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# *A NEW, SIMPLE METHOD FOR THE PREPARATION OF SUBSTITUTED 2H-1,2-THIAZINE-1,1-DIOXIDES FROM AMINOAZABUTADIENES.*

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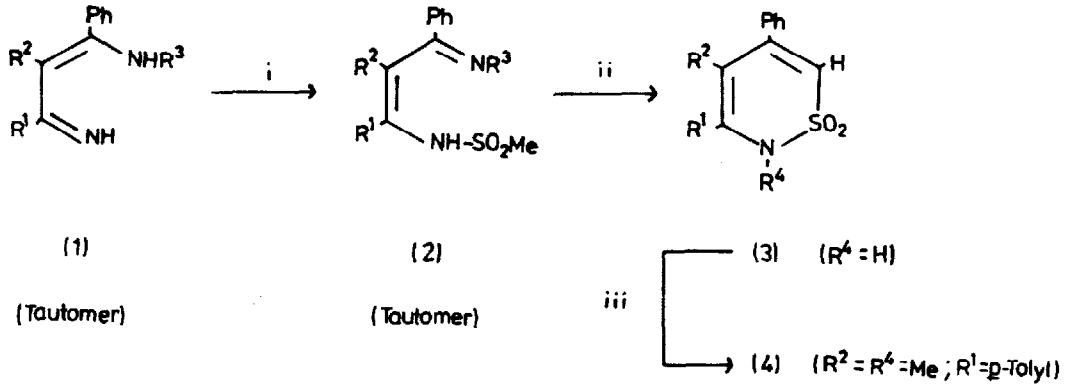
*Summary:* The synthesis of the titled compounds from aminoazabutadienes and methanesulfonyl chloride is described.

The 1,2-thiazine ring is not frecuently encountered in the literature[1]; on the other hand, some interesting recent works deal with the synthesis and utility of 2-azathiabenzene-1-oxides[2] and of tetrahydro-[3] and dihydro-1,2-thiazine-1,1-dioxides[4]. In spite that the N-substituted 3,5-dimethyl-2H-1,2-thiazine-1,1-dioxide derivatives, prepared from the corresponding sultones, appear to exhibit insecticide and fungicide properties[5], no general methods exist for synthesizing the 2H-1,2-thiazine-1,1-dioxide ring[1,6]. Recently, we have reported on the acylation reaction of 4-amino-1-azabutadienes (1) and their transformation into pyridin-2-ones by an aldol-type ring closure process[7].

We report here that substituted 2H-1,2-thiazine-1,1-dioxides are easily obtained in two steps by sulfonylation of (1) followed by a base-promoted ring closure reaction of the resulting sulfonamide derivatives (2). (Scheme 1).

Thus, treatment of compounds (1)[8] with methanesulfonyl chloride at room temperature led to pure methylsulfonamides (2) ($-SO_2-\underline{CH_3}$: $^1H$ n.m.r. $\delta$ = 2.9-3.0 ppm; $^{13}C$ n.m.r. $\delta$ = 42-44 ppm) in 85-90 % yield, after washing the crude solid with hexane; analytical samples were obtained by recrystallization from hexane-chloroform, 5:1. (Scheme 1, Table I)[9].




*Scheme 1.* Reagents: i, $ClSO_2CH_3$, $CH_2Cl_2$ or toluene, 25°C, 12 h; ii, LDA (2.5 eq.), THF, -78°C to 25°C, 12 h; iii, a) HNa, THF, 25°C, 1 h; b) MeI, 25°C, 10 h.

Compounds (2) were then reacted with 2.5 equivalents of lithium diisopropylamide (LDA) (-78°C to 25°C, THF) to afford sultams (3) by intramolecular addition of the resulting α-sulfonyl carbanion to the carbon-nitrogen double bond and loss of amine $R^3-NH_2$; pure compounds (3) were obtained in 80-92% yield by column chromatography ($SiO_2$, hexane-ether, 1:1) and analytical samples are easily available by recrystallization from hexane-chloroform 3:1 (Scheme 1, Table I)[10]. On the other hand, compounds (3) undergo normal N-alkylation reactions; thus, the reaction of (3a) with NaH (THF, 25°C, 1 h) followed by treatment with excess of methyl iodide (25°C, 10 h) furnished (4) (N-$\underline{CH_3}$: $^1H$ n.m.r. $\delta$ = 3.0 ppm; $^{13}C$ n.m.r. $\delta$ = 32.1 ppm) (94% yield; m.p. 166-168°C from hexane-ether 2:1). Compound (4) was recovered unaltered after prolonged heating in refluxing xylene.

*Table I. Sulfonamides (2) and 2H-1,2-Thiazines-1,1-dioxides (3).*

| Entry | $R^1$ | $R^2$ | $R^3$ | Compounds (2) Yield(%) | Compounds (2) m.p.(°C) | Compounds (3) Yield(%) | Compounds (3) m.p.(°C) |
|---|---|---|---|---|---|---|---|
| a | Ph | H | *p*-Tolyl | 90 | 195-197 | 92 | 170-172 |
| b | c-$C_6H_{11}$ | H | *p*-Tolyl | 85 | 191-193 | 80 | 167-169 |
| c | *p*-Tolyl | H | *p*-Tolyl | 90 | 187-189 | 92 | 178-180 |
| d | Ph | Me | *p*-Tolyl | 88 | 171-173 | 86 | 134-136 |
| e | *p*-Tolyl | Me | *p*-Tolyl | 89 | 185-187 | 87 | 148-150 |
| f | Ph | Allyl | *p*-Tolyl | 88 | 133-135 | 90 | 120-122 |
| g | *p*-Tolyl | Cl | Ph | 90 | 225-226 | 82 | 192-194 |

In conclusion, we have demonstrated that the elusive 2H-1,2-thiazine ring can be very easily formed in a regioselective manner by simple base treatment of sulfonamides (2), which in turn are readily available from azabutadienes (1)[11].

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9.- Preparation of (2): To a solution of 5 mmol of (1) and 30 mmol of $Et_3N$ in 30 ml of toluene (if $R^2$ = H) or methylene chloride (if $R^2 \neq$ H) were added at -20°C 7.5 mmol of methanesulfonyl chloride and the mixture allowed to warm to room temperature. After stirring for 12 h the mixture was hydrolyzed with 1N HCl (60 ml), extracted with $CH_2Cl_2$, washed with 5% $NaHCO_3$ and water, and dried over anhydrous $Na_2SO_4$; removing the solvents gave a solid, which was washed with hexane and recrystallized. (See table I).

Spectroscopic data of (2c): IR (KBr) 1330, 1270, 1130 $cm^{-1}$; $\delta_H$ (80 MHz, $CDCl_3$) 2.2(3H,s), 2.3(3H,s), 3.0(3H,s), 5.3(1H,s), 6.6-7.7(13H,m), 14.1(1H,NH,s broad) ppm; $\delta_C$ (20 MHz; $CDCl_3$) 19.64(q), 20.25(q), 42.16(q), 100.40(d), 121.90(d), 126.61-129.95(m), 133.94(s), 134.77(s), 135.90(s), 138.95(s), 160.37(s), 173.50(s) ppm; Ms (70 eV) m/e 404 ($M^+$, 41%), 403 (100%), 325 (60%).

10.- Preparation of (3): A solution of 12.5 mmol of LDA in 20 ml of THF was cooled to -78°C and then 5 mmol of compound (2) in 10 ml of THF were added; the mixture was allowed to warm to room temperature and stirred for 12 h. The resulting mixture was treated with 2N $H_2SO_4$ (50 ml), extracted with ether, and the organic layer washed with 5% $NaHCO_3$ and water and dried over anhydrous $Na_2SO_4$. The solution was concentrated in vacuo and the resulting crude chromatographed and recrystallized. (See table I).

Spectroscopic data of (3f): IR (nujol) 3150, 1360, 1120 $cm^{-1}$; $\delta_H$ (300 MHz ; DMSO-$d_6$) 2.9(2H,d, J 5.0 Hz), 4.5(1H,dd, J 17.2 Hz, J 1.7 Hz), 4.6(1H,dd, J 10.3 Hz, J 1.7 Hz), 5.3(1H,m), 6.2(1H,s), 7.3-7.7(10H, m), 11.2(1H,NH,s broad) ppm; $\delta_C$ (75 MHz; DMSO-$d_6$) 32.36(t), 111.60(s), 115.31(t), 116.95(d), 120.02(d), 128.46-130.07(m), 134.35(s), 137.77(s), 142.15(s), 149.96(s) ppm; Ms (70 eV) m/e 323 ($M^+$, 94%), 258 (100%), 115 (33%).

11.- All new copounds (2), (3) and (4) gave satisfactory spectroscopic and analytical data.

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