Tetrahedron. Vol. 31, pp. 597 to 600. Pergamon Press 1975. Printed in Great Britain

ON THE SYNTHESIS OF α-ARYLSULFONYL- AND α-ALKYLSULFONYLPHENYLDIAZOMETHANES[1]

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(*Received in UK 6 September 1974; Accepted for publication 3 October 1974*)

Abstract—Three general methods have been developed for the synthesis of α-diazosulfones, with special emphasis on the preparation of α-aryl substituted α-diazosulfones.

Some years ago, a method was described for the synthesis of the previously unknown α-diazosulfones[2] **1**, based on the alumina-induced cleavage of nitrosocarbamates, according to

$$RSO_2CHR'NCO_2Et \xrightarrow[Et_2O]{Al_2O_3} RSO_2C(=N_2)-R' \quad (1)$$
$$\text{(N=O)} \qquad\qquad \mathbf{1}$$

R' = H, *n*-alkyl

Although this approach was found applicable to a wide variety of substituents R, variation in R' was restricted to H and n-alkyl.[2b] For reasons explained elsewhere,[2b] reaction (1) did not apply to the case where R' = phenyl. Equally unsuccessful were attempts to employ the diazo-transfer reaction[3] to a number of benzyl sulfones:[4]

$$RSO_2CH_2Ar + TosN_3 \xrightarrow{base} RSO_2C(=N_2)-Ar \quad (2)$$
$$\mathbf{2}$$

Apparently, α-tosylphenyldiazomethane (**5**, R = *p*-tolyl, X = H) has provoked synthetic problems elsewhere too.[5a] The claim that this compound is obtained by reaction of tosyl chloride and phenyldiazomethane was recently disproven.[5b]

We wish to report the evaluation of three synthetic methods (Scheme and Table), two of which lead to the formation of α-sulfonylphenyldiazomethanes.† The yields of compounds **5** are moderate to low, however, the starting materials are available in quantity.[6] The best results, relatively speaking, were obtained by a modification of the diazo-transfer reaction to a "methylene" group activated temporarily by an additional aldehyde function[3a] (compounds **3**, reaction (3A)). The application of the Forster reaction[7] (3B) succeeded only for α-tosylphenyldiazomethane (**5a**) in low yield (6% of isolated material), whereas the same compound was not formed by reaction (3C) of sulfonyl azide with α-tosylbenzylidenetriphenylphosphorane[6d] (**7b**).

The principle of the methods (3A) and (3C) also provides useful alternative synthetic procedures for the preparation of tosyldiazomethane (**1a**, Eq. (4) and (5)).

Diazo-transfer reaction (3A). Prior to the investigation of reaction (3A), we established that the previously known unsubstituted tosyldiazomethane[2] (**1a**) can be synthesized alternatively by reaction (4). To ensure maximal conversion of **8**, an excess of sulfonyl azide **4** was necessary. Thus, 70% of **1a** was formed (as determined by NMR) using a fivefold excess of tosyl azide (**4a**). However, the separation of **1a** from the excess of the isoelectronic (and otherwise very similar) reagent **4a** was not possible by chromatography or crystallization.[8]‡ This problem could be circumvented satisfactorily by using a different azide, *p*-carboxybenzenesulfonyl azide[3b] (**4b**), the excess of which was readily removable. As a result of this variation in reagent, tosyldiazomethane (**1a**) was isolated now in a yield of 73%, which makes this method a valuable alternative for reaction (1).

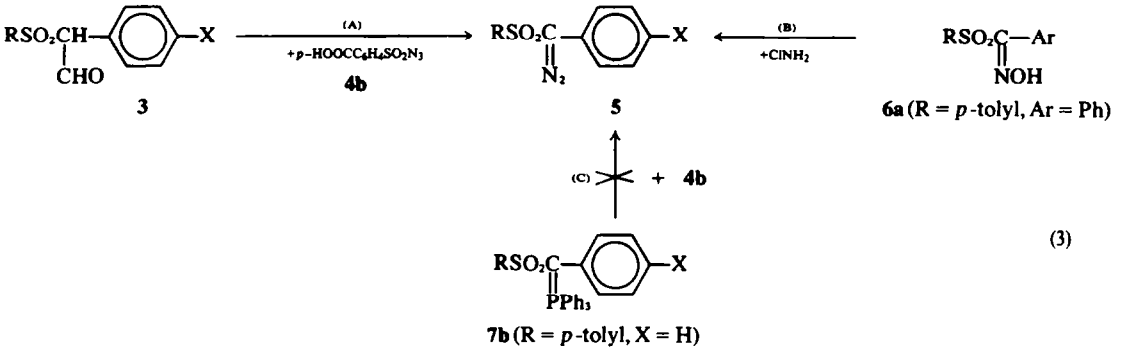
The latter method was then extended to the synthesis of the new α-aryl substituted α-diazosulfones **5a–d** (reaction (3A) and table). As a side-product in all these reactions, another sulfonyl azide RSO_2N_3 was formed, in which the group R was the same as in the starting sulfonylaldehyde **3**. For example, *ca* 30% of *tosyl* azide (**4a**) was formed in addition to α-tosylphenyldiazomethane (**5a**, 58% yield§), although the reaction was carried out with *p*-carboxybenzenesulfonyl azide (**4b**). This was quite unexpected and equally annoying, since the same tosyl azide was generated that had prevented the isolation of **1a** in the experiment discussed above, and which we wanted to avoid by using **4b** instead. However, we now were dealing with smaller quantities of the unwanted azide **4a**. Further, the two products, **5a** and **4a**, differed in molecular weight, which permitted separation by crystallization, to give α-tosylphenyldiazomethane (**5a**) in 48% yield. Comparable results were obtained for the diazosulfones **5b–d**, although the yields were lower (Table).

†The very first example of an α-sulfonylphenyldiazomethane was reported recently by *Carpino et al.*, (**5**, R = PhCH=CPh, X = H), obtained by an unsolicited ring opening of a cycloadduct of 2,3-diphenylthiirene-1,1-dioxide and phenyldiazomethane.[5c]

‡This reaction was carried out in 40% EtOH with 1 equiv triethylamine.

§Yield determined by NMR, using dimethyl sulfone as an internal standard.

Scheme and Table



3 5 6a (R = *p*-tolyl, Ar = Ph)

7b (R = *p*-tolyl, X = H) (3)

	R	X	% yield[a] by (3A)	(3B)	m.p. °C	$\nu_{C-N=N}$	ν_{SO_2} (cm^{-1})
5a	*p*-tolyl	H	48 (58)	6 (24)	79–81° (dec)	2085	1342, 1152[c]
5b	*t*-butyl	H	21 (26)		53–54°	2090	1310, 1150[c]
5c	benzyl	H	4 (10)		66–68° (dec)	2095	1335, 1165, 1135[c]
5d	*p*-tolyl	*p*-MeO	[b] (27)	—	[b]	2075	1320, 1308, 1150[d]

[a] Yield of isolated material; between brackets yield as determined by NMR using dimethyl sulfone as an internal standard.
[b] Not isolated in pure form.
[c] In nujol.
[d] Neat.

The best results in reaction (3A) were obtained in a two phase-system water-dichloromethane, using 5 equivalents of *p*-carboxybenzenesulfonyl azide (**4b**) and a large excess of ammonia (15 equiv). Similar results were found with sodium carbonate instead of ammonia. Sodium hydroxide or triethylamine gave lower yields of **5a**, but an equal amount of the by-product tosyl azide (*ca* 30%), whereas pyridine gave no reaction.

In a separate experiment it was shown that an azide function can be exchanged between sodium tosylate and *p*-carboxybenzenesulfonyl azide. We therefore tentatively explain the formation of tosyl azide in (3A), in addition to **5a** and **5d**, through such an exchange reaction with tosylate, formed by elimination from some intermediate, e.g. an intermediate similar to **9** (Eq (4)). The formation of t-butylsulfonyl azide and benzylsulfonyl azide in addition to **5b** and **5c**, respectively, are interpretable likewise.

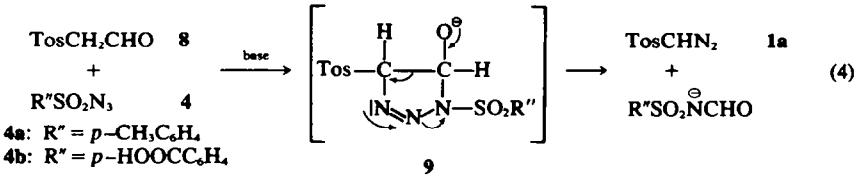
The aryl substituted α-diazosulfones **5** are red to orange coloured compounds. The thermal stability of **5a–c** and their sensitivity towards light and heat are comparable to that of unsubstituted tosyldiazomethane[2] (**1a**). Compound **5d** is somewhat exceptional since it was formed much faster (in 20 min) and, moreover, it was thermally too unstable to be isolated.

The synthetic methods leading to the starting materials **3** are dealt with in a succeeding paper.[6a]

The Forster reaction (3B). α-Tosylphenyldiazomethane (**5a**) was prepared originally by reaction of chloramine and α-hydroxyiminobenzyl *p*-tolyl sulfone (**6a**). The highest yield of **5a** was obtained by using chloramine, prepared *in situ* from ammonia (10%, 20 equiv) and sodium hypochlorite (15 equiv), in an inhomogeneous mixture of water-dichloromethane. The crude mixture consisted, as estimated by NMR, of diazosulfone **5a** (24%), benzyl *p*-tolyl sulfone* (21%) and benzonitrile[7a] (55%). Unfortunately no more than 6% of **5a** could be isolated by chromatography over alumina.

α-Tosyl-*p*-methoxyphenyldiazomethane (**5d**) could not be prepared by this method. Here, the crude mixture showed IR bands at 2248 and 2310 cm^{-1} (indicative of –C≡N and –C≡N→O, respectively), but no diazo band around 2100 cm^{-1}. Similar negative results were obtained with the oximes **6b** and **6c** (Experimental), in which

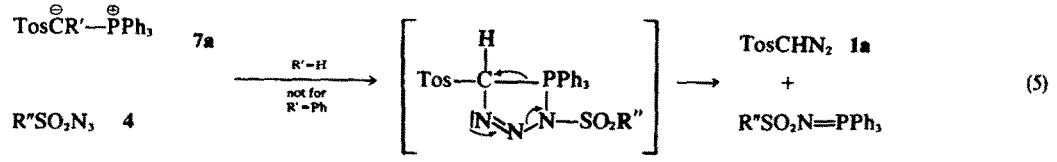
*Formed possibly by reduction of **5a**.



(4)

R = *p*-tolyl and Ar = 2,4,6-trimethylphenyl, or 2,6-dichlorophenyl, respectively.

Reaction of phosphorus ylids and sulfonyl azide (3C). Carboalkoxymethylenephosphoranes have been described to provide α-diazoesters on treatment with certain azides,[9a,b] although one erroneous claim was corrected recently.[9c] We, nevertheless, found this type of reaction applicable to tosylmethylenetriphenylphosphorane[6d] (**7a**, R' = H, Eq (5)), providing another alternative for the synthesis of tosyldiazomethane (**1a**, 60% yield). Since excess of sulfonyl azide was not required in this case, the reaction was successful with both tosyl azide (**4a**) and *p*-carboxybenzenesulfonyl azide (**4b**).



(5)

As was found previously in similar reactions[9b,c] the nature of the substituent R' is of crucial importance in these azide reactions. In our case, no reaction was observed between α-tosylbenzylidenetriphenylphosphorane[6d] (**7b**, Eq (3C)) and **4b**, not even after 2 days at room temperature in dichloromethane.*

The following conclusions can be drawn from the present work: (i) reactions (4) and (5) are useful alternatives for the previously reported[2] synthesis (Eq (1)) of sulfonyldiazo*methanes*; (ii) α-sulfonylaryldiazomethanes (**5**) are best prepared by reaction (3A).

EXPERIMENTAL

M.ps were determined in an oil bath, except for **5** which were taken on a Kofler Block. A Perkin-Elmer 257 Grating Infrared Spectrophotometer and a Varian A60 NMR apparatus were used. The elemental micro analyses were carried out in the Analytical Department of this laboratory.

Tosyldiazomethane (**1a**), by reaction (4). Compound **4b**[3b] (4·54 g, 20 mmole) was added to 2·16 g (10 mmole) of tosylacetaldehyde hemihydrate[10] in a mixture of dichloromethane (90 ml) and 1 N ammonia (50 ml). The mixture, which turned yellowish-green, was stirred overnight (16 hr) in the dark at room temp. The organic layer was dried over $MgSO_4$ and concentrated. The resulting yellow oil was chromatographed with dichloromethane (in *ca* 15 min) over a short, broad column of alumina (Merck, act. III, length 8 cm, diam 3·5 cm). Crude **1a** (80% by NMR‡) was crystallized from diethyl ether to provide 1·42 g (73%) of yellow crystals, m.p. 36–38° (lit.[2a] 34–37°).

In a similar manner **1a** was prepared in 58% yield (by NMR‡) from tosylacetaldehyde enol acetate.†

α-Tosylphenyldiazomethane (**5a**), by reaction (3). Similar to the above synthesis of **1a**, compound **5a** was prepared from α-tosylphenylacetaldehyde[6a] (2·74 g, 10 mmole) and *p*-carboxybenzenesulfonyl azide[3b] (**4b**, 11·4 g, 50 mmole) in 150 ml dichloromethane and 75 ml 2 N ammonia. After the reaction was complete (16 hr), the organic layer was filtered in *ca* 5 min over a layer of alumina (Merck, act. III, thickness 4 cm, diam 6 cm) covered with dichloromethane on a sintered glass funnel (to remove water and the remainder of **4b**), and concentrated. The resulting red oil was chromatographed on the same type of alumina (column length 15 cm, diam 1·5 cm) in CCl_4. The first coloured band provided 2·13 g of red oil, containing 58% of **5a** and 28% of tosyl azide (determined by NMR‡). The α-diazosulfone **5a** was isolated from this mixture by crystallization from diethyl ether-light petroleum 40–60°, providing 1·31 g (48%) of red crystals, m.p. 79–81° (dec); NMR (CCl_4) δ 2·38 (s, 3 H), 7·05–7·35 (br, 7 H), 7·67 (d, 2 H, *J* 8·5 c/s). (Found: C, 61·7; H, 4·5; S, 11·6; N, 9·8. Calc. for $C_{14}H_{12}N_2O_2S$ (272·3): C, 61·76; H, 4·44; S, 11·78; N, 10·29%).

α-Chlorobenzyl p-tolyl sulfone. Dry HCl was bubbled through an etheral soln of **5a** until the colour disappeared. Removal of solvent gave quantitatively the α-chlorosulfone, m.p. 200–204°, identical with an authentic sample,[12] m.p. 203°, by mixture m.p. and IR.

α-t-Butylsulfonylphenyldiazomethane (**5b**, reaction (3A)) was prepared by the method used for **5a** from α-t-butylsulfonylphenylacetaldehyde (enol tautomer,[6a] 1·20 g, 5·0 mmole) and 5·7 g (25 mmole) of azide **4b**[3b] to provide, prior to column chromatography, a red oil with IR bands at 2090 cm^{-1} ($\rangle CN_2$) and 2130 cm^{-1} (N_3), containing 26% of **5b**, 40% of t-butylsulfonyl azide and 10% of benzyl t-butyl sulfone (determined by NMR‡). Pure **5b** was obtained by chromatography followed by crystallization, as orange crystals (250 mg, 21%), m.p. 53–54°; NMR ($CDCl_3$) δ 1·38 (s, 9 H), 7·1–7·6 (m, 5 H). (Found: C, 55·5; H, 5·9; N, 11·7; S, 13·7. Calc. for $C_{11}H_{14}N_2O_2S$ (238·3): C, 55·44; H, 5·92; N, 11·75; S, 13·45%).

α-Benzylsulfonylphenyldiazomethane (**5c**, reaction (3A)) was prepared by the method used for **5b** from α-benzylsulfonylphenylacetaldehyde (a mixture of enol and keto tautomers,[6a] 2·47 g, 9·0 mmole) and 10·2 g (45 mmole) of azide **4b**[3b] in 2 hr to provide, prior to column chromatography a red oil with IR bands at 2090 ($\rangle CN_2$) and 2143 cm^{-1} (N_3), containing 10% of **5c** and 25% of benzylsulfonyl azide (determined by NMR‡). Pure **5c** was obtained after chromatography followed by fractional crystallization, as orange crystals, 98 mg (4%), m.p. 66–68° (dec); NMR (CCl_4) δ 4·28 (s, 2 H), 7·0–7·5 (m, 10 H). (Found: C, 61·5; H, 4·5; N, 10·1; S, 11·8; Calc. for $C_{14}H_{12}N_2O_2S$ (272·3): C, 61·76; H, 4·44; N, 10·29; S, 11·78%).

α-Tosyl-p-methoxyphenyldiazomethane (**5d**), reaction (3A). According to the procedure given above for **5b**, crude α-tosyl-*p*-methoxyphenylacetaldehyde (from *p*-methoxybenzyl *p*-tolyl sulfone (2·76 g, 10 mmole) by formylation with ethyl formate and BuLi[6a]) was converted with azide **4b**[3b] (7·9 g, 35 mmole) in 25 ml 2 N ammonia and 50 ml dichloromethane. After 20 min the organic layer was filtered over alumina and chromatographed, providing a red oil (1·92 g) containing 27% of **5d** and 25% of tosyl azide (by

*With R' = CH_3 no α-tosyldiazoethane is found either, although reaction did occur, presumably forming $TosCH(CH_3)P_{\oplus}Ph_3$ $TosO^{\ominus}$ (30% yield).

†Prepared by oxidation of 2-tosylethanol with dimethyl sulfoxide in acetic anhydride,[11a] m.p. Found: 102–107°; lit.[11b] 109–110°.

‡Yield determined by NMR, using dimethyl sulfone as an internal standard.

NMR). The α-diazosulfone decomposed during attempted isolation; no phosphazine derivative[2a] could be obtained.

α-Hydroxyiminobenzyl p-tolyl sulfone (**6a**). This was prepared according to the method of Hackmann *et al.*[6b] by stirring a soln of α-chlorobenzaldoxime[13] (7·78 g, 50 mmole) and sodium tosylate (8·90 g, 50 mmole) in 120 ml MeOH for 2 hr at room temp. After removal of the solid, the MeOH solution was concentrated, the residue was dissolved in ether and washed with water. After removal of the ether, the residue was crystallized from benzene, providing 5·5 g (40%) of **6a**, m.p. 149–150° (dec); IR (KBr) 3260 (br, OH), 1645, 1325 (SO_2) and 1145 cm^{-1} (SO_2); NMR ($CDCl_3$) δ 2·40 (s, 3 H), 7·1–7·4 (m, 7 H), 7·63 (d, 2 H, *J* 8 c/s), *ca* 9·7 (br, OH). (Found: C, 61·0; H, 4·8; N, 5·1; S, 11·5. Calc. for $C_{14}H_{13}NO_3S$ (275·3): C, 61·08; H, 4·76; N, 5·08; S, 11·65%).

The *syn/anti* problem of oximes **6a–c** is ignored.

α-Hydroxyimino-2,4,6-trimethylbenzyl p-tolyl sulfone (**6b**) was obtained similarly from α-chloro-2,4,6-trimethylbenzaldoxime[14] (3·95 g, 20 mmole) and sodium tosylate (10·68 g, 60 mmole) in 60 ml MeOH, yield 3·67 g (58%), m.p. 137–139° (dec) (from ether light petroleum 40–60°); IR (nujol) 3395 and 3290 (OH), 1620, 1300 (SO_2) and 1150 cm^{-1} (SO_2); NMR ($CDCl_3$) δ 2·18 (s, 6 H), 2·27 (s, 3 H), 2·40 (s, 3 H), 6·83 (s, 2 H), 7·26 (d, 2 H, J 8 c/s), 7·87 (d, *ca* 2 H, J 8 c/s). (Found: C, 64·3; H, 5·9; S, 10·2; N, 4·5. Calc for $C_{17}H_{19}NO_3S$ (317·4): C, 64·33; H, 6·03; S, 10·10; N, 4·41%).

α-Hydroxyimino-2,6-*dichlorobenzyl* p-*tolyl sulfone* (**6c**) was obtained similarly from α-2,6-trichlorobenzaldoxime[6b] (10·0 g, 45 mmole) and sodium tosylate (8·9 g, 50 mmole) in 7·1 g (46%) yield, m.p. 173–174° (dec) (from toluene); IR (nujol) 3410 and 3250 (OH), 1300 and 1140 cm^{-1} (SO_2); NMR (acetone-d_6) δ 2·47 (s, 3 H), 7·3–7·6 (m, 5 H), 8·05 (d, 2 H, *J* 8·5 c/s), 12·34 (s, 1 H); the peak at 12·34 ppm disappeared on addition of D_2O. (Found: C, 48·9; H, 3·2; Cl, 20·7; N, 4·0; S, 9·3. Calc for $C_{14}H_{11}Cl_2NO_3S$ (344·2): C, 48·85; H, 3·22; Cl, 20·60; N, 4·07; S, 9·32%).

α-Tosylphenyldiazomethane (**5a**), by Forster reaction (3B). A soln of sodium hypochlorite (360 ml, *ca* 15%) was added dropwise in 75 min to a stirred mixture of **6a** (12·0 g, 44 mmole) in dichloromethane (360 ml), conc ammonia (100 ml) and water (200 ml). After stirring for 4·5 hr at room temp in the dark, the organic layer was worked-up as described above for **5a** by reaction (3A), providing ultimately 6% of **5a**, decomposing at *ca* 80°; identical with the product described above according to IR and NMR.

Tosyldiazomethane (**1a**), by reaction (5). A soln of **7a**[6cd] (2·15 g, 5·0 mmole) in 30 ml dichloromethane was added slowly (in 4 hr) at room temp in the dark to a stirred suspension of **4b**[3b] (1·36 g, 6 mmole) in 20 ml dichloromethane. Work-up as above for **1a** by reaction (4), provided 0·59 g (60%) of yellow crystals, m.p. 35–38°.

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