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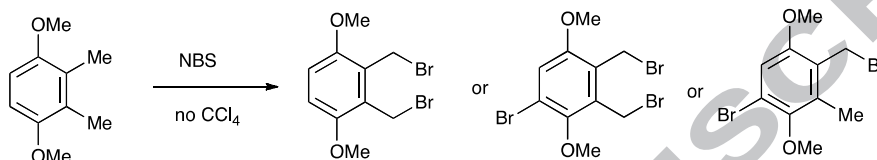
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Regioselective bromination of 1,4-dimethoxy-2,3-dimethylbenzene and conversion into sulfur-functionalised benzoquinones

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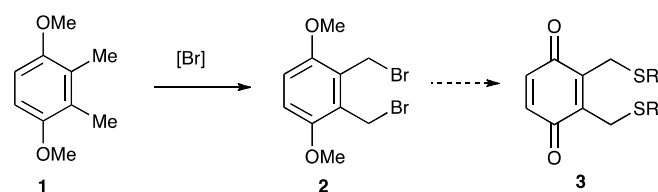
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ABSTRACT

The NBS bromination of 1,4-dimethoxy-2,3-dimethylbenzene has been examined under a variety of conditions in both 1,1,1-trichloroethane and benzotrifluoride. Four different bromination products have been isolated including the previously unknown 1-bromo-4-bromomethyl-2,5-dimethoxy-3-methylbenzene whose single crystal X-ray structure is presented. The synthetically useful 2,3-bis(bromomethyl)-1,4-dimethoxybenzene is readily prepared using either solvent and it has been converted into new sulfur-containing quinone derivatives

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In connection with our ongoing studies on electroactive compounds adsorbed onto metal surfaces,¹ we were interested in constructing simple thiol-tethered benzoquinones **3** and chose as a convenient starting material 2,3-bis(bromomethyl)-1,4-dimethoxybenzene **2** (Scheme 1). Although this compound was first obtained as early as 1959 as a minor byproduct in the monobromination of **1**,² and some nine years later in good yield by dibromination of **1**,³ these and all subsequent preparations of **2** have been conducted using *N*-bromosuccinimide (NBS) in carbon tetrachloride as solvent. Since this solvent is now essentially unavailable due to restrictions on its use under the Montreal Protocol, we were forced to examine alternative solvents and describe herein a detailed study on the regioselective bromination of **1** resulting in the identification of 1,1,1-trichloroethane and benzotrifluoride as suitable alternative solvents for formation of **2** as well as the formation, full characterisation and single crystal X-ray structure of a new dibromide isomeric with **2**. In addition, conversion of **2** into sulfur-functionalised benzoquinone derivatives is described.

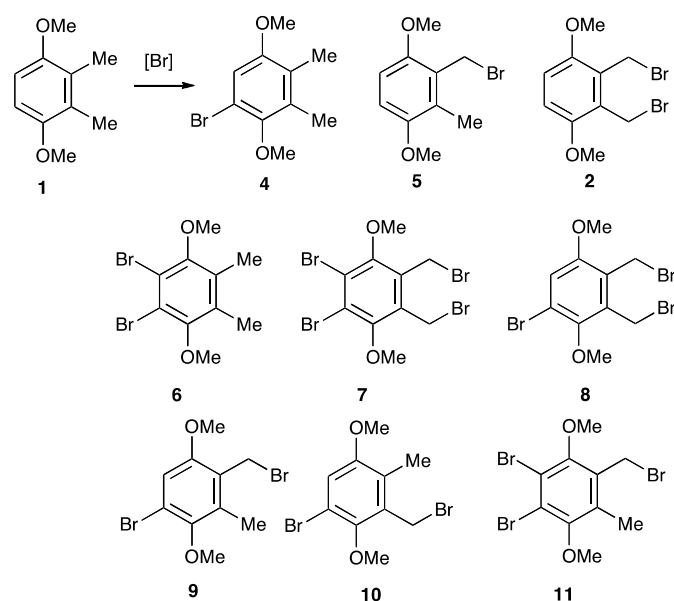


Scheme 1: Planned synthetic route

Because of the two activating methoxy groups, compound **1** is reactive towards electrophilic ring bromination as well as radical bromination of the two methyl groups and previous studies have reported the formation of various mono-, di- and tribrominated derivatives. The earliest derivative, the mono ring-brominated product **4** was reported in 1944 from reaction of **1** with bromine in chloroform,⁴ and is also formed by the reaction with bromine in acetic acid⁵ or hexafluoropropan-2-ol⁶ and with NBS in dichloromethane.⁷ In the first attempt at radical bromination,² reaction with NBS in the presence of benzoyl peroxide in boiling carbon tetrachloride for 1 h gave a 60% yield of the mono bromomethyl compound **5** accompanied by 9% of the dibromide **2**. It was noted that the NBS had to be dry otherwise ring bromination to give **4** would occur, and use of a sample of **1** slightly contaminated by the methoxyphenol resulting from incomplete methylation in its synthesis gave **4** as the only product in 60% yield. Most of the reported syntheses of **2** from **1** have used the conditions originally reported by Horner and coworkers³ involving at least 2 equivalents of NBS and catalytic benzoyl peroxide in boiling carbon tetrachloride to give the product in 71–99% yield,^{8–13} although initiation by AIBN¹⁴ and photochemically¹⁵ have also proved effective. The ring dibromo compound **6** has been prepared by treatment of **1** with two or more equivalents of bromine in chloroform,^{16–18} and this could then be further brominated on the two methyl groups to afford **7** using NBS in CCl₄.^{16,17} The first report of the tribromo compound **8** was in 2001 when it was formed in low yield by treatment of **1** with 2.5 equivalents of NBS with benzoyl peroxide in boiling carbon tetrachloride for 24 h,¹⁹ and its preparation on a 200 g scale was later reported using 4 equivalents of NBS in CCl₄ with visible light irradiation giving a 51% yield.²⁰ Neither of the possible unsymmetrical dibrominated derivatives **9** or **10** nor the

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remaining possible tribromo compound **11** have so far been reported.



Scheme 2: Possible brominated derivatives of **1**

We began by conducting a trial experiment in carbon tetrachloride using conditions similar to those reported by Horner and coworkers³ and were able to confirm that the major product was **2** (Table 1, entry 1). However NMR analysis of the crude reaction product showed the presence of two additional compounds which could be separated from **2** by column chromatography: the tribromide **8** and a dibromide resulting from one ring bromination and radical bromination of only one methyl group which was thus either **9** or **10**.²¹ In order to distinguish between these alternatives an HMBC study was carried out. Comparison of the ¹³C NMR spectra of **1**, **4**, **2** and **8** shows that ring bromination results in differentiation of the two C–OMe carbons with the one *ortho* to Br coming around 149 ppm while the one *meta* to Br comes at 154 ppm. Based on this pattern, the HMBC coupling of the CH₂Br protons at δ_{H} 4.57 with δ_{C} 154.0 but not 149.3, and the methyl protons at δ_{H} 2.37 with δ_{C} 149.3 but not 154.0 clearly favours structure **9** but this is not unambiguous since it depends on the assignment of the two C–OMe carbons.

Table 1: Bromination of **1** under different conditions

Entry	Solvent	Equiv NBS	Initiation method	Temp (°C)	Time (h)	Product % 2	composition % 8	% 9	% 4	Product isolated
1	CCl ₄	2.5	(PhCOO) ₂ (0.1 eq)	77	2.5	70	18	12	0	2 (31%)
2	MeCCl ₃	2.5	(PhCOO) ₂ (0.1 eq)	75	2.5	70	18	12	0	2 (40%)
3	MeCCl ₃	4.4	(PhCOO) ₂ (0.1 eq)	75	12		>80		0	8 (32%)
4	MeCCl ₃	2.5	visible irradiation	75	1				>80	4 (55%)
5	MeCCl ₃	2.5	visible irradiation	75	3			>80		9 (23%)
6	PhCF ₃	2.5	(PhCOO) ₂ (0.1 eq)	60	3	0	0	0	100	
7	PhCF ₃	2.5	(PhCOO) ₂ (0.1 eq)	60	20	0	65	35	0	
8	PhCF ₃	4.0	(PhCOO) ₂ (0.1 eq)	70	3	0	0	0	100	
9	PhCF ₃	4.0	(PhCOO) ₂ (0.03 eq)	102	3	33	33	33	0	
10	PhCF ₃	4.0	(PhCOO) ₂ (0.1 eq)	102	2.5	50	50	0	0	2 (35%)
11	PhCF ₃	4.0	UV irradiation	85	3	10	90	0	0	

More convincing evidence for structure **9** was provided by the observation of a weak HMBC coupling of the ring proton at δ_{H} 6.92 with the CH₂Br signal at δ_{C} 25.7 but not the methyl signal at δ_{C} 12.3. The matter was finally resolved by a single crystal X-ray diffraction study which confirmed the structure to be **9** (Figure 1).²²

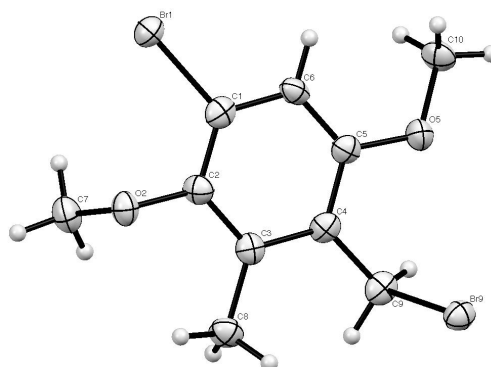


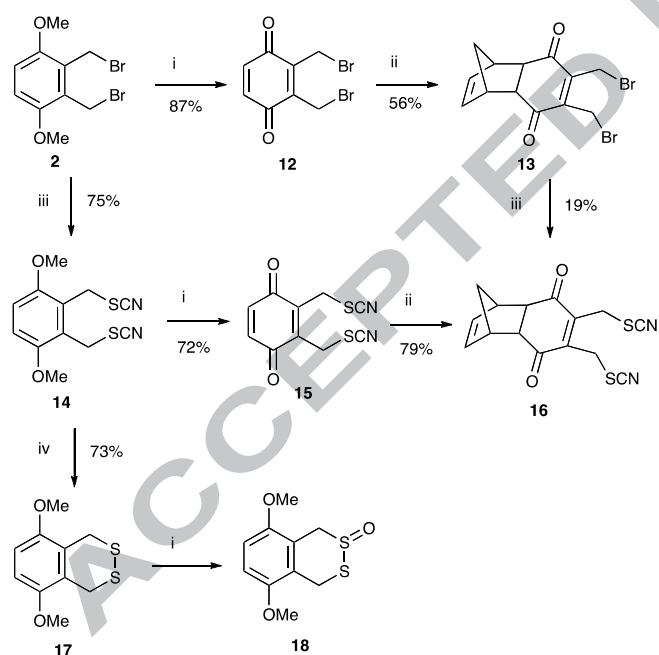
Figure 1: X-ray structure of **9** (ORTEP diagram at 50% level)

In the crystal structure the molecular dimensions are in good agreement with those determined for the tribromo compound **8**²⁰ and there are weak intermolecular OCH₂–H⁺–O and OCH₂–H⁺–BrCH₂ interactions, similar to but less extensive than those reported for **8**.

With each of the reaction products identified we examined the effect of varying the reaction solvent in the hope of identifying solvents which would allow the high yielding preparation of **2** from **1** and NBS but not suffer from the availability problems of CCl₄. Dichloromethane was discounted since it has been reported to give only the ring bromination product **4**,⁷ and this was also found to be the case for chloroform. In previous work where there was a problem of selectivity between ring and side-chain bromination in diethylthiazoles using NBS, we found 1,1,2-trichlorotrifluoroethane ("Arklone") to be a suitable substitute for CCl₄,^{23,24} but surprisingly this was not the case here. Compound **1** was recovered unreacted after prolonged treatment with 2.1 equiv. of NBS and either benzoyl peroxide or AIBN at reflux in this solvent. Two solvents were found that gave more promising results: 1,1,1-trichloroethane or methylchloroform (also a Montreal Protocol restricted solvent) and α,α,α -trifluorotoluene or benzonotrifluoride.²⁵ The results obtained using these are summarised in Table 1.

Simply substituting trichloroethane for CCl_4 gave an identical crude product composition and after chromatographic purification led to a slightly improved yield of **2** (entry 2). By varying the conditions with this solvent, conditions were found to maximise the yield of each product and thus isolate each of **8**, **9** and **4** (entries 3–5). Increasing the amount of NBS gave the tribromide **8** while ring bromination was favoured by using photochemical initiation rather than benzoyl peroxide with **4** formed after 1 h which reacted further to give **9** after 3 h. The initial attempt using benzotrifluoride and conditions otherwise similar to before gave only ring bromination (entry 6) and prolonging the reaction time (entry 7) led to **4** being further brominated to **8** and **9** but none of the desired dibromide **2** was formed. Increasing the amount of NBS (entry 8) had no effect and **4** was still the only product. Success was finally achieved by increasing the reaction temperature to the boiling point of 102°C , and conducting the reaction under reflux (entries 9 and 10) gave a substantial amount of **2** in a mixture with **8** from which it was readily isolated by recrystallisation. Finally, photochemical initiation was also tried in this solvent (entry 11) but this gave mainly the tribromide **8**.

Using benzotrifluoride, multigram quantities of compound **2** were prepared and so we have been able to investigate introducing sulfur functionality as well as unmasking the latent quinone. In connection with our previously reported method of directly constructing dihydrotetrathiafulvalenes by 1,3-dipolar cycloaddition to the strained double bond of norbornenes,²⁶ the formation of bicyclo[2.2.1] derivatives was also of interest (Scheme 3).



Scheme 3: Reagents and conditions (i) CAN, aq MeCN, rt; (ii) cyclopentadiene, MeCN, rt; (iii) KSCN, EtOH, reflux; (iv) NaBH_4 , EtOH/THF (1:20)

Oxidative removal of the *O*-methyl groups to give the quinone function was achieved by treatment with ceric ammonium nitrate (CAN) in aqueous acetonitrile¹² and this could be done before or after introduction of sulfur in the form of a thiocyanate group.²⁷ Thus the reaction of **2** with potassium thiocyanate in ethanol gave **14**,²¹ and CAN treatment of either **2**

or **14** gave the rather unstable quinones **12** and **15**,²¹ respectively, which were converted into their Diels Alder adducts **13** and **16**²¹ by reaction with cyclopentadiene. Conversion of **13** into **16** by reaction with KSCN was demonstrated but proceeded in low yield and the route from **2** via **14** and **15** to **16** is clearly preferable. It has been reported²⁴ that treatment of carbocyclic compounds bearing adjacent CH_2SCN groups with sodium borohydride results in reductive removal of cyanide and oxidative cyclisation of the resulting dithiol to give the six-membered ring 1,2-dithiin. This form is suitable for direct adsorption onto the surface of a metal such as gold. Since this reductive method is not compatible with the presence of a quinone, it was carried out with the methoxy groups still in place and **14** was converted into **17**²¹ in good yield. Unfortunately however attempted removal of the *O*-methyl groups from **17** using CAN as before instead resulted in *S*-oxidation to give the dithiin monosulfoxide **18** in impure form.²¹

In conclusion, conditions have been developed to obtain four different brominated products, including the previously unknown dibromide **9**, from reaction of compound **1** with *N*-bromosuccinimide in solvents other than the problematic CCl_4 . Benzotrifluoride is a satisfactory sustainable and non-environmentally damaging solvent for the production of the symmetrical dibromide **2**, and this product has been further transformed into several sulfur-containing intermediates aimed towards the synthesis of electroactive organic compounds suitable for direct adsorption on metal surfaces.

Supplementary data

Supplementary data (Detailed experimental procedures and copies of ^1H and ^{13}C NMR spectra for all new compounds) associated with this article can be found, in the online version, at <http://.....> These data include MOL files and InChIKeys of the most important compounds described in this article..

References and notes

- Jethwa, S. J.; Grillo, F.; Früchtel, H. A.; Simpson, G. J.; Treanor, M.-J.; Schaub, R.; Francis, S. M.; Richardson, N. V.; Aitken, R. A. *Chem. Commun.* **2014**, 50, 10140–10143.
- McHale, D.; Mamalis, P.; Marcinkiewicz, S.; Green, J. J. *Chem. Soc.* **1959**, 3358–3362.
- Horner, L.; Subramaniam, P. V.; Eiben, K. *Liebigs Ann. Chem.* **1968**, 714, 91–111.
- Smith, L. I.; Tess, R. W. H. *J. Am. Chem. Soc.* **1944**, 66, 1523–1525.
- Trost, B. M.; Shen, H. C.; Dong, L.; Surivet, J.-P.; Sylvain, C. *J. Am. Chem. Soc.* **2004**, 126, 11966–11983.
- Eberson, L.; Hartshorn, M. P.; Radner, F.; Persson, O. *J. Chem. Soc., Perkin Trans. 2* **1998**, 59–70.
- Wu, Z.; Harutyunyan, S. R.; Minnaard, A. J. *Chem. Eur. J.* **2014**, 20, 14250–14255.
- Ardecky, R. J.; Kerdesky, F. A. J.; Cava, M. P. *J. Org. Chem.* **1981**, 46, 1483–1485.
- Kotha, S.; Kuki, A. *Chem. Lett.* **1993**, 299–302.
- Eskildsen, J.; Christensen, T.; Reenberg, T.; Larsen, U.; Christensen, J. B. *Org. Prep. Proced. Int.* **2000**, 32, 398–400.
- Utey, J. H. P.; Ramesh, S.; Salvatella, X.; Szemerits, S.; Motevalli, M.; Nielsen, M. F. *J. Chem. Soc., Perkin Trans. 2* **2001**, 153–163.
- Mazzini, F.; Galli, F.; Salvadori, P. *Eur. J. Org. Chem.* **2006**, 5588–5593.
- Schneider, P.; Riedl, R.; Tigges, M.; Gitzinger, M.; Pieren, M.; Levi, A.; Sephton, M.; Schellhorn, B.; Zueger, P.; Brand, M.; Gygas, D.; Spies, P. *PCT Int. Appl. WO 2014/118361* (2014).
- Honek, J. F.; Mancini, M. L.; Belleau, B. *Tetrahedron Lett.* **1983**, 24, 257–260.
- Jansen, R. J.; de Gelder, R.; Rowan, A. E.; Scheeren, H. W.; Nolte, R. J. M. *J. Org. Chem.* **2001**, 66, 2643–2653.

16. Mendez-Rojas, M. A.; Ejsmont, K.; Watson, W. H. *J. Chem. Crystallogr.* **2002**, 32, 177–184.
17. Sandulache, A.; Silva, A. M. S.; Cavaleiro, J. A. S. *Monatsh. Chem.* **2003**, 134, 551–563.
18. Poloukhine, A.; Popik, V. V. *J. Org. Chem.* **2006**, 71, 7417–7421.
19. Rinke, K.; Grunert, R.; Bednarski, P. J. *Pharmazie*, **2001**, 56, 763–769.
20. Hammershøj, P.; Riis, E.; Christensen, J. B. *Acta Crystallogr., Sect. E* **2005**, 61, o2997–o2998.
21. **9**: colourless crystals, mp 83–84 °C (Found 324.9265. $C_{10}H_{13}^{79}Br^{81}BrO_2$ (M+H) requires 324.9262; found 322.9289. $C_{10}H_{13}^{79}Br_2O_2$ (M+H) requires 322.9282); δ_H 6.92 (1 H, s, CH), 4.57 (2 H, s, CH₂), 3.85 (3 H, s, OCH₃), 3.75 (3 H, s, OCH₃) and 2.37 (3 H, s, CH₃); δ_C 154.0 (C-5), 149.3 (C-2), 133.4 (C-3), 125.1 (C-4), 117.9 (C-1), 113.1 (C-6), 60.6 (5-OCH₃), 56.2 (2-OCH₃), 25.7 (CH₂Br) and 12.3 (CH₃); HMBC study shows correlation of δ_H 6.92 with δ_C 25.7, correlation of δ_H 4.57 with δ_C 154.0, and δ_H 2.37 with δ_C 149.3; m/z 327 ($^{81}Br_2$ -M+H, 5%), 326 ($^{81}Br_2$ -M, 4), 325 ($^{81}Br^{79}Br$ -M+H, 10), 324 ($^{81}Br^{79}Br$ -M, 7), 323 ($^{79}Br_2$ -M+H, 6), 322 ($^{79}Br_2$ -M, 3), 245 (^{79}Br -M-Br, 89) and 243 (^{81}Br -M-Br, 100). **12**: brown oil (Found 292.8811. $C_8H_7O_2^{79}Br_2$ (M+H) requires 292.8813); δ_H 6.86 (2 H, s, CH) and 4.38 (4 H, s, CH₂); δ_C 184.2 (C-1, C-4), 141.0 (C-2, C-3), 136.4 (C-5, C-6) and 19.5 (CH₂Br); m/z (CI) 297/295/293 (M^+ , 10/20/9 %), 215/213 (72/78), 134 (35), 123 (100) and 105 (76). **13**: yellow crystals, mp 68–71 °C (Found 358.9290. $C_{13}H_{13}O_2^{79}Br_2$ (M+H), requires 358.9292); δ_H 6.10 (2 H, t, J = 2, 9,10-H), 4.32 and 4.23 (4 H, AB pattern, J = 10, CH₂Br), 3.58 (2 H, m, 1,8-H), 3.34 (2 H, m, 2,7-H), 1.55 (1 H, half AB pattern of t, J = 9, 1.8, 11-H *syn*) and 1.46 (1 H, half AB pattern of m, J = 9, 11-H *anti*); δ_C 196.1 (C-3, C-6), 146.4 (C-4, C-5), 135.2 (C-9, C-10), 49.8 (C-1, C-8 or C-2, C-7), 49.1 (C-11), 48.5 (C-1, C-8 or C-2, C-7) and 20.6 (CH₂Br); m/z (CI) 363/361/359 (M^+ , 10/22/12 %), 297/295/293 (30/62/30), 281/279 (50/45), 135 (50) and 66 (100). **14**: grey solid, mp 100–102 °C (Found 303.0232. $C_{12}H_{12}N_2O_2NaS_2$ (M+Na) requires 303.0238); δ_H 6.91 (2 H, s, CH), 4.36 (4 H, s, CH₂) and 3.86 (6 H, s, CH₃); δ_C 151.6 (C-1, C-4), 123.1 (C-2, C-3), 112.3 (SCN), 111.8 (C-5, C-6), 56.0 (OCH₃) and 29.4 (CH₂); m/z (ES) 303 (M+Na, 100 %) and 222 (8). **15**: brown solid, mp 65–67 °C; δ_H 6.98 (2 H, s, CH) and 4.15 (4 H, s, CH₂); δ_C 184.1 (C-1, C-4), 139.3 (C-2, C-3), 136.8 (C-5, C-6), 111.4 (SCN) and 28.1 (CH₂). **16**: brown oil (Found 339.0233. $C_{15}H_{12}N_2O_2NaS_2$ (M+Na) requires 339.0238); δ_H 6.16 (2 H, t, J = 1.8, 9,10-H), 3.99 (4 H, d, J = 1.5, CH₂SCN), 3.63 (2 H, m, 1,8-H), 3.41 (2 H, dd, J = 2.4, 1.5, 2,7-H), 1.60 (1 H, half AB pattern of t, J = 9, 1.8, 11-H *anti*) and 1.51 (1 H, half AB pattern of m, J = 9, 11-H *syn*); δ_C 196.1 (C-3, C-6), 144.8 (C-4, C-5), 135.3 (C-9, C-10), 111.5 (SCN), 50.3 (C1, C-8 or C-2, C-7), 49.3 (C-11), 48.4 (C1, C-8 or C-2, C-7) and 29.0 (CH₂SCN); m/z (ES) 339 (M+Na, 100%). **17**: yellow solid, mp 123–130 °C (Found 229.0359. $C_{10}H_{13}O_2S_2$ (M+H) requires 229.0357); δ_H 6.71 (2 H, s, CH), 3.99 (4 H, s, CH₂) and 3.78 (6 H, s, CH₃); δ_C 151.1 (C-5, C-8), 123.5 (C-4a, C-8a), 107.6 (C-6, C-7), 55.8 (OCH₃) and 28.5 (C-1, C-4); m/z (CI) 229 (M+H, 85 %), 228 (M^+ , 54), 165 (85), 164 (100) and 151 (86). **18**: brown liquid (Found, 267.0128. $C_{10}H_{12}O_3NaS_2$ (M+Na) requires 267.0126); δ_H 6.874 (1 H, s, CH), 6.869 (1 H, s, CH), 4.57 (1 H, s), 4.53 (1 H, s), 4.21 (1 H, d, J = 14), 3.95 (1 H, d, J = 14), 3.84 (3 H, s, CH₃) and 3.83 (3 H, s, CH₃); δ_C 152.5 (C-5 or C-8), 149.3 (C-8 or C-5), 129.3 (C-4a or C-8a), 125.5 (C-8a or C-4a), 110.8 (C-6 or C-7), 110.0 (C-6 or C-7), 56.2 (-OCH₃), 55.9 (-OCH₃), 51.4 (C-1) and 25.0 (C-4); m/z (ES) 267 (M+Na, 100 %), 179 (15) and 142 (8).
22. Crystal data for **9**, $C_{10}H_{12}Br_2O_2$, M_r = 324.01, colourless prism, orthorhombic, space group $P2_12_12_1$, a = 4.2831(10), b = 15.175(4), c = 17.227(4) Å, V = 1119.7(5) Å³, Z = 4, D_c 1.922 Mg m⁻³, T = 93(2) K, R_1 = 0.0347 and wR_2 = 0.0782 for 1751 reflections [I > $2\sigma(I)$] and 130 parameters. Data were recorded using a Rigaku XtaLB P200, MoK α radiation (confocal optic, λ 0.71075 Å) and Saturn detector. The structure was solved by direct methods and refined using full-matrix least-squares methods. Crystallographic data (excluding structure factors) for the structure have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-1443548. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; email: deposit@ccdc.cam.ac.uk.
23. Aitken, K. M.; Aitken, R. A. *Tetrahedron* **2008**, 64, 4384–4386.
24. Aitken, K. M.; Aitken, R. A.; MacGregor, C. I.; Traore, M. D. M.; Slawin, A. M. Z. *J. Chem. Crystallogr.* **2015**, 45, 461–465.
25. Benzotrifluoride has previously been reported as an effective solvent for benzylic bromination using NBS, but the examples described did not include any where there was the risk of competing ring bromination. See: Suarez, D.; Laval, G.; Tu, S.-M.; Jiang, D.; Robinson, C. L.; Scott, R.; Golding, B. T. *Synthesis* **2009**, 41, 1807–1810.
26. Aitken, R. A.; Hill, L.; Lightfoot, P. *Tetrahedron Lett.* **1997**, 38, 7927–7930.
27. Oda, M.; Zhang, Y.; Thanh, N. C.; Hayashi, S.; Zuo, S.; Kuroda, S. *Heterocycles* **2006**, 68, 1031–1041.

- Four different bromination products can be prepared without using CCl_4
- Benzotrifluoride is a suitable CCl_4 replacement for radical bromination
- The X-ray structure of a new dibromination product is presented
- The target dibromide is converted to sulfur-containing quinone derivatives