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New Methods and Reagents in Organic Synthesis. 20.[1] 2-Mesitylenesulfonyl diazomethane: Synthesis and Application to the Arndt-Eistert Synthesis[2]

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2-Mesitylenesulfonyldiazomethane (**4**) was conveniently prepared from 2-mesitylenesulfonylchloride (**5**) in 4 steps. Reaction of **4** with benzoyl chloride smoothly furnished α-benzoyl α-(2-mesitylenesulfonyl)diazomethane (**9**). Thermal treatment of **9** in the presence of alcohols generally gave the Wolff rearrangement product (**10**) as the major product accompanied with the intramolecular C-H insertion product (**11**). When acetonitrile was used as a reaction solvent, a substantial amount of the desulfonylated product (**13**) was also formed.

Keywords——sulfonyldiazomethane; α-diazosulfone; Wolff rearrangement; Arndt–Eistert synthesis; α-sulfonylacetate; α-diazo-β-ketosulfone; intramolecular carbene insertion reaction; desulfonylation; thermal rearrangement

In the preceding paper of the series,[1] we showed that sulfonyldiazomethanes (**1**),[3] as stable and safe substitutes for hazardous diazomethane, are efficiently acylated with acyl chlorides in the presence of triethylamine in acetonitrile and the resulting α-acylsulfonyldiazomethanes(α-diazo-β-ketosulfones, **2**) undergo the Wolff rearrangement to give α-sulfonylacetates (**3**). The overall process is depicted in Chart 1, representing a new, safe method for the Arndt–Eistert synthesis of α-sulfonylacetates (**3**) from acyl chlorides.

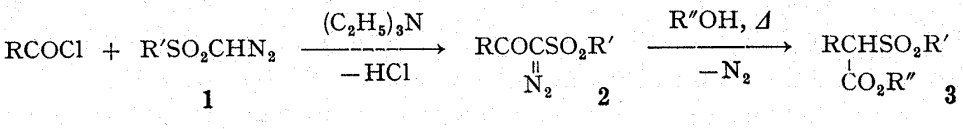


Chart 1

As an extension of this work, we now describe a facile synthesis of 2,4,6-trimethylbenzenesulfonyldiazomethane (**4**) and its application to the Arndt–Eistert synthesis.

Our preparation of 2-mesitylenesulfonyldiazomethane (**4**), shown in Chart 2, is basde on one of the general methods for the preparation of sulfonyldiazomethanes (**1**) which was developed by van Leusen and co-workers.[3a,4] 2-Mesitylenesulfonyl chloride (**5**) was first converted to the sulfinic acid salt (**6**) by treatment with aqueous sodium sulfite and sodium bicarbonate. The Mannich reaction of **6**, formalin, and ethyl carbamate afforded *N*-(2-mesitylenesulfonylmethyl)carbamate (**7**) in 52% yield from **5**. Nitrosation of **7** with nitrosyl chloride in pyridine gave the *N*-nitrosocarbamate (**8**) in 94% yield. Treatment of **8** with alumina in diethyl ether–methylene chloride furnished 2-mesitylenesulfonyldiazomethane (**4**), mp 53.5—54.5°C, in 78% yield. This crystalline sulfonyldiazomethane (**4**) is stable at room temperature in the dark for months and its stability is comparable to those of benzyl- and *tert*-butylsulfonyldiazomethanes.[4] Compound **4** does not appear to be an explosive or a skin irritant, and we have not encountered any other hazardous properties.

Benzoylation of **4** was performed with benzoyl chloride and triethylamine in acetonitrile according to the general procedure developed by us[1] for the acylation of sulfonyldiazomethanes. The yield of the product, α-benzoyl-α-(2-mesitylenesulfonyl)diazomethane (**9**), was 82%.

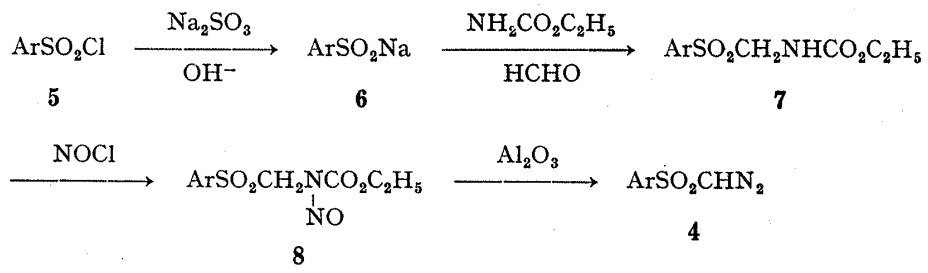


Chart 2

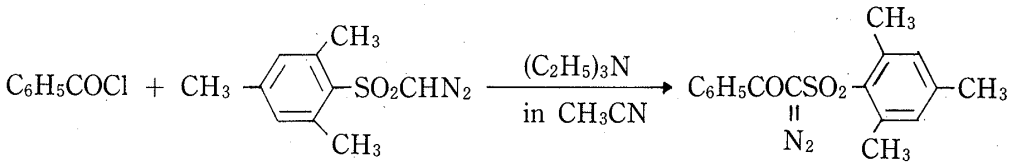
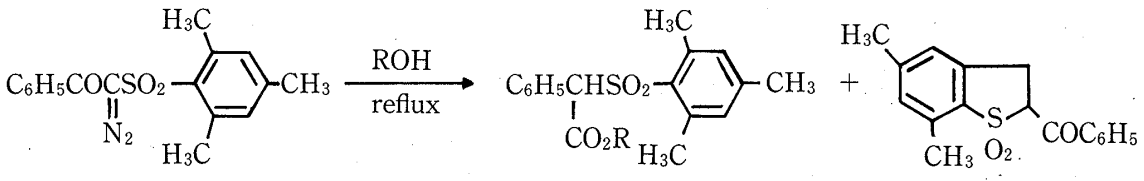


Chart 3

Since our preceding work[1] revealed that toluene is the solvent of choice for the thermal Wolff rearrangement of α-acylated sulfonyldiazomethanes (**2**), **9** was refluxed in toluene in the presence of benzyl alcohol. The desired sulfonylacetate (**10**) was obtained as the major product, but a significant amount of the benzo[*b*]thiophene derivative (**11**) was also formed. The reaction intermediate is apparently the α-benzoylsulfonylcarbene ($C_6H_5COC\ddot{S}O_2C_6H_2$-(2,4,6-tri$CH_3$), **12**), which will mainly undergo the Wolff rearrangement to give **10**. However, a part of **12** will undergo intramolecular carbene insertion with the methyl C–H bond of the mesityl function to give **11**. Changing the reaction solvent from refluxing toluene to refluxing benzene or 2,4,6-trimethylpyridine did not have any significant effect on the products, as shown in Table I. Replacement of benzyl alcohol with *tert*-butyl alcohol in 2,4,6-trimethylpyridine also furnished the Wolff rearrangement product (**10b**) and **11**. α-Benzoylsulfonyldiazomethanes, in general, have been reported[1] to undergo 1,3-dipolar addition to acetonitrile,

Table I.



9 **10a** : R=$C_6H_5CH_2$ **11**
10b : R=$(CH_3)_3C$

Run	ROH	Solvent	Reaction time (h)	Yield (%) of 10a	10b	11
1	$C_6H_5CH_2OH$	Toluene	2	48		21
2	$C_6H_5CH_2OH$	Benzene	48	43		14
3	$C_6H_5CH_2OH$	2,4,6-Trimethylpyridine	10 min	39		12
4	$C_6H_5CH_2OH$	Acetonitrile	48	45		Trace[a]
5	$(CH_3)_3COH$	2,4,6-Trimethylpyridine	31		30	13

a) 2-Mesitylacetophenone (**13**) was obtained in 32% yield.

giving 2-methyl-5-phenyl-4-sulfonyloxazoles. However, no 1,3-dipolar adduct could be isolated from **9** and acetonitrile. The main product was **10a**, accompanied by a trace amount of **11**. Furthermore, a considerable amount of the desulfonylated product, 2-mesitylacetophenone (**13**), was isolated in this case.

Experimental

General experimental procedures employed were essentially the same as described in our previous paper.[15] Infrared (IR) and nuclear magnetic resonance (NMR) spectra were measured in Nujol and deuteriochloroform, respectively.

Ethyl *N*-(2-Mesitylenesulfonylmethyl)carbamate (**7**)——To a solution of sodium sulfite heptahydrate (100.9 g, 0.4 mol) in water (200 ml) was added 2-mesitylenesulfonyl chloride (43.7 g, 0.2 mol) and sodium bicarbonate (33.6 g, 0.4 mol) at 70—80°C during 2 h. After the mixture had been stirred at 70—80°C for 48 h, it was cooled and acidified with formic acid to pH 3. Ethyl carbamate (35.6 g, 0.4 mol) and 35% formalin (130 ml, 1.6 mol) were added to the acidified mixture (containing precipitates), and the whole mixture was stirred at 60°C for 1 week. The precipitates were collected, washed with water, dried, and recrystallized from ethyl alcohol to give colorless minute needles (29.68 g, 52%), mp 118—118.5°C. IR ν_{max} cm^{-1}: 3280, 1695, 1320, 1305, 1145. NMR δ (ppm): 1.08 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.28 (3H, s, 4-CH_3), 2.68 (6H, s, 2,6-diCH_3), 3.96 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 4.54 (2H, d, J=4 Hz, $C\underline{H}_2NH$), 5.6—6.0 (1H, NH), 6.94 (2H, s, aromatic H). *Anal.* Calcd for $C_{13}H_{19}NO_4S$: C, 54.72; H, 6.71; N, 4.91. Found: C, 54.58; H, 6.82; N, 4.87.

Ethyl *N*-(2-Mesitylenesulfonylmethyl)-*N*-nitrosocarbamate (**8**)——Gaseous nitrosyl chloride prepared from sodium nitrite (43.1 g, 0.625 mol) and concentrated hydrochloric acid (250 ml, 3 mol)[6] was passed into pyridine (200 ml) at −30°C with stirring. The solution of nitrosyl chloride was added dropwise to a stirred solution of the urethane (**7**, 28.54 g, 0.1 mol) in pyridine (60 ml) at −10——15°C. After being stirred for 2 h at −10——15°C, the reaction mixture was added to ice-water (2 l). The nitroso compound readily solidified after a while, and was collected, washed well with ice-water, then dried to give **8** as a yellow solid (29.4 g, 94%). For elemental analysis, a small portion of **8** was recrystallized from diethyl ether to give yellow needles, mp 63.5—65°C. IR ν_{max} cm^{-1}: 1750, 1600, 1530, 1400, 1340, 1320, 1280, 1175, 1150. NMR δ (ppm): 1.40 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.32 (3H, s, 4-CH_3), 2.62 (6H, s, 2,6-diCH_3), 4.50 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 5.15 (2H, s, CH_2), 7.00 (2H, s, aromatic H). *Anal.* Calcd for $C_{13}H_{18}N_2O_5S$: C, 49.67; H, 5.77; N, 8.91. Found: C, 49.81; H, 5.66; N, 8.61.

2-Mesitylenesulfonyldiazomethane (**4**)——To alumina (230 g, Merck No. 1077) suspended in diethyl ether (600 ml) was added the nitrosourethane **8** (23.58 g, 0.075 mol) in methylene chloride (100 ml) at 0°C. The mixture was stirred well for 2 h at 0°C, and the solution was decanted from the alumina. Diethyl ether (400 ml) and methylene chloride (200 ml) were added to the alumina, and the mixture was stirred for 2 h at 0°C, then the solution was decanted off. This work-up was repeated twice more. The combined decanted solution was filtered and evaporated to dryness *in vacuo* without heating to give the sulfonyldiazomethane (**4**, 12.73 g, 78%). For elemental analysis, a portion of **4** was recrystallized from diethyl ether to give yellow needles, mp 53.5—54.5°C. IR ν_{max} cm^{-1}: 2100, 1600, 1330, 1260, 1155, 1135. NMR (δppm): 2.30 (3H, s, 4-CH_3), 2.60 (6H, s, 2,6-diCH_3), 5.36 (1H, s, CH), 6.96 (2H, s, aromatic H). *Anal.* Calcd for $C_{10}H_{12}N_2O_2S$: C, 53.57; H, 5.39; N, 12.48 Found: C, 53.58; H, 5.51; N, 12.89.

α-Benzoyl-α-(2-mesitylenesulfonyl)diazomethane (**9**)——To a mixture of 2-mesitylenesulfonyldiazomethane (**4**, 2.243 g, 10 mmol) and triethylamine (1.012 g, 10 mmol) in acetonitrile (80 ml) was added dropwise benzoyl chloride (1.406 g, 10 mmol) at 0°C. The mixture was stirred at room temperature for 27 h, then concentrated *in vacuo*. The residue was purified by silica gel (200 g) column chromatography with hexane–ethyl acetate (9: 1) to give **9** (2.675 g, 82%) as pale yellow crystals. Recrystallization from diethyl ether afforded yellow needles, mp 141.5—144°C. IR ν_{max} cm^{-1}: 2100, 1650, 1600, 1335, 1280, 1225, 1150. NMR δ (ppm): 2.30 (3H, s, 4-CH_3), 2.68 (6H, s, 2,6-diCH_3), 6.96 (2H, s, aromatic H), 7.20—7.70 (5H, m, aromatic H). *Anal.* Calcd for $C_{17}H_{16}N_2O_3S$: C, 62.18; H, 4.91; N, 8.53. Found: C, 62.38; H, 4.84; N, 8.53.

Wolff Rearrangement of α-Benzoyl-α-(2-mesitylenesulfonyl)diazomethane (**9**)——(a) With Benzyl Alcohol: Run 1 in Table I is described as a typical procedure. A mixture of **9** (164 mg, 0.5 mmol) and benzyl alcohol (108 mg, 1 mmol) in toluene (25 ml) was refluxed for 2 h. The solvent was evaporated off and benzyl alcohol was removed *in vacuo*. The residue was purified by silica gel preparative layer chromatography with hexane–ethyl acetate (2: 1). Benzyl 2-mesitylenesulfonyl-2-phenylacetate (**10a**, 98 mg, 48%) was obtained from the *Rf* 0.6 layer. Recrystallization from hexane–diethyl ether afforded colorless needles, mp 114—115°C. IR ν_{max} cm^{-1}: 1735, 1600, 1350, 1320, 1285, 1225, 1150. NMR δ (ppm): 2.22 (3H, s, 4-CH_3), 2.38 (6H, s, 2,6-diCH_3), 5.02 (3H, s, CH and CH_2), 6.70—7.40 (12H, m, aromatic H).

2-Benzoyl-5,7-dimethyl-2,3-dihydrobenzo[*b*]thiophene-1,1-dioxide (**11**, 31 mg, 21%) was obtained from the *Rf* 0.4 layer. Recrystallization from hexane–diethyl ether afforded colorless needles, mp 153.5—154°C. IR ν_{max} cm^{-1}: 1680, 1590, 1335, 1290, 1240, 1175, 1150, 1130. NMR δ (ppm): 2.38 (3H, s, CH_3), 2.52 (3H, s, CH_3), 3.20—4.20 (2H, m, CH_2), 5.38 (1H, q, J=6 Hz, CH), 7.0—8.40 (7H, m, aromatic H). *Anal.*

Calcd for $C_{17}H_{16}O_3S$: C, 67.98; H, 5.34. Found: C, 67.94; H, 5.54.

Runs 2 and 3 in Table I were similarly carried out using **9** (164 mg, 0.5 mmol) and benzyl alcohol (108 mg, 1 mmol) in benzene (25 ml) and 2,4,6-trimethylpyridine (2 ml), respectively.

(b) With Benzyl Alcohol in Acetonitrile (Run 4 in Table I): A mixture of **9** (164 mg, 0.5 mmol) and benzyl alcohol (108 mg, 1 mmol) in acetonitrile (25 ml) was refluxed for 48 h. The solvent was evaporated off and benzyl alcohol was removed *in vacuo*. The residue was purified by silica gel preparative layer chromatography with hexane–ethyl acetate (2: 1). 2-Mesitylacetophenone (**13**, 38 mg, 32%) was obtained from the *Rf* 0.8 layer. Recrystallization from hexane–diethyl ether afforded colorless needles, mp 147—149°C. IR ν_{max} cm^{-1}: 1675, 1610, 1590, 1470, 1410, 1330, 1220, 1200. NMR δ (ppm): 1.17 (6H, s, 2,6-diCH_3), 1.28 (3H, s, 4-CH_3), 4.32 (2H, s, CH_2), 6.80—6.82 (7H, s, aromatic H). *Anal.* Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.40; H, 7.73.

The sulfonylacetate (**10a**, 91 mg, 45%) was obtained from the *Rf* 0.6 layer. A trace of **11** was also obtained from the *Rf* 0.4 layer.

(c) With *tert*-Butyl Alcohol (Run 5 in Table I): A mixture of **9** (328 mg, 1 mmol), *tert*-butyl alcohol (4 ml), and 2,4,6-trimethylpyridine (2 ml) was refluxed for 31 h. After removal of the *tert*-butyl alcohol by evaporation, the residual oil was dissolved in chloroform and washed with 1 N hydrochloric acid. The chloroform layer was washed with water, dried, and concentrated. The residue was purified by silica gel preparative layer chromatography with hexane–diethyl ether (1: 1). *tert*-Butyl 2-mesitylenesulfonyl-2-phenylacetate (**10b**, 112 mg, 30%) was obtained from the *Rf* 0.8 layer. Recrystallization from hexane–diethyl ether furnished colorless needles, mp 127.5—128°C. IR ν_{max} cm^{-1}: 1730, 1600, 1320, 1150, 1120. NMR δ (ppm): 1.40 (9H, s, $(CH_3)_3C$), 2.28 (3H, s, 4-CH_3), 2.48 (6H, s, 2,6-diCH_3), 5.02 (1H, s, CH), 6.90—7.60 (7H, m, aromatic H). *Anal.* Calcd for $C_{21}H_{26}O_4S$: C, 67.35; H, 7.00. Found: C, 67.58; H, 7.19.

The benzo[*b*]thiophene derivative (**11**, 40 mg, 13%) was obtained from the *Rf* 0.5 layer.

References and Notes

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3) For a review, see *a*) A.M. van Leusen and J. Strating, *Quart. Rep. Sulfur Chem.*, **5**, 67 (1970); *b*) M. Regitz, "The Chemistry of Diazonium and Diazo Groups," Part 2, ed. by S. Patai, John Wiley and Sons, Chichester, 1978, Chapter 17.
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