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REACTION OF DIMETHYLOXOSULFONIUM METHYLIDE WITH N - ARYLSULFONYLAZIRIDINES - STEREOSPECIFIC CONVERSION OF N-ARYLSULFONYLAZIRIDINES TO N - ARYLSULFONYLAZETIDINES

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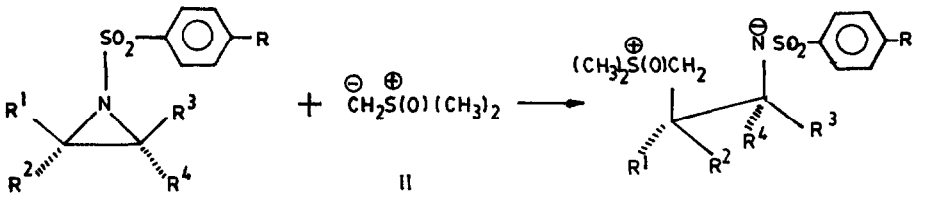
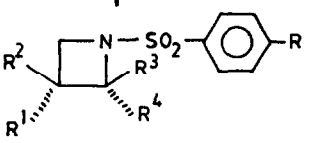
Abstract : Reaction of N-arylsulfonylaziridines with dimethyloxosulfonium methylide leads to the corresponding azetidines stereospecifically ; the cis-aziridines yielding the trans-azetidines and the trans-aziridines furnishing the cis-azetidines. This stereochemical course is interpreted in terms of an SN^2-1,4-elimination mechanism.

Recently we reported a new methodology for synthesis of azetidines involving either a single methylene transfer to an aziridine[1] or two consecutive methylene transfers to a suitable azomethine[2] from dimethyloxosulfonium methylide. Working along similar lines, Okuma et al[3] synthesized oxetanes from the corresponding oxiranes and ketones.These synthesis are believed to proceed through an SN^2 attack at the aziridine or oxirane carbon followed by a 1,4-elimination as shown in Scheme I for the aziridine case. An implication of this would be inversion at the attacked carbon thereby leading to a stereospecific conversion of the aziridines to the azetidines. It was, therefore, thought desirable to delineate the stereochemical course of these reactions.

The aziridines selected to do this, had phenyl groups at C_2 and C_3 (I_{a-f})since stereochemical assignment to the product azetidines was expected to be somewhat easier for these cases. In addition, aziridines I_{g-h}bearing methyl groups at C_2 and C_3were also subjected to the reaction conditions. All these three membered ring compounds were prepared by a British patent procedure[4] and the geometric isomers (with the C_2 and C_3 substituents cis and trans) separated by column chromatography. In the

SCHEME – I





IIIa–h

a.	R = H	R^1, R^3 = Ph	R^2, R^4 = H
b.	R = CH_3	R^1, R^3 = Ph	R^2, R^4 = H
c.	R = Cl	R^1, R^3 = Ph	R^2, R^4 = H
d.	R = H	R^1, R^4 = Ph	R^2, R^3 = H
e.	R = CH_3	R^1, R^4 = Ph	R^2, R^3 = H
f.	R = Cl	R^1, R^4 = Ph	R^2, R^3 = H
g.	R = H	R^1, R^3 = CH_3	R^2, R^4 = H
h.	R = H	R^1, R^4 = CH_3	R^2, R^3 = H

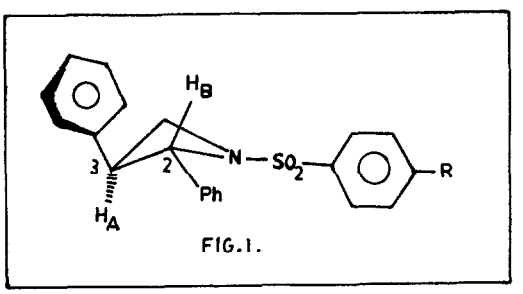


FIG. 1.

case of I_{a-f} , the geometry was assigned on the basis of the fact that the cis isomers showed a doublet at δ7.9 for the two protons ortho to the sulfonyl group whereas in the trans-isomers the corresponding protons appear at δ 7.25 as done previously by Seden and Turner[5] . Also the cis isomers showed an upfield shift of 3 to 4 ppm in relation to the trans-isomers in ^{13}C-NMR (Table I). This ^{13}C-NMR criterion was used to assign geometry in the case of I_{g-h}. Similar trends have been observed in the case of cyclopropanes[6a]

Treatment of cis - N - arylsulfonyl - 2,3-diphenylaziridines I_{a-c} (1 equiv) with dimethyloxosulfonium methylide[7] (1.5 equiv.) in an atmosphere of N_2 gas at ambient temperature for 18 hours, followed by usual work-up and chromatography on neutral alumina gave 73-81% of the corresponding trans-2,3- diphenylazetidines III_{a-c} (Scheme I). On the other hand, reaction of the trans-isomers I_{d-f} under identical reaction conditions yielded the corresponding cis-azetidines. Similar results were obtained for N-benzenesulfonyl-2,3- dimethylaziridines I_{g-h}.

The azetidine structures were established on the basis of spectral data and elemental analysis. The geometry was assigned on the basis of following NMR observations :- (a) J_{AB} in the cis-isomers (fig 1)is more ($\sim$9 Hz) than in the trans - isomers($\sim$7.5 Hz). This is in accord with observations based on the fact that the trans-isomer can exist as a mixture in which the adjacent substituents can be either pseudo-diaxial or pseudo-diequatorial whereas the cis-isomer has to have these substituents in pseudo axial - pseudo equatorial positions[6b] . Similar observations have been made by Doomes and Cromwell[8] . (b) In the trans-isomers the proton cis to the phenyl ring appears 0.5 ppm upfield of that for the cis-isomers. Such shifts have been used to assign geometry in the case of several four membered rings[6c] and (c). In the ^{13}C - NMR the isomer designated cis shows an upfield shift of $\sim$ 4 ppm in relation to the trans-compounds for the carbons bearing the cis-substituent. In the case of III_{g-h} the PMR was complex and the assignment of geometry was based on criterion (c). Additionally in III_h the two methyl groups showed an upfield shift of 4 ppm compared to the trans-isomer (III_g). These results indicate that methylene transfer to N-arysulfonylaziridines is stereospecific and leads to inversion of configuration at the attacked carbon and lend support to the rationale of this methodology.

Experimental Section

Melting points are uncorrected, IR-spectra were determined with a Pye

Unicam SP-1200 grating spectrophotometer. ^{1}H NMR and ^{13}C NMR were recorded on a JEOL FX-100 machine. Mass spectra (70 eV) were recorded on JMS D300 (JEOL) GC/MS spectrometer. Microanalysis were performed in the instrument laboratory of Department of Chemistry, I.I.T., Delhi.

Aziridines I_{a-f}

The appropriate N, N-dichloroarylsulfonamide[9a] (0.01 mole) and a suitable olefin (0.01 mole) were mixed in chloroform (100 ml) and heated under reflux for 5-6 hours under N_2 gas. To this cooled reaction mixture was added at ambient temperature aqueous sodium bisulfite (30 g in 100 ml of water) and the whole stirred for about 2-3 hours. The bishasic mixture was transferred to a separatory funnel, the organic layer separated and washed successively with aqueous sodium bicarbonate (3 x 25 ml) and water (3 x 25 ml),dried, stripped of the solvent and the solid thus obtained crystallized from chloroform - pet ether. To a solution of this sulfonamide in ethanol (95%) was added dropwise ethanolic sodium hydroxide (2 g in 10 ml aqueous ethanol). The mixture was stirred for 5-10 minutes at room temperature to give a thick precipitate, which was filtered, washed with cold aqueous ethanol and dried. This mixture of isomers was resolved by column chromatography on neutral alumina. The cis-isomer eluted first with benzene-pet ether (1:1) whereas the trans-isomer eluted later with benzene. The yield m. p., n.m.r. and elemental analysis data are shown in table I and III.

Azirıdines I_{g-h}

2-Butene[9b], prepared by the dehydration of 2-butanol with 50% conc. H_2So_4, was passed through constantly stirred solution of N, N-dichlorobenzenesulfonamide (0.02 mole, 4.52 g) in chloroform (100 ml) at 0 to -15° under an atmosphere of nitrogen for 8 - 9 hours. The reaction mixture was stirred additionally at 0 to 10°C till disappearance of the dichloride (30 hours). The diastereomeric mixture of sulfonamides obtained by treatment of the dichloroadduct with sodium bisulfite was separated by fractional crystallization using chloroform and pet-ether and cyclised with sodium hydroxide separately to cis andtrans aziridines. The yield, m.p., n.m.r. and elemental analysis data are shown in table I and III.

Azetidines III_{a-h}

A 100 ml three necked r.b. flask fitted with a dropping funnel, nitrogen

TABLE I

AZIRIDINE	M.P.(°C)	LIT.M.P. (°C.)	YIELD(%)	^{1}H-NMR ($CDCL_3$) (δ)	^{13}C-NMR ($CDCL_3$) (δ)
I_a	102-104	-	18	4.2 (S,2H), 8.1(d,2H ArH, J~8Hz), 7.6(m, 2H ArH) and 7.1 (m, 11H ArH).	47.6 (d) and 127.7 - 133.7 (ArC).
I_b	153-154	-	21	2.4 (S,3H), 4.2(S, 2H) 7.95 (d, 2H ArH, J~ 8Hz) 7.3 (d, 2H ArH, J~ 8Hz) and 7.07 (m,10H ArH).	21.6(q) 47.5(d) and 127.7-144.6 (ArC).
I_c	135-136	-	40	4.2 (S,2H), 8.0 (d, 2H ArH, J~8Hz), 7.53 (d, 2H ArH) J~8Hz) and 7.1 (m, 10H ArH).	47.8(d) and 127.7 - 140.4 (ArC).
I_d	125-126	-	70	4.21 (S,2H), 7.5 (d, 2H ArH, J~8Hz) and 7.25 (m, 13H ArH).	50.4(d) and 127.4 - 132.9 (ArC)
I_e	138-139	138-139	70	2.4 (S, 3H), 4.2 (S, 2H) 7.6 (d, 2H, ArH, J~8Hz) and 7.2 (m, 12H ArH).	21.5 (q), 50.3 (d) and 127.4 - 143.8 (ArC).
I_f	117-118	-	54	4.28 (S, 2H), 7.66 (d, 2H ArH, J~8Hz) and 7.37 (m, 12H ArH).	50.6 (d) and 127.7 - 139.5 (ArC).
I_g	41-42	42	29.9	1.2 (d, 6H, J~6Hz) 2.9 (m, 2H), 7.55 (m, 3H ArH) and 7.94 (m, 2H ArH).	11.3 (q), 40.1 (d) and 127.1 - 138.4 (ArC).
I_h	75-76	77	60.3	1.44 (d, 6H, J~6Hz) 2.74 (q, 2H, J~5Hz), 7.6 (m, 3H ArH) and 7.94 (m, 2H ArH).	15.3 (q) 45.9 (d) and 126.9 - 140.8 (ArC).

TABLE II

AZETIDINE	M.P.(°C)	YIELD(%)	^{1}H-NMR ($CDCL_3$) (δ)	^{13}C-NMR ($CDCL_3$) (δ)
III_a	117-118	80	3.8(m, 3H), 4.9 (d, 1H, J~7.5 Hz) and 7.1 (m, 15H, ArH).	39.9(d), 57.0(t), 73.4(d), and 126.2-137.2(ArC).
III_b	158-160	78	2.5 (S, 3H), 3.8 (m, 3H) 4.9 (d, 1H, J~7.5Hz) and 7.2 (m, 14H ArH).	21.4(q), 44.4(d), 53.8(t), 73.4(d), and 126.2-144(ArC).
III_c	146-147	73	3.9 (m, 3H), 4.97 (d, 1H, J~7.5Hz) and 7.3 (m, 14H ArH).	44.3(d), 53.8(t), 73.5(d), and 126.2 - 139.8 (ArC).
III_d	174-174.5	76	4.0 (complex multiplet 3H), 5.4 (d, 1H, J~9Hz) and 7.55 (m, 15H ArH).	40.4(d), 53.1(t), 69.3(d), and 126.8 - 136.8 (ArC).
III_e	160.5-161	76	2.48 (S, 3H), 4.0 (Complex multiplet, 3H), 5.35 (d, 1H, J~9Hz) and 7.4 (m, 14H ArH).	21.5(q), 40.3(d), 53.0(t), 69.1(d) and 126-144.2 (ArC).
III_f	218-219	74.4	4.0 (Complex multiplet, 3H), 5.34 (d, 1H, J~9Hz) and 7.0 - 7.8 (m, 14H ArH).	40.5(d), 53.0(t), 69.6(d) and 126.9 - 139.9 (ArC).
III_g	Oil	44	0.7 (d, 3H), 1.38 (d, 3H) 2.2 (m, 1H), 3.07 (t, 1H) 3.46 (m, 1 H), 3.8 (m, 1H, J~8Hz), and 7.3-7.98 (m, 5H ArH).	17.3(q), 20.9(q), 32.6(d), 54.8(t), 67.4(d) and 128.1-134.8 (ArC).
III_h	Oil	56	1.14 (d, 3H), 1.32 (d, 3H) 2.2 (complex multiplet, 1H), 3.29 (m, 1H) 3.65(t, 1H), 4.0 (m, 1H, J~7Hz) and 7.5 - 7.9 (m, 5H ArH).	13.9(q), 15.7(q), 27.2(d), 54.9(t), 61.7(d), and 128.1 - 134.8 (ArC).

TABLE III

AZIRIDINE	ANALYSIS FOUND (CALCD) %			AZETIDINE	ANALYSIS FOUND (CALCD) %		
	C	H	N		C	H	N
I_a	71.4 (71.64)	5.32 (5.07)	4.26 (4.18)	III_a	72.08 (72.2)	5.8 (5.44)	3.92 (4.01)
I_b	72.38 (72.2)	5.6 (5.44)	4.03 (4.01)	III_b	72.8 (72.72)	5.9 (5.78)	3.75 (3.86)
I_c	64.8 (64.95)	4.28 (4.33)	4.11 (3.79)	III_c	65.91 (65.71)	4.83 (4.69)	3.91 (3.65)
I_d	71.34 (71.64)	5.35 (5.07)	4.26 (4.18)	III_d	72.49 (72.2)	5.72 (5.44)	3.86 (4.01)
I_e	-	-	-	III_e	72.52 (72.72)	5.9 (5.78)	4.14 (3.86)
I_f	65.13 (64.95)	4.55 (4.33)	3.74 (3.79)	III_f	65.69 (65.71)	4.87 (4.69)	3.61 (3.65)
I_g	-	-	-	III_g	58.5 (58.67)	6.55 (6.67)	6.0 (6.2)
I_h	-	-	-	III_h	58.7 (58.67)	6.8 (6.67)	6.0 (6.2)

inlet and a condensor was charged with sodium hydride (0.004 - 0.006 mole, 1.5 equiv.) as a 50% dispersion in oil. The oil was washed off by swirling with dry pet ether (3 x 10 ml) under nitrogen and removing the solvent with a dropper. The whole set up was evacuated by connecting it to a vacuum pump until the last traces of pet. ether were removed. Dry nitrogen was allowed in and dry powdered trimethylsulfoxonium iodide (0.004 - 0.006 mole 1.5 equiv.) introduced into the flask through one of the necks. The contents were stirred magnetically at ambient temperature and dry DMSO (5-10 ml) added through the dropping funnel. The mixture was stirred for 15-20 minutes, when the ylide formed (with evolution of H_2 gas) as a milky white suspension. To this was added the proper N-arylsulfonylaziridine (0.0027-0.0044 mole, 1 equiv.) in dry DMSO (5-10 ml) over a period of 1 minute. The mixture was stirred additionally for 18-20 hours at ambient temperature, cold water was added to quench the reaction and the whole diluted with large excess of H_2O (150 ml). The solid obtained was filtered, washed thoroughly with water, dried and purified by column chromatography using neutral alumina as the adsorbent. The yield, m.p., n.m.r. and analysis data are given in Table II & III.

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