Vicarious Nucleophilic Substitution of Hydrogen in Nitroarenes using 1-Chloroalkanesulfonic Esters; A Simple Synthesis of 1-(Nitrophenyl)-alkanesulfonic and (Nitrophenyl)-methanesulfonic Esters[1]

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Vicarious nucleophilic substitution of hydrogen in nitroarenes with carbanions containing leaving groups at the carbanionic center is a general process of great practical value[2-5]. A variety of carbanions of the general structure

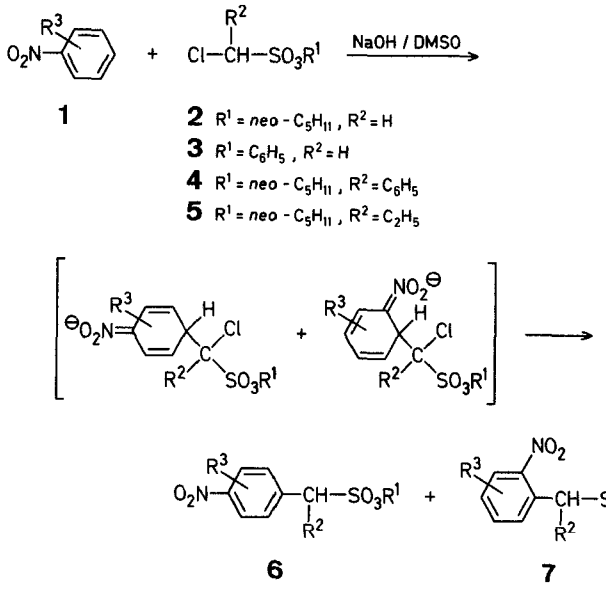
R, a substituent

X^1, a leaving group: Cl, $-OC_6H_5$, $-SC_6H_5$, etc.

X^2, a carbanion-stabilizing group: $-SO_2-C_6H_5$, $-SO_2-N$  , $-S(=O)-C_6H_5$, $-CN$, $-COOR'$, etc.

undergo this reaction[6]. There are also practically no limitations concerning substituents in the nitroaromatic ring[7]. We have obtained particularly good results with α-chlorocarbanions stabilized by phenylsulfonyl and dialkylaminosulfonyl groups[2,7]; one could therefore expect that the easily available esters of 1-chloroalkanesulfonic acids are similarly suitable for this reaction.

In preliminary experiments, methyl chloromethanesulfonate failed to react with nitrobenzene in the presence of strong alkali, apparently due to fast hydrolysis or self-alkylation of the ester. In order to eliminate this difficulty, neopentyl and phenyl sulfonates were selected for further studies since these esters are known to be very resistant toward nucleophilic substitution of the sulfonate anion and also toward base-induced β-elimination. Indeed, neopentyl and phenyl chloromethanesulfonates (**2** and **3**) were found to survive treatment with powdered sodium hydroxide in dimethyl sulfoxide and to react under these conditions with a variety of nitrobenzenes (**1**) to give mixtures of the *ortho* (**7**) and *para* (**6**) isomers of the corresponding neopentyl or phenyl nitrophenylmethanesulfonates.



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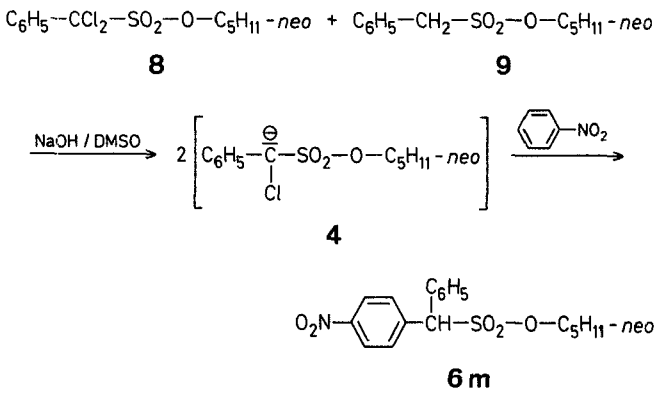
2 R^1 = *neo*-C_5H_{11}, R^2 = H
3 R^1 = C_6H_5, R^2 = H
4 R^1 = *neo*-C_5H_{11}, R^2 = C_6H_5
5 R^1 = *neo*-C_5H_{11}, R^2 = C_2H_5

6 **7**

From these results, a few conclusions can be drawn. First, the vicarious nucleophilic substitution of hydrogen occurs faster than nucleophilic substitution of halogen located *ortho*- or *para*- to the nitro group. This is a general feature of such systems which is observed in reactions of halonitroarenes with a variety of carbanions containing leaving groups. Only in the case of 4-fluoronitrobenzene, do substitution of hydrogen and halogen compete. The second interesting problem is the orientation of the substitution. As can be seen from the data in the Table the *o/p* ratio largely depends on the type of ester submitted to the reaction. In the case of nitrobenzene, the *o/p* ratios are 1.8 and 0.8 for the neopentyl and phenyl esters; similar relations are found for 2-chloronitrobenzene, the *o/p* ratios being 1.0 and 0.25, respectively. The differences in orientation between the neopentyl and phenyl esters are also observed in the reaction with 4-fluoronitrobenzene (competition between substitution of H and F). Under identical conditions, the ratio of *ortho* (H) and *para* (F) substitution of 4-fluoronitrobenzene upon reaction with neopentyl and phenyl chloromethanesulfonate is 1.0 or 0.5, respectively. We have earlier found that the orientation in vicarious substitution is sensitive to steric factors; in the present cases, the differences in orientation are due to groups (R^1) which are distant from the reaction center.

The reaction of 1-nitronaphthalene with both esters **2** and **3** leads to *ortho* substitution in spite of the general preference of ester **3** for *para* substitution. On the other hand, neopentyl 1-chloropropanesulfonate (**5**) and neopentyl phenylchloromethanesulfonate (**4**) react exclusively at the position *para* to the nitro group; this fact is in agreement with our earlier observation that tertiary carbanions replace hydrogen exclusively at the position *para* to the nitro group[2,5,6,7].

Neopentyl 1-chloropropanesulfonate (**5**) was prepared by alkylation of neopentyl chloromethanesulfonate (**2**) with bromoethane under catalytic two-phase conditions[8]. Neopentyl phenylchloromethanesulfonate (**4**) was generated *in situ* via chlorine exchange between neopentyl phenyldichloromethanesulfonate (**8**) and neopentyl phenylmethanesulfonate (**9**) in the system sodium hydroxide/dimethyl sulfoxide/nitrobenzene. Ester **4** cannot be prepared by direct chlorination of ester **9** with tetrachloromethane since dichlorination to **8** predominates.



Neopentyl Chloromethanesulfonate (2):

A solution of chloromethanesulfonyl chloride (30 g, 0.2 mol) in dichloromethane (20 ml) is added dropwise to a stirred solution of neopentyl alcohol (15.5 g, 0.2 mol) and triethylamine (24 g) in dichloromethane (20 ml) at 0°C. During the addition, the temperature of the mixture is kept below 5°C and the mixture is then stirred at room temperature for 2 h. The precipitated triethylamine hydrochloride is filtered off and the filtrate is washed with water (2 × 50 ml) and dried with

Table. Reaction of Nitroarenes (**1**) with Neopentyl and Phenyl 1-Chloroalkanesulfonates (**2–5**)

1-Chloro-alkane-sulfonic ester	R^1	R^2	R^3	Products	Total yield **6** + **7** [%]	Ratio **7** : **6**	m.p. [°C] (solvent)	Molecular formula[a]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm] of 1,1-H_2 or 1-H
2	*neo*-C_5H_{11}	H	H	**6a**	83	1.8	124–125° (hexane/benzene)	$C_{12}H_{17}NO_5S$ (287.3)	4.42
				7a			oil	$C_{12}H_{17}NO_5S$ (287.3)	5.00
3	C_6H_5	H	H	**6b**	54	0.8	137–139° (CCl_4)	$C_{13}H_{11}NO_5S$ (293.3)	4.60
				7b			oil	$C_{13}H_{11}NO_5S$ (293.3)	5.15
2	*neo*-C_5H_{11}	H	2-Cl	**6c**	80	1.0	81–82° (hexane/benzene)	$C_{12}H_{16}ClNO_5S$ (321.8)	4.41
				7c			74.5–76° (PE/benzene)	$C_{12}H_{16}ClNO_5S$ (321.8)	4.46
3	C_6H_5	H	2-Cl	**6d**	79	0.25	83–84° (methanol)	$C_{13}H_{10}ClNO_5S$ (327.7)	5.52
				7d			oil	$C_{13}H_{10}ClNO_5S$ (327.7)	5.62
2	*neo*-C_5H_{11}	H	4-Cl	**7e**	42	—	56–58° (hexane)	$C_{12}H_{16}ClNO_5S$ (321.8)	4.96
3	C_6H_5	H	4-Cl	**7f**	67	—	74–75° (CCl_4)	$C_{13}H_{10}ClNO_5S$ (327.7)	5.08
3	C_6H_5	H	4-Br	**7g**	60	—	80–81° (CCl_4)	$C_{13}H_{10}BrNO_5S$ (372.2)	5.08
2	*neo*-C_5H_{11}	H	4-F	**6h**[c] (R^2 = Cl)	62	1.0	98–99.5° (PE/benzene)	$C_{12}H_{16}ClNO_5S$ (371.8)	6.02
				7h			88–89° (PE/benzene)	$C_{12}H_{16}FNO_5S$ (305.3)	5.00
3	C_6H_5	H	4-F	**6i**[c] (R^2 = Cl)	72	0.5	oil	$C_{13}H_{10}ClNO_5S$ (327.7)	6.15
				7i			oil	$C_{13}H_{10}FNO_5S$ (311.3)	5.17
2	*neo*-C_5H_{11}	H	2,3-$(CH)_4$[b]	**7j**	74	—	88–89° (methanol)	$C_{16}H_{19}NO_5S$ (337.4)	4.58
3	C_6H_5	H	2,3-$(CH)_4$[b]	**7k**	67	—	116–117° (ethanol)	$C_{17}H_{13}NO_5S$ (343.4)	4.85
2	*neo*-C_5H_{11}	H	3-NO_2	**6l** = **7l**	47	—	82–83° (hexane/benzene)	$C_{12}H_{16}N_2O_7S$ (332.3)	5.05
4	*neo*-C_5H_{11}	C_6H_5	H	**6m**	68	—	98–99° (CCl_4)	$C_{18}H_{21}NO_5S$ (363.4)	5.63
5	*neo*-C_5H_{11}	C_2H_5	2-Cl	**6n**	59	—	52–54° (PE/benzene)	$C_{14}H_{20}ClNO_5S$ (349.8)	4.22

[a] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.3; H, ±0.23; N, ±0.36.

[b] **1** = 1-nitronaphthalene.

[c] The F-atom is replaced.

magnesium sulfate. The solvent is evaporated and the residual product **2** distilled in vacuo; yield: 29.8 g (74%); b.p. 110°C/10 torr.

$C_6H_{13}ClO_3S$	calc.	C 35.91	H 6.53
(200.7)	found	36.1	6.65

^{1}H-N.M.R. (CCl_4/TMS_{int}): δ = 1.0 (s, 9H); 3.95 (s, 2H); 4.55 ppm (s, 2H).

Phenyl Chloromethanesulfonate (3):

A solution of chloromethanesulfonyl chloride (27 g, 0.18 mol) in chloroform (50 ml) is added dropwise to a vigorously stirred cold aqueous solution of sodium phenoxide [phenol (24 g, 0.2 mol) + sodium hydroxide (8 g, 0.2 mol) + water (50 ml)] and tetrabutylammonium bromide (0.5 g). During the addition, the temperature of the mixture is kept at 0–2°C. The mixture is then stirred without cooling for 30 min, and diluted with water (150 ml). The organic layer is separated and the aqueous layer extracted with chloroform (3 × 30 ml). The combined organic layers are washed with saturated aqueous sodium hydrogen carbonate (50 ml) and dried with magnesium sulfate. The solvent is evaporated and the residual product **3** distilled in vacuo; yield: 28.9 g (78%); b.p. 98–102°C/0.04 torr.

$C_7H_7ClO_3S$	calc.	C 40.68	H 3.42
(206.7)	found	40.5	3.61

^{1}H-N.M.R. (CCl_4/TMS_{int}): δ = 4.62 (s, 2H); 7.30 ppm (s, 5H).

Neopentyl 1-Chloropropanesulfonate (5):

A mixture of neopentyl chloromethanesulfonate (**2**; 10 g, 50 mmol), bromoethane (8.6 g, 80 mmol), 50% aqueous sodium hydroxide (25 ml), and triethylbenzylammonium chloride (TEBA; 0.25 g) is vigorously stirred at room temperature for 6 h (G.L.C. shows complete reaction). The mixture is diluted with water (150 ml) and the product extracted with chloroform (3 × 30 ml), the organic extract washed with water (50 ml), and dried with magnesium sulfate. The solvent is evaporated and the product distilled in vacuo; yield: 8.9 g (78%); b.p. 80°C/0.4 torr.

$C_8H_{17}ClO_3S$	calc.	C 42.01	H 7.49
(228.7)	found	41.8	7.51

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 1–1.3 (m, 12H); 1.9–2.5 (m, 2H); 4.04 (s, 2H); 4.75 ppm (dd, 1H, J = 4.0 Hz, J = 9.6 Hz).

Neopentyl Phenyldichloromethanesulfonate (8):

A mixture of neopentyl phenylmethanesulfonate (**9**; 4.48 h, 20 mmol), tetrachloromethane (30 ml), 50% aqueous sodium hydroxide (20 ml), and TEBA (0.1 g) is vigorously stirred for 2 h at 40°C. The mixture is then diluted with water (100 ml) and product **8** extracted with chloroform (3 × 30 ml). The organic extract is washed with water (50 ml) and dried with magnesium sulfate. The solvent is evaporated and the remaining product **8** recrystallized from methanol; yield: 4.25 g (68%); m.p. 66–67°C.

$C_{12}H_{16}Cl_2O_3S$	calc.	C 46.31	H 5.18	Cl 22.78
(311.2)	found	46.3	5.19	23.0

Reaction of Nitroarenes (1) with Neopentyl or Phenyl 1-Chloroalkanesulfonates (2–5); General Procedure:

A mixture of the nitroarene (**1**; 10 mmol), the 1-chloroalkanesulfonic ester (**2–5**; 10 mmol), powdered sodium hydroxide (4 g, 100 mmol), and dimethyl sulfoxide (20 ml) is stirred for 1 h at room temperature. The mixture is then poured into water (200 ml), acidified with hydrochloric acid, and extracted with chloroform (3 × 30 ml). The combined extracts are washed with water (1 × 50 ml) and dried with magnesium sulfate. The solvent is evaporated and the products are purified and separated (*o*-, *p*-isomers) by column chromatography (silica gel, Merck 230–400 mesh, eluent chloroform).

Neopentyl (4-Nitrophenyl)-phenylmethanesulfonate (6m):

A mixture of nitrobenzene (1.56 g, 10 mmol), neopentyl phenylmethanesulfonate (**9**; 1.21 g, 5 mmol), neopentyl phenyldichloromethanesulfonate (**8**; 1.65 g, 5 mmol), sodium hydroxide (4 g, 100 mmol), and dimethyl sulfoxide (20 ml) is stirred for 1 h at 20–30°C. The mixture is then poured into water (200 ml), the resultant mixture acidified with hydrochloric acid, and extracted with chloroform (3 × 30 ml). The combined organic extract is washed with water (50 ml) and dried with magnesium sulfate. The solvent is evaporated and the remaining product purified by column chromatography (silica gel, Merck 230–400 mesh, eluent chloroform) and recrystallized from tetrachloromethane; yield: 2.5 g (68%); m.p. 98°C.

$C_{18}H_{21}NO_5S$	calc.	C 59.49	H 5.82	N 3.85
(363.4)	found	59.6	5.68	3.49

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 0.82$ (s, 9H); 3.63 (d, 1H, $J = 8$ Hz); 3.70 (d, 1H, $J = 8$ Hz); 5.62 (s, 1H); 7.3–7.55 (m, 5H); 7.72 (d, 2H, $J = 8.5$ Hz); 8.18 ppm (d, 2H, $J = 8.5$ Hz).

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