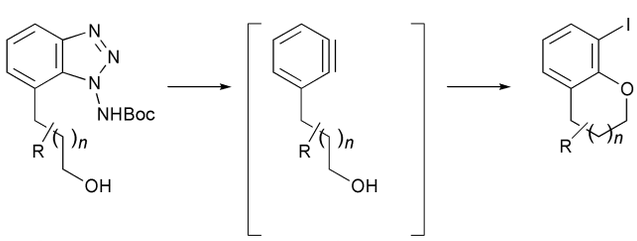
Condensations between the dianion **1** derived from 1-(*N*-butoxycarbonylamino)-1*H*-benzotriazole and silyloxysalicylaldehydes **10** give excellent yields of the expected adducts **11**. While attempts to remove the *N*-Boc function were unsuccessful, desilylation and hydrogenolysis delivered the hydroxybenzyl derivative **14** which could be efficiently deprotected to give the amine **15**. This then underwent smooth decomposition to the benzyne **16**, upon exposure to *N*-iodosuccinimide, and intramolecular trapping by the phenol group, with incorporation of iodine, to give the iodoxanthene **17**. A more efficient protocol featured condensation of dianion **1** with 2-(benzyloxy)aryl aldehydes; hydrogenolysis of the initial products **19** and **22a** served both to deprotect the phenol function and to effect hydrogenolysis of the benzylic alcohol group. A final acidic deprotection and exposure to *N*-iodosuccinimide delivered good yields of the iodoxanthenes **21** and **23**, demonstrating for the first time a viable method for the intramolecular trapping of benzynes by phenolic groups.

In our recent contributions to benzyne chemistry, we have reported the successful generation and synthetic utility of the 1-amino-1*H*-benzotriazole derived dianion **1**.[1] This can be homologated directly or converted into the iodide **2** which can



1 **2**

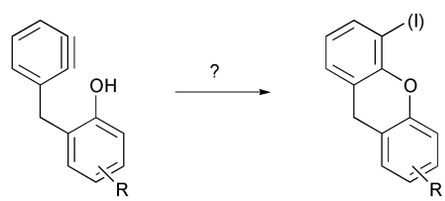
then also be manipulated through to a series of alcohol derivatives **3**. Subsequent deprotection and benzyne generation, specifically using *N*-iodosuccinimide, leads to the reactive intermediates **4** which undergo smooth intramolecular cyclisations with incorporation of iodine to give various dihydrobenzofurans and chromane derivatives **5** in good to excellent yields (Scheme 1). To the best of our knowledge, this represents



3 **4** **5**

Scheme 1

the first efficient method for the intramolecular trapping of benzynes by alcohol groups.[2] A natural extension of this was to investigate whether similar chemistry could be applied to the cyclisation of benzynes **6** having a phenolic appendage (Scheme 2). The generalised example shown, if successful, would result in a new approach to xanthenes **7** with, if the foregoing mechanism applies, incorporation of a potentially useful iodine atom. To the best of our knowledge, while efficient intermolecular reactions between benzynes and phenols have been



6 **7**

Scheme 2

reported,[2,3] there are no reports of the efficient intramolecular trapping of a benzyne by a tethered phenol. One notable exception of this was reported by Castedo's group who succeeded in isolating products arising from the trapping of a benzyne with a phenoxide anion; however, the yield was only 20%.[4] It may well be that, in common with the corresponding alcohol chemistry, the hard nature of the phenoxide species renders it unsuitable for reaction with benzyne intermediates, which are known to be soft electrophiles.[2]

Xanthenes constitute some of the oldest known dyes[5] and interest in their photochemistry continues today.[6] One notable feature of xanthenes is their flat rigid structure which has been used to advantage as a linker for peptide synthesis[7] and in unnatural amino acids and related pharmaceutical precursors.[8] There are several well established approaches to xanthenes[9] which typically feature formation of the central heterocyclic ring often by combinations of Friedel–Crafts methodology and C–O bond formation involving nucleophilic attack by a phenol residue onto an electron-deficient aryl ring.[10] Interestingly, benzyne chemistry has also been used to form a xanthene nucleus but in a very different manner to the present work. Thus, exposure of the diaryl ether **8** to two equivalents of lithium diisopropylamide causes both ester enolisation and elimination of hydrogen bromide; subsequent attack onto the benzyne by the resulting enolate then delivers a good yield of the highly substituted derivative **9** (Scheme 3).[11] Xanthenes can also be obtained by reduction of the corresponding xanthones using a number of hydride sources,[12] as well as by the Huang-Minlon modification of the Wolff–Kishner reduction.[13] Xanthones themselves can be prepared by a range of well

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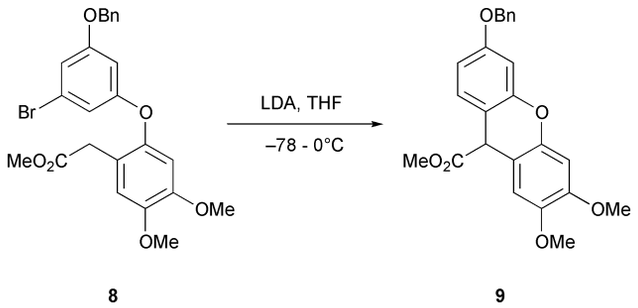
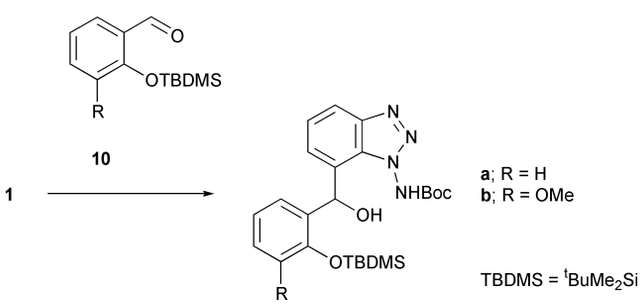


Scheme 3

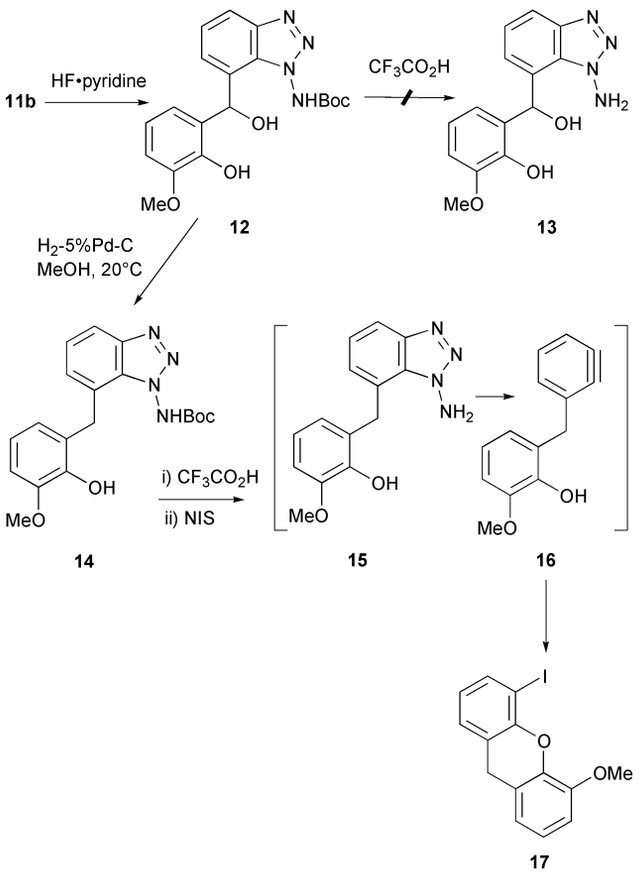
established procedures,[14,15] most notably by intramolecular Friedel–Crafts acylations or formation of the ether bond. Recent contributions to this area include the reverse of the Friedel–Crafts method developed by Snieckus in which metallated aryls cyclise by intramolecular attack onto an adjacent carboxamide function.[16] Such structures have also recently been made by the benzannelation of suitable cyclobut-2-enones.[17] Xanthones can also be accessed by oxidation of the corresponding xanthenes using a range of standard oxidizing agents.[18] In view of the foregoing results, we felt that, if successful, the ideas shown in Scheme 2 could make a useful contribution to this area, both for the initial xanthene synthesis and as an approach to xanthones, by subsequent oxidation.[19]

Our initial experiments were carried out using 2-(*tert*-butyldimethylsilyloxy)benzaldehydes **10** derived from the corresponding salicylaldehydes. Thus, condensations between these electrophiles and the benzotriazole dianion **1**, in the presence of both tetraglyme and cerium(III) chloride gave good isolated yields of the expected adducts **11**, despite concerns that the steric bulk of the silyloxy group might hinder the reaction (Scheme 4). Cleavage of the silyl group in the adduct **11b** was



Scheme 4

then readily achieved by treatment with hydrogen fluoride–pyridine complex and gave an example, **12**, of a free phenol, again in good yield (Scheme 5). However, all attempts to hydrolyse the *N*-Boc function using the standard protocol of 20% trifluoroacetic acid in dichloromethane proved fruitless and resulted in extensive decomposition; little or none of the required product **13** was obtained. This was not entirely unexpected as protonation of the secondary benzylic alcohol group and subsequent loss of water would lead to a highly stabilized benzhydryl carbocation, whose longevity might also be aided by the flanking *ortho* nitrogen and oxygen atoms. Similar problems at this deprotection stage were encountered during some of our related work on chromane synthesis.[1] Milder, Lewis-acidic reagents including aluminium(III) chloride,[20] boron tribromide,[21] trimethylsilyl iodide[22] and cerium(IV) ammonium nitrate[23] also proved unsuccessful and led to a range of unrecognizable products. As xanthenes can be readily oxidised to xanthones and the latter, in turn, reduced to xanthenes (see above), we attempted to oxidise the initial alcohols **11** to the corresponding ketones; however, using either manganese(IV) oxide or Jones reagent again led to many



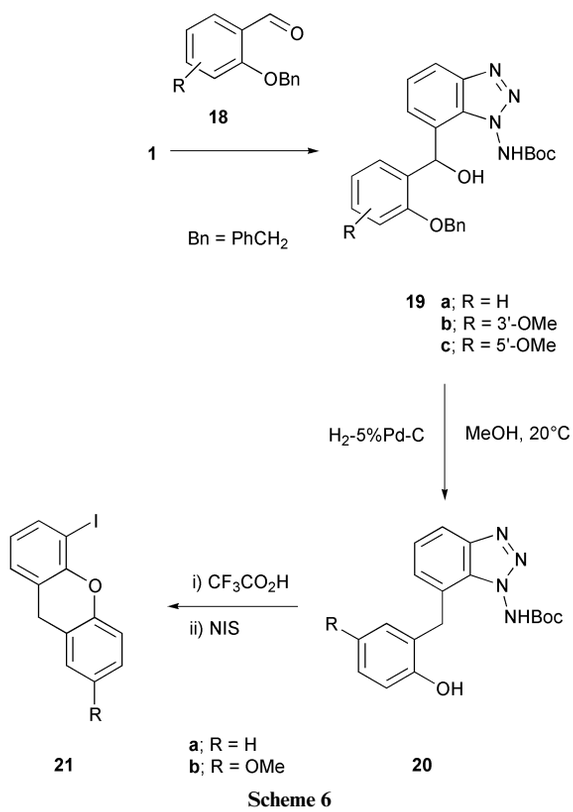
Scheme 5

products. Protection of the offending alcohol group seemed to offer limited prospects and hence we reasoned that removal was a more likely solution, by exploiting the very feature responsible for the extreme acid lability—the benzhydrylic positioning of the hydroxy group—which should also render the function amenable to hydrogenolysis. In a first model reaction, we were pleased to find both that exposure of the hydroxyphenol **12** to hydrogen and 5% Pd–C in methanol under ambient conditions led cleanly to the desired benzyl derivative **14** and that subsequent removal of the *N*-Boc group now also occurred smoothly, by brief exposure to 20% trifluoroacetic acid in dichloromethane, to give the key free amine **15**. This, due to its highly polar and somewhat sensitive nature, was not fully characterised, as attempted complete purification resulted in significant losses. In principle, a more direct approach to this type of structure in general would be by direct alkylation of the dianion **1** without competing *N*-alkylation by these particularly reactive electrophiles; however, preliminary attempts were not promising as dialkylated products were obtained, along with the desired mono-adducts.

Returning to the free amine **15**, we were delighted to find that addition of two equivalents of *N*-iodosuccinimide (NIS) to a solution of this in dichloromethane at ambient temperature resulted in the rapid and clean formation of the iodoxanthene **17**, presumably *via* the benzyne **16**, in much the same way as we were able to form iodochromanes from 1-amino-7-hydroxypropylbenzotriazoles.[1] Only traces of unidentified products were evident in the ^{1}H NMR spectrum of the crude product and the iodoxanthene **17** was readily isolated in the pure state in 81% yield. The product **17** was identified in the usual manner. Particularly characteristic was the appearance of a two-proton singlet at δ_H 3.97 due to the 9-CH_2 of the xanthene and a particularly high field sp^2 quaternary carbon at δ_C 83.6, due to the new C–I group, shifted to this position by the heavy atom effect. Molecular weight determination from mass spectral data was also unique for this structure. This successful sequence led

to the idea of using *o*-benzyloxybenzaldehydes **18** as the electrophiles in the initial condensations with the benzotriazole dianion **1**, as removal of both this alternative protecting group and the benzylic hydroxy should be possible in a single operation.

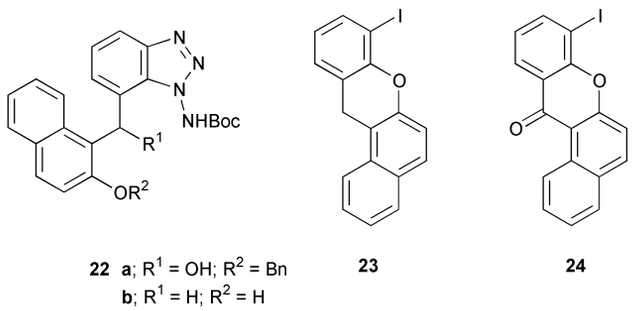
In the event, condensations between dianion **1** and representative *o*-benzyloxybenzaldehydes **18** proceeded uneventfully to give good to excellent yields of the desired alcohols **19** (Scheme 6). Subsequent hydrogenolysis then delivered the



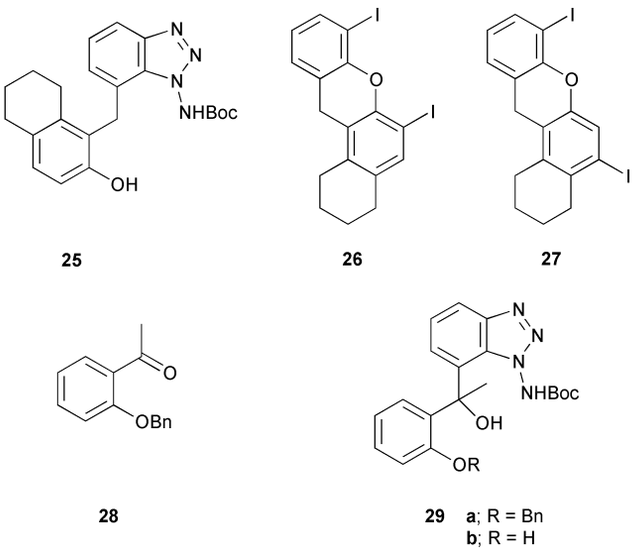
Scheme 6

required phenols **20**, again in good yields. The reaction required four hours to reach completion, but TLC and ^{1}H NMR analysis showed that the debenzylation step was complete after the first hour. The central conversion into the iodoxanthenes **21** was then carried out by a combined deprotection–cyclisation sequence which gave highly respectable overall yields in all cases. Again, there was no benefit in isolating and purifying the intermediate aminophenols (*cf*. **15**). This sequence could be extended to naphthols. Thus, 2-benzyloxy-1-naphthaldehyde underwent condensation with the dianion **1** to provide a 55% isolated yield of the expected adduct **22a**, double hydrogenolysis of which gave the phenol **22b** in 82% isolated yield. The final deprotection–cyclisation sequence then gave the iodobenzoxanthene **23** in 75% isolated yield. Unexpectedly, when the final reaction mixture was left stirring for an additional hour, the initial xanthene **23** was converted into the corresponding xanthone **24**, presumably by interaction with the excess *N*-iodosuccinimide and/or by aerial oxidation. This new product was identified by its molecular weight, along with disappearance of the xanthene 9-methylene resonances and the appearance of a carbonyl group (183.2 ppm in the ^{13}C NMR spectrum and a C=O stretch at 1644 cm^{-1} in the infrared spectrum). Traces of this xanthone could be detected in the original crude product, obtained from the shorter reaction time leading to the iodobenzoxanthene **23**.

A further example featured extended hydrogenation of the naphthaldehyde derivative **22a** which delivered an excellent yield of the tetralin (1,2,3,4-tetrahydronaphthalene) derivative **25**, which we expected would undergo cyclisation in the same



manner as the foregoing compound. We were therefore surprised to find that the product obtained following the general deprotection–cyclisation protocol was an approximately 1 : 1 mixture of the 6,8- and 6,9-diiodotetrahydrobenzo[*a*]xanthenes **26** and **27**. Fractional crystallization from dichloromethane allowed the separation of a sample of the 6,8-isomer **26**. Presumably, the tetralin ring is sufficiently electron rich to allow electrophilic iodination to occur during the cyclisation. As yet, we have not found a method to avoid this additional reaction. An extension of this methodology featured an attempt to incorporate a substituent at the 9-position of the final xanthene. To this end, the tertiary alcohol **29** was formed by condensation between the dianion **1** and 2-benzyloxyacetophenone **28**, in 72% isolated yield. Unfortunately, various attempts at hydrogenolysis failed to remove the tertiary hydroxy group, even after extended reaction times. Attempts to dehydrate this compound were similarly unproductive and, not unexpectedly, a single attempt to effect removal of the Boc group led to intractable material. Therefore, as the scheme stands, it is not amenable to preparation of 9-substituted xanthenes.



In summary, we have shown that using this aminobenzotriazole methodology it is indeed possible to secure good yields of products from the intramolecular trapping of benzynes with phenolic groups, for the first time. There are clearly some limitations, in particular the further iodination of electron-rich products (*i.e.* products **26** and **27**) and the difficulties associated with the incorporation of a 9-substituent. On the credit side, the incorporation of the additional iodine atom into the xanthenes clearly offers many opportunities for further homologation by a wide variety of functionalities using the plethora of metal-catalysed coupling reactions currently available and should allow access to many types of xanthene and xanthone derivatives. Further modifications of this overall scheme are in progress both to address these problems and also to extend this chemistry to the synthesis of other ring sizes and related heterocyclic systems.

Experimental

For general experimental details, see ref. 1.

Metallation and homologation of 1-(*tert*-butoxycarbonylamino)-1*H*-benzotriazole: general procedure

Anhydrous cerium(III) chloride was prepared from the heptahydrate by drying in a vacuum oven at 140 °C and 0.1 mmHg for 4 days with regular turning and crushing of the sample. The dry salt (1.1 equivalents) was slurried in dry tetrahydrofuran (30 ml $mmol^{-1}$) for 16 h. In a separate flask, butyllithium (2.2 equivalents of a 1.6 M solution in hexanes) was added to a stirred solution of dry tetraglyme (5 equivalents) in dry tetrahydrofuran (10 ml $mmol^{-1}$) maintained below −70 °C using a dry ice–acetone bath. After 0.5 h, a solution of 1-(*tert*-butoxycarbonylamino)-1*H*-benzotriazole[1] (1 equivalent) in dry tetrahydrofuran (10 ml $mmol^{-1}$) was added dropwise. The resulting deep purple solution of the dianion **1** was stirred at the same temperature for 0.5 h. During this period, the cerium(III) chloride suspension was cooled in a dry ice–acetone bath and titrated with butyllithium (1.6 M in hexanes) until a faint but permanent orange colour appeared; typically this required 0.1 ml $mmol^{-1}$. The purple dianion solution was then rapidly transferred *via* syringe into the cerium(III) chloride suspension. The resulting mixture was warmed to 0 °C during 3 h, then recooled to −78 °C and treated with a solution of an electrophile (1.1 equivalents) in tetrahydrofuran (1 ml $mmol^{-1}$). The mixture was then allowed to warm slowly to ambient temperature and stirred for 16 h before quenching with saturated aqueous ammonium chloride (10 ml $mmol^{-1}$ of benzotriazole), followed by acidification using 2 M hydrochloric acid. The resulting mixture was extracted with ether (3 × 30 ml $mmol^{-1}$). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (10 ml $mmol^{-1}$), water (10 ml $mmol^{-1}$) and brine (10 ml $mmol^{-1}$) then dried and evaporated. Column chromatography (CC) of the residue (*ca*. 20 g silica per mmol) in petrol–ether (7 : 3), unless otherwise stated, separated the pure product.

1-(*tert*-Butoxycarbonylamino)-7-[hydroxy(2-*tert*-butyldimethylsilyloxyphenyl)methyl]-1*H*-benzotriazole 11a. Following the general procedure, treatment of dianion **1** generated from the corresponding aminobenzotriazole (0.234 g, 1 mmol) with 2-(*tert*-butyldimethylsilyloxy)benzaldehyde **10a** (0.228 g, 1.1 mmol) yielded the *alcohol* **11a** as a beige, crystalline solid (0.389 g, 82%), mp 163–168 °C, ν_{max}/cm^{-1} 3249, 2931, 2857, 1754, 1600, 1457, 1370, 1253, 1158, 1075 and 1004; δ_H −0.1 (3H, s, $Si(CH_3)$), 0.07 (3H, s, $Si(CH_3)$), 0.94 (9H, s, $Si(CH_3)_3$), 1.37–1.58 (9H, br s, $C(CH_3)_3$), 6.77 (1H, t, *J* 6.1, 5″-H), 6.84–6.88 (2H, m, 6″-H and 1′-H), 7.08 (1H, t, *J* 6.1, 4″-H), 7.14 (1H, d, *J* 6.1, 3″-H), 7.40 (1H, t, *J* 8.0, 5-H), 7.07 (1H, d, *J* 8.0, 6-H), 7.94 (1H, d, *J* 8.0, 4-H) and 8.84 (1H, br s, NH); δ_C 14.6 (CH_3), 18.5 (CH_3), 26.1 ($Si(CH_3)_3$), 28.5 ($C(CH_3)_3$), 60.9 (CH, 1′-C), 84.5 ($C(CH_3)_3$), 117.3, 119.5, 120.7, 125.3, 128.1, 128.2, 129.5 (all CH), 145.1 (C) and 172.3 (C=O); *m*/*z* (APcI) 471 ($M^+ + 1$, 100%) [Found: C, 61.01; H, 7.20; N, 11.90. $C_{24}H_{34}N_4O_4Si$ requires C, 61.25; H, 7.29; N, 11.91%].

1-(*tert*-Butoxycarbonylamino)-7-[hydroxy(2-*tert*-butyldimethylsilyloxy-3-methoxyphenyl)methyl]-1*H*-benzotriazole 11b. Following the general procedure, treatment of dianion **1** generated from the corresponding aminobenzotriazole (0.936 g, 4 mmol) with 2-(*tert*-butyldimethylsilyloxy)-3-methoxybenzaldehyde **10b** (1.17 g, 4.4 mmol) yielded the *alcohol* **11b** as a beige, crystalline solid (1.56 g, 78%), mp 164–165 °C, ν_{max}/cm^{-1} 3342, 2928, 1747, 1480, 1251, 1158, 1064, 827 and 778; δ_H −0.02 (3H, s, CH_3Si), 0.02 (3H, s, CH_3), 3.88 (3H, s, CH_3O), 6.74 (1H, dd, *J* 8.0 and 1.9, 6″-Ar-H), 6.78 (1H, t, *J* 7.9, 4-H), 6.90 (1H, dd, *J* 8.0 and 1.9, Ar-4″-H), 7.41 (1H, t, *J* 8.0, Ar-5″-H), 7.89 (1H, br d, *J* 7.9, 6-H) and 7.93 (1H, d, *J* 7.9, 4-H); *m*/*z* (APcI) 501 ($M^+ + 1$, 100%) and 120 (100) [Found: C, 59.91; H, 7.42; N, 11.36. $C_{25}H_{36}N_4O_5Si$ requires C, 59.97; H, 7.25; N, 11.20%].

1-(*tert*-Butoxycarbonylamino)-7-[hydroxy(2-hydroxy-3-methoxyphenyl)methyl]-1*H*-benzotriazole 12. Benzotriazole **11b** (0.15 g, 0.30 mmol), in dichloromethane (10 ml), was stirred with hydrogen fluoride–pyridine complex (1 ml) for 48 h. Potassium carbonate (2 g) was added and the mixture was stirred for a further 0.5 h before being acidified with hydrochloric acid (2 M, ~10 ml). The mixture was separated and the aqueous layer extracted with dichloromethane (3 × 10 ml). The combined organic extracts were washed with water (10 ml) and brine (10 ml), then dried and evaporated to yield the *phenol* **12** as a brown solid (0.096 g, 83%), mp 155–156 °C, ν_{max}/cm^{-1} 3148, 2966, 2840, 2797, 2697, 2647, 1749, 1615, 1540, 1483, 1442, 1396, 1371, 1277, 1156, 1125, 1057, 1037, 905, 865, 816 and 759; δ_H 1.35–1.52 (9H, br s, $C(CH_3)_3$), 3.91 (3H, s, CH_3O), 6.17–6.23 (1H, br s, OH), 6.51–6.55 (1H, br s, CHOH), 6.66 (1H, d, *J* 7.5, 1 × Ar-H), 6.81–6.89 (2H, m, 2 Ar-H), 7.27–7.37 (2H, m, 2 × Ar-H), 7.98 (1H, d, *J* 7.8, 4-H) and 8.40–8.52 (1H, br s NH); δ_C 28.4 ($C(CH_3)_3$), 56.5 (CH_3O), 84.0 ($C(CH_3)_3$), 111.1 (CHOH), 120.2, 120.5, 120.7, 124.8 (all CH), 126.0 (C), 127.6 (CH), 130.2, 140.8, 143.8, 143.6, 146.2, 147.1 (all C) and 154.5 (C=O), *m*/*z* (APcI) 387 ($M^+ + 1$, 100%) and 287 (30) [Found: $M^+ + 1$, 387.1667. $C_{19}H_{23}N_4O_5$ requires *M*, 387.1668].

1-(*tert*-Butoxycarbonylamino)-7-[(2-hydroxy-3-methoxyphenyl)methyl]-1*H*-benzotriazole 14. Benzotriazole **12** (0.20 g) was subjected to the general dehydroxylation conditions described below to give the *phenol* **14** (0.18 g, 87%) as a colourless solid which showed mp 59–62 °C, ν_{max}/cm^{-1} 3296, 2978, 2941, 1746, 1616, 1480, 1442, 1394, 1370, 1275, 1275, 1254, 1158, 1118, 1077, 911 and 734; δ_H 1.31–1.63 (9H, br s, $C(CH_3)_3$), 3.91 (3H, s, MeO), 4.32–4.41 (2H, br s, $CH_2(Ar_2)$), 6.61 (1H, dd, *J* 7.8 and 6.4, 1 Ar-H), 6.71–6.80 (2H, m, 2 × Ar-H), 7.28 (1H, t, *J* 8.1, Ar-H), 7.32 (1H, t, *J* 7.4, 5-H), 7.91 (1H, d, *J* 7.4, 6-H) and 8.54–8.65 (1H, br s, NH); δ_C 29.0 ($C(CH_3)_3$), 30.4 (CH_2), 57.0 (MeO), 84.6 ($C(CH_3)_3$), 110.2, 119.0, 120.8 and 123.0 (all CH), 124.7 (C), 126.0 and 130.8 (both CH), 132.1, 144.2 and 147.4 (all C) and 154.3 (C=O), *m*/*z* (APcI) 371 ($M^+ + 1$, 100%) and 314 (30) [Found: C, 61.72; H, 6.11; N, 15.04. $C_{19}H_{22}N_4O_4$ requires C, 61.59; H, 5.99; N, 15.13%].

Material that showed identical analytical properties was given when benzotriazole **19b** (0.47 g, 1 mmol) was subjected to the general dehydroxylation conditions giving *phenol* **14** (0.30 g, 82%) as a colourless solid, mp 59–61 °C (see below).

Deprotection and cyclisation: general procedure

The *N*-*tert*-butoxycarbonylaminobenzotriazole (**14**, **20**, **22b** or **25**) (*n* mmol) was dissolved in dichloromethane (10 ml $mmol^{-1}$) containing trifluoroacetic acid (2 ml $mmol^{-1}$) and the resulting solution stirred at ambient temperature until TLC analysis showed disappearance of the starting material (*ca*. 0.5 h). The reaction mixture was then basified with aqueous sodium hydroxide (2 M, ~10 ml $mmol^{-1}$) and the pH of the solution reduced to ~5 with hydrochloric acid (2 M, ~3 ml $mmol^{-1}$). The aqueous phase was separated and saturated with sodium chloride then extracted with dichloromethane (3 × 10 ml $mmol^{-1}$). The combined organic solutions were washed with brine (10 ml $mmol^{-1}$), then dried and filtered. Solid *N*-iodosuccinimide (~2.5 eq.) was then added to the filtrate in the dark. The resulting purple solution was stirred for a further 0.5 h then washed with saturated aqueous sodium thiosulfate (5 ml $mmol^{-1}$), water (5 ml $mmol^{-1}$) and brine (5 ml $mmol^{-1}$), then dried and evaporated to give the crude product, column chromatography of which (eluent, petrol) gave the pure product.

4-Iodo-5-methoxyxanthene 17. Benzotriazole **14** (0.11 g, 0.3 mmol) was subjected to the general deprotection–cyclisation protocol described above to yield the *xanthene* **17** as a yellow

solid (0.08 g, 81%), mp 92–95 °C, ν_{max}/cm^{-1} 3055, 2983, 2926, 2848, 1594, 1497, 1446, 1240, 1089, 886, 800 and 790; δ_H 3.90 (3H, s, MeO), 3.97 (2H, s, CH_2Ar_2), 6.69–6.72 (2H, m, 2 × Ar-H), 6.76 (1H, d, *J* 8.1, Ar-H), 6.90 (1H, t, *J* 7.6, Ar-H) and 7.06 (1H, d, *J* 7.6, Ar-H); δ_C 27.6 (CH_2), 55.8 (MeO), 83.6 (C-I), 110.3, 119.3 (both CH), 120.4, 120.5 (both C), 122.3, 123.6 (both CH), 124.9 (C), 127.9, 136.5 (both CH), 150.3 and 153.2 (both C); *m*/*z* (APcI) 339 ($M^+ + 1$, 100%) [Found (EI): 337.9809. $C_{14}H_{11}IO_2$ requires 337.9806].

1-(*tert*-Butoxycarbonylamino)-7-[hydroxy(2-benzyloxyphenyl)-methyl]-1*H*-benzotriazole 19a. Following the general procedure, treatment of dianion **1** generated from the corresponding aminobenzotriazole (0.936 g, 4 mmol) with 2-(benzyloxy)-salicylaldehyde **18a** (0.827 g, 4.4 mmol) yielded the *alcohol* **19a** as a beige, crystalline solid (1.145 g, 68%), mp 67–68 °C, ν_{max}/cm^{-1} 3263, 3041, 2976, 2933, 1744, 1601, 1490, 1454, 1366, 1242, 1152, 1020 and 737; δ_H (323 K) 1.41–1.48 (9H, br s, $C(CH_3)_3$), 3.21–3.25 (1H, br d, *J* 4.4, CHO*H*), 4.98 (1H, d, *J* 11.1, CH_aAr), 5.05 (1H, d, *J* 11.1, CH_bAr), 6.62 (1H, d, *J* 4.4, C*H*OH), 7.02–7.06 (2H, m, 5 and Ar-H), 7.1 (1H, d, *J* 7.1, 6-H), 7.25–7.38 (8H, m, 8 × Ar-H), 7.80–7.85 (1H, br s, NH) and 7.99 (1H, dd, *J* 7.1 and 7.1, 4-H); δ_C 28.4 ($C(CH_3)_3$), 70.7 (CH_2), 84.0 ($C(CH_3)_3$), 112.1, 120.4, 121.8, 124.8 (all CH), 126.8 (C), 127.9, 128.0, 129.0, 129.3, 129.7 (all CH), 130.3, 136.4, 145.5, 154.2 (all C) and 156.1 (C=O); *m*/*z* (APcI) 447 ($M^+ + 1$, 100%) [Found: C, 67.04; H, 5.63; N, 12.29. $C_{25}H_{26}N_4O_4$ requires C, 67.25; H, 5.87; N, 12.55%].

1-(*tert*-Butoxycarbonylamino)-7-[hydroxy(2-benzyloxy-3-methoxyphenyl)methyl]-1*H*-benzotriazole 19b. Following the general procedure, treatment of dianion **1** generated from the corresponding aminobenzotriazole (1.18 g, 5 mmol) with 2-(benzyloxy)-3-methoxybenzaldehyde **18b** (1.33 g, 5.5 mmol) yielded the *alcohol* **19b** as a beige, crystalline solid (1.64 g, 69%), mp 59–61 °C, ν_{max}/cm^{-1} 3370, 2977, 2933, 2840, 1752, 1586, 1479, 1370, 1275, 1158, 1019, 912 and 733; δ_H 1.31–1.39 (9H, br s, $C(CH_3)_3$), 3.02–3.19 (1H, br app. s, CHO*H*), 3.85 (3H, s, MeO), 4.77 (1H, d, *J* 11.0, CH_AAr), 4.89 (1H, d, *J* 11.0, CH_BAr), 6.41 (1H, d, *J* 4.1, C*H*OH), 6.71 (1H, br d, *J* 5.6, Ar-H), 6.89 (1H, dd, *J* 8.4 and 1.3, Ar-H), 6.95–7.06 (2H, m, 2 × Ar-H), 7.12–7.26 (5H, m, 5 × Ar-H), 7.89 (2H, app. d, *J* 8.0, 2 × Ar-H); δ_C 29.4 ($C(CH_3)_3$), 57.4 (MeO), 68.7 (CHOH), 76.3 (CH_2), 85.2 ($C(CH_3)_3$), 114.0, 121.0, 121.6, 125.8, 125.9 (all CH), 128.1, 128.9 (both C), 129.7, 129.9, 130.0 (all CH), 132.1, 136.2 (both C), 138.7 (CH), 146.5, 153.9 (all C) and 154.0 (C=O); *m*/*z* (APcI) 477 ($M^+ + 1$, 100%) [Found: C, 65.60; H, 5.97; N, 11.82. $C_{26}H_{28}N_4O_5$ requires C, 65.52; H, 5.93; N, 11.76%].

1-(*tert*-Butoxycarbonylamino)-7-[hydroxy(2-benzyloxy-5-methoxyphenyl)methyl]-1*H*-benzotriazole 19c. Following the general procedure, treatment of dianion **1** generated from the corresponding aminobenzotriazole (1.18 g, 5 mmol) with 2-(benzyloxy)-5-methoxybenzaldehyde **18c** (1.33 g, 5.5 mmol) yielded the *alcohol* **19c** as a beige, crystalline solid (1.73 g, 73%), mp 65–69 °C, ν_{max}/cm^{-1} 3266, 3062, 2976, 2933, 2833, 1751, 1497, 1370, 1251, 1210, 1158, 1043, 910, 732 and 697; δ_H 1.32–1.45 (9H, br s, $C(CH_3)_3$), 3.34–3.39 (1H, br app. s, CHO*H*), 3.74 (3H, s, MeO), 4.88 (1H, d, *J* 11.0, CH_AAr), 4.95 (1H, d, *J* 11.0, CH_BAr), 6.53 (1H, d, *J* 4.4, C*H*OH), 6.76 (1H, dd, *J* 5.6 and 2.7, Ar-H), 6.88–6.93 (1H, m, Ar-H), 7.05 (2H, br app. d, *J* ~10, 2 × Ar-H), 7.25–7.40 (6H, m, 6 × Ar-H), 7.89–7.97 (1H, br s, NH) and 7.99 (1H, dd, *J* 7.7 and 1.7, 4-H); δ_C 28.4 ($C(CH_3)_3$), 56.1 (Me), 67.9 (CHOH), 71.3 (CH_2), 84.0 ($C(CH_3)_3$), 113.3, 113.8, 114.0, 120.1, 124.9, 128.0, 128.1 (all CH), 128.3 (C), 128.9, 129.2 (both CH), 129.9, 130.2, 131.9, 136.2, 145.5, 150.2 (all C) and 154.4 (C=O); *m*/*z* (APcI) 477 ($M^+ + 1$, 100%) [Found: C, 65.45; H, 6.08; N, 11.81. $C_{26}H_{28}N_4O_5$ requires C, 65.53; H, 5.92; N, 11.76%].

General hydrogenation procedure for 'one pot' debenzylation–dehydroxylation

The benzyl ether (*n* mmol) was stirred in methanol (20 ml mmol^{-1}) with 5% palladium on activated charcoal (0.05 g mmol^{-1}) under a hydrogen atmosphere for 4 h. The reaction mixture was then filtered through a plug of Celite. The solids were washed with methanol (30 ml mmol^{-1}) and dichloromethane (2 × 30 ml mmol^{-1}), and the combined filtrates dried and evaporated to give the product.

1-(*tert*-Butoxycarbonylamino)-7-[(2-hydroxyphenyl)methyl]-1*H*-benzotriazole 20a. Benzotriazole **19a** (0.16 g, 0.36 mmol) was subjected to the general hydrogenation procedure to yield the *phenol* **20a** as a colourless solid (0.095 g, 78%), mp 97–98 °C, ν_{max}/cm^{-1} 3268, 3069, 2976, 2933, 1723, 1595, 1456, 1371, 1253, 1157, 910 and 733; δ_H (323 K) 1.22–1.50 (9H, br s, $C(CH_3)_3$), 4.30–4.39 (2H, br s, CH_2Ar_2), 6.80–6.89 (2H, m, 2 × Ar-H), 6.99 (1H, d, *J* 7.5, Ar-H), 7.12 (1H, t, *J* 7.5, Ar-H), 7.19 (1H, d, *J* 7.5, 5-H), 7.19 (1H, d, *J* 7.5, 6-H), 7.25 (1H, t, *J* 7.8, Ar-H), 7.81 (1H, d, *J* 7.5, 4-H) and 8.75–8.82 (1H, br s, NH); δ_C 28.4 ($C(CH_3)_3$), 30.3 (CH_2), 84.3 ($C(CH_3)$), 116.3, 118.3, 121.0 (all CH), 124.3 (C), 125.4 (CH), 125.7 (C), 128.6, 129.9, 131.2 (all CH), 131.4, 136.2, 144.8 (all C) and 154.4 (C=O); *m*/*z* (APcI) 341 ($M^+ + 1$, 100%) [Found: $M^+ + 1$, 341.1615. $C_{18}H_{21}N_4O_3$ requires *M*, 341.1614].

1-(*tert*-Butoxycarbonylamino)-7-[(2-hydroxy-5-methoxyphenyl)methyl]-1*H*-benzotriazole 20b. Benzotriazole **19c** (0.47 g, 1.0 mmol) was subjected to the general hydrogenation procedure to yield the *title compound* **20b** as a beige, crystalline solid (0.28 g, 75%), mp 70–71 °C (EtOAc–hexane), ν_{max}/cm^{-1} 3254, 2982, 2933, 2833, 1724, 1605, 1510, 1434, 1395, 1370, 1255, 1209, 1157, 1042, 911, 871, 816 and 736; δ_H 1.20–1.49 (9H, br s, $C(CH_3)_3$), 3.56 (3H, br s, MeO), 4.09–4.21 (2H, br s, CH_2), 6.52 (1H, br s, Ar-H), 6.56 (1H, br d, *J* ~7, Ar-H), 6.68 (1H, br d, *J* ~7, Ar-H), 6.99–7.12 (2H, br m, 5- and 6-H), 7.59 (1H, br app. s, 4-H) and 9.22–9.27 (1H, br s, NH); δ_C 28.4 ($C(CH_3)_3$), 30.5 (CH_2), 56.3 (MeO), 84.3 ($C(CH_3)_3$), 110.8, 115.5, 116.8 (all CH), 122.8 (C), 124.1, 125.5, 128.5 (all CH), 129.8, 143.2, 147.0, 152.4 (all C) and 155.4 (C=O) (one aryl quaternary resonance obscured); *m*/*z* (APcI) 371 ($M^+ + 1$, 100%), 315 (40) and 271 (72) [Found: C, 61.97; H, 6.23; N, 15.20. $C_{19}H_{22}N_4O_4$ requires C, 61.59; H, 5.99; N, 15.13%].

4-Iodoxanthene 21a. Benzotriazole **20a** (0.088 g, 0.26 mmol) was subjected to the deprotection–cyclisation protocol to yield the *xanthene* **21a** as a yellow solid (0.066 g, 86%), mp 73–74 °C, ν_{max}/cm^{-1} 3062, 2962, 2926, 1622, 1597, 1445, 1426, 1246, 1099, 891 and 754; δ_H 3.95 (2H, s, CH_2Ar_2), 6.69 (1H, t, *J* 7.7, Ar-H), 6.99 (1H, t, *J* 7.6, Ar-H), 7.03–7.26 (4H, m, 4 × Ar-H) and 7.58 (1H, d, *J* 7.6, Ar-H); δ_C 27.4 (CH_2), 83.7 (C-I), 115.8 (CH), 119.6, 120.8 (both C), 122.5, 123.4, 126.7, 127.5, 128.0, 136.5 (all CH), 150.1 and 150.9 (both C); *m*/*z* (EI) 308 (M^+, 100%) and 181 (32) [Found: 307.9693. $C_{13}H_9IO$ requires 307.9700].

4-Iodo-7-methoxyxanthene 21b. Benzotriazole **20b** (0.15 g, 0.40 mmol) was subjected to cyclisation protocol to yield the *xanthene* **21b** (0.11 g, 81%), mp 99–101 °C, ν_{max}/cm^{-1} 3055, 2998, 2941, 2826, 1618, 1564, 1496, 1447, 1268, 1237, 1203, 1176, 1150, 1038, 884, 854, 807, 764 and 714; δ_H 3.81 (3H, s, MeO), 4.03 (2H, s, CH_2Ar_2), 6.72 (1H, d, *J* 7.9, Ar-H), 6.76–6.82 (2H, m, 2 × Ar-H), 7.11–7.16 (2H, m, 2 × Ar-H) and 7.65 (1H, dd, *J* 8.0 and 8.1, 2-H); δ_C 29.3 (CH_2), 56.1 (MeO), 85.1 (C-I), 113.4, 113.8, 117.9 (all CH), 121.7, 121.8 (both C), 124.6, 129.4, 137.9 (all CH), 146.4, 151.7 and 156.1 (all C); *m*/*z* (APcI) 339 ($M^+ + 1$, 100%) [Found: C, 49.51; H, 3.22. $C_{14}H_{11}IO_2$ requires C, 49.71; H, 3.28%].

1-(*tert*-Butoxycarbonylamino)-7-[hydroxy(2-benzyloxy-1-naphthyl)methyl]-1*H*-benzotriazole 22a. Following the general

procedure treatment of dianion **1** (4 mmol) with 2-(benzyloxy)-1-naphthaldehyde (1.15 g, 4.4 mmol) yielded the *alcohol* **22a** as a pale yellow, crystalline solid (1.10 g, 55%), mp 94–97 °C (ether–pentane), ν_{max}/cm^{-1} 3256, 3062, 2948, 2926, 2848, 1748, 1625, 1596, 1513, 1454, 1370, 1252, 1157, 1085, 1021, 911, 816, 734 and 697; δ_H 1.47 (9H, s, C(CH_3)$_3$), 5.12 (1H, d, *J* 11.5, CH_aAr), 5.18 (1H, d, *J* 11.5, CH_bAr), 6.66 (1H, d, *J* 7.2, C*H*OH), 6.93 (1H, d, *J* 10, Ar-H), 7.00–7.07 (3H, m, 3 × Ar-H), 7.15–7.20 (3H, m, 3 × Ar-H), 7.28–7.32 (2H, m, 2 × Ar-H), 7.38 (1H, d, *J* 8.0, Ar-H), 7.61–7.65 (1H, m, Ar-H), 7.78–7.82 (1H, m, Ar-H), 7.88 (1H, d, *J* 8.0, Ar-H), 7.93 (1H, d, *J* 8.3, Ar-H) and 8.90 (1H, s, NH); δ_C 28.5 (*C*(CH$_3$)$_3$), 68.4 (*C*HOH), 72.0 (CH_2), 83.9 (*C*(CH$_3$)$_3$), 114.9 (CH), 120.2 (C), 120.9 (CH), 122.9 (C), 124.4, 124.8 (both CH), 126.3 (C), 126.9, 127.9, 128.9, 129.1 (all CH), 129.2, 129.8 (both C), 131.1 (CH), 132.3, 135.9, 146.1 (all C) and 155.2 (C=O) (3 × CH resonances coincidental); *m*/*z* (ES) 497 (M^+ + 1, 100%) [Found: C, 70.39; H, 5.80; N, 11.41. $C_{29}H_{28}N_4O_4$ requires C, 70.13; H, 5.69; N, 11.29%].

1-(*tert*-Butoxycarbonylamino)-7-[(2-hydroxy-1-naphthyl)-methyl]-1*H*-benzotriazole 22b. Benzotriazole **22a** (0.43 g, 0.87 mmol) was subjected to the general hydrogenation procedure to yield *naphthol* **22b** as a colourless solid (0.28 g, 82%), mp 117–120 °C, ν_{max}/cm^{-1} 3263, 3062, 2984, 2833, 1720, 1629, 1513, 1439, 1370, 1272, 1252, 1157, 993, 909, 815 and 733; δ_H (323 K) 1.51–1.59 (9H, br s, C(CH_3)$_3$), 4.83 (2H, s, CH_2Ar_2), 6.00–6.30 (1H, br s, OH), 6.75 (1H, d, *J* 7.2, Ar-H), 7.01 (1H, t, *J* 7.6, 5-H), 7.20 (1H, d, *J* 7.6, 6-H), 7.35 (1H, t, *J* 7.9, Ar-H), 7.41 (1H, t, *J* 7.9, Ar-H), 7.70 (1H, d, *J* 7.6, Ar-H), 7.78 (2H, d, *J* 8.8, 2 × Ar-H), 7.84 (1H, d, *J* 7.6, 4-H) and 8.68–8.72 (1H, br s, NH); δ_C 23.0 (CH_2), 28.5 (*C*(CH$_3$)$_3$), 84.7 (*C*(CH$_3$)$_3$), 115.7 (C), 118.6, 123.4, 123.7 (all CH), 123.8, 124.4 (both C), 125.5, 128.2, 129.0, 129.5 (all CH), 129.7, 131.2, 134.1, 144.7 (all C) and 152.5 (C=O) (2 × CH coincidental); *m*/*z* (APcI) 391 (M^+ + 1, 100%) [Found: C, 67.31; H, 5.42. $C_{22}H_{22}N_4O_3$ requires C, 67.66; H, 5.68%].

8-Iodo-12*H*-benzo[*a*]xanthene 23. Benzotriazole **22b** (0.12 g, 0.31 mmol) was subjected to the deprotection–cyclisation protocol to yield the *xanthene* **23** (0.08 g, 75%), mp 131–133 °C, ν_{max}/cm^{-1} 3062, 2962, 2926, 2855, 1645, 1595, 1437, 1252, 1066 and 816; δ_H 4.33 (2H, s, CH_2Ar_2), 6.77 (1H, t, *J* 7.6, 10-H), 7.22 (1H, dd, *J* 7.5 and 7.5, 5-H), 7.31 (1H, d, *J* 7.6, 9-H), 7.39 (1H, t, *J* 7.1, 4-H), 7.52 (1H, t, *J* 7.1, 3-H), 7.64 (1H, d, *J* 8.3, 6-H), 7.70 (1H, d, *J* 8.3, 7-H) and 7.77–7.81 (2H, m, 2- and 11-H); δ_C 29.4 (CH_2), 81.2 (C-I), 117.0, 117.1 (both CH), 122.3 (C), 123.6, 124.8 (both CH), 125.2 (C), 126.2, 127.4, 127.5, 127.5 (all CH), 128.8, 129.1 (both C), 136.1 (CH), 136.7 and 142.1 (both C); *m*/*z* (APcI) 360 (M^+ + 2, 24%) and 356 (100) [Found: C, 57.11; H, 3.26. $C_{17}H_{11}IO$ requires C, 56.99; H, 3.10%].

8-Iodo-12*H*-benzo[*a*]xanthen-12-one 24. Benzotriazole **22b** (0.12 g, 0.31 mmol) was subjected to the deprotection–cyclisation protocol and the solution allowed to stir for an additional 1 h before workup, as before, to yield the *xanthone* **24** as a beige, crystalline solid (0.09 g, 84%) (^{1}H NMR showed essentially quantitative conversion), mp 110–112 °C, ν_{max}/cm^{-1} 2962, 2926, 2855, 1781, 1644, 1452, 1373, 1337, 1258, 1223, 1158, 1044 and 808; δ_H 6.73 (1H, d, *J* 8.2, 5-H), 7.36 (1H, t, *J* 7.7, 10-H), 7.74–7.85 (3H, m, 3-, 4- and 7-H), 8.20 (1H, d, *J* 7.7, 11-H), 8.60 (1H, d, *J* 7.7, 9-H), 8.79 (1H, s, 6-H) and 10.21 (1H, d, *J* 8.2, 2-H); δ_C 92.1 (C-I), 126.5 (CH), 128.4, 128.9 (both C), 129.4, 129.6, 129.7 (all CH), 130.2, 131.4 (both C), 132.4, 134.5 (both CH), 135.0, 137.7 (both C), 136.0, 147.6 (both CH) and 183.2 (C=O) (one C obscured).

1-(*tert*-Butoxycarbonylamino)-7-[(2-hydroxy-5,6,7,8-tetra-hydro-1-naphthyl)methyl]-1*H*-benzotriazole 25. Benzotriazole **22a** (0.50 g, 1.0 mmol) was subjected to the general dehydroxylation procedure for 18 h to yield the *tetrahydronaphthol* **25** as a colourless solid (0.31 g, 79%), mp 102–103 °C, ν_{max}/cm^{-1} 3254, 2976, 2934, 2862, 1724, 1592, 1488, 1455, 1395, 1370, 1253, 1158, 1056, 1019, 910, 812 and 733; δ_H 1.20–1.55 (9H, br s, C(CH$_3$)$_3$), 1.60–1.70 (4H, br res, 2 × CH_2), 2.35–2.40 (2H, br res, CH_2), 2.65–2.72 (2H, br res, CH_2), 4.15–4.20 (2H, br res, Ar_2CH_2), 6.55 (1H, br d, *J* ~8, Ar-H), 6.60 (1H, br d, *J* ~8, Ar-H), 6.78 (1H, br d, *J* ~8, 6-H), 6.98 (1H, br t, *J* ~8, 5-H), 7.52 (1H, br d, *J* ~8, 4-H) and 8.80–8.95 (1H, br s, NH); δ_C 22.9, 23.2, 25.0 and 26.6 (all CH_2), 28.1 (C(*C*H$_3$)$_3$), 29.6 (CH_2), 83.9 (*C*(CH$_3$)$_3$), 113.4, 117.7 (both CH), 122.1, 123.7 (both C), 125.0, 126.8, 128.8 (all CH), 129.8, 131.1, 137.2, 144.4, 152.3 (all C) and 153.9 (C=O); *m*/*z* (APcI) 395 (M^+ + 1, 100%) and 339 (20) [Found: C, 66.68; H, 6.88; N, 14.14. $C_{22}H_{26}N_4O_3$ requires C, 66.97; H, 6.65; N, 14.21%].

6,8- and 6,9-Diiodo-1,2,3,4-tetrahydro-12*H*-benzo[*a*]xanthene 26 and 27. Benzotriazole **25** (0.40 g, 1.0 mmol) was subjected to the general deprotection–cyclisation protocol to yield the *xanthenes* **26** and **27** (0.27 g, 77%) as an approximately 1 : 1 mixture. A sample of the 6,8-diiodide **26** was separated by fractional crystallization from dichloromethane–petrol and showed mp 87–89 °C, δ_H 1.72–1.79 (2H, br m, 8-CH_2), 1.83–1.91 (2H, br m, 9-CH_2), 2.61 (2H, br app. t, *J* 6.5, 7-CH_2), 2.72 (2H, br app. t, *J* 6.3, 10-CH_2), 3.90 (2H, s, CH_2Ar_2), 6.79 (1H, t, *J* 7.7, 2-H), 7.16 (1H, d, *J* 7.7, 1-H), 7.48 (1H, s, 6-H) and 7.69 (1H, d, *J*, 7.7, 3-H); δ_C 21.4, 21.8, 25.2, 25.3, 28.1 (all CH_2), 79.7, 83.2 (both C-I), 112.9 (C), 123.7 (CH), 124.8, 127.2 (both C), 127.9 (CH), 128.3 (C), 136.8, 136.8 (both CH), 147.9 and 150.3 (both C); *m*/*z* (APcI) 489 (M^+ + 1, 100%).

From spectra of the mixture, the *6,9-diiodide* **27** showed δ_H 1.72–1.79 (2H, br m, 8-CH_2), 1.83–1.91 (2H, br m, 9-CH_2), 2.65 (2H, br app. t, *J* 6.5, 7-CH_2), 2.77 (2H, br app. t, *J* 6.3, 10-CH_2), 3.90 (2H, s, CH_2Ar_2), 6.75 (1H, t, *J* 7.7, 2-H), 6.99 (1H, s, 6-H), 7.16 (1H, d, *J* 7.7, 1H) and 7.62 (1H, d, *J* 7.7, 3-H).

1-(*tert*-Butoxycarbonylamino)-7-[1-(2-benzyloxyphenyl)-1-hydroxyethyl]-1*H*-benzotriazole 29a. Following the general procedure, treatment of dianion **1** (5 mmol) with 2-(benzyloxy)acetophenone **28** (1.24 g, 5.5 mmol) yielded the alcohol **29a** as a beige, crystalline solid (1.65 g, 72%), mp 67–68 °C (ether–petrol), ν_{max}/cm^{-1} 3279, 3062, 2980, 2933, 1753, 1600, 1488, 1453, 1370, 1252, 1159, 1052, 911, 806, 751 and 699; δ_H 1.25–1.56 (9H, br s, C(CH$_3$)$_3$), 2.05 (3H, s, 1′-Me), 4.82–4.91 (1H, br app. s, CH_aAr), 4.95–5.05 (1H, br res., CH_bAr), 5.32–5.40 (1H, br s, OH), 6.72–7.32 (10H, br res., 10 × Ar-H), 7.40 (1H, t, *J* 7.7, Ar-H), 8.05 (1H, d, *J* 8.4, 4-H) and 9.10–9.42 (1H, br s, NH); δ_H (323 K) 1.40–1.45 (9H, br s, C(CH_3)$_3$), 2.05 (3H, s, 1′-Me), 4.90 (1H, br d, *J* ~10, CH_aAr), 5.02 (1H, br d, *J* ~10, CH_bAr), 5.27 (1H, s, OH), 6.80–6.92 (2H, br res, 2 × Ar-H), 7.01 (1H, t, *J* 7.5, 5-H), 7.09 (1H, d, *J* 7.5, 6-H), 7.11–7.19 (2H, m, 2 × Ar-H), 7.20–7.27 (4H, m, 4 × Ar-H), 7.36 (1H, t, *J* 8.2, Ar-H), 8.04 (1H, d, *J* 7.5, 4-H) and 8.81–9.00 (1H, br s, NH); δ_C 28.5 (C(*C*H$_3$)$_3$), 29.3 (CH_3), 71.3 (CH_2), 77.9 (Me*C*OH), 83.2 (*C*(CH$_3$)$_3$), 113.6, 120.6, 122.0, 124.2, 126.1, 127.8, 129.0, 129.1 (all CH), 129.7 (C), 130.1 (CH), 134.0, 135.6, 141.1, 146.8, 151.9 (all C) and 156.2 (C=O); *m*/*z* (APcI) 461 (M^+ + 1, 100%) [Found: C, 67.98; H, 6.21; N, 12.20. $C_{26}H_{28}N_4O_4$ requires C, 67.79; H, 6.13; N, 12.17%].

1-(*tert*-Butoxycarbonylamino)-7-[1-hydroxy-1-(2-hydroxy-phenyl)ethyl]-1*H*-benzotriazole 29b. Benzotriazole **29a** (0.46 g, 1.0 mmol) was subjected to the general hydrogenation procedure to yield the *phenol* **29b** as a colourless solid (0.29 g, 79%), mp 102–103 °C, ν_{max}/cm^{-1} 3279, 2976, 1713, 1581, 1496, 1366, 1287, 1225, 1151, 901, 808 and 743; δ_H 1.16–1.50 (9H, br s, C(CH_3)$_3$), 1.97–2.02 (3H, s, Me), 6.05–6.12 (1H, br d, *J* ~7, 6″-H), 6.38–6.49 (1H, br t, *J* ~7, 5″-H), 6.82–6.90 (1H, br d, *J* ~8, 6-H), 7.02–7.11 (1H, br t, *J* ~8, 5-H), 7.13–7.25 (1H, br t, *J* ~7, 4″-H), 7.35–7.42 (1H, br d, *J* ~7, 3″-H), 7.57–7.71 (1H, br

s, NH) and 7.72–7.81 (1H, br d, J ~8, 4-H); δ_C 28.3 (C(CH_3)$_3$), 28.4 (Me), 78.5 (MeCOH), 83.8 (C(CH$_3$)$_3$), 118.4, 120.2, 121.0, 124.5, 126.7 (all CH), 128.9, 129.7 (both C), 129.9 (CH), 130.1 (C), 130.5 (CH), 146.0, 153.9 (both C) and 155.5 (C=O); m/z (APcI) 371 (M^+ + 1, 100%) and 353 (55) [Found: C, 61.29; H, 5.52; N, 14.86. $C_{19}H_{22}N_4O_4$ requires C, 61.61; H, 5.99; N, 15.13%].

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