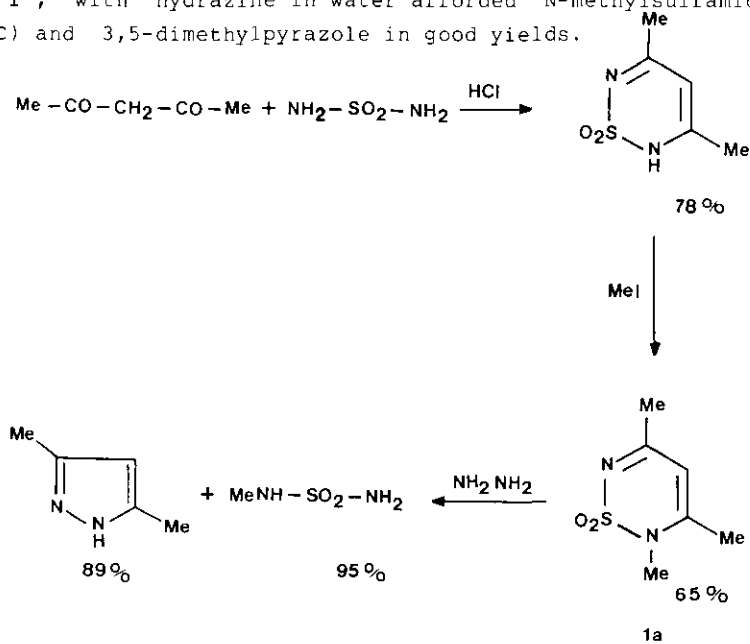


RING TRANSFORMATION OF 1,2,6-THIADIAZINE 1,1-DIOXIDES INTO PYRAZOLES. A CONVENIENT SYNTHESIS OF N-ALKYLSULFAMIDES

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Abstract -Conversion of thiadiazines into pyrazoles by the action of hydrazine represents a new example of ring transformation and provides a new entry into *N*-methylsulfamide. The latter has been used to prepare an *N*-methyl-3,5-diaminothiadiazine which cannot be obtained by direct alkylation.

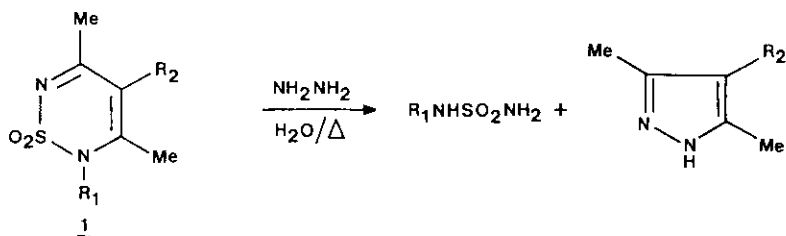
For many years, there has been considerable interest in ring transformations caused by the action of nucleophiles on heterocyclic compounds¹. We now wish to report conversion of *N*-substituted 1,2,6-thiadiazine-1,1-dioxides into pyrazoles by reaction with hydrazine. When *N*-methylthiadiazines are used, this reaction has an additional interest since it provides a very convenient synthesis of *N*-methylsulfamide, a valuable key intermediate for many heterocycles containing the *N*-SO₂-*N* moiety². The general synthesis of *N*-alkylsulfamides involves reaction of sulfamide and alkylamines³ but with methylamine this procedure does not work. Reaction of 2,3,5-trimethyl-1,2,6-thiadiazine-1,1-dioxide (**1a**) prepared according to Scheme 1⁴, with hydrazine in water afforded *N*-methylsulfamide (mp 63-65°C Lit.⁵ 63-64°C) and 3,5-dimethylpyrazole in good yields.



Scheme 1

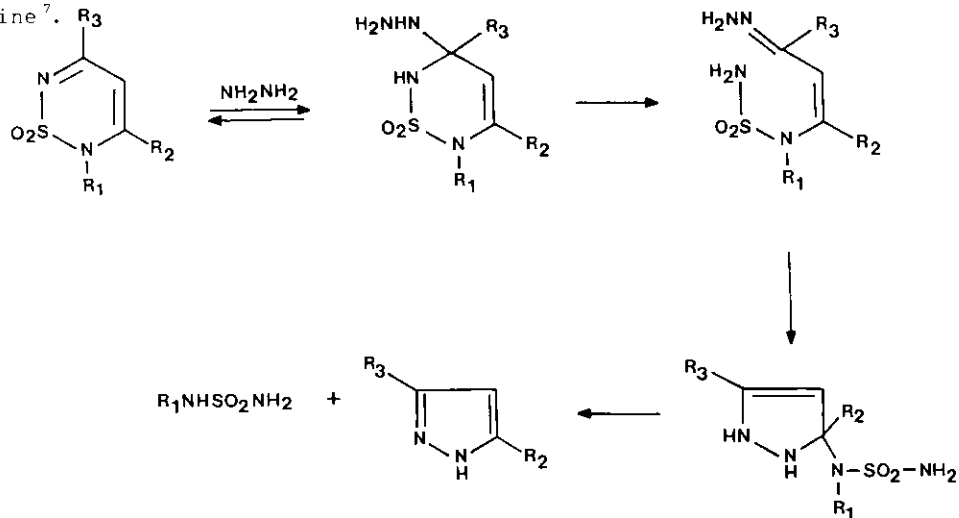
The reaction proceeded in a very clean and smooth manner and the compounds were easily separated by crystallization. Other thiadiazines were used and the results are gathered in Table 1: 3,4,5-Trimethylpyrazole was obtained from 2,3,4,5-tetramethyl-1,2,6-thiadiazine 1,1-dioxide 1b⁴, prepared in a similar way to 1a whilst 2-phenylethyl-3,5-dimethyl-1,2,6-thiadiazine-1,1-dioxide 1c⁶ afforded *N*-phenylethylsulfamide and 3,5-dimethylpyrazole. This reaction was only performed in order to check the general scope of the method, since thiadiazine 1c was synthesized from *N*-phenylethylsulfamide and 2,4-pentanedione.

TABLE 1



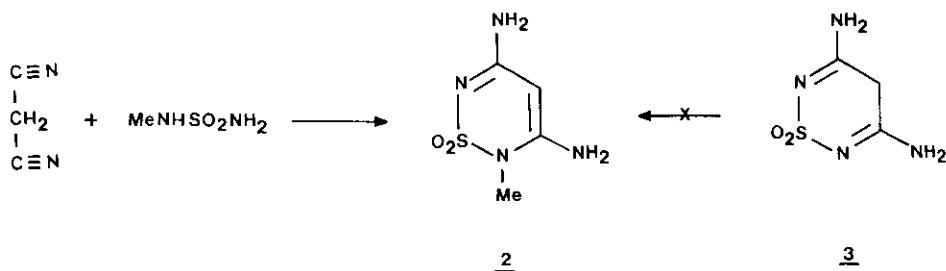
	R ₁	R ₂	%yield in sulfamide	%yield in pyrazole
a)	Me	H	95	89
b)	Me	Me	68	70
c)	CH ₂ CH ₂ Ph	H	67	59

The probable mechanism involved is depicted in Scheme 2. A similar mechanism has been postulated for the conversion of pyrimidines into pyrazoles by the action of hydrazine⁷.



Scheme 2

The structures of the pyrazoles were established by comparison with authentic samples⁸. Since no recent reports have dealt with *N*-methylsulfamide its nmr spectra have been recorded: ¹H nmr (300 MHz) (DMSO-d₆) δ: 6.46 (s, NH₂), 6.28 (d, J=3.4 Hz, NH), 2.50 (d, J=3.5 Hz, CH₃); (acetone-d₆) δ: 5.81 (s, NH₂), 5.50 (bs, NH), 2.68 (d, J=5.3 Hz, CH₃). ¹³C nmr (75 MHz) (DMSO-d₆) δ: 28.7 (q, J=137.7 Hz, CH₃). Finally, the synthetic usefulness of *N*-methylsulfamide is exemplified in the preparation of 2-methyl-3,5-diamino-1,2,6-thiadiazine-1,1-dioxide (2). The parent compound, 3,5-diamino-2H-1,2,6-thiadiazine-1,1-dioxide⁹ (3) is the starting material of many [6+6] and [6+5] fused thiadiazine derivatives¹⁰. Direct methylation of this compound afforded *C*-mono- and *C,N*-dimethyl derivatives¹¹ but the *N*-methyl derivative 2 could not be isolated. This compound can easily be obtained from *N*-methylsulfamide and malononitrile in dimethoxyethane¹² (Scheme 3).



Scheme 3

General procedure for conversion of 1,2,6-thiadiazines 1,1-dioxides into pyrazoles: An equimolar mixture of the thiadiazine and hydrazine hydrate in water (50-100 ml) was refluxed for 2h. After cooling, the precipitate (pyrazole) was collected by filtration and solvent evaporated under reduced pressure to afford the corresponding sulfamide.

ACKNOWLEDGEMENTS

The financial support from CICYT (project no. 87045) is gratefully acknowledged

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6. 2-Phenylethyl-3,5-dimethyl-1,2,6-thiadiazine-1,1-dioxide 1c.- A solution of phenylethylsulfamide (2g, 0.01 mol) and 2,4-pentanedione (1g, 0.01 mol) in ethanol (50 ml) was saturated with hydrogen chloride. The reaction mixture was refluxed for 4 h, the solvent evaporated in vacuo and the residue recrystallized from methanol to give 2.3 g (88%) of 1c, mp 185-186 C. Uv (MeOH) λ nm(ϵ): 217 (2800), 323 (4100); ir (nujol) ν cm⁻¹: 1320, 1180 (SO₂); ¹H nmr (DMSO-d₆) δ : 7.4 (m, 5H, Ar-H), 5.9 (s, 1H, H-4), 4.1 (t, J=6 Hz, 2H, N-CH₂), 3.1 (t, J=6 Hz, 2H, CH₂), 2.2 (s, 3H, CH₃-3), 2.1 (s, 3H, CH₃-5). C₁₃H₁₆N₂O₂S requires: C, 59.09; H, 6.06; N, 10.60; S, 12.12. Found: C, 59.31; H, 6.11; N, 10.64; S, 12.36.
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Received, 20th October, 1988