A New Fused Heterocyclic System: 6*H*-Pyrazolo[3,4-*c*][1,2,5]thiadiazine 2,2-Dioxide

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A base-promoted cyclodehydration of 4-nitroso-5-alkylsulfonylamidopyrazoles **3** afforded 6*H*-pyrazolo-[3,4-*c*][1,2,5]thiadiazine 2,2-dioxide (**4**). The structure of **4** was confirmed through X-ray analysis.

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Thiadiazines constitute a group of heterocycles having a wide variety of uses, in particular as biologically active compounds in medicine and in agriculture and as vulcanizing agents for rubber [1].

All six of the possible isomeric thiadiazines are described in the literature [2], but there are only a limited number of papers describing 1,2,5-thiadiazines and their benzo derivatives [3,4]. A general feature of the reported 1,2,5-thiadiazines is that they are known with the sulfur atom in its lower oxidation state or in the 1-oxide form. However, to the best of our knowledge, no 1,2,5-thiadiazine 1,1-dioxide has been up to now reported. The present work deals with a convenient route to 6*H*-pyrazolo[3,4-*c*][1,2,5]thiadiazine 2,2-dioxide, a new heterocyclic system that has received our attention as a potential antifungal agent, in parallel with the reported activity of this class of heterocycles [4].

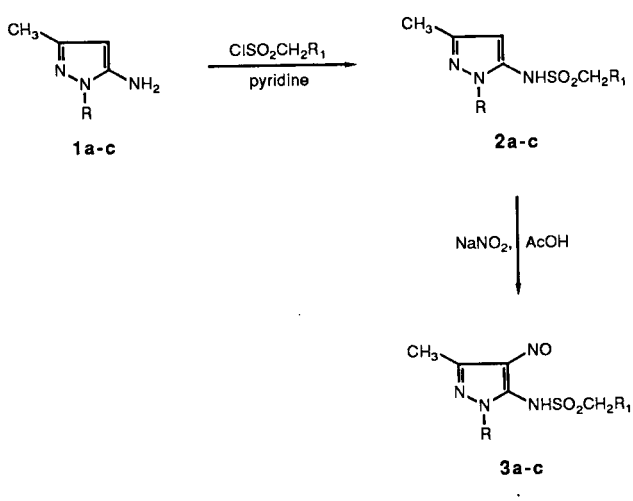
Our synthetic approach was based on the ability of the nitroso function of 4-nitrosopyrazoles to undergo nucleophilic attack by activated methylene groups, as we have shown in the synthesis of imidazo[4,5-*c*]pyrazoles [5] and pyrazolo[3,4-*b*]pyrazines [6].

The key intermediates to the target products **4** were the 4-nitroso-5-alkylsulfonamides **3**, which were cyclized to **4** through a base-promoted intramolecular nucleophilic attack by the methylene group linked to the sulfonyl function at the nitroso nitrogen.

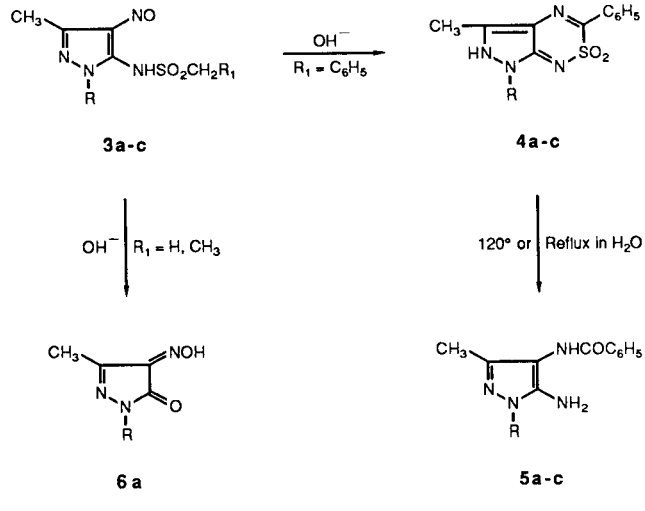
The preparative route to **3** is showed in Scheme 1.

5-Aminopyrazoles **1** were converted into the corresponding 5-alkylsulfonamido derivatives **2** by treatment with alkylsulfonylchlorides in pyridine. Nitrosation of **2** by sodium nitrite in acetic acid provided the 4-nitroso-5-alkylsulfonamidopyrazoles **3** in good yields. Cyclisation of compounds **3** to **4** occurred with some difficulties. Of the many conditions experimented, only the reflux of **3** in sodium hydroxide gave the expected results (Scheme 2).

Scheme 1



Scheme 2

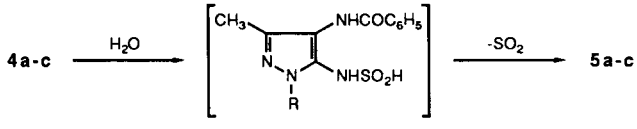


The reaction product was dependent on the nature of the substituent (R_1) linked to the methylene group. Compound **3a** (R_1 = C_6H_5) when refluxed in 1*N* sodium hydroxide afforded the required 6*H*-pyrazolothiadiazine **4a** as the only reaction product; similarly compounds **3b,c** (R_1 = C_6H_5) gave the corresponding cyclization products **4b,c**. However under the same experimental conditions, both compounds **3a** (R_1 = H) and **3a** (R_1 = CH_3) underwent hydrolysis of the alkylsulfonamido moiety yielding the same reaction product, *i.e.* the known 4-oximino-5-pyrazolone **6a** [7]. Therefore, the presence of a phenyl group increasing the methylene acidity, appears to be a crucial requirement for the cyclization process.

Compounds **4** are crystalline products, containing crystallisation water that is very difficult to be eliminated also under heating at 80° *in vacuo*, as demonstrated by analytical and ^{1}H-nmr data. On heating at 120°, compounds **4a-c** underwent ring opening to give the corresponding 4-benzoylamino-5-aminopyrazoles **5a-c**. Compounds **5a-c** were also obtained by heating the pertinent **4a-c** under reflux in water for two hours. The structure of **5** was confirmed by an alternative synthetic method, based on the regiospecific mono-acylation of 4,5-diaminopyrazole [8].

The instability of **4** at high temperature might derive from a hydrolytic process involving the attack by crystallisation water at the carbon atom linked to SO_2 group, with formation of the unstable intermediate **7** that loses sulfur dioxide to give **5** (Scheme 3).

Scheme 3



7a-c

All the spectral data agree with the proposed structures.

The ir spectra of compounds **3** and **4** show absorptions at 1350-1250 and near 1100 cm^{-1} attributable to sulfonamido group. Both the ^{1}H and the ^{13}C-nmr spectra show the disappearance of the methylene group absorptions of compounds **3** after their cyclization to **4**. As the definitive assignment of structure **4** by nmr techniques was prevented by the low number of hydrogen and carbon atoms, a single-crystal X-ray analysis was performed on a sample of **4c** recrystallized from ethanol.

Crystal Structure Determination.

Intensity data were collected at room temperature on an Enraf-Nonius CAD4 diffractometer with monochromated Mo-Kα radiation and ω-2θ scan technique. Cell parameters were obtained from least-squares refinement of the setting angles of 25 centered reflections in the range $9<\theta<13°$. Crystal data are reported in Table 1.

Table 1

Crystal Data for **4c**

formula	$C_{12}H_{12}N_4O_3S \cdot H_2O$
formula weight	294.32
crystal size (mm)	0.26 x 0.50 x 0.55
crystal system	orthorhombic
space group	$Pna2_1$
a(Å)	14.132(2)
b(Å)	7.180(1)
c(Å)	13.534(4)
V(Å^3)	1373.3(5)
Z	4
D_c(g cm^{-3})	1.42
F(000)	616
μ(MoKα) (cm^{-1})	2.37
θmin-θmax(°)	2-27
Independent reflections	1557
Reflections with $I>3\sigma(I)$	1231
R	0.032
Rw	0.039
S = Error in on observation of unit weight	1.37
Langest peak (e/Å^3) in final difference map	0.2

Intensities were corrected for Lorentz and polarization. Scattering factors were taken from reference [9]. The intensities of three standard reflections measured after every 2 hours showed no significant variation during data collection. The structure was solved by direct methods (MULTAN 81) [10] and refined by full-matrix least-squares analysis with anisotropic temperature factors for all non-H atoms and isotropic ones for hydrogens. Weights were applied according to the scheme: $w = 4Fo^2/[\sigma^2(Fo^2) + (0.04\,Fo^2)^2]$ and final statistical parameters are: $R = \Sigma|\,|\Delta Fo|\,|/\Sigma|Fo| = 0.032$, $R_w = (\Sigma w\,|\,\Delta Fo\,|^2/\Sigma w\,|\,Fo^2\,|)^{1/2} = 0.039$. Final positional and equivalent isotropic vibrational parameters are reported in Table 2.

Bond distances and angles are given in Tables 3 and 4.

All calculations were done with the CAD-4 SDP system of programs [11] and PARST [12]. An ORTEP [13] view of the molecule with the atom-labeling scheme is shown in Figure 1.

The crystal is built up by **4c** and water molecules, in the ratio 1/1, connected by a net of hydrogen bonds. Each water molecule, surrounded by three molecules of the heterocyclic compound, acts as an acceptor of an hydrogen bond from N-H group and as a donor of two hydrogens to oxygens of the SO_2 groups belonging to two different mol-

Table 2

Table of Positional Parameters and Their Estimated Standard Deviations

Atom	x	y	z	B(Å²)
S	0.08323(4)	0.43134(9)	0.000	3.65(1)
O1	0.0450(1)	0.6174(3)	0.0052(2)	5.05(4)
O2	0.0262(1)	0.2956(3)	0.0497(2)	4.89(5)
N1	0.0975(2)	0.3676(4)	−0.1110(2)	4.40(5)
N2	0.2739(2)	0.4617(3)	0.0028(2)	3.70(4)
N3	0.2968(2)	0.4469(3)	−0.2560(2)	4.12(5)
N4	0.2031(2)	0.4026(4)	−0.2453(2)	4.13(5)
C1	0.1990(2)	0.4440(4)	0.0560(3)	3.55(6)
C2	0.2660(2)	0.4551(4)	−0.0979(3)	3.64(6)
C3	0.1823(2)	0.4100(4)	−0.1483(3)	3.70(6)
C4	0.3363(2)	0.4765(4)	−0.1674(3)	3.93(6)
C5	0.1416(2)	0.3693(6)	−0.3295(3)	5.37(8)
C6	0.4380(2)	0.5210(5)	−0.1571(3)	5.00(7)
C7	0.2076(2)	0.4383(4)	0.1641(3)	3.71(6)
C8	0.2946(2)	0.3865(5)	0.2061(3)	4.51(7)
C9	0.3064(2)	0.3917(5)	0.3073(3)	5.13(8)
C10	0.2335(3)	0.4446(5)	0.3682(3)	5.58(8)
C11	0.1478(3)	0.4920(6)	0.3281(3)	5.55(8)
C12	0.1349(3)	0.4888(5)	0.2272(3)	4.81(8)
OW	0.1124(2)	0.9497(4)	0.0736(2)	6.91(7)
HW1	0.071(2)	0.869(6)	0.071(3)	11(1)*
HW2	0.080(3)	1.034(6)	0.054(5)	9(1)*
HN3	0.319(2)	0.439(4)	−0.303(3)	5.8(9)*
H51	0.179(2)	0.295(6)	−0.373(3)	9(1)*
H52	0.141(3)	0.471(4)	−0.360(3)	5.4(8)*
H53	0.092(3)	0.293(9)	−0.332(5)	13(2)*
H61	0.463(2)	0.419(4)	−0.127(3)	5.8(8)*
H62	0.454(2)	0.619(5)	−0.115(3)	7.0(9)*
H63	0.466(3)	0.522(7)	−0.219(5)	10(1)*
H8	0.346(2)	0.354(4)	0.158(2)	3.3(6)*
H9	0.371(3)	0.356(6)	0.321(3)	6.5(9)*
H10	0.246(3)	0.451(5)	0.431(3)	7(1)*
H11	0.091(2)	0.542(5)	0.367(4)	7(1)*
H12	0.068(2)	0.526(4)	0.192(3)	4.7(8)*

Starred atoms were refined isotropically. Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $Beq = 4/3\Sigma_i\Sigma_j\beta_{ij}a_ia_j$.

ecules. The hydrogen bonding parameters are: HW1....O1 (x,y,z) = 2.05(4), OW....O1 = 2.731(4)Å, OW-HW1....O1 = 140(3)°; HW2....O2(x,y+1,z) = 2.03(4), OW....O2 = 2.785(4)Å, OW-HW2....O2 = 157(5)°; HN3....OW(½-x,-y-½,z-½) = 1.93(4), N3....OW = 2.639(4)Å, N3-HN3-....OW = 172(3)°.

The five membered ring is almost planar ($\Sigma(\Delta/\sigma)^2$ = 34.7) with a maximum deviation from the mean plane of 0.011(3)Å of the N4 atom, whereas the six membered ring (S, N1, C3, C2, N2, C1) is not planar assuming a conformation intermediate between envelope ^1E and half-chair $^1H_2$ with puckering parameters [14]: Q = 0.255(2), ϕ = 16.6(7), θ = 61.6(6).

The analysis of the bond distances indicates the existence of a delocalization on the heterocyclic system with a contribution of the two canonical forms (Figure 2):

Table 3

Table of Bond Distances in Angstroms

Atom1	Atom2	Distance	Atom1	Atom2	Distance	Atom1	Atom2	Distance
S	O1	1.443(2)	C1	C7	1.468(5)	C8	C9	1.379(5)
S	O2	1.433(2)	C2	C3	1.403(4)	C8	H8	1.00(3)
S	N1	1.583(3)	C2	C4	1.376(4)	C9	C10	1.373(5)
S	C1	1.805(3)	C4	C6	1.479(4)	C9	H9	0.97(4)
N1	C3	1.336(4)	C5	H51	0.95(4)	C10	C11	1.370(5)
N2	C1	1.287(4)	C5	H52	0.84(3)	C10	H10	0.87(4)
N2	C2	1.369(5)	C5	H53	0.89(5)	C11	C12	1.377(5)
N3	N4	1.369(3)	C6	H61	0.91(3)	C11	H11	1.02(4)
N3	C4	1.339(5)	C6	H62	0.94(4)	C12	H12	1.10(3)
N3	HN3	0.71(4)	C6	H63	0.93(6)	OW	HW1	0.83(4)
N4	C3	1.345(4)	C7	C8	1.404(4)	OW	HW2	0.81(4)
N4	C5	1.453(5)	C7	C12	1.383(5)			

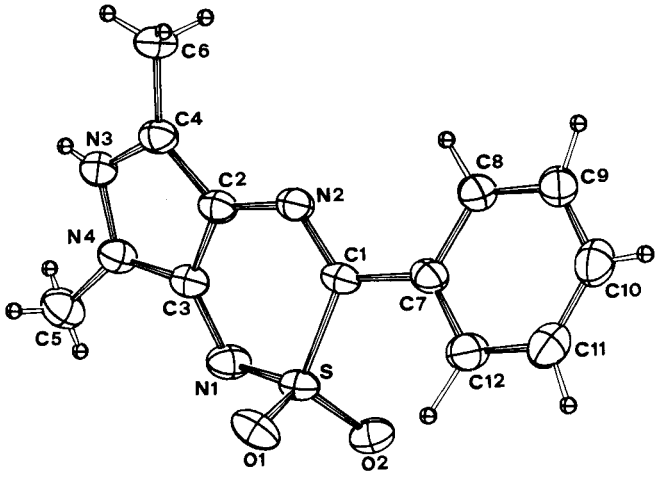


Figure 1. An ORTEP [12] view of **4c** showing the termal ellipsoid at 30% probability.

Figure 2

Moreover the distribution of the charges on the form **II** is suitable to involve both N-H and SO_2 groups in the formation of strong hydrogen bonds, as observed in the crystal packing. The inclusion of water molecules in the crystal is probably due to a balancing of the H bonding donors and H bonding acceptors groups, with a lowering of the interaction energy with respect to a crystal built up only by pyrazolothiadiazines molecules.

EXPERIMENTAL

Melting points were determined using a Buchi capillary apparatus and are uncorrected. The ir spectra were recorded from potassium bromide discs on a Hitachi-Perkin 157G spectrometer. The ^{1}H-nmr and ^{13}C-nmr spectra were recorded on a Bruker AC 200 spectrometer; chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane as internal standard.

General Procedure for 5-Alkylsulfonamidopyrazoles **2a-c.**

A solution of **1** (30 mmoles) in anhydrous pyridine (30 ml) was treated with the pertinent alkylsulfonyl chloride (30 mmoles). The mixture was heated on a steam bath for 2 hours and poured into ice water. The aqueous solution was made alkaline with concentrated ammonium hydroxide, washed with dichloromethane (5-10 ml), acidified with hydrochloric acid and extracted with ethyl acetate. The combined organic extracts were dried over magnesium sulfate and evaporated to give a white solid that was crystallized from the indicated solvent. By using this procedure the following compounds were obtained as pure products:

1,3-Dimethyl-5-benzylsulfonamidopyrazole (**2c**, $R_1 = C_6H_5$).

This compound was obtained in a yield of 55%, mp 160-162° (ethyl acetate/light petroleum); ir: 3040 (br), 2780 (br), 1550, 1330, 1160 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.10 (s, 3H, CH_3), 3.56 (s, 3H, CH_3N), 4.48 (s, 2H, CH_2), 5.97 (s, 1H, CH), 7.38 (s, 5H, aromatic), 9.83 (br, 1H, NH, deuterium oxide exchangeable); ^{13}C-nmr (hexadeuteriodimethyl sulfoxide): δ 13.6 (q, J = 127 Hz, CH_3), 34.7 (q, J = 139 Hz, NCH_3), 57.14 (t, J = 139.2 Hz, CH_2), 100.2 (d, J = 176 Hz, CH), 128.2 (d, J = 158 Hz, CH aromatic), 128.35 (d, J = 158 Hz, 2 CH, aromatic), 129.35 (s, aromatic), 130.90 (d, J = 160 Hz, 2 CH, aromatic), 134.9 (s, C-NH), 145.6 (s, C=N).

Anal. Calcd. for $C_{12}H_{15}N_3O_2S$: C, 54.32; H, 5.70; N, 15.84; S, 12.08. Found: C, 54.28; H, 5.69; N, 15.77; S, 11.77.

Table 4

Table of Bond Angles in Degrees

Atom1	Atom2	Atom3	Angle	Atom1	Atom2	Atom3	Angle	Atom1	Atom2	Atom3	Angle
O1	S	O2	113.4(1)	C3	C2	C4	107.6(3)	C1	C7	C8	118.9(3)
O1	S	N1	111.2(2)	N1	C3	N4	123.8(3)	C1	C7	C12	123.1(3)
O1	S	C1	105.8(1)	N1	C3	C2	128.7(3)	C8	C7	C12	118.0(3)
O2	S	N1	108.7(1)	N4	C3	C2	107.4(3)	C7	C8	C9	120.0(3)
O2	S	C1	110.3(1)	N3	C4	C2	107.0(3)	C7	C8	H8	115.(2)
N1	S	C1	107.3(1)	N3	C4	C6	121.6(3)	C9	C8	H8	125.(2)
S	N1	C3	114.0(2)	C2	C4	C6	131.4(3)	C8	C9	C10	120.8(3)
C1	N2	C2	119.1(3)	N4	C5	H51	104.(2)	C8	C9	H9	107.(2)
N4	N3	C4	110.2(3)	N4	C5	H52	104.(3)	C10	C9	H9	132.(2)
N4	N3	HN3	120.(3)	N4	C5	H53	127.(5)	C9	C10	C11	119.6(4)
C4	N3	HN3	129.(3)	H51	C5	H52	101.(4)	C9	C10	H10	116.(3)
N3	N4	C3	107.8(3)	H51	C5	H53	94.(5)	C11	C10	H10	124.(3)
N3	N4	C5	122.2(3)	H52	C5	H53	121.(5)	C10	C11	C12	120.4(4)
C3	N4	C5	129.8(3)	C4	C6	H61	104.(2)	C10	C11	H11	125.(3)
S	C1	N2	121.0(3)	C4	C6	H62	117.(2)	C12	C11	H11	114.(3)
S	C1	C7	119.5(2)	C4	C6	H63	110.(3)	C7	C12	C11	121.2(3)
N2	C1	C7	119.5(3)	H61	C6	H62	104.(3)	C7	C12	H12	116.(2)
N2	C2	C3	124.2(3)	H61	C6	H63	104.(4)	C11	C12	H12	123.(2)
N2	C2	C4	128.1(3)	H62	C6	H63	116.(4)	HW1	OW	HW2	97.(4)

1-Phenyl-3-methyl-5-benzylsulfonamidopyrazole (**2a**, R_1 = C_6H_5).

This compound was obtained in a yield of 31%, mp 163-165° (ethyl acetate); ir: 3050 (br), 2820 (br), 1600, 1560, 1505, 1330, 1135 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.21 (s, 3H, CH_3), 4.44 (s, 2H, CH_2), 6.25 (s, 1H, CH), 7.35-7.57 (m, 10H, 2 aromatic), 9.83 (br, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{17}H_{17}N_3O_2S$: C, 62.37; H, 5.24; N, 12.83; S, 9.79. Found: C, 61.88; H, 5.16; N, 12.76; S, 9.51.

1-(3-chloro)Phenyl-3-methyl-5-benzylsulfonamidopyrazole (**2b**, R_1 = C_6H_5).

This compound was obtained in a yield of 41%, mp 161-162° (ethyl acetate/light petroleum); ir: 3020 (br), 2770 (br), 1600, 1560, 1330, 1135 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.22 (s, 3H, CH_3), 4.50 (s, 2H, CH_2), 6.30 (s, 1H, CH), 7.36 (s, 5H, aromatic), 7.42-7.63 (m, 4H, aromatic), 9.96 (br, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{17}H_{16}ClN_3O_2S$: C, 56.43; H, 4.46; N, 11.61; S, 8.86. Found: C, 56.72; H, 4.32; N, 11.48; S, 8.55.

1-Phenyl-3-methyl-5-methanesulfonamidopyrazole (**2a**, R_1 = H).

This compound was obtained in a yield of 58%, mp 162-163° (ethyl acetate); ir: 3020 (br), 2800 (br), 1600, 1560, 1500, 1330, 1150 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.29 (s, 3H, CH_3), 2.85 (s, 3H, CH_3SO_2), 6.15 (s, 1H, CH), 6.93 (s, 1H, NH, deuterium oxide exchangeable), 7.42-7.45 (m, 5H, aromatic).

Anal. Calcd. for $C_{11}H_{13}N_3O_2S$: C, 52.57; H, 5.21; N, 16.72; S, 12.76. Found: C, 52.48; H, 5.11; N, 16.39; S, 12.56.

1-Phenyl-3-methyl-5-ethanesulfonamidopyrazole (**2a**, R_1 = CH_3).

This compound was obtained in a yield of 13%, mp 128-129° (ethyl acetate); ir: 3000 (br), 2800 (br), 1600, 1565, 1505, 1335, 1145 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 1.14 (t, J = 7.3 Hz, 3H, CH_3), 2.21 (s, 3H, CH_3), 3.07 (q, J = 7.3 Hz, 2H, CH_2), 6.3 (s, 1H, CH), 7.49-7.6 (m, 5H, aromatic), 9.8 (s, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{12}H_{15}N_3O_2S$: C, 54.32; H, 5.70; N, 15.84; S, 12.08. Found: C, 54.75; H, 5.86; N, 16.14; S, 11.74.

General Procedure for 4-Nitroso-5-alkylsulfonamidopyrazoles **3a-c**.

Sodium nitrite (2.11 g, 30 mmoles) was added to a solution of **2** (30 mmoles) in acetic acid (100 ml). The reaction mixture was stirred at room temperature for 10 minutes. When the reaction product was insoluble in the medium, the resulting red precipitate (**3a**, R_1 = H, CH_3, C_6H_5; **3b**, R_1 = C_6H_5) was collected, washed with light petroleum and crystallized. When the product was soluble (**3c**, R_1 = C_6H_5), the reaction mixture was neutralized with ammonium hydroxide and repeatedly extracted with ethyl acetate; the combined organic extracts were dried over magnesium sulfate and evaporated to give a solid red residue that was crystallized from the indicated solvent. By using this procedure the following compounds were obtained as pure products:

1,3-Dimethyl-4-nitroso-5-benzylsulfonamidopyrazole (**3c**, R_1 = C_6H_5).

This compound was obtained in a yield of 92%, mp 167-168° (ethyl acetate/light petroleum); ir: 3200-2600, 1650, 1600, 1295, 1120 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.27 (s, 3H, CH_3), 3.34 (s, 3H, CH_3), 4.43 (s, 2H, CH_2), 7.33-7.47 (m, 5H, aromatic), 15.5 (br, 1H, NH, deuterium oxide exchangeable);

^{13}C-nmr (hexadeuteriodimethyl sulfoxide): δ 16.39 (q, J = 129 Hz, CH_3), 33.5 (q, J = 140 Hz, N-CH_3), 59.9 (t, J = 136 Hz, CH_2), 127.7 (d, J = 155 Hz, CH, aromatic), 127.8 (d, J = 156 Hz, 2 CH, aromatic), 131.1 (d, J = 160 Hz, 2 CH, aromatic), 131.2 (s, C, aromatic), 140.9 (s), 145.2 (s), 152.6 (s) (C-3, C-4, C-5).

Anal. Calcd. for $C_{12}H_{14}N_4O_3S$: C, 48.97; H, 4.79; N, 19.04; S, 10.89. Found: C, 48.85; H, 4.69; N, 19.09; S, 10.46.

1-Phenyl-3-methyl-4-nitroso-5-benzylsulfonamidopyrazole (**3a**, R_1 = C_6H_5).

This compound was obtained in a yield of 98%, mp 200-201° (ethyl acetate/light petroleum); ir: 3300 (br), 1640, 1590, 1570, 1300, 1120 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.36 (s, 3H, CH_3), 4.46 (s, 2H, CH_2), 7.30-7.64 (m, 10H, 2 aromatic), 12 (v br, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{17}H_{16}N_4O_3S\cdot\frac{1}{2}H_2O$: C, 55.88; H, 4.69; N, 15.33; S, 8.77. Found: C, 55.51; H, 4.20; N, 15.5; S, 8.55.

1-(3-chloro)Phenyl-3-methyl-4-nitroso-5-benzylsulfonamidopyrazole (**3b**, R_1 = C_6H_5).

This compound was obtained in a yield of 90%, mp 180-181° (ethyl acetate/light petroleum); ir: 3200 (br), 1590, 1530, 1250, 1055 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.34 (s, 3H, CH_3), 4.51 (s, 2H, CH_2), 7.28-7.84 (m, 9H, 2 aromatic), 12.0 (v br, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{17}H_{15}ClN_4O_3S\cdot\frac{1}{2}H_2O$: C, 51.07; H, 4.03; N, 14.01; S, 8.02. Found: C, 50.95; H, 3.75; N, 14.02; S, 7.88.

1-Phenyl-3-methyl-4-nitroso-5-methanesulfonamidopyrazole (**3a**, R_1 = H).

This compound was obtained in a yield of 83%, mp 195-196° (ethyl acetate/light petroleum); ir: 3300 (br), 1630, 1560, 1420, 1280, 1145, 1100 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.40 (s, 3H, CH_3), 3.12 (s, 3H, CH_3), 7.32-7.85 (m, 5H, aromatic), 12.0 (v br, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{11}H_{12}N_4O_3S\cdot\frac{1}{2}H_2O$: C, 45.67; H, 4.53; N, 19.37; S, 11.08. Found: C, 45.59; H, 4.40; N, 19.33; S, 10.94.

1-Phenyl-3-methyl-4-nitroso-5-ethanesulfonamidopyrazole (**3a**, R_1 = CH_3).

This compound was obtained in a yield of 90%, mp 166-167° (ethyl acetate/light petroleum); ir: 3150 (br), 1635, 1565, 1420, 1275, 1145, 1100 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 1.26 (t, J = 7.2 Hz, 3H, CH_3), 2.36 (s, 3H, CH_3), 3.15 (q, J = 7.2 Hz, 2H, CH_2), 7.3-7.86 (m, 5H, aromatic), 12 (v br, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{12}H_{14}N_4O_3S\cdot\frac{1}{2}H_2O$: C, 47.51; H, 4.98; N, 18.47; S, 10.57. Found: C, 47.76; H, 4.56; N, 18.77; S, 10.21.

General Procedure for 6*H*-Pyrazolo[3,4-*c*][1,2,5]thiadiazine 2,2-Dioxide **4a-c**.

3-Methyl-4-nitroso-5-alkylsulfonamidopyrazole **3** (1.5 mmoles) was heated under reflux in 1*N* sodium hydroxide (40 ml). The solution turned from dark red to yellow. The reaction mixture was acidified with hydrochloric acid and the resulting pale yellow precipitate was characterized as 6*H*-pyrazolo[3,4-*c*][1,2,5]thiadiazine 2,2-dioxide **4**. By using this procedure the following compounds were obtained as pure products:

3-Phenyl-5,7-dimethyl-6*H*-pyrazolo[3,4-*c*][1,2,5]thiadiazine 2,2-Dioxide **4c**.

This compound was obtained in a yield of 50%, mp 133-134° (ethanol); ir: 3450 (br), 2600 (v br), 1560, 1235, 1115 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.19 (s, 3H, CH_3), 3.42 (s, 3H, N-CH_3), 3.58 (br, 3H, H_2O) 7.30-7.37 (m, 3H, aromatic), 8.04 (d, J = 7.3 Hz, 2H, aromatic); ^{13}C-nmr (hexadeuteriodimethyl sulfoxide): 10.9 (q, J = 126 Hz, CH_3), 32.0 (q, J = 137 Hz, CH_3), 113.4 (s, 1 C), 127.2 (d, J = 167 Hz, 1 CH, aromatic) 127.7 (d, J = 159 Hz, 2 CH, aromatic), 127.8 (d, J = 159 Hz, 2 CH, aromatic), 134.6 (s, 1 C), 136.2 (s, 1 C), 141.4 (s, 1 C), 144.0 (s, 1 C).

Anal. Calcd. for $C_{12}H_{12}N_4O_2S\cdot H_2O$: C, 48.97; H, 4.79; N, 19.04; S, 10.89. Found: C, 48.86; H, 4.79; N, 19.03; S, 10.52.

3,7-Diphenyl-5-methyl-6*H*-pyrazolo[3,4-*c*][1,2,5]thiadiazine 2,2-Dioxide **4a**.

This compound was obtained in a yield of 68%, mp 166-167° (ethyl acetate); ir: 3200 (br), 1605, 1590, 1510, 1260, 1115 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.40 (s, 3H, CH_3), 5.0 (br, 3H, NH + H_2O, deuterium oxide exchangeable), 7.28-8.12 (m, 10H, aromatic), the position of NH + water absorption is strongly dependent on the amounts of water.

Anal. Calcd. for $C_{17}H_{14}N_4O_2S$: C, 60.34; H, 4.17; N, 16.56; S, 9.47. Found: C, 60.55; H, 4.05; N, 16.61, S, 9.35.

3-Phenyl-5-methyl-7-(3-chloro)phenyl-6*H*-pyrazolo[3,4-*c*][1,2,5]-thiadiazine 2,2-Dioxide **4b**.

This compound was obtained in a yield of 70%, mp 136-137° (ethanol); ir: 3450 (br), 2700 (v br), 1600, 1490, 1250, 1130 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.31 (s, 3H, CH_3), 4.7 (v br, NH + 3 water, deuterium oxide exchangeable), 7.2-8.2 (m, 9H, aromatic).

Anal. Calcd. for $C_{17}H_{13}ClN_4O_2S\cdot 3H_2O$: C, 47.83; H, 4.49; N, 13.13; S, 7.51. Found: C, 47.75; H, 4.33; N, 13.05; S, 7.39.

Reflux of **3a** (R_1 = H, CH_3) for 5 minutes in sodium hydroxide gave an orange precipitate (yield 96%) that was identified as 1-phenyl-3-methyl-4-oximino-pyrazol-5-one **6a**, from ir and ^{1}H-nmr [8].

Decomposition of 6*H*-Pyrazolo[3,4-*c*][1,2,5]thiadiazines 2,2-Dioxide **4a-c**. Formation of 4-Benzamido-5-aminopyrazoles **5a-c**.

Method A.

Compounds **4a-c** were heated *in vacuo* at 120° over phosphorus pentoxide for 4 hours. The resulting white solides were characterized as 3-methyl-4-benzamido-5-aminopyrazoles **5a-c**.

Method B.

Compounds **4a-c** (1 mmole) were refluxed in water (300 ml) for 2 hours. The aqueous solution was extracted with ethyl acetate (2 x 100 ml), the combined organic layers were anhydrified over magnesium sulfate and the solvent was removed to give a quantitative yield of solid residues which were identical with the corresponding samples of **5a-c** obtained by the termal decomposition. By using either of the above described procedures the following compounds were obtained as pure products:

1,3-Dimethyl-4-benzamido-5-aminopyrazole **5c**.

This compound had mp 156-158° (ethyl acetate/light petroleum); ir: 3250 (br), 1625, 1530 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 1.93 (s, 3H, CH_3), 3.48 (s, 3H, CH_3), 4.8 (v br, 2H, NH_2, deuterium oxide exchangeable), 7.4-7.6 (m, 3H, aromatic), 7.96 (d, J = 7 Hz, 2H, aromatic), 9.30 (s, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{12}H_{14}N_4O$: C, 62.59, H, 6.13, N, 24.33. Found: C, 62.44; H, 6.19; N, 24.48.

1-Phenyl-3-methyl-4-benzamido-5-aminopyrazole **5a**.

This compound had mp 198°; ir: 3390, 3280 (br), 1640, 1620, 1550, 1520 cm^{-1}; ^1H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.04 (s, 3H, CH_3), 5.1 (br, 1H, NH, deuterium oxide exchangeable), 7.29-7.63 (m, 8H, aromatic), 8.01 (dd, J = 7.8 and 1.5 Hz, 2H, aromatic), 9.42 (s, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{17}H_{16}N_4O$: C, 69.84, H, 5.52; N, 19.17. Found: C, 70.23; H, 5.60; N, 19.51.

1-(3-Chloro)Phenyl-3-methyl-4-benzamido-5-aminopyrazole **5b**.

This compound had mp 179-180°; ir: 3400, 3280, 3200, 1660, 1630, 1520 cm^{-1}; ^1H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.04 (s, 3H, CH_3), 5.2 (s, 2H, NH_2, deuterium oxide exchangeable), 7.36-7.20 (m, 7H, aromatic), 8.01 (dd, J = 7.6 and 1.5 Hz, 2H, aromatic), 9.42 (s, 1H, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_{17}H_{15}ClN_4O$: C, 62.48; H, 4.63; N, 17.15. Found: C, 62.77; H, 4.41; N, 16.90.

Alternative Synthesis of 1-Phenyl-3-methyl-4-benzamido-5-aminopyrazole **5a**.

Benzoyl chloride (0.6 ml, 5.3 mmoles) in ethyl acetate (15 ml) was added dropwise to a vigorously stirred mixture of 1-phenyl-3-methyl-4,5-diaminopyrazole (1.0 g, 5.3 mmoles) in ethyl acetate (30 ml) and sodium hydrogen carbonate (0.45 g, 5.3 mmoles) in water (15 ml). Stirring was continued for 1 hour at room temperature. The organic layer was extracted with hydrochloric acid (30 ml), the aqueous solution was made alkaline with sodium hydroxide and extracted with ethyl acetate (2 x 20 ml). The combined organic extracts were dried over magnesium sulfate and evaporated to give a solid residue that was crystallized from ethyl acetate/light petroleum (1.1 g, yield 71%, mp 198°). The product was identical with a sample of **5a** obtained by the above described procedure.

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