where X is concentration of inositol (mg/ml) and Y is ratio of peak height (inositol/methyl arachidate). The limit of determination was 0.1 mg/ml. The variation and average recovery of 5 samples are shown in Table I, indicating that the present method is enough accurate for quantitative analysis of inositol in MPCS.

Influences of Sugars

In order to examine the interference with large amounts of various sugars, 13 kinds of synthetic mixture which contained inositol and 1000-fold amount of each sugars (see Table II) were prepared and treated according to the above procedure. As a result, the sugars except maltose and sorbitol had no influences on the recovery of inositol, whereas maltose and sorbitol made the recovery of inositol a little higher, as shown in Table II. It was found that 500-fold amount of maltose or 200-fold amount of sorbitol did not interfere any more.

From these results, it was proved that the present method is applicable to the determination of inositol in samples containing large amounts of sugars.

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Reaction of N,N-Dialkylaminomethyl Arenesulfonates with Diazoalkanes

Yoshitaka Akasaka, Toshiaki Morimoto, and Minoru Sekiya

Shizuoka College of Pharmacy[1)]

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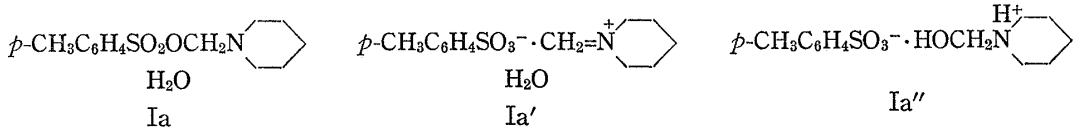
The present paper describes our finding that diazoalkanes react with N,N-dialkylaminomethyl arenesulfonates affecting the insertion of alkylidenes into the methylene carbon-oxygen bond.

Keywords——diazoalkane; methyleniminium salt; N,N-dialkylaminomethyl arenesulfonate; insertion reaction; aziridinium intermediate; anion exchange; piperidineethanol

We describe here a new reaction of diazoalkanes with N,N-dialkylaminomethyl arenesulfonates affecting the insertion of alkylidenes into the methylene carbon-oxygen bond.

The reactions of N,N-dialkyl-N-chloromethylamines with methyl *p*-toluenesulfonate and of methylenebisamines with benzenesulfonic benzoic anhydride have been reported by Böhme *et al.*[2)] to give N,N-dialkyl-N-methyleniminium arenesulfonates without description of their melting points. In an attempt to synthesize 1-methylenepiperidinium *p*-toluenesulfonate according to the former method, recrystallization of the product from benzene, however, gave crystals of mp 85—87°, which were analyzed as a compound corresponding to its monohydrate. For this hydrate the following three structures, Ia, Ia′ and Ia″, can be

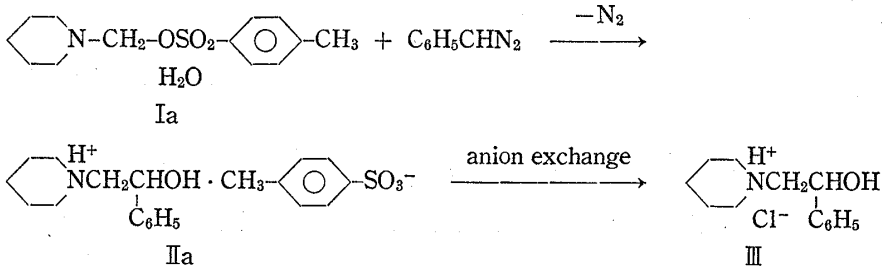


1) Location: *2-2-1, Oshika, Shizuoka, 422, Japan.*

2) H. Böhme and E. Köhler, *Stizber. Ges. Beförd. Ges. Naturw. Marburg*, **83/84**, 535 (1961) [*C.A.*, **59**, 11416 (1963)]; H. Böhme and K.-H. Meyer-Dulheuer, *Ann. Chem.*, **688**, 78 (1965).

possibly written. In its nuclear magnetic resonance (NMR) spectrum, the signal of the methylene protons, however, appeared at δ 4.5—4.75 ppm, in contrast to those of the previously known methyleniminium salts at δ 8.01 ppm (CD_3CN),[3] δ 8.03 ppm (CF_3CO_2H),[4] δ 8.18 ppm (DMSO).[5] It has also been reported[6] that the chemical shift, δ 4.9 ppm, of the methylene protons of dimethylaminomethyl acetate indicates a covalent C–O bond. From these data it is considered that the structure of covalent C–O bond is rather favorable for the hydrate. To the best of our knowledge, in the literature there has not been isolated N-hydroxymethylated secondary amine which is presumably unstable in pure state. Although further investigation is necessary for determination of the structure, the hydrate structure, 1-piperidinomethyl *p*-toluenesulfonate monohydrate (Ia), may be most probable. A similarly prepared 1-piperi dinomethyl benzenesulfonate (Ib), mp 73—74°, recrystallized from benzene also gave the similar analytical data corresponding to its monohydrate.

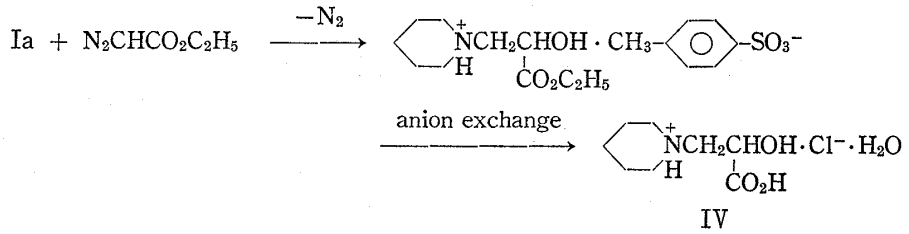
We have found that, by allowing Ia to react with phenyldiazomethane in benzene at room temperature, the reaction proceeded with evolution of nitrogen to give crystals, mp 153—155°. This product was assigned as α-phenyl-1-piperidineethanol *p*-toluenesulfonate (IIa) by noting well correspondence of its analytical data and NMR spectrum. Its structure was evidenced as piperidinium salt by the anion exchange into its hydrochloride, III, on



passing its aqueous solution through Amberlite IRA-400 (chloride form). The compound, Ib, similarly gave the corresponding product, α-phenyl-1-piperidineethanol benzenesulfonate (IIb) by the reaction with phenyldiazomethane.

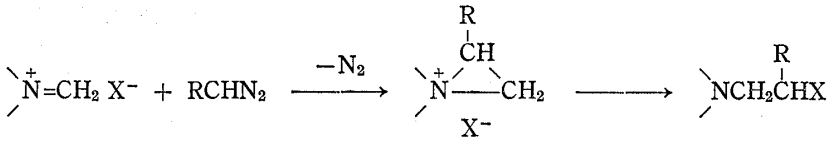
As for the reaction with Ia, control experiments were made using some other solvents in place of benzene (yield, 57%), resulting in the following yields; tetrahydrofuran (THF) (50%), toluene (48%), dichloromethane (32%), ether (28%).

When diazomethane and ethyl diazoacetate were allowed to react with Ia, the former was unreactive, but the latter gave the corresponding insertion product on carrying out the reaction in toluene at 85°. The insertion product was identified by converting into its hydrochloride, IV, on passing its aqueous solution through Amberlite IR-120-B and eluting with hydrochloric acid.



It has been known that iminium salts react with diazoalkanes to give aziridinium salts.[7] The reaction of methyleniminium halides with diazoalkanes has been reported to result in the

3) F. Knoll and U. Krumm, *Chem. Ber.*, **104**, 31 (1971).
4) A.F. McDonagh and H.E. Smith, *J. Org. Chem.*, 33, 8 (1968).
5) J. Schreiber, H. Maag, N. Hashimoto, and A. Eschenmoser, *Angew. Chem.*, **83**, 355 (1971).
6) H. Böhme and P. Backhaus, *Ann. Chem.*, **1975**, 1790.
7) N.J. Leonard and K. Jann, *J. Am. Chem. Soc.*, **82**, 6418 (1960); *idem, ibid.*, **84**, 4806 (1962).



production of β-haloamines through aziridinium intermediates.[8] In this reaction, electrophilicity of the iminium salts may be a driving force. When the iminium structure, Ia′, is taken up for the substrate, the present reaction can be illustrated in analogy with the above reaction.

Experimental[9]

1-Piperidinomethyl Arenesulfonate Monohydrates (Ia and Ib)——To a suspension of N-chloromethylpiperidine (6.7 g, 0.05 mol) in 40 ml of acetonitrile was added methyl *p*-toluenesulfonate (13.0 g, 0.07 mol). The mixture was refluxed for 30 min. After evaporation of the solvent under reduced pressure, the residue was triturated with isopropyl ether to give a solid material which was collected by filtration. Recrystallization from benzene gave 1-piperidinomethyl *p*-toluenesulfonate monohydrate (Ia). Yield, 76%. Prisms, mp 85—87°. NMR ($CDCl_3$) δ ppm: 1.22—2.12 (6H, m, $(CH_2)_3$), 2.35 (3H, s, CH_3), 2.50—3.90 (4H, m, $(CH_2)_2$-N), 4.50—4.75 (2H, br, NCH_2O), 7.23, 7.75 (4H, ABq, J=7 Hz, C_6H_4), 5.6—6.5, 9—9.6 (2H, br, H_2O). *Anal.* Calcd. for $C_{13}H_{21}NO_4S$: C, 54.34; H, 7.37; N, 4.88. Found: C, 54.69; H, 7.28; N, 4.99. 1-Piperidinomethyl benzenesulfonate monohydrate (Ib) was obtained by the same procedure as for Ia. Yield, 78%. Prisms, mp 73—74°. NMR ($CDCl_3$) δ: 1.05—2.05 (6H, m, $(CH_2)_3$), 2.15—3.65 (4H, m, $(CH_2)_2N$), 4.30—4.70 (2H, br, NCH_2O), 7.10—7.96 (5H, m, C_6H_5), 6.4—7.2, 8.7—9.5 (2H, br, H_2O). *Anal.* Calcd. for $C_{12}H_{19}NO_4S$: C, 52.74; H, 7.01; N, 5.13. Found: C, 52.81; H, 6.98; N, 5.18.

Reaction of 1-Piperidinomethyl Arenesulfonate Monohydrates (Ia and Ib) with Phenyldiazomethane——To a stirred suspension of Ia (5.7 g, 0.02 mol) in 40 ml of benzene was added dropwise a solution of phenyldiazomethane (0.02 mol) in 10 ml of benzene. The mixture was stirred overnight at room temperature. Process of the reaction was indicated by evolution of N_2, while the suspending Ia was brought into a solution and then the product was gradually deposited. Filtration and recrystallization from THF gave α-phenyl-1-piperidineethanol *p*-toluenesulfonate (IIa) as prisms, mp 153—155°. Yield, 57%. NMR ($CDCl_3$) δ: 1.15—2.00 (6H, m, $(CH_2)_3$), 2.30 (3H, s, CH_3), 2.50—3.80 (6H, m, $(CH_2)_3N$), 5.15 (1H, t, J=7 Hz, $-CH_2\underline{C}\underline{H}-$), 6.95—7.45 (5H, m, C_6H_5), 7.12, 7.68 (4H, ABq, J=7 Hz, C_6H_4), 6.4—6.7, 8.2—9.5 (2H, br, OH, NH). *Anal.* Calcd. for $C_{20}H_{27}NO_4S$: C, 63.64; H, 7.21; N, 3.71. Found: C, 63.55; H, 7.06; N, 3.71. By passing an aqueous solution of this material through an anion-exchange resin, Amberlite IRA-400 (chloride form), α-phenyl-1-piperidineethanol hydrochloride (III) was obtained as prisms (EtOH), mp 187—189° (lit.[10] mp 200—202°).

The reaction of Ib with phenyldiazomethane was processed by the same procedure as described above to give α-phenyl-1-piperidineethanol benzenesulfonate (IIb) as prisms (THF), mp 143—145°. Yield, 25%. NMR (DMSO-d_6) δ: 1.10—2.12 (6H, m, $(CH_2)_3$), 2.60—3.80 (6H, m, $(CH_2)_3N$), 4.90—5.30 (1H, br, $-CH_2\underline{C}\underline{H}-$), 7.10—7.80 (10H, m, $2\times C_6H_5$), 6.1—7.0, 8.9—9.4 (2H, br, OH, NH). *Anal.* Calcd. for $C_{19}H_{25}NO_4S$: C, 62.79; H, 6.93; N, 3.85. Found: C, 62.82; H, 7.00; N, 3.86.

Reaction of 1-Piperidinomethyl *p*-Toluenesulfonate Monohydrate (Ia) with Ethyl Diazoacetate——To a stirred suspension of Ia (5.7 g, 0.02 mol) in 40 ml of toluene was added a solution of ethyl diazoacetate (2.3 g, 0.02 mol) in 10 ml of toluene. The mixture was heated with stirring at 85° for 3.5 hr, while the evolution of N_2 was observed. After removal of the precipitated piperidine *p*-toluenesulfonate by filtration, the filtrate was evaporated to dryness under reduced pressure. The residue was treated with 50 ml of 3% aq. HCl on a boiling water bath for 1 hr. After washed with ether, the aqueous layer was evaporated to dryness under reduced pressure. An aqueous solution of the residue was passed through a cation-exchange resin (Amberlite IR-120-B) and elution with hydrochloric acid gave 0.88 g (19%) of α-hydroxy-β-piperidinopropionic acid hydrochloride monohydrate (IV) as prisms (iso-PrOH), mp 104—106°. IR ν_{max}^{KBr} cm^{-1}: 2700—3400 (OH), 1735 (C=O), 1115 (>C–OH). *Anal.* Calcd. for $C_8H_8ClNO_4$: C, 42.20; H, 7.97; N, 6.15. Found: C, 42.19; H, 7.87; N, 6.21.

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8) H. Böhme, E. Mundlos, W. Lehners, and O.-E. Herboth, *Chem. Ber.*, **90**, 2008 (1957); H. Böhme and M. Haake, "Advances in Organic Chemistry : Methods and Results," Vol. 9, ed. by E. C. Taylor, John Wiley and Sons, Inc., New York, 1976, p. 205.
9) All melting points are uncorrected.
10) J. Klosa, *J. Prakt. Chem.*, **21**, 1 (1963).