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Smiles-type free radical rearrangement of aromatic sulfonates and sulfonamides: syntheses of arylethanols and arylethylamines

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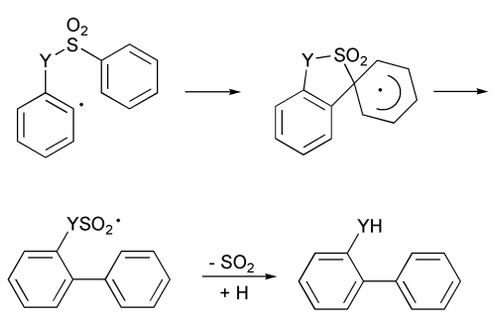
Smiles-type free radical rearrangements of arenesulfonates and arenesulfonamides are exploited for synthetic purposes. 4-Substituted benzenesulfonates cause Smiles-type rearrangement only when substituted by an electron withdrawing group. Therefore, *ipso*-attack by an alkyl radical on arenesulfonates takes place in an electrophilic manner. Arenesulfonamides rearrange only when the amide nitrogen is substituted by an alkoxycarbonyl group, due to the electron withdrawing nature of this group. Sulfonates and the *N*-ethoxycarbonylsulfonamide derivatives of naphthalene, quinoline, and thiophene cause more rearrangement and show synthetic utility. Aromatic amino acid analogues were synthesized by Smiles-type rearrangement with moderate yields. The radical Smiles-type rearrangement of sulfonate and sulfonamide derivatives can be a useful synthetic route when we understand the electronic character of these reactions.

Introduction

The ionic Smiles rearrangement[1] has a broad utility in the organic syntheses of aromatic compounds. However, Smiles-type free radical rearrangement has rarely been observed in previous synthetic studies. Aromatic sulfonates and sulfonamides are readily available substrates that are expected to yield phenols or aromatic amines. Motherwell and Pannell,[2] Ryokawa and Togo,[3] and Caddick *et al.*[4] reported the syntheses of biphenyl derivatives by radical Smiles-type rearrangements of aryl radicals, and they discussed the effect of the *ipso*-substitution on the ring and the conformational effect of the amide moiety on the Smiles-type rearrangement (Scheme 1).



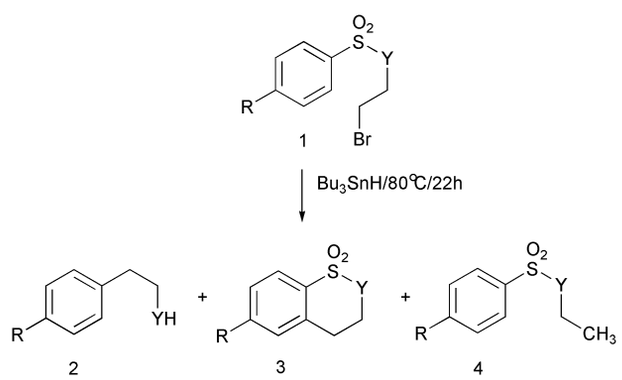
Scheme 1

Although a vinyl radical can be a substrate for Smiles-type rearrangement in some cases,[5] rearrangement starting from an alkyl radical has been reported only for some sulfonates[6] and sulfonamides[7] and only a few synthetic discussions have covered the structure–reactivity relationship.

In free radical *ipso*-substitution, the position substituted by the sulfone or the sulfoxide group is more reactive than non-substituted or thio-substituted aromatics[6,8] and we have studied the free radical rearrangement of aromatic sulfonates and sulfonamides. In this paper, we report the Smiles-type radical rearrangement of arenesulfonates and arenesulfonamides, where the expected products are 2-arylethanols and 2-arylethylamine derivatives including aromatic α-amino acid analogues. The rearrangement is triggered by free radical attack at the *ipso*-position of the sulfonates or sulfonamides in a nucleophilic manner. *N*-Ethoxycarbonylsulfonamide derivatives yield 20–76% of the rearranged products although the free forms of sulfonamide (SO_2NH-) are not suitable substrates for the Smiles-type rearrangement.

Results and discussion

Para-substituted benzenesulfonyloxyethyl bromides, **1a**–**1c** are expected to yield the corresponding 2-phenylethanols, **2a**–**2c** by a Smiles-type rearrangement. Similarly, sulfonamide **1d** and its derivatives, **1e** and **1f** are expected to yield 2-phenylethylamine derivatives, **2d**–**2f** *via* the radical rearrangement (Scheme 2).



Scheme 2

The sulfonates or the sulfonamides in benzene were treated with tributyltin hydride and the reaction conditions were kept identical throughout all the reactions described in this paper. The tributyltin hydride was added slowly over a period of 10 hours using a syringe pump under reflux, and then the reaction mixture was refluxed for a further 12 hours.

The *para*-substituted benzenesulfonyloxyethyl radical from the bromides (**1**) gave Smiles-type rearrangement products (**2**) as well as *ortho*-substitution products (**3**) and reduction products (**4**) in varying yields (Table 1). *Para*-substituted 2-phenylethanols, **2b** and **2c** were formed by *ipso*-substitution followed by the loss of sulfur dioxide and hydrogen abstraction from the tin hydride. Free radical substitution at the *ortho*-position gave the cyclisation products **3**, and the direct reduction of the radical intermediate with tributyltin hydride gave reduction products **4**. As shown in Table 1, the radical reactions yielded 4-chlorophenylethanol (**2b**) (8%) and 4-cyanophenyl-

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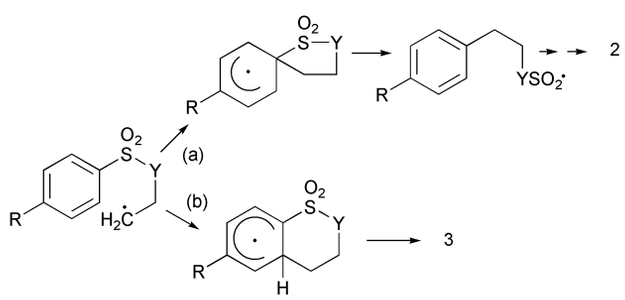
Table 1 Free radical reaction of benzenesulfonyl derivatives

Bromide	R	Y	Yield (%) 2	3	4	2 : 4
1a	CH_3	O	0.0	22	43	0.0
1b	Cl	O	8.0	13	37	0.22
1c	CN	O	31	8.0	38	0.82
1d	Cl	NH	0.0	15	49	0.0
1e	Cl	NMe	0.0	30	21	0.0
1f	Cl	NCO_2Et	16	20	44	0.34

Table 2 Free radical reaction of naphthalene- and quinoline-sulfonyl derivatives

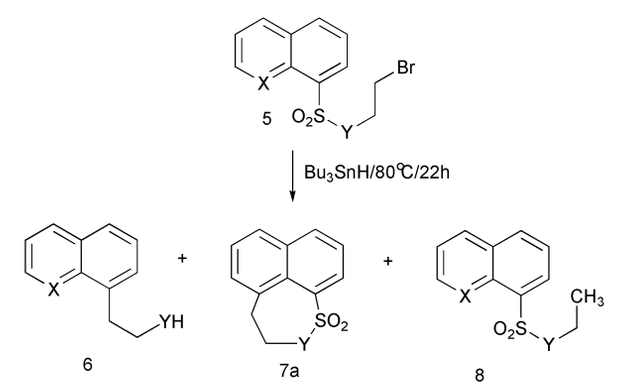
Bromide	X	Y	Yield (%) 6	7	8	6 : 8
5a	CH	O	53	2.0	12	4.4
5b	N	O	63	0.0	14	4.5
5c	CH	NCO_2Et	51	0.0	13	3.9
5d	N	NCO_2Et	76	0.0	10	7.6



Scheme 3

ethanol (**2c**) (31%). The carbamate derivative **2f** (16%) was formed in poor yield, but there were no rearrangement products from bromides **1a**, **1d** and **1e**. These substitution effects indicate that the radical Smiles-type rearrangement takes place through an *ipso*-substitution characterized by nucleophilic attack of the radical centre (Scheme 3). The radical intermediate giving **3** is considered to aromatise in one of two reported processes. One is the reaction with the tin hydride to produce molecular hydrogen and the substrate radical,[9] and the other is the reaction with AIBN to produce the (AIBN)-H radical.[10] Therefore, Smiles-type rearrangement is not a practical synthetic process for phenylethyl alcohols and phenylethylamines, even under the high dilution conditions described here.

Bromides with larger aromatic systems, such as the 1-naphthyl or 8-quinolyl moieties, gave better results, as shown in Scheme 4 and Table 2. Only the sulfonate **5a** gave the cyclisation product **7a** resulting from *peri*-substitution, and its structure was assigned from ^{1}H-NMR. The protons on the ring bearing the sulfonate group resonate downfield, δ 8.36 (J = 1.4 and 7.4 Hz); 8.08 (J = 1.2 and 8.4 Hz), and both of these appear as a double-doublet. The alternative structure resulting from *ortho*-substitution leaves two hydrogens on the same ring, which would result in no *meta*-hydrogen being available for long-range coupling to induce the double-doublet.

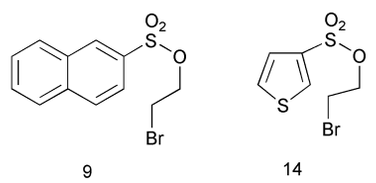


Scheme 4

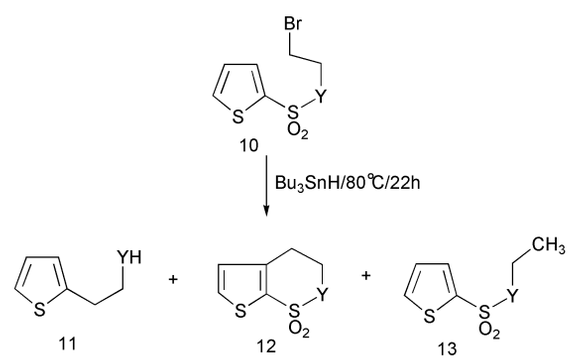
Table 3 Free radical reaction of thiophenesulfonyl derivatives

Bromide	Y	Yield (%) 11	12	13	11 : 13
10a	O	74	9.0	13	5.7
10b	NMe	Trace	0.0	42	~0
10c	NCO_2Et	51	0.0	13	3.9

The rearrangement becomes a major reaction process in the cases of 1-naphthyl or 8-quinolyl derivatives (**5a**–**5d**). However, the 2-naphthyl derivative **9** gave a complex mixture of products, which contained only 4% of the rearrangement product, 2-(2-naphthyl)-ethanol (Scheme 4).



The 2-thiophenesulfonyl derivatives (**10a** and **10c**) gave reasonable yields of the rearranged products **11a** and **11c** (Scheme 5 and Table 3), whereas the 3-thiophenesulfonyl derivative (**14**) gave the rearranged product, 2-(3-thienyl)-ethanol, in poor yield (5%), along with a complex mixture .



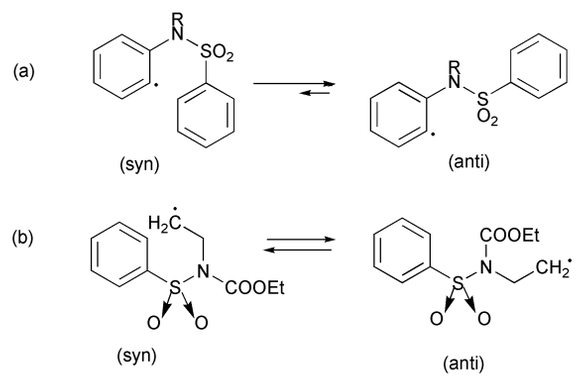
Scheme 5

N-(2-bromoethyl)-4-chlorophenylsulfonamides gave the Smiles-type rearrangement product only when the amide nitrogen was substituted by an ethoxycarbonyl group (**1f**). Throughout the phenyl, naphthyl, and thiophenyl sulfonamide derivatives, the free N–H forms gave either no yield or poor yield of the rearranged products. This property was also reported for the *ortho*-(benzenesulfonamidyl)-phenyl radical[3] and was accounted for by the distance between the radical centre and the *ipso*-position. Lower population of the *syn*-conformer in the present study is predicted from an analogy with the reported case of benzoanilide (Scheme 6a).[11] The corresponding *N*-methyl derivatives **1e** and **10b** do not improve the rearrangement process, and this behaviour cannot be explained by the conformational population effect of the intermediate radical. The substitution of sulfonamide with the ethoxycarbonyl group (**1f**, **5c**, **5d** and **10c**) gave better yields of the rearranged product. Simple molecular model inspection and MOPAC (PM3) calculations[12] suggest that the *syn*-form is less stable (Scheme 6b) due to the Coulomb repulsion between the sulfonyl oxygen and the ethoxycarbonyl group, though the rearrangement requires the *syn*-conformation. Experimental results, however, show that substitution of the amide nitrogen

Table 4 Free radical reaction of *N*-ethoxycarbonyl-sulfonamide derivatives

Bromide	Product yield (%) 16	17	16 : 17
15a	25	31	0.80
15b	18	41	0.44
15c	21[a]	6.6[a]	3.10

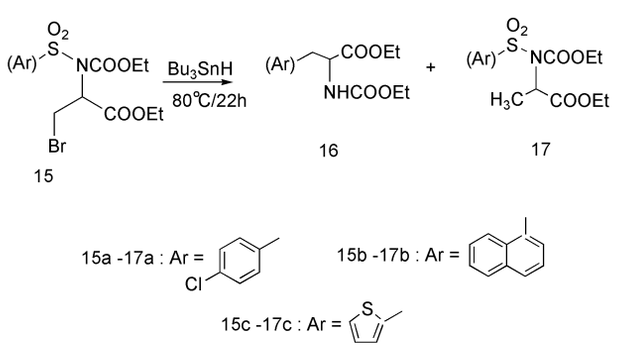
[a] Most of the starting material remained intact.



Scheme 6

by an ethoxycarbonyl group leads to Smiles-type rearrangement as the main radical process. This must be due to the electron withdrawing effect of the ethoxycarbonyl group, and this concept is in accord with the comparable reactivity of the sulfonate derivatives and the corresponding *N*-ethoxycarbonylamide derivatives. Thus, corresponding sulfonate derivatives and *N*-ethoxycarbonylsulfonamide derivatives show comparable yields of Smiles-type rearrangement products; **1b** (8.0%) and **1f** (16%), **5a** (53%) and **5c** (51%), **5b** (63%) and **5d** (76%), **10a** (74%) and **10c** (51%).

Amides **5c**, **5d**, and **10c** containing the *N*-ethoxycarbonyl group give reasonable yields of the rearrangement products (51–76%), and we attempted the radical rearrangement of esters **15a**–**15c**, which contain β-ethoxycarbonyl-substituted radical centres, because the expected rearrangement products, **16a**–**16c**, are analogues of aromatic α-amino acids such as tyrosine, tryptophane, and histidine. However, reactions under the same conditions as for **1d** resulted in rather poor yields of the rearrangement products (**16**) (Scheme 7 and Table 4) and no *ortho*-cyclisation took place. One of the reasons of the results must be the steric hindrance of the ester group near the radical centre for both *ipso*- and *ortho*-substitution, and another reason may be the reduction of the nucleophilicity of the radical centre by the ester substitution.



Scheme 7

The trends seen in the reactions of the sulfonates and sulfonamides indicate a nucleophilic *ipso*-attack of the alkyl radical on the aromatic system. The formation rate of the reduction products must essentially be the same for all of the reactions except in the case of **15a**–**c**, since the reaction centre is located far from the aromatic moiety. This means that the formation of the reduction products, **4**, **8** and **13** can be an internal clock for other radical processes, and the ratio [rearrangement product] : [reduction product] is an intrinsic index of the ease of Smiles-type radical rearrangement. Benzene derivatives (**1a**–**1f**) give smaller values of **2 : 4**, and rearrangement is a minor process in this system. The rather higher ratios of **6 : 8**, **11a : 13a**, and **11c : 13c** indicate that position-1 on naphthalene, position-8 on quinoline and position-2 on thiophene are susceptible to radical *ipso*-substitution.

The present experimental results show us the scope and the limitations of Smiles-type free radical rearrangement as a synthetic utility, and also that radical *ipso*-substitution is controlled by a polar effect . Thus the 5-*exo* cyclisation leading to the rearrangement and the 6-*exo* cyclisation leading to the *ortho*-substitution take place competitively in the present systems. We have seen that the benzene derivative is not suitable for this type of transformation ($ArSO_2XCH_2CH_2Br$ to $ArCH_2$-CH_2XH) but that naphthalene and heteroaromatic systems such as thiophene and quinoline are suitable. These features must be a consequence of a low-lying LUMO to accept nucleophilic free radicals and the easy break of aromaticity by the formation of intermediates. Larger π-systems or heteroaromatics are favourable for the free radical Smiles-type rearrangement and they may be promising synthetic substrates if we keep the factors described in this paper in mind and seek an alternative non-harmful method of free radical generation.

Experimental

All the ^{1}H-NMR spectra were measured by a JEOL AL-400 spectrometer (400 MHz) in deuteriochloroform. Chemical shifts and coupling constants are recorded in δ-values and Hz respectively. ^{13}C-NMR spectra were measured by a Bruker AVANCE-600 spectrometer (150 MHz). IR spectra were measured by a HORIBA FT-700 spectrometer in chloroform of 0.1 mm thickness. High resolution mass spectra were measured by a JEOL SX-162A spectrometer by FAB ionization unless otherwise mentioned using 3-nitrobenzyl alcohol as matrix. Preparative TLC was performed on Merck Kieselgel 60PF_{254} plate (20 × 20 × 0.2 cm).

Preparation of the starting materials

a) 2-Bromoethylarenesulfonates. One of the arenesulfonates (6.0×10^{-3} mol) and 2-bromoethanol (649 mg, 5.2×10^{-3} mol) were dissolved in 10 ml of dry dichloromethane under nitrogen atmosphere. Triethylamine (1.4 ml, 1.0×10^{-2} mol) was added dropwise to the mixture under ice-cooling and stirred overnight under cooling. Diethyl ether (30 ml) was added and the mixture washed twice with 40 ml 2 M hydrochloric acid and 40 ml saturated sodium chloride solution. Evaporation of the solvents after drying over magnesium sulfate gave the crude products, which were separated by silica gel column chromatography (4.0(ϕ) × 10 cm) eluted with hexane–ethyl acetate (4 : 1) for **1a** (28%), dichloromethane–hexane (1 : 5) for **1e** (83%), dichloromethane–hexane (1 : 3) for **1f** (60%) and **5a** (78%), dichloromethane for **5b** (36%), and ethyl acetate–hexane (1 : 5) for **10a** (45%).

1a, bp 155 °C/1.8 Torr.[13] ^{1}H-NMR 2.46(3H, s), 3.47(2H, t, J = 6.6), 4.29(2H, t, J = 6.), 7.35(2H, d, J = 8.8), 7.82(2H, d, J = 8.8).

1b, mp 32–33 °C (lit. 33 °C).[14] ^{1}H-NMR 3.50(2H, t, J = 6.4), 4.33(2H, t, J = 6.4), 7.56(2H, d, J = 8.8), 7.88(2H, d, J = 8.8).

1c, mp 53–54 °C. ^{1}H-NMR 3.52(2H, t, J = 6.2), 4.40(2H, t, J = 6.2), 7.89(2H, d, J = 8.8), 8.07(2H, d, J = 8.8); IR 3030, 3014, 2234, 1362, 1199 cm^{-1}; MS (EI/70 eV) *m*/*z* 210(17), 166(36), 102(100), 75(42).

Anal. C, 37.23; H, 2.41; N, 4.70. $C_9H_8BrNO_3S$ requires C, 37.26; H, 2.78; N, 4.83%.

5a, oil. ^{1}H-NMR 3.43(2H, t, J = 6.8), 4.27(2H, t, J = 6.8), 7.58(1H, dd, J = 8.4 and 7.6), 7.64(1H, dd, J = 8.0 and 7.6), 7.73(1H, dd, J = 8.8 and 7.6), 7.97(1H, d, J = 8.0), 8.16(1H, d, J = 8.4), 8.30(1H, d, J = 7.6), 8.63(1H, d, J = 8.8); ^{13}C-NMR 27.12, 68.96, 123.92, 124.92, 127.31, 128.29, 128.74, 128.79, 130.45, 130.82, 134.10; IR 3030, 1558, 1509, 1060, 981, 963 cm^{-1}.

HRMS m/z = 313.9584. $C_{12}H_{11}BrO_3S$ requires m/z = 313.9612.

5b, mp 89–90 °C. ^{1}H-NMR 3.56(2H, t, J = 6.8), 4.75(2H, t, J = 6.8), 7.59(1H, dd, J = 4.0 and 8.4), 7.68(1H, dd, J = 8.2 and 7.4), 8.14(1H, dd, J = 8.2 and 1.4), 8.29(1H, dd, J = 8.4 and 1.8), 8.54(1H, dd, J = 7.4 and 1.4), 9.15(1H, dd, J = 4.0 and 1.8); ^{13}C-NMR 27.79, 70.21, 122.32, 125.13, 128.83, 132.88, 133.72, 134.76, 136.43, 143.65, 151.66; IR 3034, 1615, 1598, 1565, 1058, 989, 962 cm^{-1}.

Anal C, 41.70; H, 2.84; N, 4.27. $C_{11}H_{10}BrNO_3S$ requires C, 41.79; H, 3.19; N, 4.43%.

10a, oil, bp 110–120 °C/1.0 Torr (Kugelrohr). ^{1}H-NMR 3.51(2H, t, J = 6.6), 4.38(2H, t, J = 6.6), 7.17(1H, dd, J = 5.0 and 4.0), 7.74(1H, dd, J = 5.0 and 1.2), 7.77(1H, dd, J = 4.0 and 1.2); ^{13}C-NMR 27.07, 69.49, 127.58, 134.04, 134.56, 135.07; IR 3030, 1559, 1508, 1455, 1095, 1021, 988, 965 cm^{-1}.

Anal C, 26.60; H, 2.42. $C_6H_7BrO_3S_2$ requires C, 26.58; H, 2.62%.

b) *N*-(2-Bromoethyl)-arenesulfonamides. One of the arenesulfonyl chlorides (9.9×10^{-3} mol) and 2-bromoethylammonium bromide (2.23 g, 1.1×10^{-2} mol) were dissolved in 15 ml dry dichloromethane under a nitrogen atmosphere. The mixture was treated dropwise with 3.2 ml triethylamine under ice-cooling and then stirred for 5 min under cooling. The reaction mixture was washed twice with 25 ml 2 M hydrochloric acid and 25 ml saturated sodium chloride solution. Evaporation of the organic solvent after drying over magnesium sulfate gave the crude product, which was purified by silica gel column chromatography (4(ϕ) × 17 cm) eluted with dichloromethane–hexane (4 : 1) to give **1d** (96%).

1d, mp 88–89 °C. ^{1}H-NMR 3.34–3.41(4H, m), 5.03(1H, s, NH), 7.49(2H, d, J = 8.8), 7.80(2H, d, J = 8.8); ^{13}C-NMR 31.59, 44.57, 128.39, 129.50, 138.35, 139.45; IR 3388, 3029, 1588, 1478, 1412, 1095, 1015, 912 cm^{-1}.

HRMS m/z = 297.9268. $C_8H_9BrClNO_2S$ requires m/z = 297.9304.

Anal. C,32.23; H, 2.91; N, 4.69. $C_8H_9BrClNO_2S$ requires C, 32.18; H, 3.04; N, 4.96%.

c) *N*-(2-Bromoethyl)-*N*-methyl-arenesulfonamides. The *N*-methyl-arenesulfonamides were prepared using the same method for arenesulfonamides but using 2-bromoethyl-methyl-ammmonium bromide instead of 2-bromoethylammonium bromide. Silica gel chromatography was performed using dichloromethane to give **1e** (83%) and using dichloromethane–hexane (2 : 1) to give **10b** (73%).

1e, mp 85–86 °C. ^{1}H-NMR 2.86(3H, s), 3.40–3.50(4H, m), 7.52(2H, d, J = 8.4), 7.75(2H, d, J = 8.4); ^{13}C-NMR 28.77, 36.03, 51.82, 128.62, 129.47, 136.17, 139.37; IR 3033, 1587, 1348, 1228, 1209, 1165, 1093, 994, 950 cm^{-1}.

Anal. C, 34.65; H, 3.42; N, 4.40. $C_9H_{11}BrClNO_2S$ requires C, 34.58; H, 3.55; N, 4.48%.

10b, mp 68–69 °C. ^{1}H-NMR 2.90(3H, s), 3.40–3.52(4H, m), 7.14(1H, dd, J = 5.2 and 4.0), 7.59(1H, dd, J = 4.0 and 1.2), 7.62(1H, dd, J = 5.2 and 1.2); ^{13}C-NMR 29.01, 36.43, 52.17, 127.52, 131.93, 132.14, 137.55; IR 3032, 1559, 1507, 1091, 993, 949 cm^{-1}.

Anal. C, 29.57; H, 3.38; N, 4.85. $C_7H_{10}BrNO_2S_2$ requires C, 29.58; H, 3.55; N, 4.93%.

d) *N*-(2-Bromoethyl)-*N*-ethoxycarbonyl-arenesulfonamides. Sodium hydride mineral dispersion (198 mg, 4.8×10^{-3} mol) and 3 ml of THF were placed in a nitrogen flushed flask and treated with *N*-(2-bromoethyl)-arenesulfonamide (4.0×10^{-3} mol) in 5 ml of dry THF under ice-cooling. The mixture was stirred until hydrogen evolution ceased and then treated with ethyl chloroformate (520 mg, 4.5×10^{-3} mol) in 3 ml dry THF. After stirring for 5 min, the reaction was quenched by adding 5 ml 1 M tartaric acid solution and extracted three times with 10 ml dichloromethane. Evaporation of the solvent after drying over magnesium sulfate gave the crude product, which was purified by silica gel column chromatography (2.6(ϕ) × 21 cm) eluted with dichloromethane (**1f**), dichloromethane–hexane (2 : 3) (**5c**), and dichloromethane–hexane (3 : 1) (**5d**). Compound **10c** was purified by Kugelrohr distillation without chromatography.

1f, oil. ^{1}H-NMR 1.23(3H, t, J = 7.0), 3.59(2H, t, J = 7.2), 4.16–4.21(4H, m), 7.52(2H, d, J = 8.8), 7.92(2H, d, J = 8.8): ^{13}C-NMR 14.10, 28.66, 47.74, 64.07, 129.05, 129.90, 137.49, 140.46, 151.63; IR 3034, 1734, 1586, 1478, 1445, 1093, 1014, 954 cm^{-1}.

Anal. C, 35.70; H, 3.46; N, 3.69. $C_{11}H_{13}BrClNO_4S$ requires C, 35.65; H, 3.54; N, 3.78%.

5c, mp 74–74 °C. ^{1}H-NMR 1.00(3H, t, J = 7.2), 3.69(2H, t, J = 7.8), 4.11(2H, q, J = 7.2), 4.40(2H, t, J = 7.8), 7.60(1H, dd, J = 8.4 and 7.2), 7.62(1H, dd, J = 8.0 and 7.2), 7.71(1H, dd, J = 8.4 and 7.2), 7.97(1H, d, J = 8.0), 8.14(1H, d, J = 8.4), 8.23(1H, d, J = 8.4), 8.43(1H, d, J = 7.2); ^{13}C-NMR 13.78, 28.28, 47.58, 63.74, 123.40, 123.87, 126.89, 128.01, 128.71, 129.24, 132.40, 133.94, 134.00, 135.32, 151.64; IR 3034, 3013, 1734, 1595, 1569, 1035, 1033, 1010, 974, 952 cm^{-1}.

Anal. C, 46.64; H, 4.18; N, 3.36. $C_{15}H_{16}BrNO_4S$ requires C, 46.59; H, 4.06; N, 3.52%.

5d, mp 125–127 °C. ^{1}H-NMR 0.98(3H, t, J = 7.0), 3.77(2H, t, J = 8.0), 3.99(2H, q, J = 7.0), 4.59(2H, t, J = 8.0), 7.55(1H, dd, J = 4.2 and 8.4), 7.69(1H, dd, J = 8.0 and 7.8), 8.11(1H, dd, J = 8.0 and 1.4), 8.26(1H, dd, J = 8.4 and 1.4), 8.60(1H, dd, J = 7.8 and 1.4), 9.04(1H, dd, J = 1.4 and 4.2); ^{13}C-NMR 13.80, 29.42, 49.00, 63.40, 122.22, 125.19, 128.64, 133.73, 134.31, 136.17, 136.46, 143.43, 151.39, 152.11; IR 3033, 3013, 1734, 1616, 1597, 1565, 1144 cm^{-1}.

Anal. C, 43.33; H, 3.68; N, 7.08. $C_{14}H_{15}BrN_2O_4S$ requires C, 43.42; H, 3.90; N, 7.23%.

10c, bp 140–150 °C/0.35 Torr (Kugelrohr). ^{1}H-NMR 1.30(3H, t, J = 7.2), 3.58(2H, t, J = 7.6), 4.18(2H, t, J = 7.6), 4.26(2H, q, J = 7.2), 7.12(1H, dd, J = 4.0 and 5.2), 7.70(1H, dd, J = 1.6 and 5.2), 7.82(1H, dd, J = 4.0 and 1.6); ^{13}C-NMR 14.17, 28.53, 48.11, 64.13, 127.03, 133.76, 134.99, 143.47, 151.80; IR 3035, 3012, 1739, 1507, 1466, 1092, 1016 cm^{-1}.

HRMS m/z = 343.9436. ($C_9H_{12}{}^{81}BrNO_4S_2$ + H) requires m/z = 343.9449.

e) *N*-(2-Bromo-1-ethoxycarbonyl)ethyl-*N*-ethoxycarbonyl-arenesulfonamides. The three amides (**15a**, **15b**, and **15c**) were prepared by the same method and the procedure for **15a** is described as an example. Into a pre-dried two-necked flask were placed *N*-(2-bromo-1-ethoxycarbonyl)ethyl-4-chlorobenzenesulfonamide (2.2 g, 6.0×10^{-3} mol) and 9 ml dry THF, and the mixture was treated under cooling with sodium hydride (310 mg, 7.2×10^{-3} mol) dispersed in 3 ml THF. After hydrogen evolution ceased, 1.20 ml (1.2×10^{-2} mol) ethyl chloroformate was slowly added and the mixture was stirred for 100 h. After neutralization with tartaric acid solution, the mixture was condensed to remove most of the THF, 30 ml water was added and the mixture was extracted with chloroform (30 ml × 3). The condensate of the extract was subjected to chromatography on silica gel (10(ϕ) × 45 cm) eluted with chloroform to give amide **15a** (960 mg, 36.2%).

15a, oil. ^{1}H-NMR 1.06(3H, t, J = 7.2), 1.26(3H, t, J = 6.8), 3.95(1H, dd, J = 10.4 and 11.2), 4.10–4.17(3H, m), 4.26(2H, q,

J = 6.8), 5.39–5.43(1H, m), 7.52(2H, d, J = 8.7), 8.05(2H, d, J = 8.7); ^{13}C-NMR 13.87, 14.00, 29.45, 60.71, 62.52, 64.16, 128.59, 130.73, 137.09, 140.33, 150.84, 166.88; IR 1741, 1397, 1375, 1351, 1280, 1171, 1093, 1015, 854, 829 cm^{-1}.

HRMS m/z = 441.9730. ($C_{14}H_{17}ClNO_6S$ + H) requires m/z = 441.9727.

15b, oil. ^{1}H-NMR 1.09(3H, t, J = 7.3), 1.23(3H, t, J = 7.3), 3.98(1H, dd, J = 10.0 and 11.2), 4.08–4.19(3H, m), 4.24(2H, q, J = 7.3), 5.50(1H, dd, J = 4.8 and 10.0), 7.50–7.80(2H, m), 7.91–8.02(3H, m), 8.07(1H, dd, J = 1.8 and 8.6), 8.67(1H, d, J = 1.6); ^{13}C-NMR 13.88, 14.07, 29.58, 60.77, 62.50, 64.06, 123.78, 127.50, 127.84, 128.41, 129.34, 129.38, 131.48, 131.57, 135.24, 135.60, 151.15, 167.13; IR 1740, 1394, 1376, 1289, 1161, 1074, 1020, 858 cm^{-1}.

HRMS m/z = 458.0275. ($C_{18}H_{20}BrNO_5S$ + H) requires m/z = 458.0273.

15c, oil. ^{1}H-NMR 1.24(3H, t, J = 7.3), 1.25(3H, t, J = 7.1), 3.94(1H, dd, J = 10.2 and 11.2), 4.10(1H, dd, J = 4.6 and 11.2), 4.10–4.17(4H, m), 5.39(1H, dd, J = 4.6 and 10.2), 7.12(1H, dd, J = 3.9 and 4.9), 7.71(1H, dd, J = 1.5 and 4.9), 7.90(1H, dd, J = 1.5 and 3.9); ^{13}C-NMR 13.93, 29.48, 61.20, 62.37, 64.22, 65.89, 126.78, 134.14, 135.68, 138.48, 151.07, 166.80; IR 1740, 1401, 1376, 1353, 1287, 1235, 1169, 1093, 1020, 859 cm^{-1}.

HRMS m/z = 413.9699. ($C_{12}H_{16}BrNO_6S_2$ + H) requires m/z = 413.9681.

Radical reaction of 2-bromoethyl-arenesulfonates

All the radical reactions were carried out under the same reaction conditions described below. One of the 2-bromoethyl-arenesulfonates (3.0×10^{-4} mol) was placed in a two-necked flask equipped with a condenser and a rubber septum. The vessel was then flushed with argon and dry benzene was added, which was deaerated by bubbling argon for 30 min in an ultrasonic bath. Under reflux, tributyltin hydride (174 mg, 6.0×10^{-4} mol) and AIBN (24.7mg, 1.5×10^{-4}mol) in 0.6 ml dry benzene were added slowly over 9–10 h using a syringe pump, and the mixture was heated for a further 12 h.

The reactions of sulfonates, **1a**–**1c**, **5a**, **5b**, and **10a** were worked up as follows: the reaction mixture was condensed under reduced pressure, dissolved in 10 ml ethyl acetate, treated with 5 ml saturated aqueous potassium fluoride and 1.0 g of powdered potassium fluoride, and stirred for 5 h at room temperature. The organic layer of the reaction mixture was evaporated after drying over magnesium sulfate to give the product mixture. The mixture was passed through a short column of silica gel using dichloromethane–hexane to remove polar by-products. The condensed eluate was subjected to preparative TLC developed with dichloromethane–hexane to give products **2**–**4**, **6**–**8**, and **11**–**13**.

3a, solid. ^{1}H-NMR(90 MHz) 2.39(3H, s), 3.15(2H, t, J = 5.7), 4.87(2H, t, J = 5.7), 7.07(1H, s), 7.12(1H, d, J = 7.9), 7.72(1H, d, J = 7.9); ^{13}C-NMR 21.50, 28.03, 69.95, 124.96, 128.41, 129.45, 132.78, 134.12, 143.42; IR 3033, 1351, 1187, 1079, 1016, 889 cm^{-1}.

HRMS m/z = 199.0404. ($C_9H_{10}O_3S$ + H) requires m/z = 199.0429.

4a, mp 33 °C.[15] ^{1}H-NMR 1.30(3H, t, J = 7.0), 2.46(3H, s), 4.11(2H, q, J = 7.0), 7.33(2H, d, J = 8.5), 7.80(2H, d, J = 8.5).

2b, oil.[13] ^{1}H-NMR 2.27(2H, t, J = 6.4), 3.78(2H, t, J = 6.4), 7.10(2H, d, J = 8.2), 7.21(2H, d, J = 8.2).

3b, white powder. ^{1}H-NMR 3.20(2H, t, J = 6.1), 4.91(2H, t, J = 6.1), 7.30(1H, s), 7.42(1H, d, J = 8.0), 7.79(1H, d, J = 8.0); ^{13}C-NMR 28.97, 69.99, 126.57, 128.51, 129.11, 134.06, 136.07, 138.90; IR 3035, 1593, 1565, 1474, 1373, 1358, 1186, 1010, 952 cm^{-1}.

HRMS m/z = 218.9894. ($C_8H_7ClO_3S$ + H) requires m/z = 218.9883.

4b, white solid.[14] ^{1}H-NMR 1.33(3H, t, J = 7.0), 4.15(2H, q, J = 7.0), 7.54(2H, d, J = 8.8), 7.86(2H, d, J = 8.8).

2c, oil.[16] ^{1}H-NMR 2.93(2H, t, J = 6.4), 3.90(2H, t, J = 6.4), 7.36(2H, d, J = 8.0), 7.61(2H, d, J = 8.0).

3c, solid. ^{1}H-NMR 3.28(2H, t, J = 6.0), 4.96(2H, t, J = 6.0), 7.63(1H, s), 7.74(1H, d, J = 8.4), 7.97(1H, d, J = 8.4); ^{13}C-NMR 27.79, 69.81, 116.58, 116.73, 126.03, 131.34, 132.82, 135.48, 139.25; IR 3016, 2240, 1374, 1362, 1190, 1011, 957 cm^{-1}.

HRMS (EI/70eV) m/z = 209.0181. $C_9H_7NO_3S$ requires m/z = 209.0147.

4c, solid. ^{1}H-NMR 1.35(3H, t, J = 7.2), 4.21(2H, q, J = 7.2), 7.87(2H, d, J = 8.0), 8.04(2H, d, J = 8.0); ^{13}C-NMR 14.86, 67.98, 116.94, 117.40, 128.37, 132.92, 140.55; IR 3030, 2238, 1375, 1363, 1189, 1177, 1002, 924 cm^{-1}.

HRMS (EI/70eV) m/z = 211.0340. $C_9H_9NO_3S$ requires m/z = 211.0303.

6a, oil.[17] ^{1}H-NMR 3.33(2H, t, J = 6.8), 3.96(2H, t, J = 6.8), 7.36(1H, d, J = 6.4), 7.41(1H, dd, J = 6.4 and 8.4), 7.46–7.53(2H, m), 7.74(1H, d, J = 8.4), 7.85(1H, d, J = 7.6), 8.04(1H, d, J = 8.4).

7a. ^{1}H-NMR 3.93(2H, t. J = 6.4), 4.74(2H, t, J = 6.4), 7.50–7.59(3H, m), 7.89(1H, dd, J = 2.4 and 7.2), 8.08(1H, dd, J = 1.4 and 8.4), 8.36(1H, dd, J = 1.4 and 7.4); ^{13}C-NMR 35.42, 72.67, 124.44, 126.79, 129.11, 129.32, 131.06, 134.78; IR 3029, 1599, 1350, 1176, 1014, 908, 827 cm^{-1}.

HRMS m/z = 235.0425. ($C_{12}H_{10}O_3S$ + H) requires m/z = 235.0429.

8a.[18] ^{1}H-NMR 1.25(3H, t, J = 7.2), 4.09(2H, q, J = 7.2), 7.57(1H, dd, J = 8.4 and 7.6), 7.63(1H, dd, J = 8.0 and 7.2), 7.71(1H, dd, J = 8.8 and 7.2), 7.96(1H, d, J = 8.0), 8.13(1H, d, J = 8.4), 8.29(1H, d, J = 7.6), 8.63(1H, d, J = 8.8).

6b, oil. ^{1}H-NMR 3.48(2H, t, J = 5.6), 4.01(2H, t, J = 5.6), 4.22(1H, s, OH), 7.44(1H, dd, J = 4.2 and 8.2), 7.49(1H, t, J = 7.6), 7.58(1H, d, J = 7.6), 7.73(1H, d, J = 7.6), 8.21(1H, dd, J = 8.2 and 1.8), 8.88(1H, dd, J = 4.2 and 1.8); ^{13}C-NMR 36.76, 63.84, 120.84, 126.56, 128.55, 130.43, 136.90, 139.35, 146.84, 148.93; IR 3240, 1597, 1580, 1503, 1235, 949 cm^{-1}.

HRMS m/z = 147.0911. ($C_{11}H_{11}NO$ + H) requires m/z = 147.0919.

8b.[19] ^{1}H-NMR 1.35(3H, t, J = 7.2), 4.44(2H, q, J = 7.2), 7.57(1H, dd, J = 8.4 and 4.4), 7.66(1H, dd, J = 8.0 and 7.2), 8.12(1H, dd, J = 8.0 and 1.2), 8.27(1H, dd, J = 8.4 and 1.8), 8.51(1H, dd, J = 7.2 and 1.2), 9.16(1H, dd, J = 4.4 and 1.8).

11a.[20] ^{1}H-NMR 3.01(2H, t, J = 6.0), 3.79(2H, t, J = 6.0), 6.08(1H, dd, J = 3.6 and 1.2), 6.89(1H, dd, J = 3.6 and 5.2), 7.10(1H, dd, J = 5.2 and 1.2).

12a, solid. ^{1}H-NMR 3.10(2H, t, J = 5.8), 4.93(2H, t, J = 5.8), 6.93(1H, d, J = 5.2), 7.57(1H, d, J = 5.2); ^{13}C-NMR 26.12, 71.16, 126.25, 128.51, 129.65, 130.14; IR 3031, 3015, 1358, 1184 cm^{-1}.

HRMS m/z = 190.9842. ($C_6H_6O_3S$ +H) requires m/z = 190.9837.

13a, oil. ^{1}H-NMR 1.35(3H, t, J = 7.2), 4.21(2H, q, J = 7.2), 7.14(1H, dd, J = 5.0 and 4.0), 7.69(1H, dd, J = 5.0 and 1.2), 7.72(1H, dd, J = 4.0 and 1.2); ^{13}C-NMR 14.73, 67.82, 127.38, 133.31, 133.97, 136.11; IR 3032, 3016, 1509, 1373, 1180, 1093 cm^{-1}.

HRMS m/z = 193.0013. ($C_6H_8O_3S_2$ + H) requires m/z = 192.9993.

Radical reaction of *N*-(2-bromoethyl)-arenesulfonamides and *N*-(2-bromoethyl)-*N*-methyl-arenesulfonamides

The reaction of 4-chlorobenzenesulfonamide **1d** and *N*-methyl-arenesulfonamides, **1e** and **10b** were worked up in the following manner: the condensed residue from the reaction mixture was dissolved in 5 ml dichloromethane and washed five times with 5 ml 1 M hydrochloric acid. The combined aqueous layer was treated with 10% sodium hydroxide solution until the pH was alkaline and extracted five times with 15 ml ethyl acetate. Condensation of the ethyl acetate extract after drying over magnesium sulfate gave the crude basic products. The neutral

products (**3d**, **4d**, **3e**, **4e**, **11b**, and **13b**) from the first dichloromethane extract were separated by preparative TLC using ethyl acetate–hexane (1 : 2). We attempted to purify the basic products from the ethyl acetate extract by GPC (gel permeation chromatography) using JAIGEL-1H (Japan Analytical Industry) but the products were a complex mixture in most cases.

3d, solid. ^{1}H-NMR 2.91(2H, t, J = 6.3), 3.74(2H, dt, J = 6.3 and 7.6), 4.45(1H, t, J = 7.6, NH), 7.19(1H, s), 7.30(1H, d, J = 8.4), 7.69(1H, d, J = 8.4); ^{13}C-NMR 28.24, 41.81, 125.79, 128.10, 129.41, 136.57, 137.17, 138.17; IR 3342, 1592, 1562, 1471, 1401, 1338, 1327, 1169 cm^{-1}.

HRMS m/z = 218.0043. ($C_8H_8ClNO_2S$ + H) requires m/z = 218.0044.

4d,[21] solid. ^{1}H-NMR 3.13(3H, t, J = 7.2), 2.99–3.07(2H, m), 4.33(1H, br s, NH), 7.50(2H, d, J = 8.4), 7.81(2H, d, J = 8.4).

3e, oil. ^{1}H-NMR 2.81(3H, s), 2.94(2H, t, J = 6.4), 3.80(2H, t, J = 6.4), 7.18(1H, s), 7.30(1H, d, J = 8.4), 7.71(1H, d, J = 8.4); ^{13}C-NMR 22.91, 35.14, 47.92, 126.53, 127.93, 129.16, 134.24, 136.56, 137.98; IR 3022, 3014, 1592, 1470, 1336, 1167, 1098, 977, 950 cm^{-1}.

HRMS m/z = 232.0194. ($C_9H_{10}ClNO_2S$ + H) requires m/z = 232.0199.

4e, oil. ^{1}H-NMR 1.14(3H, t, J = 7.2), 2.75(3H, s), 3.11(2H, q, J = 7.2), 7.49(2H, d, J = 8.8), 7.73(2H, d, J = 8.8); ^{13}C-NMR 12.86, 33.74, 44.67, 128.41, 129.01, 136.00, 138.53; IR 3027, 1587, 1476, 830 cm^{-1}.

HRMS m/z = 234.0375. ($C_9H_{12}ClNO_2S$ + H) requires m/z = 234.0356.

11b.[21] ^{1}H-NMR 2.40(1H, s), 2.58(3H, s), 3.07(2H, t, J = 7.6), 3.21(2H, t, J = 7.6), 6.88(1H, d, J = 3.2), 6.94(1H, dd, J = 3.2 and 5.2), 7.17(1H, d, J = 5.2).

13b, oil. ^{1}H-NMR 1.17(3H, t, J = 7.2), 2.78(3H, s), 3.13(2H, q, J = 7.2), 7.12(1H, dd, J = 5.2 and 4.4), 7.55(1H, dd, J = 4.4 and 1.2); ^{13}C-NMR 12.87, 33.94, 44.92, 127.25, 131.39, 131.47, 137.39; IR 3020, 1347, 1261, 1153, 916 cm^{-1}.

HRMS m/z = 206.0285. ($C_7H_{11}NO_2S_2$ + H) reqires m/z = 206.0309.

Radical reaction of *N*-(2-bromoethyl)-*N*-ethoxycarbonyl-arenesulfonamides

The reactions of *N*-ethoxycarbonyl-sulfonamides (**1d**, **5c**, **5d**, and **10c**) were carried out in the same manner as mentioned above and worked up as follows: the condensed reaction mixture was passed through a short column of silica gel to remove polar by-products using dichloromethane–ether and the residue from the eluate was subjected to preparative TLC with dichloromethane to give products **2f**, **3f**, **4f**, **6c**, **8c**, **6d**, **8d**, **11c**, and **13c**.

2f, solid. ^{1}H-NMR 1.23(3H, t, J = 7.0), 2.78(2H, t, J = 6.8), 3.41(2H, t, J = 6.8), 4.10(2H, q, J = 7.0), 4.65(1H, br s, NH), 7.12(2H, d, J = 8.2), 7.27(2H, d, J = 8.2); ^{13}C-NMR 14.61, 35.54, 41.94, 60.79, 128.70, 130.11, 132.30, 137.25, 156.52; IR 3455, 3026, 3014, 1717, 1517 cm^{-1}.

HRMS m/z = 228.0800. ($C_{11}H_{14}ClNO_2$ + H) requires m/z = 228.0791.

3f, solid. ^{1}H-NMR 1.37(3H, t, J = 7.2), 3.13(2H, t, J = 6.2), 4.27(2H, t, J = 6.2), 4.35(2H, q, J = 7.2), 7.30(1H, d, J = 1.6), 7.41(1H, dd, J = 8.4 and 1.6), 7.84(1H, d, J = 8.4); ^{13}C-NMR 14.18, 27.74, 45.43, 64.29, 126.06, 128.09, 129.09, 136.63, 137.59, 138.99, 152.07; IR 3033, 3020, 1728, 1591, 1564 cm^{-1}.

HRMS m/z = 290.0235. ($C_{11}H_{12}ClNO_4S$ + H) requires m/z = 290.0254.

4f, oil. ^{1}H-NMR 1.21(3H, t, J = 7.2), 1.35(3H, t, J = 7.2), 3.92(2H, q, J = 7.2), 4.15(2H, q, J = 7.2), 7.49(2H, d, J = 8.8), 7.90(2H, d, J = 8.8): ^{13}C-NMR 13.96, 15.50, 42.64, 63.41, 128.96, 129.84, 138.19, 139.99, 151.99; IR 3035, 1731, 1585 cm^{-1}.

HRMS m/z = 292.0399. ($C_{11}H_{14}ClNO_4S$ + H) requires m/z = 292.0410.

6c, solid.^{1}H-NMR 1.24(3H, t, J = 7.2), 3.30(2H, t, J = 6.8), 3.55(2H, t, J = 6.8), 4.13(2H, q, J = 7.2), 4.72(1H, s, NH), 7.33(1H, d, J = 7.0), 7.41(1H, dd, J = 7.0 and 8.0), 7.49(1H, dd, J = 8.0 and 7.2), 7.54(1H, dd, J = 8.0 and 7.2), 7.75(1H, d, J = 8.0), 7.86(1H. d, J = 8.0), 8.10(1H, d, J = 8.0); ^{13}C-NMR 14.65, 33.40, 41.57, 60.75, 123.62, 125.48, 125.68, 126.16, 126.77, 127.31, 128.79, 131.92, 133.92, 134.89, 156,67; IR 3455, 3027, 3013, 1715, 1517 cm^{-1}.

HRMS m/z = 244.1355. ($C_{15}H_{17}NO_2$ + H) requires m/z = 244.1337.

8c, oil. ^{1}H-NMR 0.97(3H, t, J = 7.2), 1.45(3H, t, J = 7.2), 3.97(2H, q, J = 7.2), 4.12(2H, q, J = 7.2), 7.57(1H, dd, J = 8.0 and 7.6), 7.58(1H, dd, J = 8.0 and 7.2), 7.65(1H, dd, J = 8.0 and 7.2), 7.94(1H, d, J = 8.0), 8.09(1H, d, J = 8.4), 8.34(1H, d, J = 8.0), 8.40(1H, d, J = 7.6); ^{13}C-NMR 13.76, 15.52, 42.37, 63.16, 123.76, 123.96, 126.79, 128.17, 128.46, 129.18, 132.08, 134.02, 134.87, 134.97, 152.13; IR 3020, 1728, 1351, 1260 cm^{-1}.

HRMS m/z = 308.0966. ($C_{15}H_{17}NO_4S$ + H) requires m/z = 308.0956.

6d, oil. ^{1}H-NMR 1.19(3H, t, J = 7.0), 3.46(2H, t, J = 6.4), 3.61(2H, t, J = 6.4), 4.06(2H, q, J = 7.0), 7.41(1H, dd, J = 4.0 and 8.2), 7.48(1H, dd, J = 6.8 and 8.2), 7.59(1H, dd, J = 6.8 and 1.4), 7.71(1H, dd, J = 8.2 and 1.4), 8.15(1H, dd, J = 8.2 and 1.6), 8.93(1H, dd, J = 4.0 and 1.6); ^{13}C-NMR 14.64, 31.80, 42.22, 60.83, 121.00, 126.43, 126.77, 128.46, 130.01, 136.54, 138.04, 146.89, 149.43, 156.68; IR 3451, 3026, 3010, 1700, 1517 cm^{-1}.

HRMS m/z = 245.1274. ($C_{14}H_{16}N_2O_2$ + H) requires m/z = 245.1290.

8d, solid. ^{1}H-NMR 0.99(3H, t, J = 7.0), 1.49(3H, t, J = 7.0), 3.98(2H, q, J = 7.0), 4.29(2H, q, J = 7.0), 7.52(1H, dd, J = 4.0 and 8.4), 7.67(1H, dd, J = 7.6 and 8.0), 8.08(1H, dd, J = 1.4 and 8.0), 8.24(1H, dd, J = 1.8 and 8.4), 8.60(1H, dd, J = 7.6 and 1.4), 9.01(1H, dd, J = 4.0 and 1.8); ^{13}C-NMR 13.79, 15.94, 43.97, 62.82, 122.11, 125.21, 128.63, 133.63, 134.02, 136.39, 136.88, 143.70, 151.36, 152.59; IR 3034, 3015, 1726, 1350 cm^{-1}.

HRMS m/z = 309.0880. ($C_{14}H_{16}N_2O_4S$ + H) requires m/z = 309.0909.

11c, oil. ^{1}H-NMR 1.33(3H, t, J = 7.2), 3.03(2H, t, J = 8.4), 3.45(2H, t, J = 8.4), 4.11(2H, q, J = 7.2), 4.80(1H, br s, NH), 6.83(1H, dd, J = 4.4 and 1.2), 6.94(1H, dd, J = 4.4 and 6.8), 7.16(1H, dd, J = 6.8 and 1.2); ^{13}C-NMR 14.60, 30.34, 42.23, 60.78, 123.90, 125.33, 126.99, 141.20, 156.49; IR 3451, 3027, 3013, 1717, 1517 cm^{-1}.

HRMS m/z = 200.0733. ($C_9H_{13}NO_2S$ + H) requires m/z = 200.0745.

13c, oil. ^{1}H-NMR 1.28(3H, t, J = 7.2), 1.33(3H, t, J = 7.2), 3.91(2H, q, J = 7.2), 4.23(2H, q, J = 7.2), 7.09(1H, dd, J = 3.8 and 5.0), 7.65(1H, dd, J = 5.0 and 1.4), 7.78(1H, dd, 3.8 and 1.4); ^{13}C-NMR 12.87, 33.94, 44.92, 127.25, 131.39, 131.47, 137.39; IR 3020, 1347, 1261, 1153, 916 cm^{-1}.

HRMS m/z = 206.0285. ($C_7H_{11}NO_2S_2$+H) requires m/z = 206.0309.

Radical reaction of *N*-(2-bromo-1-ethoxycarbonyl)ethyl-*N*-ethoxycarbonyl-arenesulfonamides

The reactions of sulfonamides **15a**–**15c** were carried out and worked up in the same manner as the *N*-ethoxycarbonyl-sulfonamides mentioned above.

16a, oil. ^{1}H-NMR 1.16(3H, t, J = 7.1), 1.17(3H, t, J = 7.1), 2.93–3.10(2H, m), 4.03(2H, q, J = 7.1), 4.05–4.20(2H, m), 4.53(1H, dd, J = 6.4 and 13.2), 5.08(1H, NH), 7.00(2H, d, J = 8.8), 7.18(2H, d, J = 8.8); ^{13}C-NMR 14.18, 14.57, 37.78, 54.56, 61.21, 61.57, 128.55, 130.58, 132.87, 134.33, 155.70, 171.25; IR 3024, 1733, 1717, 1509, 1494, 1375, 1340, 1201, 1093, 1064 cm^{-1}.

HRMS m/z = 300.1028. ($C_{14}H_{18}NO_4$ + H) requires m/z = 300.1003.

17a, oil. ^{1}H-NMR 1.15(3H, t, J = 6.8), 1.21(3H, t, J = 7.2), 1.69(3H, d, J = 7.6), 4.09–4.23(4H, m), 5.19(1H, q, J = 7.6),

7.50(2H, d, J = 8.6), 7.98(2H, J = 8.6); ^{13}C-NMR 13.91, 14.09, 17.04, 55.39, 61.79, 63.71, 128.74, 130.09, 137.56, 140.14, 151.05, 169.65; IR 3019, 1737, 1479, 1375, 1349, 1279, 1173, 1093, 1016, 855, 824 cm^{-1}.

HRMS m/z = 364.0531. ($C_{14}H_{18}ClNO_6S$ + H) requires m/z = 364.0543.

16b, oil. ^{1}H-NMR 1.21(6H, t, J = 7.3), 3.24–3.29(2H, m), 4.10(2H, q, J = 7.3), 4.17(2H, q, J = 7.3), 4.70(1H, dd, J = 4.4 and 14.0), 5.14(1H, d, J = 4.4, NH), 7.27(1H, dd, J = 4.0 and 8.4), 7.43–7.49(3H, m); ^{13}C-NMR 14.17, 14.58, 38.56, 54.73, 61.15, 61.53, 121.89, 125.64, 126.05, 127.24, 127.46, 127.55, 128.01, 132.37, 133.29, 155.79, 171.55; IR 3431, 3027, 1717, 1509, 1376, 1340, 1234, 1198, 1064, 1033, 864 cm^{-1}.

HRMS m/z = 380.1130. ($C_{18}H_{21}NO_2$ + H) requires m/z = 380.1168.

17b, ^{1}H-NMR 1.08(3H, t, J = 6.8), 1.17(3H, t, J = 6.8), 1.73(3H, d, J = 6.8), 4.03–4.12(2H, m), 4.13–4.21(2H, m), 5.28(1H, q, J = 6.8), 7.59–7.70(2H, m), 7.90–8.02(4H, m), 8.62(1H, d, J = 1.2); ^{13}C-NMR 13.89, 14.08, 17.04, 55.31, 61.70, 63.56, 123.14, 127.48, 127.83, 128.61, 129.20, 129.33, 131.66, 135.13, 136.02, 151.21, 169.79; IR 3019, 1739, 1736, 1375, 1346, 1170, 860 cm^{-1}.

HRMS m/z = 316.1514. ($C_{18}H_{21}NO_6S$ + H) requires m/z = 316.1549.

16c, oil.^{1}H-NMR 1.25(3H, t, J = 7.2), 1.28(3H, t, J = 6.8), 3.37(2H, d, J = 4.8), 4.13(2H, q, J = 7.2), 4.20(2H, q, J = 7.2), 4.59–4.66(1H, m), 5.28(1H, d, J = 8.0), 6.81(1H, dd, J = 1.2 and 3.6), 6.93(1H, dd, J = 3.6 and 4.8), 7.17(1H, dd, J = 1.2 and 4.8); ^{13}C-NMR 14.56, 14.99, 32.85, 54.89, 61.58, 62.07, 125.12, 127.07, 127.25, 137.54, 156.11, 171.23; IR 3432, 3028, 1734, 1507, 1376, 1339, 1236, 1196, 1064, 701 cm^{-1}.

HRMS m/z = 272.0950. ($C_{12}H_{17}NO_4S$ + H) requires m/z = 272.0957.

17c, oil. ^{1}H-NMR 1.09(3H, t, J = 7.2), 1.15(3H, t, J = 6.8), 1.60(3H, d, J = 7.2), 4.06(2H, q, J = 7.2), 4.08–4.18(2H, m), 5.08(1H, q, J = 7.2), 7.04(1H, dd, J = 1.2 and 3.4), 7.63(1H, dd, J = 3.4 and 5.1), 7.77(1H, dd, J = 1.2 and 5.1); ^{13}C-NMR 13.92, 13.95, 16.89, 55.91, 61.59, 63.70, 126.77, 133.54, 134,92, 138.95, 151.18, 169.49; IR 3027, 1740, 1735, 1376, 1261, 1172, 1093, 1019, 859 cm^{-1}.

HRMS m/z = 336.0573. ($C_{12}H_{17}NO_6S_2$ + H) requires m/z = 336.0576.

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