Ambient temperature method for the generation and Diels–Alder trapping of benzofuran-2,3-quinodimethane (2,3-dimethylidene-2,3-dihydrobenzofuran)

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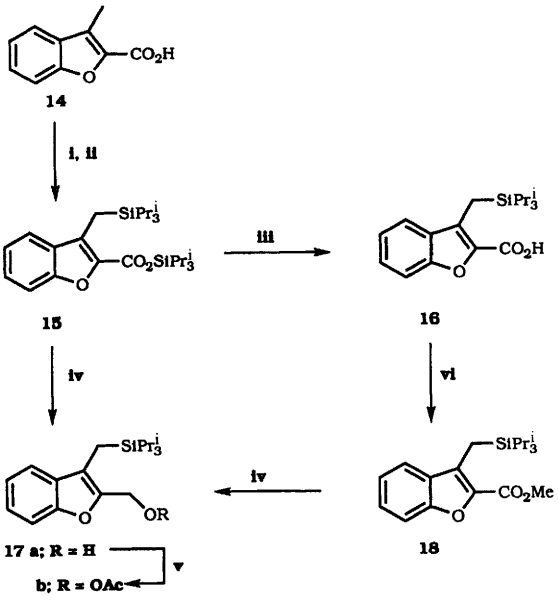
The Ito–Saegusa method has been used to generate benzofuran-2,3-quinodimethane 10 from the corresponding silyl acetate 17b in solution at −4 °C. The intermediate reacts efficiently with a range of reactive Diels–Alder dienophiles with moderate to good levels of regioselection; the structure of the major diastereoisomer has been determined by X-ray analysis.

The generation of heteroquinodimethanes **1** has attracted considerable attention during recent times,[1] to such an extent that these reactive intermediates are becoming as available as the corresponding quinodimethane (*o*-xylylene) derivatives of benzenoid systems.[2] To date, their synthetic potential has been little explored, beyond Diels–Alder cycloadditions; in some respects, this may be associated with the relatively harsh, pyrolytic conditions often used in the generation of these intermediates. Flash vacuum pyrolysis (FVP) of aryl esters or the related chloromethyl derivatives **2**[3] and reductive debromination of vicinal bromomethyl derivatives **3** by heating with sodium iodide in a variety of solvents (the Cava method)[4] are two older but still popular methods for obtaining intermediates **1**. More recently, thermal extrusion of sulfur dioxide from 3-sulfolenes **4**[5] has been shown to be a very versatile alternative while a milder method features fluoride-induced expulsion of the silicon and leaving groups (L = OAc or NR_3^+) from substrates **5**,[6] based on the original Ito–Saegusa idea for the generation of quinodimethanes from the corresponding benzenoid derivatives.[7] Less commonly used approaches include retro-Diels–Alder reactions at ~950 °C[8] and cycloreversion of furanocyclobutanes.[9] A highlight of this general area is the method devised by the Magnus group whereby indole-2,3-quinodimethanes are generated from 2-methylindole-3-carbaldehydes by sequential imine and iminium ion formation followed by proton loss;[10] a mechanistically related deprotonation method has also recently been reported.[11] Stable analogues of the intermediates **1** are also known, for example, an intramolecular dehydration protocol (**6** ⟶ **7**), which generates the equivalent of a thiophene-quinodimethane;[12] similar species have also been obtained by an enolisation–trapping method.[13] Other stable versions of heteroaromatic quinodimethanes are the pyranones **8**, which undergo smooth Diels–Alder reactions with, for example, alkynes or alkyne equivalents; subsequent loss of carbon dioxide results in the generation of a benzene ring.[14]

It was against this background that we wondered whether the dianionic intermediate **9**,[15] derived from 3-methylbenzofuran-2-carboxylic acid, could provide a rapid entry to benzofuran-2,3-quinodimethane **10** using the Ito–Saegusa method.[7] Potential attractions of this approach would be ease of access to the starting material and the anticipated mild protocol for generation of this reactive intermediate in solution. The only previous report of the generation of quinodimethane **10**, by FVP of the corresponding benzoate **11** at 620–640 °C and 10^{-4} Torr, is illustrative of a drawback often associated with this methodology: condensation of intermediate **10** into an extremely large excess of a dienophile (methyl acrylate) was necessary to secure a modest 35% yield of the expected Diels–Alder adducts.[16,17] We had previously prepared and fully characterized the trimethylsilyl derivative **12**[15] and this therefore seemed an appropriate starting material for the preparation of an Ito–Saegusa-type quinodimethane precursor **13**. However, all attempts to manipulate this compound resulted in extensive or complete loss of the trimethylsilyl group, returning either unreacted acid or the corresponding alcohol, from attempted reduc-

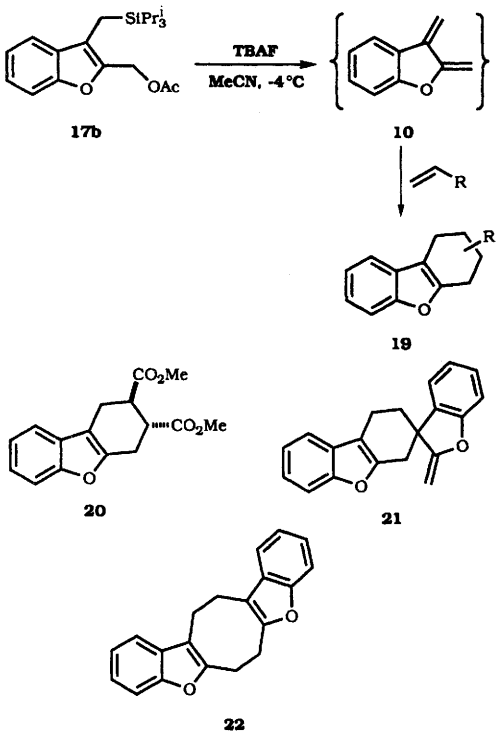
tions. This problem had previously been encountered in related indole chemistry by the Magnus group and was responsible for their development of an elegant alternative strategy.[10] We reasoned that a more hindered silyl group might prove more robust, but were disappointed to find the same loss of silicon occurred with the *tert*-butyldimethylsilyl group. It was only when we turned to the triisopropylsilyl group that we were able to achieve our aim. Thus, deprotonation of 3-methylbenzofuran-2-carboxylic acid **14**[18,19] using two equivalents of lithium diisopropylamide (LDA) followed by addition of two equivalents of triisopropylsilyl chloride delivered a good yield of the expected silyl ester **15** which subsequently underwent a smooth acid-induced hydrolysis to the corresponding acid **16** (Scheme 1). Subsequent treatment with diazomethane



Scheme 1 *Reagents:* i, 2 equiv. LDA, THF, −78 °C, 0.5 h; ii, 2 equiv. Pr^i_3SiCl, warm to 0 °C, 3 h then aq. NH_4Cl; iii, 2 M aq. HCl, 0.5 h, 20 °C; iv, $LiAlH_4$, Et_2O, 0 °C; v, Ac_2O, DMAP (cat.), 0 °C; vi, CH_2N_2

gave the corresponding methyl ester **18** which could be readily reduced to the alcohol **17a**, with minimal loss of the silyl group, using lithium aluminium hydride in ice-cold diethyl ether. Subsequently, we found that there was no advantage in this route, as the silyl ester **15** could be directly reduced equally efficiently, under the same conditions, to the desired alcohol **17a** which was then converted into the key acetate **17b** upon treatment with acetic anhydride and a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) in dichloromethane, again with only minimal loss of the silyl group, although attempts to rigorously purify this compound did lead to some desilylation.

Initial attempts to effect the Diels–Alder sequence outlined in Scheme 2 to give adducts **19**, using dimethyl fumarate (2 equiv.) as the dienophile and the original Ito–Saegusa conditions[7] consisting of caesium fluoride in refluxing acetonitrile resulted in disappearance of the starting silyl acetate **17b** within 4 h, but led to poor yields of the hoped-for adduct **20**, along with large amounts of polymeric material. We presume that the latter was formed from the fumarate by a series of fluoride-initiated Michael additions. Replacing caesium fluoride with tetrabutylammonium fluoride (TBAF) required several further additions of both the dienophile and TBAF during 4 h to the refluxing acetonitrile solution to effect complete consumption of the starting material **17b**. However, chromatographic separation of the crude product afforded an encouraging 63% yield of the desired adduct **20** along with much reduced amounts of polymeric material. Also isolated were the interesting dimeric products **21** and **22**, formally the [4 + 2] and [4 + 4] dimers of



Scheme 2

the quinodimethane **10**, in a combined yield of 29% and in a 4:1 ratio, identical to that previously obtained under FVP conditions.[16] It is probable that these compounds arise *via* a Diels–Alder dimerisation of the quinodimethane **10**, followed by a [1,3]-carbon shift.[3,6,16] Diradical intermediates have been proposed in the FVP method,[3,16] although these seem less likely to be formed under the present conditions unless the intermediate **10** has considerable diradical character, as has been suggested.[3,6,16] While the identical 4:1 ratio might be coincidental, it is perhaps suggestive of a common mechanism involving quinodimethane **10**, relatives of which have been observed spectroscopically.[20]

We next examined changes of solvent, with the aim of reducing formation of polymers and the dimeric products **21** and **22**. Tetrahydrofuran at reflux provided a marginal improvement in the yield of the desired adduct **20** during 4 h. Reasoning that this might be due to a reduced reaction temperature, we further lowered the latter, ultimately to −4 °C, under which conditions polymer formation from dimethyl fumarate was almost completely suppressed and the isolated yield of adduct **20** improved to 73%, accompanied by only small traces of the dimers **21** and **22**. Two equivalents each of TBAF and the dienophile were necessary to obtain this yield, a significant improvement on the large excesses of the latter which are usually required when FVP is used to generate quinodimethanes, although the reaction was, as expected, much slower, taking typically 48 h to go to completion. The outcomes of similar reactions with typical Diels–Alder dienophiles are summarized in Scheme 3. Cycloaddition to dimethyl maleate unfortunately produced a mixture of the *trans*- **20** and the expected *cis*-adduct **23**. This was due to subsequent epimerisation of the latter as indicated when a pure sample of *cis*-**23** was stirred with TBAF in THF at −4 °C, resulting in formation of a similar *trans*:*cis* ratio of **20** and **23**. Reaction with methyl acrylate gave an excellent yield of cycloadduct, but unfortunately as a mixture of regioisomers **24** and **25**, in a ratio of 2:1, similar to the 3:1 ratio obtained using the FVP approach.[16] The structural assignments were based on the earlier deductions of Chou and Trahanovsky.[16] Similarly when methyl vinyl ketone was the dienophile, an excellent combined yield of the two expected regioisomers **26** and **27** was obtained.

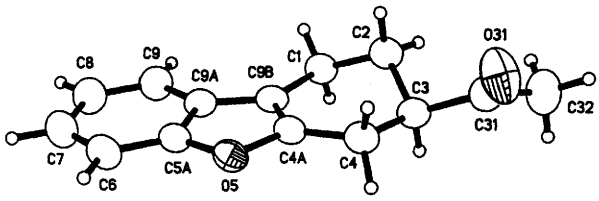
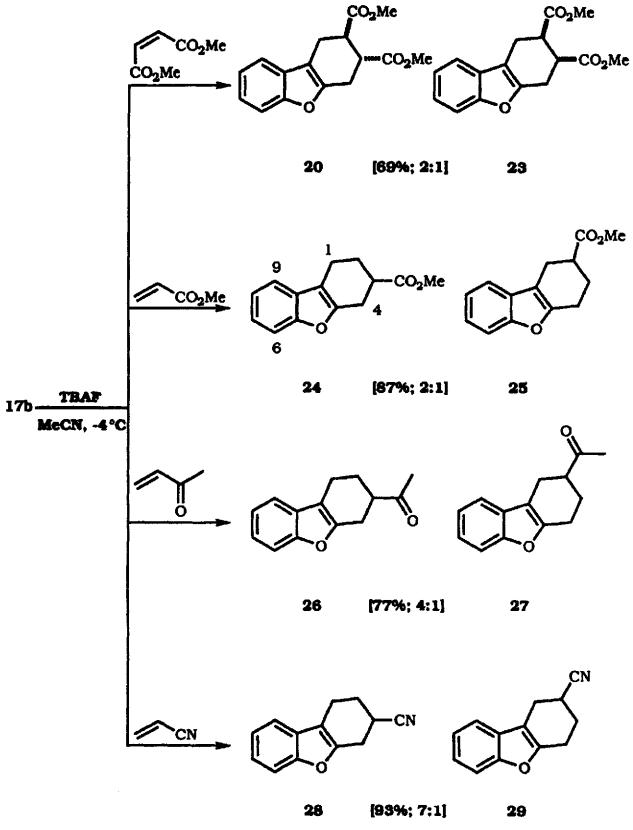


Fig. 1



Scheme 3

Structural assignments were based on comparisons of ^{1}H and ^{13}C NMR spectral data, with the foregoing examples. Due to its greater propensity to undergo Michael addition of fluoride, four equivalents each of methyl vinyl ketone and TBAF were necessary to secure the high yield. Finally, reaction with acrylonitrile was the most regioselective of the series, giving an excellent yield of the adducts **28** and **29** in a 7:1 ratio; comparisons of ^{1}H and ^{13}C NMR spectral data were again used to assign these structures.

While we did not doubt the veracity of Chou and Trahanovsky's structural assignments,[16] we felt it would be worthwhile to obtain further confirmation of these; in the general area of heteroquinodimethane Diels–Alder chemistry, structural assignments have always been based on such comparative spectral data. Fortunately, slow crystallisation of the adduct mixture (**26** and **27**) derived from methyl vinyl ketone gave single crystals of the major adduct **26**, X-ray analysis of which confirmed the structure, which is shown in Fig. 1.

The foregoing results suggest, but do not prove, that the adducts **23**–**29** are formed by a conventional Diels–Alder cyclisation. We have therefore carried out AM1 calculations, using a MOPAC package[21] on the reaction between quinodimethane **10** and methyl vinyl ketone. Perhaps unsurprisingly, the calculations indicated that the reaction was a typical $HOMO_{diene}$ controlled cycloaddition, $E_{LUMO\,(dienophile)} - E_{HOMO\,(diene)} = 8.785$ eV, in contrast to ΔE [$HOMO_{(dienophile)}$/$LUMO_{(diene)}$] = 10.246 eV. However, calculations of the coefficients of the p_z atomic orbitals did not provide such an unambiguous answer (Fig. 2);

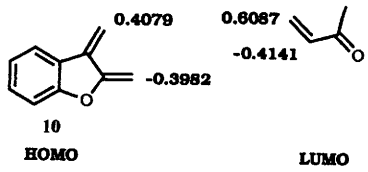
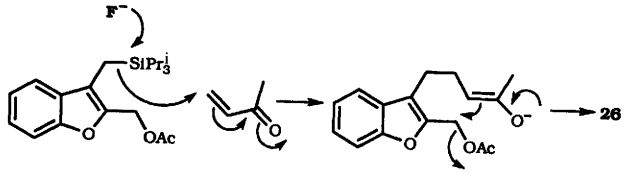


Fig. 2

the relevant values for quinodimethane **10** indicating an almost equal size for the pertinent coefficients. At least the trend is consistent with the observed regiochemical results, but is hardly definitive. Despite the fact that the regiochemical results from FVP[16] and the present solution method are quite similar, it is possible that a portion of the major isomers formed in solution arise from a Michael addition–trap sequence, outlined in Scheme 4, along the lines of the recently reported approach



Scheme 4

to carbazoles from deprotonated 2-methylindole-3-carbaldehyde.[11] The lack of stereoselection when dimethyl maleate is the dienophile is consistent with this idea, although it can also be explained by subsequent epimerisation (*vide supra*). Further experiments will be necessary to fully define this. However, we failed to observe formation of Diels–Alder adducts between the quinodimethane **10** and cyclohexene when the latter was present as a co-solvent; instead, high yields of the dimers **21** and **22** were isolated, suggesting that a 'simple' Diels–Alder mechanism may not be operating, although cyclohexene is a notoriously poor dienophile.

Experimental

General details

^{1}H NMR spectra were obtained using a Perkin-Elmer R32a instrument operating at 90 MHz (90), a Bruker WM-250 instrument operating at 250 MHz (250) or a Bruker WM-400 spectrometer operating at 400 MHz (400). The latter instrument was also used to measure ^{13}C NMR spectra (at 100 MHz). All spectra were recorded using dilute solutions in deuteriochloroform unless otherwise stated, with tetramethylsilane as the internal standard; in the reporting of the data app. = apparent. All J values are given in Hz. Mass spectra were obtained using an AEI MS 902 or VG 7070E instrument at 70 eV.

All reactions were performed under dry nitrogen and all organic solutions from aqueous work-ups were dried by brief exposure to anhydrous magnesium sulfate followed by filtration. SG chromatography refers to column chromatography using silica gel (Merck 9385) and the eluents specified. Petrol refers to light petroleum with bp 60–80 °C. Ether refers to diethyl ether.

3-Methylbenzofuran-2-carboxylic acid 14

Ethyl 2-phenoxy-3-oxobutanoate (84 g, 0.4 mol) prepared as previously described from ethyl 2-chloroacetoacetate and sodium phenoxide[18] was added dropwise during *ca.* 2 h to well-stirred sulfuric acid (12 M, 84 ml), maintained at −10 °C using a propan-2-ol–solid carbon dioxide bath. The resulting red solution was stirred for an additional hour then carefully poured into a stirred mixture of crushed ice and water (500 ml, 1:1) with external cooling to maintain the temperature at ~0 °C. The mixture was then extracted with ethyl acetate

(3 × 100 ml). The combined extracts were washed with water (3 × 50 ml), 2 M sodium hydrogen carbonate (3 × 50 ml) then dried and evaporated. Distillation of the residue gave ethyl 3-methylbenzofuran-2-carboxylate (49 g, 65%) bp 165–170 °C/17 mmHg (lit.,[18] 162–167 °C/16 mmHg) as a yellow oil which rapidly solidified (often in the condenser during distillation), mp 50–51 °C (lit.,[18] 49–51 °C); ν_{max}(KBr)/cm^{-1} 1741; δ_H(90) 1.40 (3 H, t, *J* 7, OCH_2CH_3), 2.61 (3 H, s, 3-Me), 4.45 (2 H, q, *J* 7, OCH_2CH_3) and 7.10–7.71 (4 H, m) (Found: C, 70.7; H, 5.9. Calc. for $C_{12}H_{12}O_3$: C, 70.6; H, 5.9%).

To an ice-cold, stirred solution of the foregoing ester (6.12 g, 30 mmol) in methanol (20 ml) was slowly added a solution of potassium hydroxide (2.0 g, 36 mmol) in methanol (10 ml) and the resulting solution stirred without further cooling for 24 h then evaporated. The residue was dissolved in water and ether and the separated aqueous layer acidified with 2 M hydrochloric acid. The liberated acid was extracted into ether (3 × 30 ml); the combined extracts were dried and evaporated. Crystallisation of the residue from ether–petrol or toluene gave the acid **14** (5.1 g, 97%) as a colourless solid, mp 191–193 °C (lit.,[18] 192–193 °C); ν_{max}(KBr)/cm^{-1} 3300–2400 and 1690; δ_H[90; $(CD_3)_2CO$] 2.61 (3 H, s, 3-Me) and 7.20–7.91 (4 H, m).

Triisopropylsilyl 3-(triisopropylsilylmethyl)benzofuran-2-carboxylate 15

To a solution of 3-methylbenzofuran-2-carboxylic acid **14** (0.18 g, 1 mmol) in anhydrous tetrahydrofuran (20 ml) stirred and cooled to −78 °C was added a solution of lithium diisopropylamide (2.4 ml of a 1 M solution in tetrahydrofuran) in tetrahydrofuran (4 ml).[15] The resulting deep red solution was stirred at this temperature for 0.5 h then a solution of triisopropylsilyl chloride (0.46 g, 2.4 mmol) in tetrahydrofuran (2 ml) was added dropwise. The resulting solution was slowly warmed to 0 °C during 3 h, then quenched by the addition of saturated aqueous ammonium chloride (10 ml). Ether (30 ml) was added and the upper organic layer separated, washed with water and dried. Evaporation of the solvents left the *ester* **15** (0.34 g, 69%) as an orange oil; ν_{max}(film)/cm^{-1} 1680; δ_H(90) 1.05–1.17 (42 H, app. br s, 6 × Pr^i), 2.78 (2 H, s, CH_2Si) and 7.10–7.80 (4 H, m); *m/z* 488 (M^+, 0.2%), 445 (100, M − Pr^i), 315 (13), 287 (21), 157 (7) and 131 (43) (Found: M^+, 488.3148. $C_{28}H_{48}O_3Si_2$ requires *M*, 488.3142).

3-(Triisopropylsilylmethyl)benzofuran-2-carboxylic acid 16

The foregoing reaction was repeated on a 4 mmol scale. After the 3 h warming period, the mixture was quenched by the addition of 2 M hydrochloric acid (20 ml) and left stirring for 0.5 h, then poured into ether (100 ml). The resulting mixture was washed with brine (3 × 40 ml) and the separated organic layer dried and evaporated. Crystallisation of the residue from pentane–ether (80:20) gave the *silyl acid* **16** (0.70 g, 53%) as a colourless solid, mp 216–217 °C; ν_{max}(KBr)/cm^{-1} 3200–2400 and 1670; δ_H[90; $(CD_3)_2CO$] 1.05 (21 H, app. br s, 3 × Pr^i), 2.74 (2 H, s, CH_2Si) and 7.00–7.81 (4 H, m); *m/z* 332 (M^+, 0.2%), 289 (100, M − Pr^i), 203 (5), 175 (4), 144 (5) and 130 (7) (Found: C, 68.7; H, 8.6. $C_{19}H_{28}O_3Si$ requires C, 68.6; H, 8.5%).

Methyl 3-(triisopropylsilylmethyl)benzofuran-2-carboxylate 18

An excess of ethereal diazomethane was added to an ice-cold solution of the foregoing acid **16** (1 g) in ether (10 ml). After 1 h without cooling, the solution was flushed with nitrogen then diluted with ether (20 ml) and washed with 2 M aqueous sodium hydroxide (2 ml) and water (2 ml) then dried and evaporated. Crystallisation of the residue from pentane–ether (~4:1) gave the *methyl ester* **18** (0.96 g, 92%) as an off-white solid, mp 71–73 °C; ν_{max}(KBr)/cm^{-1} 1718; δ_H(90) 1.07 (21 H, app. br s, 3 × Pr^i), 2.55 (2 H, s, CH_2Si), 3.92 (3 H, s, OMe) and 7.25–7.91 (4 H, m) (Found: C, 69.4; H, 8.7. $C_{20}H_{30}O_3Si$ requires C, 69.3; H, 8.7%).

3-(Triisopropylsilylmethyl)benzofuran-2-methanol 17a

A solution of the silyl ester **15** (0.73 g, 1.5 mmol) in dry ether (15 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (0.06 g, 1.5 mmol) in ether (5 ml), cooled in an ice bath. After the addition, the mixture was stirred for 0.25 h then quenched by the addition of ethyl acetate (2 ml). The mixture was washed with 2 M aqueous sodium hydroxide then dried and evaporated. SG chromatography [hexanes–ethyl acetate (4:1)] of the residue gave the *alcohol* **17a** (0.34 g, 71%) as an off-white solid, mp 69–70 °C; ν_{max}(KBr)/cm^{-1} 3350 and 1460; δ_H(90) 1.05 (21 H, app. br s, 3 × Pr^i), 2.12 (2 H, s, CH_2Si), 4.75 (2 H, s, CH_2O) and 7.11–7.70 (4 H, m); *m/z* 318 (M^+, 4%), 275 (17), 157 (16), 144 (100) and 131 (62) (Found: C, 71.7; H, 9.8; M^+, 318.2013. $C_{19}H_{30}O_2Si$ requires C, 71.7; H, 9.5%; *M*, 318.2015).

The product of desilylation, 3-methylbenzofuran-2-methanol (0.043 g, 8%) was also isolated, as a colourless solid, mp 82–83 °C (from 1:1 pentane–ether) [lit.,[22] 83–84 °C (from petrol)]; ν_{max}(KBr)/cm^{-1} 3236, 1454 and 1357; δ_H(90) 1.94 (1 H, br s, OH), 2.56 (3 H, s, 3-Me), 4.75 (2 H, s, CH_2O) and 7.10–7.60 (4 H, m); *m/z* 162 (M^+, 100%), 145 (97), 144 (10), 131 (12) and 115 (19) (Found: C, 74.5; H, 5.9. Calc. for $C_{10}H_{10}O_2$: C, 74.1; H, 6.2%).

2-Acetyloxymethyl-3-(triisopropylsilylmethyl)benzofuran 17b

To an ice-cold, stirred solution of the alcohol **17a** (0.95 g, 3 mmol) in acid-free dichloromethane (20 ml) were added 4-(*N*,*N*-dimethylamino)pyridine (3 crystals) and acetic anhydride (0.34 ml, 3.6 mmol).[23] After 1 h, the solvent was evaporated and the residue dissolved in ether (30 ml) and washed with water (2 × 15 ml). The resulting solution was dried then filtered through a pad of alumina. Evaporation of the filtrate left the *acetate* **17b** (0.92 g, 86%) as an off-white solid, mp 41–43 °C; ν_{max}(KBr)/cm^{-1} 1746 and 1458; δ_H(400) 1.03–1.15 (18 H, app. br s, 6 × Me), 1.16–1.23 (3 H, m, 3 × C*H*Me$_2$), 2.01 [3 H, s, OC(O)Me], 2.18 (2 H, s, CH_2Si), 5.20 (2 H, s, CH_2O), 7.21 [1 H, dd, *J* 7.5 and 7.5, 5(6)-H], 7.29 [1 H, dd, *J* 7.5 and 7.5, 6(5)-H], 7.40 (1 H, br d, *J* ~7.3, 4-H) and 7.50 (1 H, br d, *J* ~7.4); δ_C 5.26 (CH_2Si), 11.61 (3 × CHSi), 18.60 (6 × Me), 20.83 [MeC(O)O], 57.20 (CH_2OAc), 111.27 (CH), 118.98 (C), 120.32 (CH), 122.15 (CH), 124.88 (CH), 129.47 (C), 144.99 (C), 154.47 (C) and 170.77 (CO); *m/z* 360 (M^+, 7%), 301 (6), 173 (94) and 144 (100) (Found: M^+, 360.2182. $C_{21}H_{32}O_3Si$ requires *M*, 360.2121).

Careful recrystallisation did not yield material which gave correct microanalytical data, due to some desilylation. Attempts at further purification resulted in significant desilylation to give 2-acetyloxymethyl-3-methylbenzofuran, mp 73–76 °C (lit.,[24] oil); ν_{max}(KBr)/cm^{-1} 1746 and 1450; δ_H(90) 2.01 [3 H, s, OC(O)Me], 2.09 (3 H, s, 3-Me), 5.21 (CH_2O) and 7.22–7.50 (4 H, m), as a byproduct.

Generation of benzofuran-2,3-quinodimethane (2,3-dimethylidene-2,3-dihydrobenzofuran) 10 and Diels–Alder reactions

General procedure. Preparation of *trans*-dimethyl 1,2,3,4-tetrahydrodibenzofuran-2,3-dicarboxylate 20. To a stirred solution of the silyl acetate **17b** (0.36 g, 1 mmol) and dimethyl fumarate (0.3 g, 2.08 mmol) in dry, acid-free acetonitrile (20 ml) maintained at −4 °C was added tetrabutylammonium fluoride (TBAF) [1 ml of a 1.0 M solution in tetrahydrofuran (Aldrich), 1 mmol]. After 60 h at this temperature, a further aliquot of TBAF (1 ml) was added and stirring continued for another 60 h. The bulk of the solvent was evaporated and the residue purified by SG chromatography [hexanes–ethyl acetate (4:1)] to give the trans-*diester* **20** (0.21 g, 73%) which crystallized from pentane–ether (9:1) as a yellow solid, mp 96–97 °C; ν_{max}(KBr)/cm^{-1} 1735, 1460 and 1440; δ_H(400) 2.85 (1 H, dddd, *J* 16.0, 9.5, 2.6 and 1.9, 1-H_a), 2.98 (1 H, dddd, *J* 16.0, 9.5, 2.6 and 1.9, 4-H_a), 3.10 (1 H, dddd, *J* 16.0, 6.0, 1.6 and *ca.* 1.6, 1-H_b), 3.18 (1 H, partly obscured, dddd, *J* 16.0, 6.0, 1.6 and *ca.* 1.6, 4-H_b),

3.21 (1 H, ddd, *J* 9.5, 9.5 and 6.0, C*H*CO_2Me), 3.32 (1 H, ddd, *J* 9.5, 9.5 and 6.0, C*H*CO_2Me), 3.75 (6 H, s, 2 × OMe), 7.21 [1 H, dd, *J* 8.3 and 6.5, 8(7)-H], 7.23 [1 H, dd, *J* 8.3 and 6.5, 7(8)-H], 7.39 (1 H, d, *J* 6.5, 9-H) and 7.41 (1 H, d, *J* 6.5, 6-H); δ_C 22.9 [1(4)-CH_2], 25.5 [4(1)-CH_2], 41.6 [2(3)-*C*HCO_2Me], 41.8 [3(2)-*C*HCO_2Me], 52.2 (OMe), 52.3 (OMe), 111.1 (CH), 118.4 (9b-C), 118.5 (CH), 122.6 (CH), 123.7 (CH), 127.8 (9a-C), 150.7 (4a-C), 154.9 (5a-C), 174.0 (CO) and 174.4 (CO); *m/z* 288 (M^+, 28%), 257 (12), 228 (33), 196 (9), 169 (100), 144 (16) and 115 (10) (Found: C, 67.0; H, 5.9; M^+, 288.1000. $C_{16}H_{16}O_5$ requires C, 66.7; H, 5.6%; *M*, 288.0998).

Also isolated was a mixture of the [4 + 2] and [4 + 4] adducts **21** and **22**, R_f ~0.9, from this and the following reactions, which accounted for between 1–10% of the material balance. The two isomers could be separated by SG chromatography (hexanes) to give samples of the [4 + 4] *adduct* **22** as a pale yellow oil; ν_{max}(film)/cm^{-1} 1474 and 1452; δ_H(250) 3.41 (4 H, s, 2 × CH_2), 3.20 (4 H, s, 2 × CH_2) and 6.90–7.21 (8 H, m); *m/z* 288 (11%, M^+), 144 (100) and 115 (6) (Found: M^+, 288.1144. $C_{20}H_{16}O_2$ requires *M*, 288.1149) and the [4 + 2] *adduct* **21** as a yellow, unstable oil; ν_{max}(film)/cm^{-1} 1472 and 1450; δ_H(250)[16] 2.05–2.14 (2 H, m), 2.81–2.91 (2 H, m), 3.03 (2 H, s), 4.19 (1 H, d, *J* 3.0, =CH_a), 4.68 (1 H, d, *J* 3.0, =CH_b) and 7.20–7.71 (8 H, m); *m/z* 288 (17%, M^+), 144 (100) and 115 (15) (Found: M^+, 288.1157).

trans- and *cis*-Dimethyl 1,2,3,4-tetrahydrodibenzofuran-2,3-dicarboxylate 20 and 23

By the general procedure and on the same scale, reaction between the silyl acetate **17b** and dimethyl maleate for 48 h at −4 °C followed by addition of a further portion of TBAF (1 ml), continued stirring for 24 h and the usual work-up gave an unseparated 2:1 mixture of the trans- and cis-*diesters* **20** and **23** (0.20 g, 69%) as a pale solid, mp 94–99 °C; ν_{max}(KBr)/cm^{-1} 1736, 1460 and 1440; δ_H(400) 2.85–3.40 (6 H, m), 3.71 (1 H, s, *cis*-CO_2Me), 3.72 (1 H, s, *cis*-CO_2Me), 3.75 (4 H, 2 × *trans*-CO_2Me) and 7.19–7.43 (4 H, m); δ_C(*cis*-isomer **23**) 21.5 [1(4)-CH_2], 24.4 [4(1)-CH_2], 40.7 [2(3)-*C*HCO_2Me], 41.0 [3(2)-*C*HCO_2Me], 52.3 (OMe), 52.4 (OMe), 111.0 (9b-C), 111.2 (CH), 118.6 (CH), 122.5 (CH), 123.7 (CH), 128.0 (9a-C), 141.0 (4a-C), 151.8 (5a-C), 173.1 (CO) and 173.4 (CO), together with the resonances given in the foregoing experiment for the *trans*-isomer **20**; *m/z* 288 (M^+, 28%), 257 (11), 228 (39), 196 (8), 169 (100), 144 (12) and 115 (8) (Found: *M*, 288.0985).

Methyl 1,2,3,4-tetrahydrodibenzofuran-3- and -2-carboxylate 24 and 25

By the general procedure, reaction between the silyl acetate **17b** (1 mmol) and methyl acrylate (0.2 ml, 2 mmol) for 48 h followed by the addition of more TBAF (1 ml) and a further 48 h reaction period gave, after SG chromatography [hexanes–ethyl acetate (9:1)], an unseparated 2:1 mixture of the 3- and 2-*carboxylates* (**24** and **25**) (0.2 g, 87%) as a yellow, low-melting solid (mp ~30 °C); ν_{max}(film)/cm^{-1} 1740, 1650, 1620 and 1460; δ_H(400) 1.95–2.00 (1.33 H, m, 2-CH_2), 2.05–2.14 (0.66 H, m, 3-CH_2), 2.25–2.30 (1.33 H, m, 1-CH_2), 2.34–2.42 (0.66 H, m, 1-CH_2), 2.61–2.63 (0.66 H, m, 4-CH_2), 2.65–2.67 (1.33 H, m, 4-CH_2), 2.70–3.10 (1 H, m, C*H*CO_2Me), 3.74 (3 H, s, OMe), 7.11–7.16 (2 H, m), 7.31 (0.66 H, d, *J* 7.5), 7.33 (0.33 H, d, *J* 5.1), 7.34 (0.66 H, d, *J* 7.4) and 7.35 (0.33 H, d, *J* 5.3); δ_C(major 3-isomer **24**) 19.4, 25.6, 25.8 (all CH_2), 39.9 (*C*HCO_2Me), 51.9 (OMe), 110.9 (CH), 112.4 (C), 118.3, 122.3, 123.6 (all CH), 128.2, 151.9, 152.9, 154.6 (all C) and 174.9 (CO); (minor 2-isomer **25**) 22.4, 23.2, 25.4 (all CH_2), 39.5 (*C*HCO_2Me), 51.8 (OMe), 110.9 (CH), 111.4 (C), 118.4, 122.3, 123.3 (all CH), 128.3, 152.9, 154.9 (all C) and 174.3 (CO); *m/z* (mixture) 230 (M^+, 59%), 185 (7), 170 (100), 144 (59) and 115 (21) (Found: C, 73.0; H, 6.4; M^+, 230.0941. Calc. for $C_{14}H_{14}O_3C$, 73.0; H, 6.1%; *M*, 230.0943).

3- and 2-Acetyl-1,2,3,4-tetrahydrodibenzofuran 26 and 27

By the general procedure, reaction between the silyl acetate **17b** (0.72 g, 2 mmol), methyl vinyl ketone (0.56 g, 8 mmol) and TBAF (2 ml of a 1 M solution in tetrahydrofuran, 2 mmol) at −4 °C for 72 h with the addition of further aliquots of TBAF (2 ml) at 24 h intervals gave, after SG chromatography [hexanes–ethyl acetate (9:1)], a 4:1 mixture of the 3- and 2-*methyl ketones* **26** and **27** (0.33 g, 77%) as a yellow oil; ν_{max}(film)/cm^{-1} 1715 and 1450; δ_H(400) 1.85–2.28 (4 H, m), 2.29 (3 H, s, 2- and 3-MeCO), 2.68–2.71 (2 H, m), 2.75–3.05 (1 H, m, 2- and 3-CHCO), 7.17–7.31 (2 H, m), 7.40 (0.8 H, d, *J* 5.7, 3-isomer, 9-H), 7.41 (0.2 H, d, *J* 5.1, 2-isomer, 9-H), 7.42 (0.8 H, d, *J* 5.7, 3-isomer, 6-H) and 7.43 (0.2 H, d, *J* 5.3, 2-isomer, 6-H); δ_C(major 3-isomer **26**) 19.9, 25.0, 25.3 (all CH_2), 28.3 (*C*H_3CO), 48.0 (*C*HCO), 111.0 (CH), 112.1 (C), 118.5, 122.4, 123.4 (all CH), 128.0, 152.0, 155.0 (all C) and 209.1 (CO). Many resonances in the ^{13}C spectrum due to the minor 2-isomer **27** were coincident or obscured, but it was detected by resonances at δ_C 22.6 (CH_2), 22.8 (CH_2), 47.7, 118.7 and 123.6 (all CH). The mixture also showed *m/z* 214 (M^+, 71%), 199 (21), 171 (100), 144 (61) and 115 (17) (Found: M^+, 214.0975. $C_{14}H_{14}O_2$ requires *M*, 214.0994).

Crystal data for compound 26. Slow crystallisation of a concentrated solution of the mixture in pentane–ether gave a single crystal of the major 3-isomer **26**, mp 43–44 °C, suitable for X-ray analysis. Compound **26**, mp 43–44 °C, $C_{14}H_{14}O_2$, crystallized from pentane–ether in the monoclinic space group $P2_1/c$ (No. 14), with cell dimensions $a = 12.018(6)$, $b = 11.303(6)$, $c = 8.574(4)$ Å, $\beta = 100.19(5)°$, $U = 1146(1)$ Å (from centring angles for 25 reflections) determined using graphite-monochromated Mo-Kα X-radiation, $\lambda = 0.710\,73$ Å, $Z = 4$, $D_c = 1.241$ mg m^{-3}, $F(000) = 456$, μ(Mo-Kα) = 0.082 mm^{-1}, and an Enraf-Nonius CAD4 diffractometer, data collecting range $5 \leq 2\theta \leq 53°$, $+h$, $+k$, $\pm l$, 5% decay, which was corrected for during processing; 2397 unique reflections were measured, of which 2361 were used in all calculations. No corrections were required for absorption or extinction effects. The structure was solved by automatic direct methods[25] and refined on F^2 using SHELXL-93[26] with the non-hydrogen atoms allowed anisotropic thermal motion. Hydrogen atoms were initially placed in geometrically calculated positions and thereafter allowed to ride on their parent carbon atoms, with $U_{iso}(H) = xU_{eq}(C)$, where $x = 1.5$ for methyl H atoms and 1.2 for others. The weighting scheme $w^{-1} = \sigma^2(F_a^2) + (0.096P)^2 + 0.36P$, $P = 1/3[\max(F_a^2, 0) + 2F_c^2]$, led to final convergence with $wR(F^2) = 0.2309$ and conventional $R(F)^{46} = 0.0650$ for 145 refined parameters, GOF on $F^2 = 1.06$, maximum $\Delta/\sigma < 0.001$, maximum $\Delta\rho = 0.28$ e $Å^{-3}$. Fig. 1 was produced using SHELXTL/PC.†[27]

3- and 2-Cyano-1,2,3,4-tetrahydrodibenzofuran 28 and 29

Reaction, by the general procedure, between the silyl acetate **17b** (1 mmol), acrylonitrile (0.2 ml, 2 mmol) and TBAF (1 ml) in acetonitrile (10 ml) for 48 h at −4 °C followed by the addition of more TBAF (1 ml), a further 48 h at −4 °C and the usual work-up gave the *nitriles* **28** and **29** (0.18 g, 93%), in a 7:1 ratio as a colourless solid, mp 83–85 °C; ν_{max}(film)/cm^{-1} 2240, 1474 and 1451; δ_H(400) 2.10–2.29 (1.76 H, m, 2-CH_2, major 3-isomer), 2.30–2.37 (0.24 H, m, 3-CH_2, minor 2-isomer), 2.77 (0.88 H, ddddd, *J* 16.4, 6.1, 6.1, 2.0 and 2.0, 1-H_{ax}, major 3-isomer), 2.91 (0.88 H, ddddd, *J* 16.4, 6.1, 6.1, 2.0 and 2.0, 4-H_{ax}, major 3-isomer), 3.02–3.10 (0.24 H, m, 4-CH_2, minor 2-isomer), 3.14 (1.76 H, m, 1- and 4-CH_{eq}, major 3-isomer), 3.21 (0.88 H, ddd, *J* 8.7, 6.1 and 6.1, 2-CHCN, major 3-isomer) and 7.25–

† Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/55.

7.45 (4 H, m) (the resonances due to the remainder of the minor 2-isomer protons were partly obscured); δ_C(major 3-isomer **28**) 18.5 (CH_2), 25.5 (*C*HCN), 25.9, 27.0 (both CH_2), 111.1 (CH), 112.6 (C), 118.7 (CH), 121.2 (CN), 122.6, 124.0 (both CH), 127.7, 149.0 and 154.6 (all C); the minor isomer **29** could be detected by resonances at 18.5, 21.5, 24.6 (all CH_2), 25.1, 118.4, 123.9 (all CH) and 154.0 (C); *m/z* 197 (M^+, 44%), 163 (44), 144 (100) and 101 (40) (Found: C, 79.4; H, 5.7; N, 6.9; M^+, 197.0848. $C_{13}H_{11}NO$ requires C, 79.2; H, 5.6; N, 7.1%; *M*, 197.0841).

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