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A New Approach to Dihydrobenzofurans and Dihydrobenzopyrans (Chromans) Based on the Intramolecular Trapping by Alcohols of Benzynes Generated from 7-Substituted-1-aminobenzotriazoles

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Abstract—1-Aminobenzotriazoles **9** having 7-hydroxyalkyl substituents are efficiently converted into the corresponding benzynes **4** when treated with *N*-iodosuccinimide which then undergo highly efficient intramolecular trapping by the pendant hydroxyl groups leading to dihydrobenzofurans **24**–**26** and dihydrobenzopyrans (chromans) **27**, with incorporation of a synthetically useful iodine atom adjacent to the new ether bond, which allows subsequent and high-yielding homologations using Stille, Sonogashira and Heck couplings.

Classical methods for benzyne generation are generally related to the original method involving the elimination of hydrogen halides from halobenzenes under strongly basic conditions.[1] Related methods include halogen–metal exchange, typically by treatment of a 1,2-dihalobenzene with an alkyl lithium followed by the same type of elimination of halide;[1] similar but milder methodology features fluoride-induced desilylation of an *ortho*-silylhalobenzene and, again, elimination of halide.[2] Alternatives which avoid strongly basic conditions during benzyne generation include the use of another classical benzyne precursor, anthranilic acid, together with more exotic vicinally functionalised benzenes and a variety of heteroaromatic systems, such as benzothiadiazole-*S*,*S*-dioxide and 1-aminobenzotriazole.[1,2] As has recently been succinctly emphasised: 'An important drawback of the aryne routes starting with bidentate or cyclic precursors can be the effort needed to prepare the precursor itself, especially for substituted arynes. However, these have the advantage that the arynic bond can be generated without positional ambiguity.'[2] Certainly, a number of relatively complex benzyne precursors have been prepared, most often from bromobenzenes wherein the very complexity renders both the synthesis and subsequent benzyne generation unambiguous. Very little has been reported on the preparation of substituted 1-aminobenzotriazoles in this context, beyond the original seminal studies by Campbell and Rees,[3] and a few more recent, usually symmetrical examples and higher homologues, together with a benzene fused to two aminotriazole rings, which effectively acts as a bis-benzyne precursor although, presumably, the process occurs in a stepwise fashion.[4]

The use of 1-aminobenzotriazole **1** as a benzyne precursor was highlighted by Campbell and Rees who demonstrated the ease of formation of the parent benzyne **3** by oxidation to the intermediates **2**, which rapidly disintegrates presumably by the spectacular cascade shown, rather than via an *N*-nitrene species, as was originally thought.[3] Two of the best methods identified for achieving this rely on direct oxidation by lead(IV) acetate, in which case X=OAc, or using *N*-bromosuccinimide, when X=Br; nickel peroxide and iodobenzene diacetate were also shown to be effective oxidants. Alternative methods include decompositions of various lithium salts of 1-tosylamidobenzotriazole and related species,[5] along with deoxygenation of *N*-nitrosobenzotriazole using ethyl diphenylphosphinite, a process which may involve a true *N*-nitrene intermediate.[6] The extremely mild conditions associated with the oxidation methods stand in stark contrast to the alternatives outlined above which employ various strong base-induced eliminations from halo- or dihalo-benzenes. It occurred to us that these oxidative conditions might be compatible with hydroxyl groups and perhaps enable these to act as intramolecular traps for the benzynes so generated, as indicated in formula **4** (Fig. 1). In great contrast to related intramolecular

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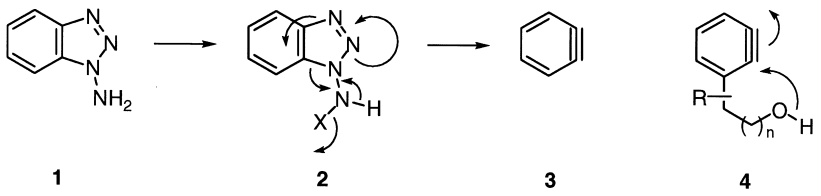


Figure 1.

cyclisations using amino- and enolate nucleophiles, such trapping by hydroxyl functions is virtually unknown and then using only very simple types of alcohol.[1,2] As arynes are soft electrophiles, alcohols and alkoxides, the latter inevitably formed in base-induced aryne formation, would be expected to be less reactive partners. While intermolecular trapping of benzynes by phenols is well precedented,[1,2] related intramolecular reactions were almost unknown[7] until very recently.[8]

Our starting point was the thought that it might be possible to apply the often used principle of lateral deprotonation[9] to enable generation of the dianionic species **7** from *N*-Boc-1-aminobenzotriazole **6** and hence provide a contribution to the availability of diversely substituted 1-aminobenzotriazoles. If successful, one series of products [**8**; n=1,2], derived from reactions of dianion **7** with carbonyls or epoxides, would also present the opportunity to test the idea of intramolecular trapping of arynes by hydroxyl functions (Fig. 2).

In the event, intermediate **7** turned out to be relatively straightforward to generate and, as expected of an sp^3-centred carbanion, reacted smoothly with a wide range of electrophiles, including aldehydes, ketones and epoxides, to provide access to the required substrates **8**.[10] The starting material **6** was readily prepared from the commercially available nitroaniline **5** in five steps, using a slight modification of the original Campbell and Rees method.[3,10]

Our first task was therefore to remove the *N*-Boc protecting group from derivatives **8**, for which we used the now standard procedure of brief exposure to a 20% solution of trifluoroacetic acid in dichloromethane at ambient temperature, followed by basification and chromatographic purification when necessary, to give representative examples of the free 7-hydroxyl-1-aminobenzotriazoles **9**. The rather sensitive benzaldehyde adduct [**8**; R=Ph, n=1] gave a relatively modest return of the expected 1-aminobenzotriazole **10a**, due to partial dehydration, whereas the hexanal adduct [**8**; R=*n*-C_5H_{11}, n=1] gave a respectable 75% isolated yield of the free amine **10b**. Fears that a tertiary alcohol function would also undergo dehydration proved unfounded when the acetone and cyclohexanone adducts of dianion **7** were deprotected to give the free amines **11** and **12** in excellent yields. However, the sensitive citral adduct derived from dianion **7** failed to give more than traces of the free amine **13**. Addition of anisole[11] as a *t*-butyl cation scavenger did not improve the situation whereas use of thioanisole, a better carbocation scavenger,[12] did lead to 40–50% isolated yields of material which was largely the desired product **13** but which we could never completely separate from some of the many other products formed, presumably, by rearrangement and dehydration, initiated by protonation of the hydroxy group (Scheme 1).

Using the same method, the epoxide adducts [**8**; R=Et, (*S*)-Me, (*R*)-Ph, n=2] derived from dianion **7** were converted into the free amines **14** in good yields in the former two examples but, again, with some loss of material due to dehydration in the case of the secondary benzylic alcohol **14c**.

Although lead(IV) acetate seems often to be regarded as the standard oxidant for triggering benzyne generation from 1-aminobenzotriazoles,[1,2] we felt that the less commonly used *N*-bromosuccinimide (NBS) would be more compatible with the potentially oxidisable secondary alcohol functions in the amines **10**–**14** and would offer the benefit of milder conditions. Treatment of the parent 1-aminobenzotriazole **1** with NBS in the absence of a trap had been found by Campbell and Rees to give a 52% yield of 1,2-dibromobenzene **15**; that benzyne **3** was a true intermediate was indicated by the formation of the Diels–Alder adduct **16**, (Fig. 3), in an excellent isolated yield of 88%, when tetraphenylfuran was added as a trap.[3]

We found that when a dichloromethane solution of the benzaldehyde-derived 1-aminobenzotriazole **10a** was slowly added to a solution of NBS in the same solvent at ambient temperature, nitrogen evolution ensued rapidly together with formation of an orange colouration, presumably due to the generation of molecular bromine.[13] A simple work-up provided an ominously multi-component mixture of products, according to TLC analysis. Fortunately, column chromatography resulted in the separation of a single

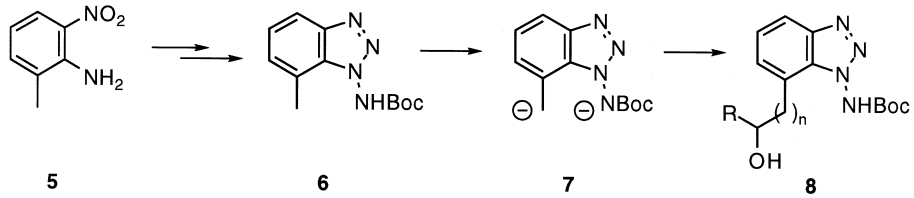
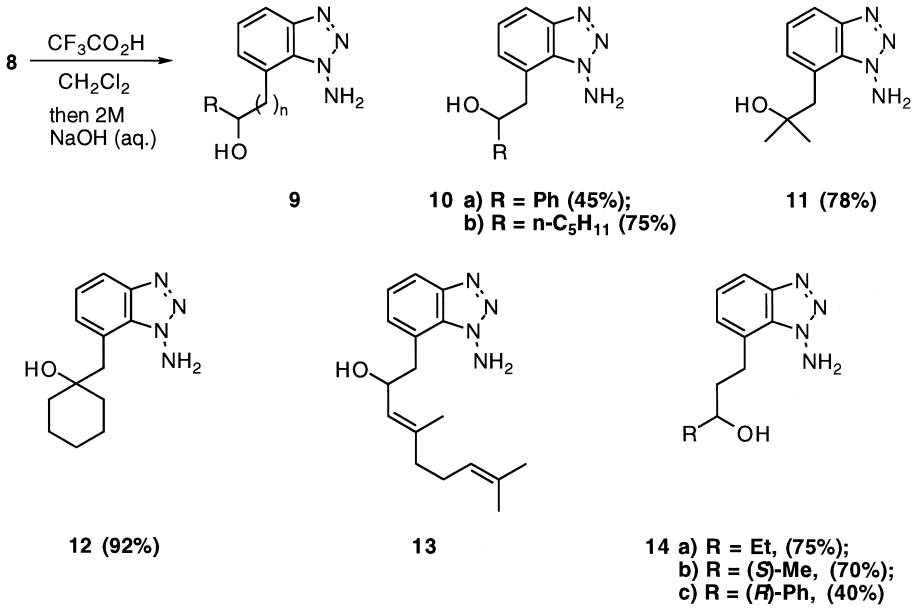


Figure 2.



Scheme 1.

component in 41% yield which appeared to be a 2-phenyl-2,3-dihydrobenzofuran, indicated particularly by the presence of geminal diastereotopic protons at δ_H 3.10 (1H, dd, J=13.0 and 8.3 Hz, 3-H_a) and 3.44 (1H, dd, J=13.0 and 7.5 Hz, 3-H_b) and the absence of any O–H or N–H absorbances in the infrared spectrum of this non-polar compound. However, it was plain from the NMR spectra of this material that only three aromatic protons were present, indicating that something more than simple addition of the hydroxyl oxygen and proton to the presumed intermediate benzyne [cf. **4**] had occurred.

That the product was actually the 7-bromo derivative **17a** was deduced from the NMR data, which was consistent with a 1,2,3-trisubstituted benzene, along with mass spectral analysis which clearly showed incorporation of a bromine atom. Similarly, treatment of the hexanal-derived 1-amino-benzotriazole **10b** gave a comparable isolated yield of the 7-bromo-2-pentyldihydrobenzofuran **17b**. Although not fully characterised, NMR and mass spectral data indicated in both cases that major by-products were the vicinal dibromides **18**, formed presumably by direct reaction between molecular bromine and the benzyne intermediates (Fig. 4).

This side reaction predominated in the more stringent tests of such intramolecular cyclisations involving the tertiary hydroxyl groups in both the acetone- and cyclohexanone adducts **11** and **12**. In both cases, only small amounts of the anticipated dihydrobenzofurans were formed, the major products now being the dibromides **19**. Evidently, steric hindrance rather than a potentially beneficial Thorpe–Ingold effect operates in these examples. Reasoning that molecular bromine could be responsible for this, the reaction of the acetone adduct **11** was repeated in the presence of 30 equiv. of 1-pentene. The idea proved correct: a 45% isolated of the bromo-dihydrobenzofuran **20** was obtained. However, this was a limited success as the related

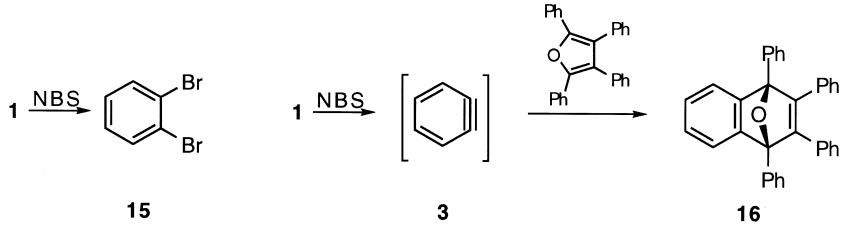


Figure 3.

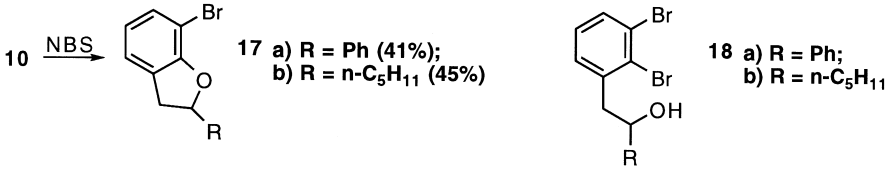


Figure 4.

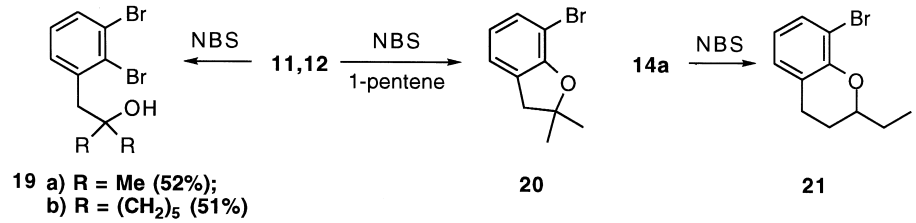


Figure 5.

cyclohexanone adduct **12** delivered very largely the 1,2-dibromo derivative **19b** even in the presence of 1-pentene. NMR and mass spectral analysis indicated the presence of the desired dihydrobenzofuran, but only to an extent of some 10–15%. Finally, in this series, we established that similar cyclisations were viable for the formation of six-membered rings. Thus, exposure of the epoxybutane adduct **14a** to NBS under the usual conditions led to a 53% isolated yield of the 8-bromo-benzopyran (chroman) **21** (Fig. 5). Again, the corresponding uncyclised dibromide could be detected by a combination of NMR and mass spectral analysis, albeit in much lower yield.

Despite the obvious benefits of bromine incorporation in the successful cyclisations described above, at this stage we briefly examined the reaction of this type of 1-amino-benzotriazole with lead(IV) acetate, again using dichloro-methane as solvent at ambient temperature. These proceeded somewhat more efficiently and without interference from any unexpected processes to give the dihydro-benzofurans **22** and **23**,[14] the latter in a remarkably high yield considering the foregoing results, indicating that this particular method is rather clean and does not result in the generation of other species which react readily with benzynes (Fig. 6). However, hopes that useful acetoxy functions would be incorporated, along the same lines as bromine, evidently proved groundless. It thus seems clear that the failure of the tertiary alcohols **19** to undergo at least reasonably clean cyclisations is associated with a rate retardation due to steric hindrance, which allows other species to attack the intermediate benzyne species, rather than an intrinsic inability to cyclise.

We had thus established a novel approach to both dihydro-benzofurans and -benzopyrans (chromans), with the bonus, in terms of synthetic potential, that an additional bromine atom is incorporated which could be useful as a handle for further elaborations of the initial cyclisation products. However, the uniformly moderate 40–50% isolated yields rather mitigated against the utility of this methodology. The formation of varying amounts of the corresponding, uncyclised vicinal dibromides [e.g. **18** and **19**], together with the desired cyclisation products, indicated that the benzyne pathway was being followed but that other reagents present during the reaction, especially molecular bromine, were seriously diminishing the efficiency of what appeared to be a rather smooth intramolecular trapping process. We reasoned that an iodonium source might prove more effective; Houghton and Rees[3,15] had found that oxidation of 1-aminobenzotriazole itself with iodobenzene diacetate, in the absence of an additional trap, led to the isolation of 1,2-diiodobenzene in 70% yield [cf. **33** below]. However, we felt that molecular iodine, if formed, would be less reactive than bromine and hence might not compete as well as bromine with the desired intramolecular trapping reactions. In view of the foregoing, it seems most reasonable to try *N*-iodosuccinimide (NIS) in place of NBS to examine this idea.

We were delighted to find that treatment of the 1-aminobenzotriazole **10a** derived from benzaldehyde with 2.5 equiv. of NIS in dichloromethane resulted in the formation of essentially a single product, which was isolated in 86% yield, spectroscopic and analytical data for which showed this to be the 7-iododihydrofuran **24a**. Similarly, the amino-benzotriazole **10b** derived from hexanal gave the 2-pentyl analogue **24b** in 92% isolated yield.

Remarkably, the 1-aminobenzotriazoles **11** and **12** containing tertiary hydroxyl groups also underwent smooth cyclisation when exposed to NIS to give the 7-iododihydro-benzofurans **25** and **26** in 95 and 82% isolated yields, respectively, in contrast to the much poorer yields obtained with NBS. Similarly, the homologous 1-aminobenzotriazoles **14** gave improved returns of the 8-iodo-dihydro-benzopyrans **27** as indicated (Fig. 7). Along with all other data, these iodides were identified by molecular weight values and also especially diagnostic quaternary carbon resonances in the ranges of 74–77 ppm in the benzofurans and 86–88 ppm in the benzopyrans, due to the 7-C and 8-C, respectively, moved to these unusual positions for aromatic sp^2 carbons by the iodine-induced heavy atom effect.[16] Given the known availability of homochiral monoepoxides, clearly this approach has much potential for the synthesis of single enantiomers of 2-substituted dihydro-benzopyrans.

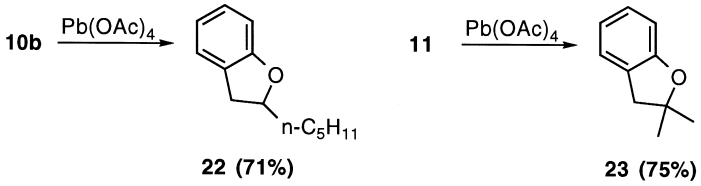


Figure 6.

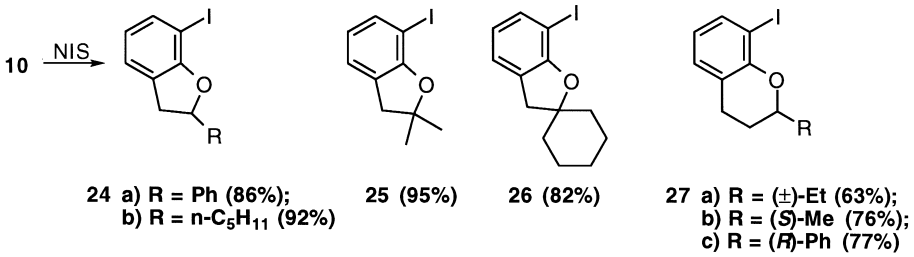


Figure 7.

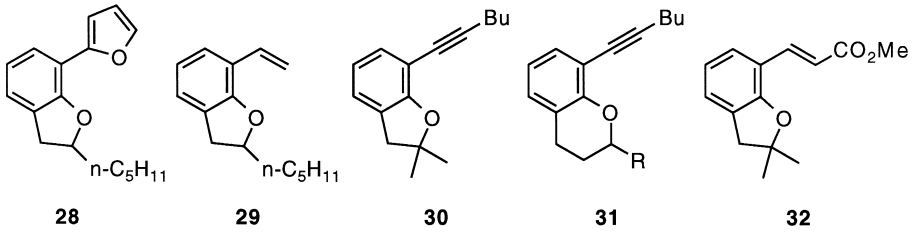


Figure 8.

While the incorporation of a bromine atom offered possibilities for further elaboration of the initial cyclisation products described above, the iodides were expected to show enhanced reactivities and hence represent even more attractive intermediates. We have briefly illustrated some of these possibilities by conducting a short, unoptimised series of palladium-catalysed coupling reactions of the representatives of the foregoing iodides. Thus, the 2-pentyl derivative **24b** underwent Stille coupling[17] with 2-tributylstannylfuran and tributylvinylstannane to give the expected homologues **28** and **29**, respectively. Both the 2,2-dimethyldihydrobenzofuran **25** and the 2-ethyldihydrobenzopyran **27a** underwent smooth Sonogashira coupling[18] with 1-hexyne leading to the alkynyl homologues **30** and **31**. The former also underwent a successful Heck reaction[19] with methyl acrylate and gave a 65% unoptimised return of the (*E*)-cinnamate **32** (Fig. 8). No doubt, other related couplings will prove possible (for example, the Suzuki method[20] with boronic acids and carbonylations may well be successful) and it may even possible to effect halogen–metal exchange and also useful radical trapping reactions.

The key step in which a presumed benzyne intermediate is generated from a 1-aminobenzotriazole and NIS was very similar in physical appearance to the related NBS reactions: evolution of nitrogen was very rapid and, to judge from the development of a distinct purple colouration, so was liberation of molecular halogen, in this case iodine. Evidently, the very high yields preclude the formation of significant amounts of the 1,2-diodides, which proved a limitation in the NBS method. Evidence that benzynes were true intermediates came from two experiments. When the parent 1-aminobenzotriazole **1** was treated with NIS in the absence of other trapping agents, only 1,2-diiodobenzene **33** was isolated in 54% yield, comparable with that previously obtained using iodobenzene diacetate (see above).[3,15] Further, when furan was used as solvent in place of dichloromethane, the Diels–Alder adduct **34**[21] was isolated in 49% yield. Hence, it seems that iodine, while able to react with benzyne, must do so at a significantly slower rate than molecular bromine, which appears to react at a rate comparable with the intramolecular trapping by pendant hydroxyl groups (Fig. 9).

Finally, we were intrigued by the possibility of trapping the benzyne so generated by cyclic ethers with a view to generating intermediates **35** which might be expected to rearrange as shown, resulting in annulation of the benzene ring, if such a dipole were really to be formed. In the event, only the diiodides **36** were isolated in moderate yields when oxetane, tetrahydrofuran and tetrahydropyran were used as solvents, respectively. Clearly, if dipoles **35** are true intermediates, then either or both anion trapping by iodonium ions and ring opening by attack of iodide are faster processes. Related results have been obtained earlier for benzyne generated from anthranilic acid, for example.[22]

All the evidence points to a true benzyne intermediate being involved in the foregoing trapping reactions; however, dipoles related to **35** appear as rather high energy intermediates which seem less likely under the rather gentle reaction conditions. In addition, a related species **37**, formed by intramolecular addition of a hydroxyl group to benzyne, would appear very well set up to undergo simple proton

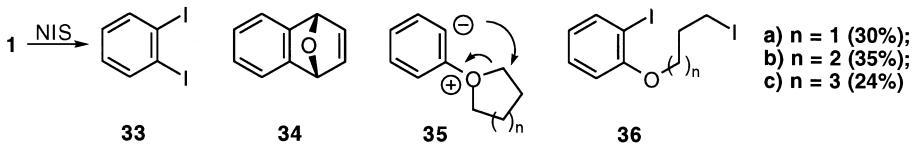


Figure 9.

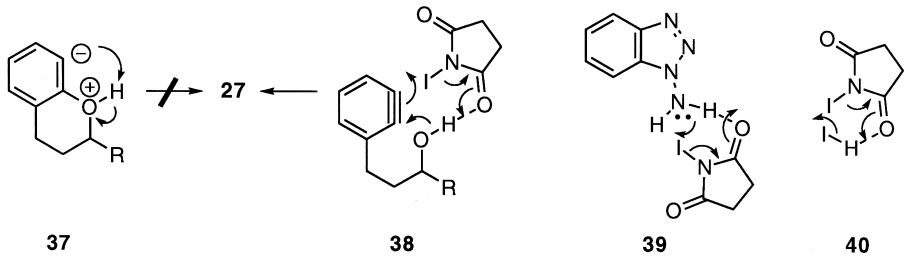


Figure 10.

transfer and not the very efficient trapping by iodine which is observed. At present therefore, a detailed mechanistic rationale is not clear; perhaps a hydrogen-bonded association between the reactants, as depicted in formula **38**, plays a key role in activating the key nucleophilic attack, the subsequent trapping by iodine and also proton transfer to succinimide in a concerted but non-synchronous manner as indicated. There may be a commonality between this and two other reactions in this overall sequence. Firstly, the initial, presumed iodination of the 1-aminobenzotriazoles can be depicted as proceeding via a similar hydrogen-bonded species **39**. Secondly, the hydrogen halide produced during benzyne formation [cf. **2**] could interact with a second molecule of the *N*-halosuccinimide, again by formation of an initial hydrogen bond, as shown in formula **40**, followed by a similar proton transfer, leading to generation of molecular halogen, either bromine or iodine (Fig. 10).

In any event, the excellent yields of the NIS step, coupled with the good to excellent yields which can be obtained from the initial metallation chemistry leading to the precursors **8**[10] suggests that this approach should be useful for the elaboration of a wide range of these types of oxygen heterocycles and does point the way towards the elaboration of even more highly substituted derivatives.

Experimental

General details

Optical rotations were measured using an Optical Activity AA-10 polarimeter. Infrared spectra were obtained using a Perkin–Elmer 1720 FTIR spectrometer using liquid films on sodium chloride plates or, if solids, chloroform solutions. ^{1}H NMR spectra were obtained using a Perkin–Elmer R32a instrument operating at 90 MHz (90) or a Bruker WM-250 instrument operating at 250 MHz. ^{13}C NMR spectra were determined using a JEOL EX270 spectrometer operating at 67.8 MHz or the Bruker AM-400 instrument operating at 100 MHz. All spectra were recorded using dilute solutions in deuteriochloroform, with tetramethylsilane as the internal standard. Coupling constants are quoted in Hertz. Mass spectra were obtained in the EI mode using either an AEI MS 902 or a VG 7070E instrument operating at 70 eV. Unless stated otherwise, all reactions were performed under dry nitrogen in anhydrous solvents, which were obtained by the usual methods.[23] All organic solutions from aqueous work-ups were dried by brief exposure to anhydrous magnesium sulphate followed by filtration. CC refers to column chromatography using silica gel (SORBSIL® C60-H [40–60 mm]) and the eluents specified. Petrol refers to light petroleum with bp 60–80°C and ether refers to diethyl ether.

Deprotection of 7-substituted 1-(*t*-butoxycarbonylamino)-benzotriazoles: general procedure

To a stirred solution of the 1-[*t*-butyloxycarbonyl(Boc)-amino]benzotriazole **8**[10] (1 equiv.) in dichloromethane (10 ml mmol^{-1}) at ambient temperature was added dropwise, via syringe, trifluoroacetic acid to give a 20% v/v solution. After 0.5 h, the solution was evaporated to near-dryness and basified by the addition of excess aqueous sodium hydroxide. The resulting mixture was extracted with ether (3×30 ml) and the combined extracts dried and evaporated to leave the crude 1-aminobenzotriazole, usually as a colourless gum, which was purified if necessary by CC [EtOAc–petrol, 1:1].

7-(2′-Hydroxy-2′-phenylethyl)-1H-benzotriazol-1-amine 10a. By the general procedure, deprotection of the benzaldehyde-derived *N*-Boc aminobenzotriazole [**8**; R=Ph, *n*=1] (75 mg) gave the *amine* **10a** (24 mg, 45%) as a colourless gum, ν_{max}/cm^{-1} 3245, 2814, 1606, 1455, 1114, 910 and 644, δ_H (250) 1.59 (1H. br s, OH), 3.47–3.56 (2H, m, 1′-CH$_2$), 4.98 (1H, dd, *J*=8.0 and 4.6 Hz, 2′-H), 5.94 (2H, s, NH$_2$), 7.09 (1H, dd, *J*=7.8 and 1.0 Hz, 6-H), 7.15 (1H, dd, *J*=7.8 and 7.8 Hz, 5-H), 7.16–7.26 (5H, m, Ph) and 7.76 (1H, dd, *J*=7.8 and 1.0 Hz, 4-H), δ_C (67.5) 40.3 (1′-CH$_2$), 75.2 (2′-CH), 118.5 (CH), 122.4 (C), 124.4 (CH), 125.8 (2×CH), 127.9 (CH), 128.5 (2×CH), 129.8 (CH), 130.9, 143.8 and 145.3 (all C), *m/z* [FAB] 255 (M$^+$+H, 100%), 237 (18) and 189 (21). HRMS Calcd for $C_{14}H_{15}N_4O$: 255.1246 (M$^+$+H). Found 255.1263.

7-(2′-Hydroxyhept-1′-yl)-1H-benzotriazol-1-amine 10b. By the general procedure, deprotection of the hexanal-derived *N*-Boc aminobenzotriazole [**8**; R=*n*-C$_5$H$_{11}$, *n*=1] (164 mg) gave the *amine* **10b** (88 mg, 75%) as a colourless gum, ν_{max}/cm^{-1} 3363, 2931, 2858, 1603, 1459, 1118 and 947, δ_H (250) 1.03 (3H, br t, *J*=ca. 6.1 Hz, 7′-Me), 1.20–1.60 (8H, m, 4×CH$_2$), 3.20–3.29 (2H, m, 1′-CH$_2$), 3.90–3.94 (1H, m, 2′-H), 6.21 (2H, s, NH$_2$), 7.18–7.22 (2H, m, 5- and 6-H) and 7.63–7.67 (1H, m, 4-H), δ_C (67.5) 14.0 (7′-Me), 22.6, 25.4, 31.8, 37.2, 38.2 (all CH$_2$), 72.6 (2′-CH), 117.7 (CH), 123.3 (C), 124.2, 129.2 (both CH), 131.3 and 144.3 (both C), *m/z* [FAB] 249 (M$^+$+H, 100%), 234 (5), 148 (5) and 134 (3). HRMS Calcd for $C_{13}H_{21}N_4O$: 249.1715 (M$^+$+H). Found 249.1721.

7-(2′-Hydroxy-2′-methylpropyl)-1H-benzotriazol-1-amine 11. By the general procedure, deprotection of the acetone-derived *N*-Boc aminobenzotriazole (53 mg) gave the *amine* **11** (28 mg, 78%) as a colourless gum, ν_{max}/cm^{-1} 3348, 2928, 2855, 1619, 1457, 1092, 962 and 885, δ_H (250) 1.33 (6H, s, 2×Me), 2.76 (1H, br s, OH), 3.33 (2H, s, 1′-CH_2), 6.36 (2H, s, NH_2), 7.17 (1H, dd, *J*=7.3 and 1.0 Hz, 6-H), 7.26 (1H, dd, *J*=7.3 and 7.3 Hz, 5-H) and 7.78 (1H, dd, *J*=7.3 and 1.0 Hz, 4-H), δ_C (100) 29.7 (2×Me), 43.2 (1′-CH_2), 71.0 (2′-C), 118.2 (CH), 122.8 (C), 123.9, 130.4 (both CH), 131.3 and 143.3 (both C), *m/z* [FAB] 207 (M^++H, 100%), 191 (5) and 189 (10). HRMS Calcd for $C_{10}H_{15}N_4O$: 207.1246 (M^++H). Found 207.1250.

7-[(1-Hydroxycyclohex-1-yl)methyl]-1H-benzotriazol-1-amine 12. By the general procedure, deprotection of the cyclohexanone-derived *N*-Boc aminobenzotriazole (250 mg) gave the *amine* **12** (167 mg, 92%) as a colourless gum, ν_{max}/cm^{-1} 3244, 2934, 2845, 1432, 964 and 910, δ_H (250) 1.40–1.60 (10H, m, 5×CH_2), 3.24 (2H, s, 1′-CH_2), 6.28 (2H, s, NH_2), 7.07–7.20 (2H, m, 5- and 6-H) and 7.73 (1H, dd, *J*=7.3 and 1.0 Hz, 4-H), δ_C (67.5) 22.0, 25.6, 37.7, 42.4 (all CH_2), 71.6 (1″-C), 117.8 (CH), 121.4 (C), 123.9, 130.3 (both CH), 130.9 and 144.3 (both C), *m/z* [FAB] 247 (M^++H, 100%), 231 (6) and 229 (5). HRMS Calcd for $C_{13}H_{19}N_4O$: 247.1559 (M^++H). Found 247.1549.

7-(3′-Hydroxypentyl)-1H-benzotriazol-1-amine 14a. By the general procedure, deprotection of the epoxybutane-derived *N*-Boc aminobenzotriazole (100 mg) gave the *amine* **14a** (52 mg, 75%) as a colourless gum, ν_{max}/cm^{-1} 3360, 2930, 1647, 1470, 1118, 985, 913, 882 and 864, δ_H (250) 0.91 (3H, t, *J*=7.5 Hz, 5′-Me), 1.43–1.57 (2H, m, 4′-CH_2), 1.73–1.96 (2H, m, 2′-CH_2), 3.35 (2H, t, *J*=7.5 Hz, 1′-CH_2), 3.49–3.62 (1H, m, 3′-H), 6.30 (2H, s, NH_2), 7.21–7.38 (2H, m, 5- and 6-H) and 7.70–7.80 (1H, m, 4-H), δ_C (100) 9.8 (5′-Me), 26.1, 30.1, 38.5 (all CH_2), 72.0 (3′-CH), 117.0, 124.4 (both CH), 126.6 (C), 127.8 (CH), 130.3 and 144.7 (both C), *m/z* [FAB] 221 (M^++H, 100%) and 207 (25). HRMS Calcd for $C_{11}H_{17}N_4O$: 221.1402 (M^++H). Found 221.1403.

(*S*)-(+)-7-(3′-Hydroxybutyl)-1H-benzotriazol-1-amine 14b. Deprotection of the *N*-Boc aminobenzotriazole (200 mg) derived from (*S*)-propylene oxide by the general procedure gave the *amine* **14b** (94 mg, 70%) as a colourless gum, $[\alpha]_D^{25}$ +9.9 (*c* 1.9, CH_2Cl_2), ν_{max}/cm^{-1} 3367, 2928, 2854, 1635, 1457, 1121, 950 and 903, δ_H (250) 1.24 (3H, d, *J*=4.2 Hz, 4′-Me), 1.74–1.89 (2H, m, 2′-CH_2), 3.21 (2H, t, *J*=7.6 Hz, 1′-CH_2), 3.75–3.83 (1H, m, 3′-H), 5.75 (2H, br s, NH_2), 7.12–7.22 (2H, m, 5- and 6-H) and 7.61–7.75 (1H, m, 4-H), δ_C (67.5) 23.3 (4′-Me), 26.4 (2′-CH_2), 40.8 (1′-CH_2), 66.9 (3′-CH), 117.1, 124.5 (both CH), 126.5 (C), 128.1 (CH), 130.4 and 144.1 (both C), *m/z* [FAB] 207 (M^++H, 100%), 191 (8) and 189 (11). HRMS Calcd for $C_{10}H_{15}N_4O$: 207.1246 (M^++H). Found 207.1241.

(*R*)-(+)-7-(3′-Hydroxy-3′-phenylpropyl)-1H-benzotriazol-1-amine 14c. Deprotection of the *N*-Boc aminobenzotriazole (129 mg) derived from (*S*)-styrene oxide by the general procedure gave the *amine* **14c** (38 mg, 40%) as a colourless gum, $[\alpha]_D^{25}$ +66.7 (*c* 0.65, CH_2Cl_2), ν_{max}/cm^{-1} 3360, 2927, 2854, 1635, 1463, 1124, 1013, 977 and 900, δ_H (250) 2.04–2.24 (2H, m, 2′-CH_2), 3.27 (2H, t, *J*=7.9 Hz, 1′-CH_2), 4.64–4.70 (1H, m, 3′-H), 7.19–7.37 (7H, m) and 7.71–7.75 (1H, m, 4-H), δ_C (67.5) 26.5 (2′-CH_2), 40.6 (1′-CH_2), 73.4 (3′-CH), 117.5, 124.4, 125.8 (all CH), 126.0 (C), 126.4, 127.6, 128.0, 128.1 (all CH), 128.4, 131.2 and 144.3 (all C), *m/z* [FAB] 269 (M^++H, 100%), 253 (15) and 251 (10). HRMS Calcd for $C_{15}H_{17}N_4O$: 269.1402 (M^++H). Found 269.1404.

Reactions of 1-aminobenzotriazoles with *N*-bromosuccinimide: general procedure

To a stirred solution of *N*-bromosuccinimide (NBS; 2 equiv.) in dichloromethane (10 ml $mmol^{-1}$) at ambient temperature was added dropwise, via syringe, a solution of the 1-aminobenzotriazole (1 equiv.) in dichloromethane (1 ml $mmol^{-1}$) which resulted in vigorous effervescence, a mild exotherm and the development of an orange colouration. After 1 h, the solvent was evaporated and the residue purified using CC [ether–petrol, 1:9].

7-Bromo-2,3-dihydro-2-phenylbenzofuran 17a. By the general procedure, treatment of the 7-(2′-hydroxy-2′-phenylethyl)-1-aminobenzotriazole **10a** (50 mg, 0.2 mmol) with NBS gave the *2-phenyl-2, 3-dihydrobenzofuran* **17a** (21.5 mg, 41%) as a colourless oil, ν_{max}/cm^{-1} 2980, 2914, 1624, 1480, 1119 and 970, δ_H (400) 3.10 (1H, dd, *J*=13.0 and 8.3 Hz, 3-H_a), 3.44 (1H, dd, *J*=13.0 and 7.5 Hz, 3-H_b), 4.98 (1H, dd, *J*=8.3 and 7.5 Hz, 2-H), 7.05 (1H, dd, *J*=7.6 and 7.6 Hz, 5-H), 7.21–7.49 (6H, m, Ph and 6-H) and 7.46 (1H, dd, *J*=7.6 and 1.8 Hz, 4-H), δ_C (100) 48.0 (3-CH_2), 73.3 (2-CH), 125.8 (CH), 126.1 (C), 127.9, 128.1, 128.4, 128.6, 128.9 (all CH), 130.8 (C), 131.0, 132.3 (both CH), 140.7 and 143.8 (both C), *m/z* [EI] 276 (M^+ (^{81}Br), 7%), 274 (6), 258 (48), 256 (47), 194 (12), 177 (26), 176 (28), 165 (21), 163 (21), 151 (28), 149 (25), 105 (100), 88 (33), 82 (19) and 77 (37). HRMS Calcd for $C_{14}H_{11}{}^{79}BrO$: 273.9994 (M^+). Found 273.9992.

7-Bromo-2,3-dihydro-2-pentylbenzofuran 17b. Following the general procedure, treatment of the 7-(2′-hydroxyheptyl)-1-aminobenzotriazole **10b** (51 mg, 0.2 mmol) with NBS gave the *2-pentyl-2,3-dihydrobenzofuran* **17b** (25 mg, 45%) as a colourless oil, ν_{max}/cm^{-1} 2930, 2856, 1642, 1580, 1459, 1122 and 1009, δ_H (250) 0.90 (3H, t, *J*=6.8 Hz, 5′-Me), 1.29–1.45 (4H, m, 2×CH_2), 1.48–1.62 (4H, m, 2×CH_2), 2.81 (1H, dd, *J*=13.7 and 8.8 Hz, 3-H_a), 3.11 (1H, dd, *J*=13.7 and 8.9 Hz, 3-H_b), 3.83–4.01 (1H, m, 2-H), 7.12 (1H, dd, *J*=7.7 and 7.7 Hz, 5-H), 7.22 (1H, dd, *J*=7.7 and 1.7 Hz, 6(4)-H) and 7.52 (1H, dd, *J*=7.7 and 1.7 Hz, 4(6)-H), δ_C (100) 14.1 (5′-Me), 22.7, 25.4, 31.9, 37.4, 45.4 (all CH_2), 71.1 (2-CH), 126.0, 127.0 (both C), 128.2, 130.4, 132.1 (all CH) and 141.4 (C), *m/z* [EI] 270 (M^+(^{81}Br), 61%), 268 (M^+(^{79}Br), 64%), 200 (63), 198 (66), 187 (97), 185 (100), 172 (51), 170 (52), 132 (87), 118 (61), 105 (25), 91 (47), 90 (31), 89 (50), 83 (91) and 77 (38). HRMS Calcd for $C_{13}H_{17}{}^{79}BrO$: 268.0463 (M^+). Found 268.0458.

1,2-Dibromo-3-(2′-hydroxy-2′-methylpropyl)benzene 19a. Following the general procedure, treatment of the 1-aminobenzotriazole **11** (48 mg, 0.27 mmol) with NBS

gave the *1,2-dibromobenzene* **19a** (36 mg, 52%) as a pale yellow oil [Found: C, 40.3; H, 4.4. $C_{10}H_{12}Br_2O$ requires C, 39.2; H, 4.0%], ν_{max}/cm^{-1} 3592, 3400–3200, 2929, 2853, 1580, 1462, 1410, 1110, 970 and 899, δ_H (250) 1.29 (6H, s, 2×Me), 1.51 (1H, br res, OH), 3.13 (2H, s, 1′-CH_2), 7.12 (1H, dd, *J*=7.8 and 7.8 Hz, 5-H), 7.31 (1H, dd, *J*=7.8 and 1.7 Hz, 6-H) and 7.53 (1H, dd, *J*=7.8 and 1.7 Hz, 4-H), δ_C (100) 29.7 (2×Me), 49.6 (1′-CH_2), 72.0 (2′-C), 126.2, 126.7 (both C), 127.7, 131.0, 132.2 and 140.7 (C), (all CH), *m*/*z* [EI] 295 (M^+-Me, (2×^{81}Br), 3%), 293 (6), 291 (3), 252 (11), 250 (23), 248 (12; M^+-Me_2CO; Found: 247.8842. $C_7H_6{}^{79}Br_2$ requires M, 247.8837), 130 (9), 89 (14) and 59 (100). HRMS Calcd for $C_9H_9{}^{79}Br_2O$: 290.9021 (M^+-Me). Found 290.8984.

7-Bromo-2,3-dihydro-2,2-dimethylbenzofuran 20. Following the general procedure, except that 1-pentene (420 mg, 6 mmol) was added prior to the aminobenzotriazole **11** (50 mg, 0.2 mmol), reaction between the latter and NBS gave the *dimethyl-2,3-dihydrobenzofuran* **20** (25 mg, 45%) as a colourless oil, ν_{max}/cm^{-1} 2930, 2855, 1603, 1582, 1462, 1372, 1329, 1294, 1144, 1122, 1101, 971 and 904, δ_H (250) 1.45 (6H, s, 2×Me), 3.03 (2H, s, 3-CH_2), 6.70 (1H, dd, *J*=7.7 and 7.7 Hz, 5-H), 7.06 (1H, dd, *J*=7.7 and 1.3 Hz, 6-H) and 7.27 (1H, dd, *J*=7.7 and 1.3 Hz, 4-H), δ_C (67.5) 28.3 (2×Me), 43.8 (3-CH_2), 87.8 (2-C), 102.8, 112.7 (both C), 121.3, 124.1 (both CH), 128.6 (C) and 131.1 (CH), *m*/*z* [EI] 228 (M^+(^{81}Br), 100%), 226 (98), 213 (9), 211 (10), 147 (67), 120 (15) and 104 (20). HRMS Calcd for $C_{10}H_{11}{}^{79}BrO$: 225.9994 (M^+). Found 225.9991.

1,2-Dibromo-3-[(1-hydroxycyclohex-1-yl)methyl]benzene 19b. By the foregoing procedure, with the addition of 30 equiv. of 1-pentene, reaction between the cyclohexylmethyl-l-aminobenzotriazole **12** (35 mg) gave the *1,2-dibromobenzene* **19b** (25 mg, 51%), ν_{max}/cm^{-1} 3591, 2933, 2854, 1579, 1450, 1410, 1127, 1096, 979, 956, 905 and 806, δ_H (250) 1.35–1.65 (10H, 5×CH_2), 3.07 (2H, s, 1′-CH_2), 7.08 (1H, dd, *J*=7.7 and 7.7 Hz, 5-H), 7.27 (1H, dd, *J*=7.7 and 1.6 Hz, 6-H) and 7.49 (1H, dd, *J*=7.7 and 1.6 Hz, 4-H), δ_C (100) 21.8 (2×CH_2), 25.6 (CH_2), 37.4 (2×CH_2), 49.6 (1′-CH_2), 72.5 (1″-C), 126.6 (C), 127.6 (CH), 128.0 (C), 131.0, 132.0 (both CH) and 139.3 (C), *m*/*z* [FAB] 333 (M^+-H_2O, (2×^{81}Br), 14%), 331 (30), 329 (13), 267 (20), 250 (30), 249 (42) and 248 (25). HRMS Calcd for $C_{13}H_{15}{}^{79,81}Br_2$: 331.0725 ($M^+-H_2O$). Found 331.0719.

8-Bromo-3,4-dihydro-2-ethyl-2H-1-benzopyran 21. By the general procedure, reaction between the 3′-hydroxypentyl-1-aminobenzotriazole **14a** (45 mg, 0.2 mmol) and NBS gave the *8-bromo-benzopyran* **21** (26 mg, 53%), ν_{max}/cm^{-1} 2929, 1602, 1458, 1409, 1097, 981 and 908, δ_H (250) 0.97 (3H, t, *J*=7.5 Hz, 2′-Me), 1.46–1.83 (4H, m, 1′- and 3-CH_2), 2.84–3.02 (2H, m, 4-CH_2), 3.55–3.64 (1H, m, 2-H), 7.09 (1H, dd, *J*=7.7 and 7.7 Hz, 6-H), 7.20 (1H, dd, *J*=7.7 and 1.7 Hz, 7-H) and 7.48 (1H, dd, *J*=7.7 and 1.7 Hz, 5-H), δ_C (100) 10.0 (2′-Me), 30.4, 34.4, 38.9 (all CH_2), 72.3 (2-CH), 126.1, 126.7 (both C), 128.4, 129.0, 131.6 (all CH) and 144.6 (C), *m*/*z* [EI] 242 (M^+, (^{81}Br), 11%), 240 (15), 211 (72), 209 (67), 185 (24), 183 (25), 171 (15), 169 (15), 167 (25), 102 (15) and 77 (15). HRMS Calcd for $C_{11}H_{13}{}^{79}BrO$: 240.0149 (M^+). Found 240.0142.

2,3-Dihydro-2-pentylbenzofuran 22. To a stirred suspension of lead(IV) acetate (487 mg, 1.1 mmol) in dichloromethane (10 ml) at ambient temperature was added dropwise via syringe a solution of the 7-(2′-hydroxyheptyl)-1-aminobenzotriazole **10b** (248 mg, 1.0 mmol) in dichloromethane (2 ml), resulting in vigorous effervescence and a mild exotherm. After 1 h, the mixture was filtered through celite and the solid washed with ether (2×30 ml). The combined filtrates were evaporated and the residues separated by CC [ether–petrol, 1:9] to give the *dihydrofuran* **22** (135 mg, 71%) as a colourless oil, ν_{max}/cm^{-1} 2928, 2854, 1650, 1463, 1100 and 1009, δ_H (250) 0.91 (3H, t, *J*=6.8 Hz, 5′-Me), 1.33–1.71 (7H, m), 1.77–1.86 (1H, m, 1′-H_a), 2.84 (1H, dd, *J*=15.5 and 7.9 Hz, 3-H_a), 3.26 (1H, dd, *J*=15.5 and 8.9 Hz, 3-H_b), 4.74–4.79 (1H, m, 2-H), 6.75 (1H, dd, *J*=7.6 and 1.0 Hz, 4-H), 6.81 (1H, dd, *J*=7.6 and 7.6 Hz, 5-H), 7.10 (1H, dd, *J*=7.6 and 7.6 Hz, 6-H) and 7.14 (1H, dd, *J*=7.6 and 1.0 Hz, 7-H), δ_C (100) 14.1 (5′-Me), 22.7 25.2, 31.6, 35.6, 36.2 (all CH_2), 83.5 (2-CH), 109.3, 120.1, 125.0 (all CH), 127.1 (C), 128.0 (CH) and 159.7 (C), *m*/*z* [EI] 190 (M^+, 31%), 133 (54), 120 (44), 119 (51), 108 (14), 107 (100), 91 (22) and 77 (10). HRMS Calcd for $C_{13}H_{18}O$: 190.1358 (M^+). Found 190.1344.

2,3-Dihydro-2,2-dimethylbenzofuran 23. By the foregoing method, oxidation of the 1-aminobenzotriazole **11** (21 mg, 0.12 mmol), derived from acetone, using lead(IV) acetate gave the dihydrobenzofuran **23**[14] (11 mg, 75%) as a colourless oil, ν_{max}/cm^{-1} 2928, 2854, 1590, 1459, 1100 and 1009, δ_H (250) 1.48 (6H, s, 2×Me), 3.01 (2H, s, 3-CH_2), 6.98 (1H, dd, *J*=7.6 and 1.0 Hz, 4-H), 7.07 (1H, dd, *J*=7.6 and 7.6 Hz, 5-H) and 7.33–7.40 (2H, m, 6- and 7-H), *m*/*z* [EI] 148 (M^+, 4%), 147 (16), 133 (10), 120 (60), 107 (25), 105 (18), 97 (23), 95 (22), 93 (30), 83 (40), 77 (21) and 69 (100). HRMS Calcd for $C_{10}H_{12}O$: 148.0888 (M^+). Found 148.0863.

Reactions of 1-aminobenzotriazoles with *N*-iodosuccinimide: general procedure

To a solution of *N*-iodosuccinimide (NIS; 2.5 equiv.) in dichloromethane (10 ml $mmol^{-1}$) stirred in the dark at ambient temperature was added dropwise, via syringe, a solution of the 1-aminobenzotriazole (1 equiv.) in dichloromethane (1 ml $mmol^{-1}$) which resulted in vigorous effervescence, a mild exotherm and the development of a purple colouration. After 1 h, the mixture was washed with saturated aqueous sodium thiosulphate (10 ml $mmol^{-1}$), water (10 ml $mmol^{-1}$) and brine (10 ml $mmol^{-1}$), then dried, filtered and evaporated. The residue was purified using CC [ether–petrol, 1:9].

2,3-Dihydro-7-iodo-2-phenylbenzofuran 24a. Following the general procedure, treatment of the 1-aminobenzotriazole **10a** (96 mg, 0.39 mmol) with NIS gave the *7-iodo-2,3-dihydrobenzofuran* **24a** (107 mg, 86%) as a colourless oil, ν_{max}/cm^{-1} 2928, 2854, 1600, 1580, 1491, 1120, 973, 909 and 871, δ_H (250) 3.31 (1H, dd, *J*=15.8 and 9.5 Hz, 3-H_a), 3.40 (1H, dd, *J*=15.7 and 8.0 Hz, 3-H_b), 5.85 (1H, dd, *J*=9.5 and 8.0 Hz, 2-H), 6.65 (1H, dd, *J*=7.7 and 7.7 Hz, 5-H), 7.12 (1H, dd, *J*=7.7 and 1.1 Hz, 6-H), 7.32–7.44 (5H, m, Ph) and 7.52 (1H, dd, *J*=7.7 and 1.1 Hz, 4-H), δ_C (67.5) 39.8 (3-CH_2), 74.1

(7-C), 83.2 (2-CH), 122.5, 124.7 (both CH), 125.6 (2×CH), 127.8 (C), 128.1 (CH), 128.7 (2×CH), 137.0 (CH), 142.9 and 144.1 (both C), *m/z* [EI] 322 (M^+, 100%), 244 (5), 194 (20), 165 (27), 152 (11), 89 (10) and 77 (5). HRMS Calcd for $C_{14}H_{11}IO$: 321.9857 (M^+). Found 321.9844.

2,3-Dihydro-7-iodo-2-pentylbenzofuran 24b. By the general procedure, reaction between NIS and the 1-aminobenzotriazole **10b** (30 mg, 0.12 mmol) gave the *7-iodo-2,3-dihydrobenzofuran* **24b** (35 mg, 92%) as a colourless oil, ν_{max}/cm^{-1} 2981, 2858, 1599, 1579, 1457, 1117, 984, 897 and 869, δ_H (250) 0.94 (3H, t, *J*=6.6 Hz, 5′-Me), 1.10–1.70 (7H, m), 1.81–1.90 (1H, m, 1′-H_a), 2.97 (1H, dd, *J*=15.5 and 7.6 Hz, 3-H_a), 3.40 (1H, dd, *J*=15.5 and 8.8 Hz, 3-H_b), 4.75–4.90 (1H, m, 2-H), 6.58 (1H, dd, *J*=7.8 and 7.8 Hz, 5-H), 7.10 (1H, d, *J*=7.8 Hz, 6-H) and 7.45 (1H, d, *J*=7.8 Hz, 4-H), δ_C (100) 14.0 (5′-Me), 22.5, 24.6, 31.7, 35.8, 36.6 (all CH_2), 73.6 (7-C), 83.3 (2-CH), 121.9, 124.8 (both CH), 127.8 (C), 136.6 (CH) and 148.0 (C), *m/z* [EI] 316 (M^+, 89%), 246 (50), 233 (100), 132 (58), 118 (44), 105 (28) and 77 (18). HRMS Calcd for $C_{13}H_{17}IO$: 316.0326 (M^+). Found 316.0302.

2,3-Dihydro-2,2-dimethyl-7-iodobenzofuran 25. By the general procedure, reaction between NIS and the 1-aminobenzotriazole **11** (100 mg, 0.49 mmol) gave the *7-iodo-2,3-dihydrobenzofuran* **25** (126 mg, 95%) as a colourless oil, ν_{max}/cm^{-1} 2929, 2854, 1599, 1577, 1459, 1142, 1099, 970, 890 and 871, δ_H (250) 1.44 (6H, s, 2×Me), 3.04 (2H, s, 3-CH_2), 6.49 (1H, dd, *J*=7.5 and 7.5 Hz, 5-H), 7.00 (1H, dd, *J*=7.5 and 1.0 Hz, 6-H) and 7.38 (1H, dd, *J* 4-H), δ_C (67.5) 28.2 (2×Me), 44.1 (3-CH_2), 74.1 (7-C), 88.1 (2-C), 121.7, 124.9 (both CH), 125.7 (C), 136.7 (CH) and 144.1 (C), *m/z* [EI] 274 (M^+, 100%), 259 (16), 147 (10), 132 (72), 131 (32), 119 (23), 91 (15), 89 (17) and 77 (17). HRMS Calcd for $C_{10}H_{11}IO$: 273.9857 (M^+). Found 273.9830.

7-Iodo-spiro[benzofuran-2(3H)]-1′-cyclohexane 26. By the general procedure, reaction between NIS and the cyclohexanone-derived aminobenzotriazole **12** (35 mg, 0.14 mmol) gave the *spiro derivative* **26** (37 mg, 82%) as a colourless oil, ν_{max}/cm^{-1} 2940, 2856, 1598, 1577, 1457, 1126, 1110, 946, 916 and 860, δ_H (250) 1.27–1.91 (10H, m), 3.08 2H, s, 3-CH_2), 6.59 (1H, dd, *J*=7.7 and 7.7 Hz, 5-H), 7.07 (1H, dd, *J*=7.7 and 1.1 Hz, 6-H) and 7.44 (1H, dd, *J*=7.7 and 1.1 Hz, 4-H), δ_C (67.5) 22.9, 23.0, 25.1, 36.9, 37.0, 42.2 (all CH_2), 76.5 (7-C), 88.3 (2-C), 121.5, 125.0 (both CH), 126.8 (C), 136.6 (CH) and 138.2 (C), *m/z* [EI] 314 (M^+, 75%), 246 (10), 234 (16), 233 (66), 105 (18), 81 (100), 80 (34) and 77 (18). HRMS Calcd for $C_{13}H_{15}IO$: 314.0169 (M^+). Found 314.0161.

3,4-Dihydro-2-ethyl-8-iodo-2H-1-benzopyran 27a. By the general procedure, reaction between NIS and the 1-aminobenzotriazole **14a** (83 mg, 0.38 mmol), derived from 1,2-epoxybutane, gave the *pyran* **27a** (65 mg, 63%) as a colourless oil, ν_{max}/cm^{-1} 2939, 2848, 1594, 1562, 1459, 1119, 979, 944, 904, 863 and 837, δ_H (250) 1.14 (3H, t, *J*=7.4 Hz, 2′-Me), 1.58–1.88 (3H, m, 1′-CH_2 and 3-H_a), 1.96–2.06 (1H, m, 3-H_b), 2.68–2.93 (2H, m, 4-CH_2), 3.96–4.06 (1H, m, 2-H), 6.58 (1H, dd, *J*=7.7 and 7.7 Hz, 6-H), 7.02 (1H, dd, *J*=7.7 and 0.6 Hz, 7-H) and 7.57 (1H, dd, *J*=7.7 and 0.6 Hz, 5-H), δ_C (67.5) 9.9 (2′-Me), 25.0, 27.1, 28.3 (all CH_2), 78.5 (2-CH), 85.7 (8-C), 121.4 (CH), 123.1 (C), 129.6, 136.9 (both CH) and 153.1 (C), *m/z* [EI] 288 (M^+, 69%), 259 (8), 233 (100), 132 (28), 105 (19) and 77 (14). HRMS Calcd for $C_{11}H_{13}IO$: 288.0013 (M^+). Found 288.0011.

(*S*)-(−)-3,4-Dihydro-8-iodo-2-methyl-2H-1-benzopyran 27b. By the general procedure, reaction between NIS and the aminobenzotriazole **14b** (102 mg, 0.49 mmol), derived from (*S*)-propylene oxide, gave the *(S)-2-methylpyran* **27b** (103 mg, 76%) as a colourless oil, $[\alpha]_D^{25}$ −44.1 (*c* 0.32, CH_2Cl_2), ν_{max}/cm^{-1} 2935, 2848, 1595, 1562, 1461, 1121, 1103, 1076, 949, 940, 906 and 848, δ_H (250) 1.46 (3H, d, *J*=6.3 Hz, 1′-Me), 1.74 (1H, dddd, *J*=13.6, 11.1, 9.9 and 5.7 Hz, 3-H_a), 2.03 (1H, dddd, *J*=13.6, 6.1, 3.5 and 2.3 Hz, 3-H_b), 2.72 (1H, ddd, *J*=16.5, 5.7 and 3.5 Hz, 4-H_a), 2.85 (1H, ddd, *J*=16.5, 11.1 and 6.1 Hz, 4-H_b), 4.24 (1H, dqd, *J*=9.8, 6.3 and 2.3 Hz, 2-H), 6.58 (1H, dd, *J*=7.6 and 7.6 Hz, 5-H), 7.02 (1H, dd, *J*=7.6 and 1.0 Hz, 6-H) and 7.58 (1H, dd, *J*=7.6 and 1.0 Hz, 4-H), δ_C (67.5) 21.1 (1′-Me), 25.0 (3-CH_2), 29.1 (4-CH_2), 73.5 (2-CH), 88.3 (8-C), 121.5 (CH), 122.1 (C), 129.7, 137.0 (both CH) and 143.4 (C), *m/z* [EI] 274 (M^+, 100%), 233 (56), 232 (16), 132 (27), 131 (40), 118 (10), 105 (19), 83 (14) and 77 (13). HRMS Calcd for $C_{10}H_{11}IO$: 273.9857 (M^+). Found 273.9861.

(*R*)-(+)-3,4-Dihydro-8-iodo-2-phenyl-2H-1-benzopyran 27c. By the general procedure, reaction between NIS and the aminobenzotriazole **14c** (33 mg, 0.12 mmol), derived from (*S*)-styrene oxide, gave the *(S)-2-phenylpyran* **27c** (32 mg, 77%) as a colourless oil, $[\alpha]_D^{25}$ +25.6 (*c* 0.36, CH_2Cl_2), ν_{max}/cm^{-1} 2926, 2854, 1595, 1564, 1494, 1450, 1128, 1092, 997 and 904, δ_H (250) 1.95–2.20 (1H, m, 3-H_a), 2.26–2.40 (1H, m, 3-H_b), 2.75 (1H, ddd, *J*=16.3, 4.4 and 4.4 Hz, 4-H_a), 3.00 (1H, ddd, *J*=16.3, 10.8 and 5.7 Hz, 4-H_b), 5.24 (1H, dd, *J*=9.5 and 2.5 Hz, 2-H), 6.64 (1H, dd, *J*=7.6 and 7.6 Hz, 6-H), 7.05 (1H, d, *J*=7.6 Hz, 7-H), 7.24–7.58 (5H, m, Ph) and 7.64 (1H, d, *J*=7.6 Hz, 5-H), δ_C (67.5) 25.6 (3-CH_2), 29.1 (4-CH_2), 77.8 (2-CH), 88.2 (8-C), 122.7 (C), 125.5 (2×CH), 126.5 (CH), 128.5 (2×CH), 129.3, 136.4 (both CH), 142.7 and 143.7 (both C), *m/z* [EI] 336 (M^+, 100%), 245 (10), 244 (10), 232 (20), 209 (29), 118 (31), 105 (84), 104 (49), 91 (38) and 77 (48). HRMS Calcd for $C_{15}H_{13}IO$: 336.0013 (M^+). Found 336.0016.

2,3-Dihydro-7-(2-furyl)-2pentylbenzofuran 28. To a solution of the 7-iodo-dihydrobenzofuran **24b** (115 mg, 0.35 mmol), in dry tetrahydrofuran (10 ml) was added dichloro-bis-triphenylphosphinepalladium(0) (8 mg) and (2-furyl)tributylstannane (140 mg, 0.40 mmol). The resulting solution was refluxed for 14 h then cooled and evaporated. The residue was dissolved in ether (50 ml) and filtered through alumina. The solid was washed with ether (2×50 ml) and the combined filtrates evaporated. CC of the residue [petrol–EtOAc, 99:1] separated the *furyl-dihydrobenzofuran* **28** (54 mg, 48%) as a colourless oil, ν_{max}/cm^{-1} 2931, 2858, 1598, 1464, 1156, 1014, 987, 908, 886 and 870, δ_H (250) 0.95 (3H, t, *J*=6.9 Hz, 5′Me), 1.36–1.78 (7H, m), 1.82–1.96 (1H, m, 1′-H_b), 2.88 (1H, dd, *J*=15.3 and 7.8 Hz, 3-H_a), 3.32 (1H, dd, *J*=15.3 and 8.9 Hz, 3-H_b), 4.84–4.96 (1H, m, 2-H), 6.50 (1H, dd, *J*=3.2 and 1.8 Hz, furyl 4-H), 6.88 (1H, dd, *J*=7.5 and

7.5 Hz, 5-H), 6.90 (1H, d, *J*=3.2 Hz, furyl 3-H), 7.06 (1H, dd, *J*=7.5 and 0.5 Hz, 4-H), 7.45 (1H, d, *J*=1.8 Hz, furyl 5-H) and 7.58 (1H, dd, *J*=7.5 and 0.5 Hz, 6-H), δ_C (67.5) 15.0 (5′-Me), 23.5, 26.3, 32.1, 36.4, 37.2 (all CH_2), 84.9 (2-CH), 109.5, 112.6 (both CH), 115.2 (C), 121.2, 123.9, 124.3 (all CH), 128.5 (C), 142.0 (CH), 152.2 and 156.1 (both C), *m/z* [EI] 256 (M^+, 100%), 199 (32), 186 (15), 173 (87), 172 (30), 157 (11), 144 (13), 128 (10) and 115 (15). HRMS Calcd for $C_{17}H_{20}O_2$: 256.1463 (M^+). Found 256.1455.

2,3-Dihydro-7-ethenyl-2-pentylbenzofuran 29. By the foregoing method, reaction between the 7-iodo-dihydrobenzofuran **24b** (87 mg, 0.33 mmol) and tributylvinylstannane (120 mg, 0.38 mmol) gave the *7-ethenyl derivative* **29** (60 mg, 87%) as a colourless oil, ν_{max}/cm^{-1} 2932, 2858, 1624, 1598, 1570, 1453, 995, 912 and 863, δ_H (250) 0.93 (3H, t, *J*=6.9 Hz, 5′-Me), 1.34–1.92 (8H, m), 2.83 (1H, dd, *J*=15.4 and 8.8 Hz, 3-H_a), 3.25 (1H, dd, *J*=15.4 and 8.8 Hz, 3-H_b), 4.76–4.88 (1H, m, 2-H), 5.28 (1H, dd, *J*=11.3 and 1.6 Hz, :CH_c), 5.92 (1H, dd, *J*=17.6 and 1.6 Hz, :CH_t), 6.74 (1H, dd, *J*=17.6 and 11.3 Hz, :CH), 6.78 (1H, dd, *J*=7.5 and 7.5 Hz, 5-H), 7.04 (1H, dd, *J*=7.5 and 0.5 Hz, 6-H) and 7.13 (1H, dd, *J*=7.5 and 0.5 Hz, 4-H), δ_C (100) 14.0 (5′-Me), 22.6, 25.2, 31.7, 35.3, 36.2 (all CH_2), 83.6 (2-CH), 115.3 (:CH_2), 120.0 (CH), 120.2 (C), 123.9, 126.1 (both CH), 127.5 (C), 132.2 (CH) and 157.3 (C), *m/z* [EI] 216 (M^+, 77%), 159 (41), 145 (24), 133 (100), 131 (60), 117 (22), 115 (23), 91 (9) and 77 (7). HRMS Calcd for $C_{15}H_{20}O$: 216.1514 (M^+). Found 216.1503.

2,3-Dihydro-2,2-dimethyl-7-(hexyn-1-yl)benzofuran 30. To a solution of the 2,2-dimethyl-7-iododihydorbenzofuran **25** (45 mg, 0.14 mmol) in diethylamine (3 ml) was added copper(I) iodide (7 mg, 4 mol%), dichloro-bis-triphenylphosphinepalladium(0) (15 mg, 1 mol%) and 1-hexyne (14 mg, 0.17 mmol). The resulting mixture was stirred and gently refluxed for 16 h then cooled and evaporated. CC [petrol] separated the *7-hexynly-dihydrobenzofuran* **30** (26 mg, 80%) as a pale yellow oil, ν_{max}/cm^{-1} 2932, 2858, 2216, 1592, 1443, 1167, 1137, 969 and 881, δ_H (250) 0.91 (3H, t, *J*=7.1 Hz, 6′-Me), 1.46–1.66 (4H, m, 4′- and 5′-CH_2), 1.50 (6H, s, 2×2-Me), 2.45 (2H, t, *J*=7.0 Hz, 3′-CH_2), 2.99 (2H, s, 3-CH_2), 6.72 (1H, dd, *J*=7.6 and 7.6 Hz, 5-H), 7.30 (1H, dd, *J*=7.6 and 1.0 Hz, 6-H) and 7.14 (1H, dd, *J*=7.6 and 1.0 Hz, 4-H), δ_C (67.5) 13.7 (6′-Me), 19.5, 22.0 (4′- and 5′-CH_2), 28.2 (2×2-Me), 30.9, 42.9 (3- and 3′-CH_2), 87.1 (2-C), 93.8, 106.0 (1′- and 2′-C), 119.6, 124.5 (both CH), 127.1 (C), 131.6 (CH) and 158.1 (C), *m/z* [EI] 228 (M^+, 100%), 213 (28), 199 (13), 185 (64), 171 (24), 157 (13), 145 (19), 128 (11) and 115 (17). HRMS Calcd for $C_{16}H_{20}O$:228.1514 (M^+). Found 228.1527.

3,4-Dihydro-2-ethyl-8-(hexyn-1-yl)-2H-1-benzopyran 31. By the foregoing method, Sonogashira coupling between the 7-iodo-dihydrobenzofuran **27a** (101 mg, 0.35 mmol) and 1-hexyne (38 mg, 0.47 mmol) gave the *8-hexynylbenzopyran* **31** (70 mg, 84%) as a pale yellow oil, ν_{max}/cm^{-1} 2900, 2860, 2226, 1590, 1464, 1140, 908 and 880, δ_H (250) 0.95 (3H, t, *J*=7.5 Hz, 6′-Me), 1.10 (3H, t, *J*=7.1 Hz, 2-CH_2CH_3), 1.45–2.06 (8H, m), 2.48 (2H, t, *J*=6.7 Hz, 3′-CH_2), 2.67–2.90 (2H, m, 4-CH_2), 3.92–4.03 (1H, m, 2-H), 6.72 (1H, dd, *J*=7.5 and 7.5 Hz, 5-H), 6.96 (1H, dd, *J*=7.5 and 1.0 Hz, 6-H) and 7.28 (1H, dd, *J*=7.5 and 1.0 Hz, 4-H), δ_C (67.5) 9.8, 13.7 (both Me), 19.5, 21.9, 24.8, 26.8, 28.3, 30.9 (all CH_2), 77.7 (2-CH), 93.2, 112.4 (1′- and 2-C), 119.3 (CH), 121.5 (C), 128.9, 131.6 (both CH) and 153.3 (C), *m/z* [EI] 242 (M^+, 100%), 213 (16), 212 (16), 199 (18), 187 (93), 171 (18), 157 (20), 145 (38), 144 (23), 115 (29) and 113 (25). HRMS Calcd for $C_{17}H_{22}O$: 242.1671 (M^+). Found 242.1659.

Methyl (*E*)-3-(2,3-dihydro-2,2-dimethyl-7-benzofuranyl)-2-propenoate 32. To a solution of palladium(II) acetate (1 mg) and triphenylphosphine (4 mg) in dimethylformamide (5 ml) was added the 7-iododihydrobenzofuran **27a** (45 mg, 0.16 mmol), anhydrous sodium acetate (15 mg, 0.18 mmol) and methyl acrylate (18 mg, 0.18 mmol). The resulting solution was stirred and heated at 120°C for 20 h then cooled, diluted with water (5 ml) and extracted with petrol (3×10 ml). The combined extracts were washed with water (2×3 ml) then dried and evaporated. CC [petrol–EtOAc, 99:1] of the residue separated the *unsaturated ester* **32** (25 mg, 65%) as a pale yellow oil, ν_{max}/cm^{-1} 2951, 1704, 1630, 1606, 1450, 1322, 1294, 1174, 1137, 988 and 879, δ_H (250) 1.52 (6H, s, 2×2′-Me), 3.02 (2H, s, 3′-CH_2), 3.81 (3H, s, OMe), 6.71 (1H, d, *J*=16.2 Hz, 2-H), 6.83 (1H, 1H, dd, *J*=7.6 and 7.6 Hz, 5′-H), 7.14 (1H, dd, *J*=7.6 and 1.0 Hz, 6′-H), 7.19 (1H, dd, *J*=7.6 and 1.0 Hz, 4′-H) and 7.70 (1H, d, *J*=16.2 Hz, 3-H), δ_C (67.5) 28.5 (2×2′-Me), 42.5 (3′-CH_2), 51.6 (OMe), 88.0 (2′-C), 117.3 (C), 118.9, 120.2, 126.8 (all CH), 128.2 (C), 128.9 (CH), 130.4 (C), 141.2 (CH) and 168.3 (CO), *m/z* [EI] 232 (M^+, 100%), 200 (23), 199 (13), 185 (9), 113 (10), 97 (8) and 85 (12). HRMS Calcd For $C_{14}H_{16}O_3$: 232.1099 (M^+). Found 232.1085.

1,2-Diiodobenzene 33. By the general procedure for benzyne formation using NIS, reaction between 1-aminobenzotriazole **1** (150 mg, 1.2 mmol) and NIS (630 mg, 2.8 mmol) gave the diiodide **33**[3,15] (199 mg, 54%) as a light-sensitive oil which displayed spectral data identical to an authentic sample (Aldrich).

1,4-Dihydro-1,4-epoxynaphthalene 34. By the general procedure for benzyne generation using NIS, but with freshly distilled furan as the solvent in place of dichloromethane, reaction between 1-aminobenzotriazole **1** (100 mg, 0.68 mmol) and NIS (380 mg, 1.69 mmol) gave the 1,4-epoxynaphthalene **34** (48 mg, 49%) as an off-white solid, mp 52–53°C [lit.[21] mp 53–55°C]. An authentic sample (Aldrich) showed mp 54–55°C (mixed mp 52–53°C) together with identical spectroscopic and chromatographic characteristics.

1-Iodo-2-(3′-iodopropyloxy)benzene 36a. By the general procedure for benzyne generation using NIS, but with freshly distilled oxetane as the solvent in place of dichloromethane, reaction between 1-aminobenzotriazole **1** (50 mg, 0.37 mmol) and NIS (210 mg, 0.93 mmol) gave the *diiodide* **36a** (43 mg, 30%) as a yellow gum, ν_{max}/cm^{-1} 3002, 2930, 2877, 1582, 1478, 1464, 1440, 1179, 1162, 1120, 1054, 1018, 914 and 651, δ_H (250) 2.20–2.31 (2H, m, 2′-CH_2), 3.42 (2H, t, *J*=6.7 Hz, 3′-CH_2), 4.10 (2H, t, *J*=5.6 Hz, 1′-CH_2), 6.74 (1H, dd, *J*=7.6 and 7.6 Hz, 5-H), 6.85 (1H, dd, *J*=7.6 and 1.1 Hz, 6-H), 7.31 (1H, dd, *J*=7.6 and 7.6 Hz,

4-H) and 7.78 (1H, dd, J=7.6 and 1.1 Hz, 3-H), δ_C (67.5) 4.4 (3′-CH_2), 32.8 (2′-CH_2), 68.3 (1′-CH_2), 84.2 (1-C), 112.2, 122.8, 129.5, 139.4 (all CH) and 153.1 (2-C), *m/z* [EI] 388 (M^+, 76%), 220 (72), 203 (17), 191 (10), 169 (100), 134 (17), 106 (21), 92 (23) and 76 (21). HRMS Calcd for $C_9H_{10}I_2O$: 387.8825 (M^+). Found 387.8778.

1-Iodo-2-(4′-iodobutyloxy)benzene 36b. By the general procedure for benzyne generation using NIS, but with tetrahydrofuran as the solvent in place of dichloromethane, reaction between 1-aminobenzotriazole **1** (100 mg, 0.74 mmol) and NIS (420 mg, 1.86 mmol) gave the *diiodide* **36b** (104 mg, 35%) as a yellow oil, ν_{max}/cm^{-1} 3001, 2945, 2875, 1582, 1455, 1440, 1162, 1121, 1051, 1018, 942, 908 and 650, δ_H (250) 1.89–2.20 (4H, m, 2′- and 3′-CH_2), 3.30 (2H, t, J=6.3 Hz, 4′-CH_2), 4.02 (2H, t, J=6.3 Hz, 1′-CH_2), 6.68 (1H, dd, J=7.7 and 7.7 Hz, 5-H), 6.80 (1H, dd J=7.7 and 1.0 Hz, 6-H), 7.29 (1H, dd, J=7.7 and 7.7 Hz, 4-H) and 7.78 (1H, dd, J=7.7 and 1.0 Hz, 3-H), δ_C (67.5) 8.0 (4′-CH_2), 30.3, 30.6 (2′- and 3′-CH_2), 68.3 (1′-CH_2), 88.2 (1-C), 112.5, 122.8, 129.5, 139.4 (all CH) and 152.1 (2-C), *m/z* [EI] 402 (M^+, 8%), 220 (49), 203 (10), 183 (100), 155 (10), 106 (7), 93 (10), 92 (10) and 76 (11) [Found: M^+, 401.8937. $C_{10}H_{12}I_2O$ requires M, 401.8981]. HRMS Calcd for $C_{10}H_{12}I_2O$: 401.8981 (M^+). Found 401.8937.

1-Iodo-2-(5′-iodopentyloxy)benzene 36c. By the general procedure for benzyne generation using NIS, but with tetrahydropyran as the solvent in place of dichloromethane, reaction between 1-aminobenzotriazole **1** (50 mg, 0.37 mmol) and NIS (210 mg, 0.93 mmol) gave the *diiodide* **36c** (34 mg, 24%) as a yellow oil, ν_{max}/cm^{-1} 3002, 2944, 2876, 1644, 1582, 1479, 1465, 1439, 1162, 1122, 1051, 1018, 980, 908, 865 and 650, δ_H (250) 2.14–2.51 (6H, m, 2′-, 3′- and 4′-CH_2), 3.74 (2H, t, J=7.0 Hz, 5′-CH_2), 4.52 (2H, t, J=6.1 Hz, 1′-CH_2), 6.72 (1H, dd, J=7.7 and 7.7 Hz, 6-H), 6.83 (1H, dd, J=7.7 and 7.7 Hz, 5-H), 7.31 (1H, dd, J=7.7 and 7.7 Hz, 4-H) and 7.77 (1H, dd, J=7.7 and 1.0 Hz, 3-H), δ_C (67.5) 6.8 (5′-CH_2), 27.8, 28.0, 33.1 (2′-, 3′- and 4′-CH_2), 68.6 (1′-CH_2), 85.1 (1-C), 112.0, 122.4, 129.4, 139.4 (all CH) and 153.1 (2-C), *m/z* [EI] 416 (M^+, 26%), 220 (100), 197 (65), 162 (12), 151 (33), 113 (27), 106 (8), 92 (10), 76 (9) and 69 (69). HRMS Calcd for $C_{11}H_{14}I_2O$: 415.9134 (M^+). Found 415.9117.

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