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Bromination by means of sodium monobromoisocyanurate (SMBI)

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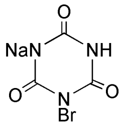
A variety of aromatic compounds with both activating and deactivating substituents were brominated with sodium monobromoisocyanurate (SMBI) **1**, diethyl ether, diethyl ether–methanesulfonic acid, trifluoroacetic acid, or sulfuric acid were employed as solvents. Thus nitrobenzene was conveniently brominated in sulfuric acid, benzene was readily monobrominated in diethyl ether–methanesulfonic acid, and phenol was selectively brominated at the *ortho* position under mild conditions in refluxing diethyl ether. With substituents that are easily protonated, trifluoroacetic acid may be employed as solvent in the reaction with **1**, in contrast NBS was ineffective in trifluoroacetic acid. This renders **1** a superior reagent relative to NBS. In addition to aromatics, alkenes, ketones and esters were also brominated with **1**. Diethyl malonate was brominated with **1** and then subjected to a Bingel reaction with NaH to afford the desired methanofullerene in reasonable yield.

Introduction

Bromination is a fundamental transformation in organic chemistry and brominated aromatics are of paramount importance as building blocks in organic synthesis.

The development of modern coupling reactions,[1] such as Tamao–Kumada, Suzuki–Miyaura, Migita–Kosugi–Stille, Negishi, Hiyama–Hatanaka, Sonogashira, and Mizorogi–Heck reactions, has greatly increased the demand for brominated aromatics as starting materials.

Although a variety of brominating reagents capable of brominating both electron-rich and electron-deficient target molecules[2] are available ranging from Br_2 itself to *N*-bromosuccinimide (NBS), there is a continuing need to utilize new and improved brominating reagents and improved reaction conditions to provide superior selectivity.[3]



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Recently, sodium monobromoisocyanurate **1** (SMBI),[4] a bromonium-fixed reagent similar to NBS and dibromoisocyanurate (DBI), has become commercially available as a white powder. SMBI is almost odorless, practically insoluble in most organic solvents, and therefore easily handled in the laboratory. As a urea trimer, compound **1** is also expected to be environmentally friendly. Following the discovery of SMBI as a brominating reagent, we have undertaken a systematic study of the scope of bromination, in particular with aromatics, and found that it selectively monobrominates both electron-deficient aromatics and electron-rich substrates in reasonable yields as well as ketones and esters. In this paper, we report facile, regioselective bromination of arenes, as well as alkene and carbonyl compounds under appropriate reaction conditions.

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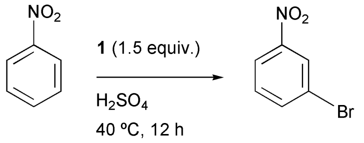
Results and discussion

Selective monobromination of aromatics

For electrophilic aromatic substitution, the arene substrates are classified into three groups: 1) those bearing electron withdrawing, deactivating substituents such as nitrobenzene, 2) those that are moderately active like parent benzene itself and 3) the highly reactive arenes such as phenol.

The products obtained were identified by their ^1H NMR spectra in comparison with those of commercially available authentic samples (see Experimental section).

Electron-deficient aromatics such as nitrobenzene and methyl benzoate can be brominated by bromine in sulfuric acid in the presence of silver nitrate.[5] NBS and DBI have also been applied successfully for this purpose in sulfuric acid.[6] Reagent **1**, which readily dissolves in sulfuric acid, was employed in bromination of nitrobenzene in sulfuric acid. The reaction proceeds smoothly at around 40 °C as shown in eqn. (1). Bromination data for the electron-deficient aromatics are summarized in Table 1 and eqn. (2).



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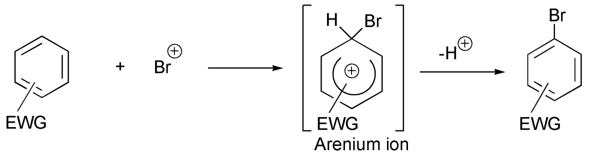


EWG=electron-withdrawing group

(2)

Attempted monobromination of *o*-dichlorobenzene and trifluoromethylbenzene under these conditions resulted in multibromination (see below).

Table 1 Bromination of electron-deficient aromatics by means of **1**[a]

Entry	Substrate	Product	Yield (%)
1	Dimethyl phenylphosphonate	Dimethyl *m*-bromophenylphosphonate	91
2	Benzaldehyde	*m*-Bromobenzaldehyde	70[b]
3	Methyl benzoate	Methyl *m*-bromobenzoate	70[c]
4	Benzoic acid	*m*-Bromobenzoic acid	40
5	Dimethyl isophthalate	Dimethyl 5-bromoisophthalate	75
6	Nitrobenzene	*m*-Bromonitrobenzene **2**	95
7	*m*-Dinitrobenzene	1-Bromo-3,5-dinitrobenzene	65

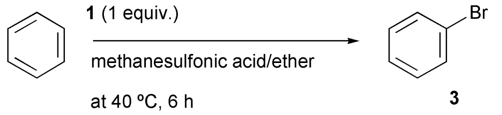
[a] Reaction conditions: at 40 °C for 12 h in sulfuric acid. The ratio of substrate and **1** was 1 : 1.5. [b] Dibrominated products were obtained in 17% yield. [c] Dibrominated products were obtained in 22% yield.

Table 2 Bromination of intermediate reactive aromatics by means of **1**

Entry	Substrate[a]	Product	Yield (%)
1	Anisole	*p*-Bromoanisole	75
2	Toluene	Bromotoluene[b]	60
3	Benzene	Bromobenzene **3**	79
4	*o*-Dichlorobenzene	1-Bromo-3,4-dichlorobenzene	60
5	*m*-Dichlorobenzene	1-Bromo-2,4-dichlorobenzene	65
6	Benzonitrile[c]	*m*-Bromobenzonitrile	40
7	Trifluoromethylbenzene[c]	*m*-Bromotrifluoromethylbenzene	85

[a] In methanesulfonic acid–ether mixed solvent, unless otherwise noted. [b] A mixture of *o*- and *p*-isomers in the ratio of 60 : 40. [c] In trifluoroacetic acid. In sulfuric acid, not only monobromide and multibromides but also hydrated products were produced.

For anisole, benzene, and toluene the aforementioned conditions applied to bromination of nitrobenzene are unsuitable and bromination is typically carried out with Br_2 in the presence of iron.[7] However, NBS in combination with methanesulfonic acid[8] has been reported recently to be a useful brominating reagent. We, therefore, studied the reaction of **1** with benzene in this solvent system and found it to be comparable with NBS (54% *vs*. 79%, respectively) (eqn. (3)). We postulate that the mechanism of this reaction proceeds through activated **1** *via* protonation at the carbonyl group, for example see **4** in eqn. (4)



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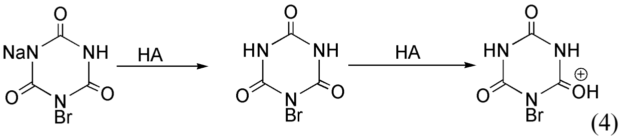
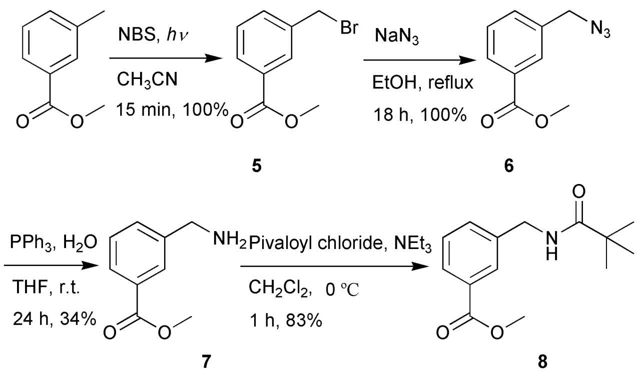


(4)

4

The molar ratio of methanesulfonic acid : **1** was changed from 0.5 to 3 and the highest yield of bromobenzene was obtained at the 1 : 1 ratio. When the ratio was larger than 1, further bromination occurred (up to 15% of the mixture). Thus keeping the reagent to acid ratio at 1 : 1 ensures that the reaction can be controlled at the monosubstitution level. The data are summarized in Table 2. Dichlorobenzenes successfully afforded monobrominated products under these conditions. The reaction did not proceed in the solvents ether or CH_2Cl_2 without the addition of acid.

The data indicate that there is no appreciable difference in reactivity and selectivity between **1** and NBS. We believe that this is because of a leveling effect due to the high reactivity of the arene substrate and "Br^+" species generated. However, if both reactivities are appropriately reduced, then, the difference between the two reagents (**1** *versus* NBS) can be studied. Therefore aminomethylbenzoic acid derivative **8** was chosen as a substrate, because it is moderately more reactive than the electron-deficient benzoic acid, but is less reactive than toluene; moreover it has several sites for protonation which would reduce its reactivity further in strong acids. The intriguing compound **8** was prepared by the sequence shown in Scheme 1 and the overall yield from methyl *m*-methylbenzoate was 28%.



Scheme 1

The reactivity of "Br^+" generated from **1** or NBS can be manipulated *via* the acidity of solvents, as mentioned above. Therefore, **8** was first subjected to reactions with **1** and NBS in sulfuric acid as solvent. Reagent **1** gave the monobrominated product **9a** together with multibrominated products (eqn. (5)), while NBS exhibited more regioselectivity towards monobromination. The result showed that in the acidic media **1** produces a more reactive (less selective) electrophile ("Br^+") relative to that *via* NBS. Since the optimum reaction conditions for the reaction of **1** with aromatics are already determined, we examined the effect of temperature and acidity on the reaction of **8** and **1**. Changing the reaction temperature in the range of 0 to 40 °C did not have much effect on the reaction, but changing the solvent from sulfuric acid to trifluoroacetic acid had a pronounced effect, as shown in Table 3.

The reaction of **1** with **8** in trifluoroacetic acid gave an entirely different product from that in sulfuric acid. The product was isolated and characterized by several spectroscopic methods including ^1H NMR spectroscopy and was determined to be **9b**, a regioisomer of **9a**. Under identical reaction conditions no reaction was observed for NBS with **8**. It was found that NBS in trifluoroacetic acid produces less bromine[9] than **1** as shown in Fig. 1. Although the mechanism for bromine

Table 3 Bromination of **8** by **1** and NBS

Entry	Reagent[a]	Solvent	Time/h	Temp.	Yield (%)[b] **9a**	**9b**	Dibromide
1	**1** (1.5)	H_2SO_4	2	rt	45(40[c])	0	41
2	NBS(1.5)	H_2SO_4	5	rt	50	0	13
3	**1** (1.1)	H_2SO_4	3	0 °C	47	0	26
4	**1** (1.5)	Methanesulfonic acid–ether	24	40 °C	0	0	0
5	**1** (1.5)	CF_3COOH	4	rt	0	51(41[c])	0
6	NBS(1.5)	CF_3COOH	24	rt	0	0	0

[a] The amount of reagent (eq.) is shown in parentheses. [b] Obtained by gas chromatography. [c] Isolated yield.

Table 4 Bromination of phenol by means of **1** in CH_2Cl_2

Entry	Ratio[a]	Time/h	Conv.[b] (%)	Product yield (%)[c] *o*-(**10**)	*p*-(**11**)	2,4-(**12**)	2,6-(**13**)	2,4,6-(**14**)	Ratio[d] *o*-/*p*-
1	0.5	1	32(71)[e]	69	19	3	6	3	79 : 21
2	0.5	2.5	32	69	19	3	5	4	78 : 22
3	1.0	1	55(70)[e]	65	13	5	9	7	84 : 16
4[f]	1.0	1	28	78	10	4	5	3	89 : 11
5[g]	1.0	1	77(100)[e]	46	26	10	13	5	64 : 36
6	2.0	1	89	45	15	9	17	17	75 : 25
7	3.0	1	100	29	8	9	21	34	78 : 22
8	4.0	5	100					100	—

[a] The ratio of **1** and phenol. [b] Based on the phenol. [c] Based on the conversion. Determined by GC. [d] The ratio of *o*-bromophenol and *p*-bromophenol. [e] Yield of bromides, based on **1** in the parentheses. [f] Diethyl ether was used as solvent. [g] NBS was used instead of **1**.

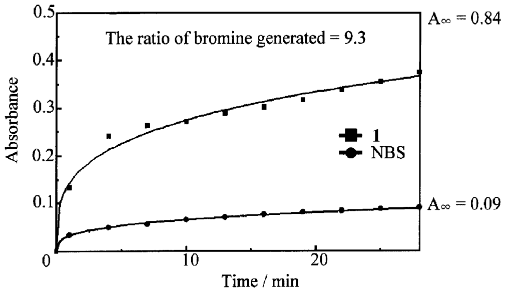
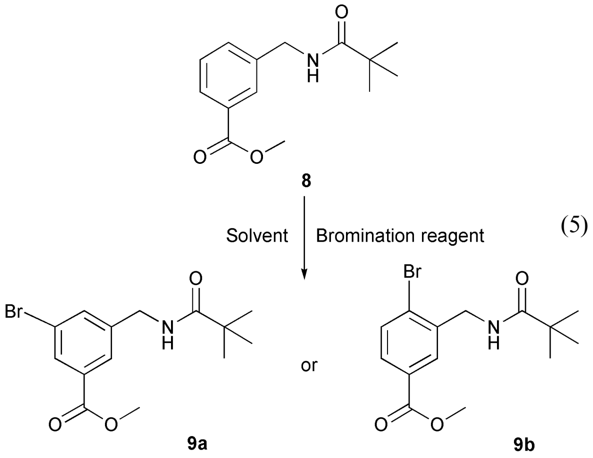


Fig. 1 Time-course of bromine formation in trifluoroacetic acid. Absorbance at 405 nm is plotted. [**1**] = [NBS] = 4.4 × 10^{-2} mol L^{-1}.



(5)

formation is not known in this system, it is believed that NBS generates the Br^+ cation more slowly than **1** or does not produce bromine through the cation.

The formation of **9a** is considered to stem from protonation of the amide-nitrogen and/or carboxylate-oxygen thus making the substituent(s) more electron-withdrawing and hence attack is directed to the 3-position (*meta* to both strong deactivating groups). On the other hand, **8** does not appear to be appreciably protonated in the relatively weak trifluoroacetic acid, resulting in bromination on the relatively activated *ortho*-position. Consequently for the preparation of the isomer **9a**, NBS or **1** in sulfuric acid is useful as a brominating reagent, while **1** in trifluoroacetic acid is highly recommended, when the isomer **9b** is the target.

Trifluoromethylbenzene and benzonitrile were unreactive to **1** in ether containing methanesulfonic acid. Therefore, trifluoroacetic acid was used as a solvent for these substrates. Both gave the desired monobromides *via* bromination by **1** as shown in Table 2 (entries 6 and 7).

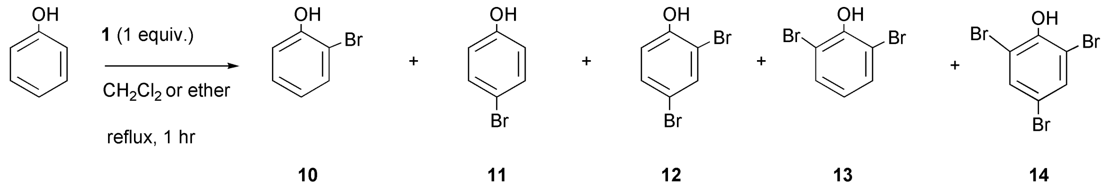
Phenol, an electron-rich aromatic compound, can easily react with bromine in water and the reaction is apt to give tribromophenol, and monobromination is difficult to control. Among several methods to make monobromophenol,[10] Pearson's method is practical for *o*-bromophenol, although it has to be carried out at −70 °C with bromine.[10b] On the other hand, recently Oberhauser reported a convenient method to make *p*-bromophenol.[10d]

As shown in Table 4 and eqn. (6), the reaction of **1** and phenol was found to give *o*-bromophenol selectively. NBS, soluble in both dichloromethane and diethyl ether, was used instead of **1**, but *o*-/*p*-isomer ratio (64 : 36) was lower than that for **1** under the same reaction conditions (see Table 4, entry 5).

Monobromination of phenol with **1** was usually complete within 1 h and further heating did not change the products composition. The ratio of starting materials influences the product ratio or selectivity. The conditions outlined in entry 2 in Table 4 are recommended as the optimized ones to synthesize *o*-bromophenol selectively.

The effect of water on this reaction was significant. When the reaction was carried out under sufficiently anhydrous conditions, it did not proceed at all. Hence, it is recommended to add a few drops of water to the solvent (100 mg per 100 mL of solvent), even though the commercially available **1** has 10% water in the crystal or powder. The data infer that water contained in the reagent is not active in the reaction.

p-Cresol was also brominated to give 2-bromo-4-methylphenol in 37% yield under the same conditions as above. Hydroquinone, however, was not only brominated, but also oxidized to 2-bromo-*p*-benzoquinone **15** in 15% yield



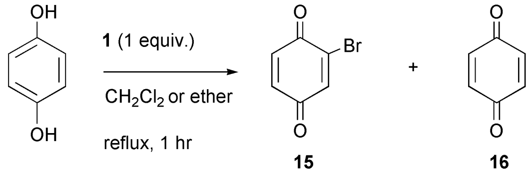
(6)

Table 5 Bromination of **18** by **1** and subsequent Bingel reaction

	18		
Entry	R$_1$	R$_2$	Yield of **19** (%)[a]
1	COOEt	COOEt	49(37)
2	COOMe	COOMe	12 (2)
3	CN	COOMe	16 (4)

[a] The monoadduct yield was based on fullerene used. All runs also afforded bisadducts whose yields are given in parentheses.

(eqn. (7)).[11] During the reaction, the starting hydroquinone was also oxidized to *p*-benzoquinone **16** exclusively.

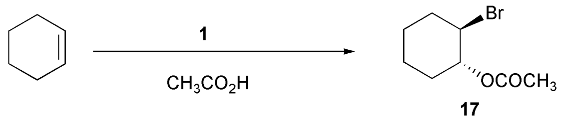


(7)

N,N-Dimethylaniline and aniline reacted with **1** under the same conditions as those used for phenol and gave *p*-bromoanilines in 45 and 50% yields, respectively.

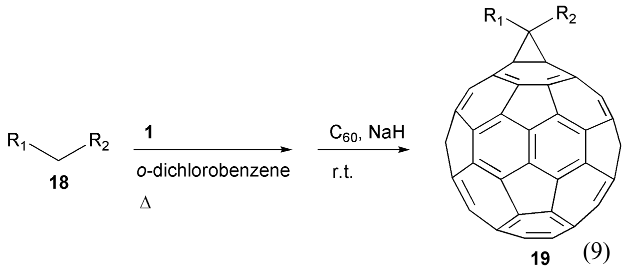
Bromination of alkene, ketone, and ester functionalities

Cyclohexene was readily brominated by **1** in acetic acid to give *trans*-1-acetoxy-2-bromocyclohexane **17** in 70% yield (eqn. (8)).[12]



(8)

The α-position of cyclohexanone was readily brominated by **1**. Diethyl malonate was converted to the corresponding bromomalonate by **1**, and with a subsequent Bingel reaction[13] was designed as a one-pot reaction: *i.e.*, the malonate was brominated in *o*-dichlorobenzene by **1** *in situ* with stirring overnight, [60]fullerene and NaH were added, and the reaction mixture was stirred for several hours.[13] Filtration of the precipitates gave the crude reaction products (eqn. (9)). The results are summarized in Table 5.



(9)

Conclusion

Commercially available powdered **1** has proven to be a useful as a bromination reagent. Electron-rich, intermediate reactivity, and electron-deficient aromatics were brominated by **1** in diethyl ether, in diethyl ether containing methanesulfonic acid or in trifluoroacetic acid, and in sulfuric acid, respectively: *i.e.*, phenol was selectively brominated at the *o*-position in refluxing diethyl ether. Benzene was readily monobrominated in diethyl ether containing methanesulfonic acid. Nitrobenzene was conveniently converted to bromonitrobenzene in sulfuric acid. The reactivity of **1** can be lowered by protonation in sulfuric acid, trifluoroacetic acid or methanesulfonic acid–ether, and using ether containing a trace of water. It is noteworthy that **1** can be used in trifluoroacetic acid while NBS cannot. Alkenes, ketones and esters were also brominated by **1**. Diethyl malonate was brominated by **1** and then subjected to Bingel reaction with NaH to afford a methanofullerene in reasonable yield.

Experimental

General

Gas mass spectra were taken by a GCMS spectrometer with a gas chromatograph equipped by an SE capillary column. HPLC analysis was carried out with an HPLC apparatus (ODS, methanol). NMR spectra were recorded on a 500 MHz FT NMR spectrometer using TMS as internal standard.

Reagent **1** was kindly provided by Nissan Chemical Ind., Co. Ltd., and used without further purification. Other materials and reagents were commercially available and were used without further purification.

Bromination of nitrobenzene in sulfuric acid (general procedure)

Nitrobenzene (1.23 g, 10 mmol) and **1** (3.45 g, 15 mmol, 1.5 equiv.) were dissolved in sulfuric acid (9.8 g) and heated to 40 °C for 12 h with stirring. After cooling, the reaction mixture was poured on to ice–water (20 mL), and extracted by ether (10 × 3 mL). The combined organic extracts were washed with 5% NaOH (10 mL) and then with water (10 × 3 mL), dried over Na$_2$SO$_4$, and distilled under reduced pressure. Yield of *m*-bromonitrobenzene **2** was 1.95 g (95%). ^{1}H NMR (CDCl$_3$):[14] **2**, δ 7.45 (1H, t, $J = 8.2$ Hz), 7.84 (1H, d, $J = 8.2$ Hz), 8.19 (1H, d, $J = 8.2$ Hz), 8.40 (1H, s); MS(M$^+$, *m*/*z*), 201, 203.

^{1}H NMR spectra (CDCl$_3$) of products from dimethyl phenylphosphonate, benzaldehyde, methyl benzoate, dimethyl isophthalate, *m*-dinitrobenzene: dimethyl *m*-bromophenylphosphonate,[15] δ 3.78 (6H, d, $J = 2.1$ Hz), 7.37 (1H, dt, $J = 4.9$ & 10.4 Hz), 7.71 (1H, d, $J = 29.6$ Hz), 7.74 (1H, t, $J = 4.9$ Hz), 7.93 (1H, d, $J = 29.6$ Hz); MS(M$^+$, *m*/*z*), 264, 266. *m*-Bromobenzaldehyde,[16] δ 7.43 (1H, t, $J = 7.9$ Hz), 7.77 (1H, d, $J = 7.9$ Hz), 7.82 (1H, d, $J = 7.9$ Hz), 8.03 (1H, s), 9.97 (1H, s); MS(M$^+$, *m*/*z*), 184, 186. Methyl *m*-bromobenzoate,[16] δ 3.93 (3H, s), 7.32 (1H, t, $J = 8.0$ Hz), 7.69 (1H, d, $J = 8.0$ Hz), 7.98 (1H, d, $J = 7.6$ Hz), 8.18 (1H, s); MS(M$^+$, *m*/*z*), 214, 216. Dimethyl 5-bromoisophthalate,[17] δ 8.36 (2H, s), 8.61 (1H, s); MS(M$^+$, *m*/*z*), 272, 274. 1-Bromo-3,5-dinitrobenzene,[18] δ 8.71 (2H, s), 9.01 (1H, s).

Bromination of benzene in ether containing methanesulfonic acid (general procedure)

Benzene (0.78 g, 10 mmol) and **1** (2.30 g, 10 mmol, 1 equiv.) were heated at 40 °C (bath temperature) in ether (5 mL) containing methanesulfonic acid (0.96 g, 10 mmol, 1 equiv.) for 6 h under stirring. After cooling, the reaction mixture was poured on to ice water (20 mL), and extracted with ether (10 × 3 mL).

The combined organic solution was washed by 5% NaOH (20 mL) and then with water (10 × 3 mL), dried over Na_2SO_4, and distilled by a ball distillation apparatus. Yield of bromobenzene **3** was 1.25 g (79%). ^1H NMR ($CDCl_3$): **3**, δ 7.24 (2H, t, J = 8.2 Hz), 7.29 (1H, t, J = 8.2 Hz), 7.50 (2H, d, J = 8.2 Hz).

Products from anisole, toluene, *o*-dichlorobenzene, and *m*-dichlorobenzene were also identified by the comparison of their ^1H NMR spectra with those of authentic samples. ^1H NMR ($CDCl_3$): *p*-bromoanisole,[16] δ 3.81 (3H, s), 6.79 (2H, d, J = 8.8 Hz), 7.38 (2H, d, J = 8.8 Hz). *o*-Bromotoluene,[16] δ 2.40 (3H, s), 7.04 (1H, t, J = 8.2 Hz), 7.20 (1H, t, J = 8.2 Hz), 7.23 (1H, d, J = 8.2 Hz), 7.52 (1H, d, J = 8.2 Hz). *p*-Bromotoluene,[16] δ 2.30 (3H, s), 7.05 (2H, d, J = 8.2 Hz), 7.37 (2H, d, J = 8.2 Hz). 1-Bromo-3,4-dichlorobenzene,[16] δ 7.32 (1H, d, J = 8.6 Hz), 7.35 (1H, d, J = 8.6 Hz), 7.62 (1H, s). 1-Bromo-2,4-dichlorobenzene,[19] δ 7.12 (1H, d, J = 8.6 Hz), 7.47 (1H, s), 7.55 (1H, d, J = 8.6 Hz).

Synthesis of methyl *m*-(*N*-pivaloylaminomethyl)benzoate 8

Methyl *m*-methylbenzoate (5.12 g, 34 mmol) and NBS (7.29 g, 1.2 equiv.) in acetonitrile (680 mL) were irradiated with a 400 W high-pressure mercury lamp in a Pyrex vessel for 15 min at room temperature. The reaction mixture was concentrated under reduced pressure. The residue was added to excess hexane and the precipitates were removed. The solution was evaporated to give a yellow liquid (7.82 g, 100%). ^1H NMR ($CDCl_3$): **5**, δ 3.93 (3H, s), 4.52 (2H, s), 7.43 (1H, t, J = 7.7 Hz), 7.59 (1H, d, J = 7.9 Hz), 7.97 (1H, d, J = 7.7 Hz), 8.07 (1H, s).

Compound **5** (7.82 g, 34 mmol) and NaN_3 (8.87 g, 4.0 equiv.) were heated in EtOH (140 mL) for 18 h under reflux and with stirring. The reaction mixture was filtrated, evaporated, poured into water (50 mL), and extracted with ether (50 × 3 mL). The combined organic extracts were washed with water (50 × 3 mL), dried over $MgSO_4$, and evaporated. Yield of compound **6** was 6.52 g (100%). ^1H NMR ($CDCl_3$): **6**, δ 3.94 (3H, s), 4.41 (2H, s), 7.47 (1H, t, J = 7.7 Hz), 7.53 (1H, d, J = 7.7 Hz), 8.00 (1H, s), 8.02 (1H, d, J = 7.5 Hz).

Compound **6** (3.82 g, 20 mmol), PPh_3 (5.76 g, 1.1 equiv.), and H_2O (3.60 g, 10 equiv.) were dissolved in THF (770 mL) and the mixture was stirred at room temperature for 24 h. It was poured into 1 M HCl (100 mL), and extracted with ether (100 mL). The aqueous phase was made basic by 5% NaOH (50 mL) and then extracted with ether (100 × 3 mL), dried over $MgSO_4$, and evaporated. The product was separated by GPC. Yield of compound **7** was 1.12 g (34%). ^1H NMR ($CDCl_3$): **7**, δ 3.92 (3H, s), 3.94 (2H, s), 7.41 (1H, t, J = 7.6 Hz), 7.53 (1H, d, J = 7.7 Hz), 7.92 (1H, d, J = 7.7 Hz), 8.01 (1H, s).

Pivaloyl chloride (3.27 g, 2.0 equiv.) was added to **7** (2.23 g, 14 mmol) and NEt_3 (2.73 g, 2.0 eq.) in dichloromethane (400 mL) at 0 °C for 1 h with stirring. The reaction mixture was poured into water (50 mL), and extracted with ether (50 × 3 mL). The combined organic extracts were washed with 1 M HCl (100 × 2 mL), aqueous NaCl (100 × 2 mL), dried over $MgSO_4$, and evaporated. The product was separated by silica gel column chromatography. Yield of **8** was 2.79 g (83%). ^1H NMR ($CDCl_3$): **8**, δ 1.24 (9H, s), 3.92 (3H, s), 4.49 (2H, d, J = 5.9 Hz), 5.97 (1H, s), 7.41 (1H, t, J = 7.5 Hz), 7.48 (1H, d, J = 7.9 Hz), 7.93 (1H, s), 7.95 (1H, d, J = 7.5 Hz).

Bromination of 8 and moderately electron-deficient aromatics by means of 1

Reagent **1** (14 mg, 0.6 mmol, 1.5 equiv.) was added to **8** (0.10 g, 0.4 mmol) dissolved in sulfuric acid (4 mL) and the mixture was stirred at room temperature for 2 h. It was then poured onto ice– water (20 mL), and extracted with $CHCl_3$ (50 × 3 mL). The combined organic extract was washed with 5% $Na_2S_2O_3$ (50 mL) and then with water (50 mL), dried over $MgSO_4$, and evaporated. The product was separated by GPC. Yield of **9a** was 52 mg (40%). ^1H NMR ($CDCl_3$): **9a**, δ 1.25 (9H, s), 3.92 (3H, s), 4.45 (2H, d, J = 5.9 Hz), 5.99 (1H, s), 7.59 (1H, s), 7.85 (1H, s), 8.07 (1H, s). Anal. Calcd. C, 51.23%; H, 5.53%; N, 4.27%. Found C, 50.92%; H, 5.43%; N, 4.17%.

The same reaction in trifluoroacetic acid gave **9b** in 54 mg (41% isolated yield). ^1H NMR ($CDCl_3$): **9b**, δ 1.24 (H, s), 3.90 (3H, s), 4.53 (2H, d, J = 5.9 Hz), 6.15 (1H, s), 7.63 (1H, d, J = 8.3 Hz), 7.80 (1H, dd, J = 2.0 & 8.4 Hz), 7.98 (1H, d, J = 2.2 Hz). Anal. Found C, 51.50%; H, 5.75%; N, 3.99% for C, 51.23%; H, 5.53%; N, 4.27%.

Benzonitrile and trifluoromethylbenzene also gave the monobromides by the reaction in trifluoroacetic acid: *m*-bromobenzonitrile,[16] δ 7.36 (1H, t, J = 8.0 Hz), 7.60 (1H, dt, J = 1.4 & 8.0 Hz), 7.75 (1H, dt, J = 1.4 & 8.0 Hz), 7.80 (1H, d, J = 1.4 Hz). *m*-Bromo(trifluoromethyl)benzene,[16] δ 7.37 (1H, t, J = 8.0 Hz), 7.57 (1H, d, J = 8.0 Hz), 7.69 (1H, d, J = 8.0 Hz), 7.78 (1H, s).

Bromination of phenol in CH_2Cl_2 or ether (general procedure)

Phenol (1.0 g) and **1** (0.5 to 3 equiv.) were heated in CH_2Cl_2 (40 mL with a drop of water) under reflux. After the prescribed period, the reaction mixture was cooled, filtered, passed through a short column of sodium thiosulfate, and then analyzed by gas chromatography (GC), using naphthalene as an internal standard. The products were identified by comparison with authentic samples:[16] Actually, *o*-bromo- (**10**), *p*-bromo-(**11**), 2,4-dibromo- (**12**), 2,6-dibromo- (**13**), and 2,4,6-tribromophenol (**14**), showed ^1H NMR peaks at δ 5.53 (1H, s), 6.80 (1H, dt, J = 1.5 & 7.9 Hz), 7.02 (1H, dd, J = 1.5 & 8.2 Hz), 7.23 (1H, dt, J = 1.5 & 7.9 Hz), 7.44 (1H, dd, J = 1.5 & 8.3 Hz), 4.79 (1H, s), 6.73 (2H, d, J = 8.9 Hz), 7.34 (2H, d, J = 8.9 Hz), 5.49 (1H, s), 6.91 (1H, d, J = 8.9 Hz), 7.33 (1H, dd, J = 2.5 & 8.9 Hz), 7.60 (1H, d, J = 2.5 Hz), 5.86 (1H, s), 6.71 (1H, t, J = 8.0 Hz), 7.44 (2H, d, J = 7.9 Hz), 5.88 (1H, s) and 7.59 (2H, s), respectively. MS(M^+, *m*/*z*) for **10** (or **11**), **12** (or **13**), and **14** were 172 and 174, 250, 252, and 254, 328, 330, 332, and 334, respectively.

Other products from *p*-cresol and hydroquinone show the following data: ^1H NMR ($CDCl_3$): 2-bromo-4-methylphenol,[16] δ 5.37 (1H, s), 6.91 (1H, d, J = 8.3 Hz), 7.02 (1H, dd, J = 1.5 & 8.3 Hz), 7.27 (1H, d, J = 1.5 Hz). **15**,[16] δ 6.84 (1H, dd, J = 2.1 & 10.3 Hz), 6.98 (1H, d, J = 10.3 Hz), 7.32 (1H, d, J = 2.1 Hz). **16**,[16] δ 6.98 (4H, s).

N,*N*-Dimethylaniline and aniline were brominated under the same conditions. ^1H NMR ($CDCl_3$): *p*-bromo-*N*,*N*-dimethylaniline,[16] δ 2.92 (6H, s), 6.59 (2H, d, J = 8.8 Hz), 7.29 (2H, d, J = 8.8 Hz); *p*-bromoaniline, δ 4.10 (2H, s), 6.56 (2H, d, J = 7.5 Hz), 7.23 (2H, d, J = 7.5 Hz).

Reaction of 1 with cyclohexene

Cyclohexene (0.41 g, 5.0 mmol) and **1** (1.74 g, 7.5 mmol, 1.5 equiv.) were stirred in acetic acid (50 mL) at room temperature for 7 h. The reaction mixture was poured on to ice water (50 mL), and extracted with ether (50 × 3 mL). The combined organic extract was washed with 5% $Na_2S_2O_3$ (10 mL), 10% $NaHCO_3$ (100 × 5 mL) and then with water (100 × 3 mL), dried over Na_2SO_4, and evaporated. Yield of *trans*-1-acetoxy-2-bromocyclohexane[12] **17** was 0.77 g (70%). ^1H NMR ($CDCl_3$): **17**, δ 1.39 (3H, m), 1.75 (2H, m), 1.87 (1H, m), 2.07 (3H, s), 2.13 (1H, m), 2.36 (1H, m), 3.96 (1H, m), 4.89 (1H, m).

Bromination of cyclohexanone

Cyclohexanone (1.96 g, 20 mmol) and **1** (6.90 g, 30 mmol, 1.5 equiv.) were heated in ether solvent (30 mL) containing methanesulfonic acid (2.88 g, 30 mmol, 1.5 equiv.) at 40 °C for 24 h with stirring. After cooling, the reaction mixture was poured onto ice–water (20 mL), and extracted with ether (50 × 3 mL). The combined organic extract was washed with 5% NaOH (20 mL) and then with water (50 × 3 mL), dried over Na_2SO_4, and distilled by a ball distillation apparatus. Yield of

2-bromocyclohexanone was 1.11 g (31%), although gas-chromatographic yield was 72%. ^{1}H NMR (CDCl$_3$): 2-bromocyclohexanone,[20] δ 1.73 (1H, m), 1.81 (1H, m), 1.95 (1H, m), 2.02 (1H, m), 2.24 (1H, m), 2.34 (2H, m), 2.99 (1H, m), 4.45 (1H, m).

Bingel reaction through bromination of diethyl malonate by 1

Diethyl malonate **18** (32 mg, 0.2 mmol) and **1** (46 mg, 0.2 mmol) were heated to 40 °C in *o*-dichlorobenzene (10 mL) for 24 h with stirring. After cooling, C_{60} (72 mg, 0.1 mmol) and NaH (0.1 g, excess) in *o*-dichlorobenzene (10 mL) were added to the reaction mixture. After stirring for 2 h at room temperature, the mixture was evaporated and subjected to column chromatography (silica gel, toluene). Yield of methanofullerene **19** was 43 mg (49%). ^{1}H NMR (CDCl$_3$): **19**,[13] δ 1.49 (6H, t, J = 7.2 Hz), 4.57 (4H, q, J = 7.0 Hz).

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