

Note

Sulfonyl pyrazoles and isoxazoles: Cycloaddition of nitrile imines and nitrile oxides to aryl styryl sulfones

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Nitrile imines and nitrile oxides by intermolecular cycloaddition reaction with aryl styryl sulfones **1** lead to the formation of tetrasubstituted pyrazolines **3** and trisubstituted isoxazolines **6**. The **3** and **6** on dehydrogenation with chloranil in xylene gave pyrazoles **4** and isoxazoles **7**. The IR and ¹H NMR spectral data have been used to ascertain the structures of the new compounds.

The chemistry of five membered heterocycles have more than one heteroatoms has gained importance in recent times, as many of them exhibit pronounced bioactive nature. One of the important general methods to accomplish this, is the 1,3-dipolar cycloaddition of ylide to an alkene involving 3+2 principle-nitrile ylides to activated olefins. Although, different methods were reported for the synthesis of pyrazolines and isoxazolines¹⁻⁵, the utility of nitrile imines and nitrile oxides for the same are relatively less⁶⁻⁸. Furthermore, these cycloadducts may serve as precursors for various class of compounds including natural product synthesis^{9,10}.

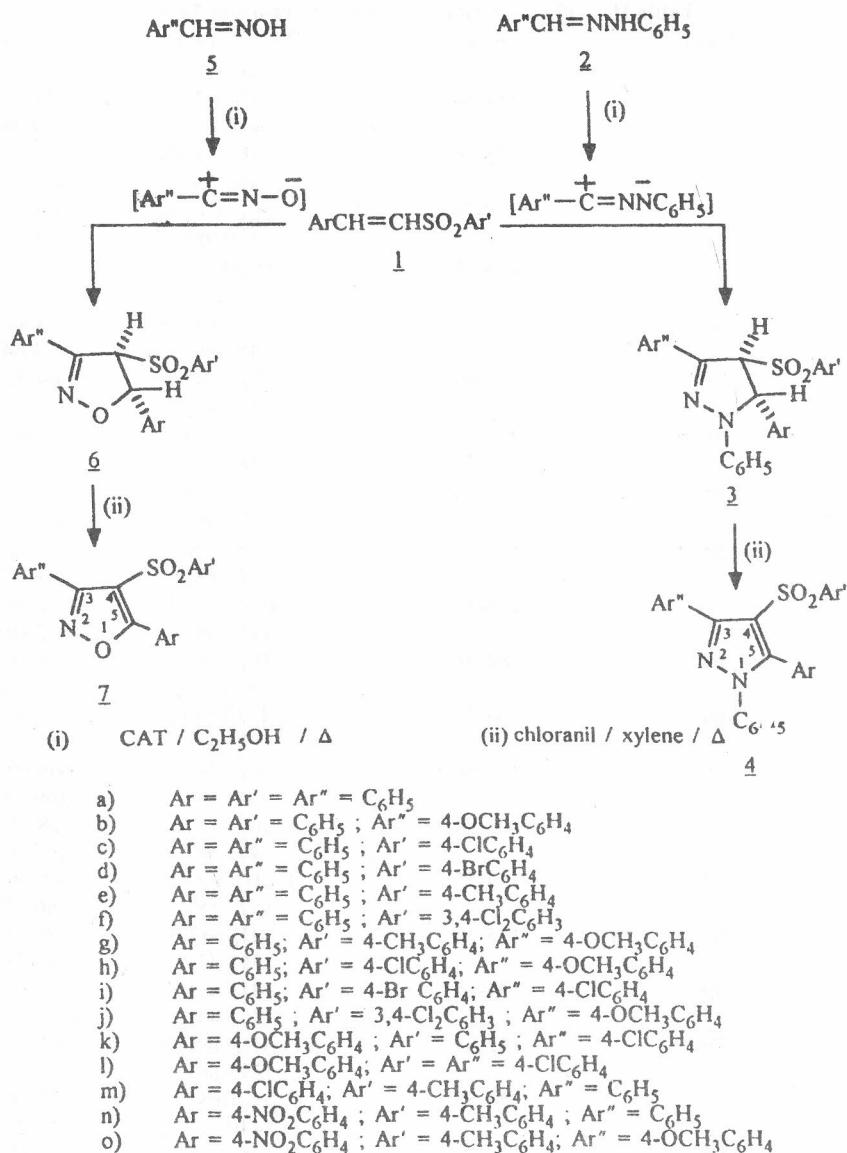
In continuation of our work on aryl styryl sulfones¹¹⁻¹³, we thought it fit to develop five membered heterocyclic systems, 2-pyrazolines and 2-isoxazolines with the former as a substrate. Earlier, disubstituted pyrazolines were reported by the cycloaddition of diazomethane to unsaturated sulfones⁵ or by the cyclocondensation of unsaturated keto sulfones with hydrazine hydrate³. However, there are no reports to our knowledge on sulfonyl isoxazolines. At present, we are reporting tetrasubstituted 2-pyrazolines and trisubstituted 2-isoxazolines by the reaction of aryl styryl sulfones with hydrazones and oximes of araldehydes. The dehydrochlorination of the latter in the presence of chloramine-T (CAT) generates *in situ* the nitrile

imines and nitrile oxides. Thus, a series of 1,3,5-triaryl-4-arylsulfonyl-4,5-dihydro-2-pyrazolines **3** and 3,5-diaryl-4-arylsulfonyl-4,5-dihydro-2-isoxazolines **6** have been prepared by the reaction of equimolecular mixture of arylhydrazones **2** or araldoximes **5**, aryl styryl sulfones **1** and CAT in refluxing ethanol for 4hr (Scheme I and Table I). The aromatization of these 2-pyrazolines and 2-isoxazolines by autoxidation or thermal dehydrogenation or by treatment with tetrachloro-1,4-benzoquinone (chloranil) and perchloric acid led to corresponding pyrazoles and isoxazoles¹⁴. Thus, 1,3,5-triaryl-4-arylsulfonyl pyrazoles **4** and 3,5-diaryl-4-arylsulfonyl isoxazoles **7** have been prepared by refluxing **3** and **6** with chloranil in xylene (Table II).

The structures of **3,4,6,7** have been assigned on the basis of IR and PMR spectral data. The compounds showed strong absorption bands at 1360-1335 and at 1145-1120 for asymmetric and symmetric stretching vibrations of SO₂ group. They also exhibited two medium absorption bands in the region 1458-1433 for C=N. The PMR spectra of **3** and **6** exhibited two doublets at 5.25-5.35 and at 5.70-5.80 for C₅-H and C₄-H protons of pyrazoline and isoxazoline ring systems (Table III). The coupling constants (*J*=6.2-6.5 Hz) of the pyrazoline and isoxazoline protons indicate that they possess *trans* geometry¹⁴. The ¹³C NMR spectra of **4a** and **7a** indicated signals for C-3, C-4 and C-5 at 149.24, 152.72 and 150.87 and at 148.91, 153.45 and 152.38 ppm respectively¹⁵. This confirms that dehydrogenation of **3** and **6** indeed has taken place leading to aromatization.

Experimental Section

Melting points were determined in open capillaries and are uncorrected. The purity of the compounds was checked by TLC. (Silica gel-G, hexane: ethyl acetate, 3:1 as eluents). IR spectra were run as KBr pellets using Perkin-Elmer 993 infrared spectrometer (λ_{max} in cm⁻¹) and ¹H NMR spectra were recorded in CDCl₃ using varian EM-360 spectrophotometer with TMS as an internal standard (chemical shifts in δ , ppm), Microanalytical data were obtained from Indian



Scheme I

Table I—Physical data of compounds 3a-o and 6a-o

Compd.	Yield (%)	m.p. (°C)	Compd	Yield (%)	m.p. (°C)
3a	74	170-72	6a	65	120-21
3b	66	148-50	6b	68	138-39
3c	71	180-82	6c	64	134-35
3d	68	176-78	6d	73	142-43
3e	63	168-70	6e	62	130-31
3f	75	170-72	6f	67	126-27
3g	82	136-38	6g	70	162-64
3h	80	168-70	6h	62	110-11
3i	71	162-64	6i	66	170-72
3j	72	184-86	6j	65	168-69
3k	66	168-69	6k	71	134-35
3l	68	174-76	6l	70	146-47
3m	82	154-56	6m	66	138-40
3n	73	188-90	6n	72	146-47
3o	75	138-40	6o	63	162-63

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1,3,5-Triaryl-4-arylsulfonyl-4,5-dihydro-2-pyrazolines 3: General procedure. A mixture of aryl styryl sulfone (0.001 mole), arylhydrazine (0.001 mole) and chloramine-T (0.0015 mole) in ethanol was refluxed for 3 hr. Salts were filtered off and the filtrate was concentrated. The residue was extracted with ether. The ethereal layer was washed with 1N NaOH (2 × 15 mL), brine solution (2 × 20 mL) and dried over anhyd. Na₂SO₄. The solvent was removed on rotary evaporator. The resultant solid was purified by column chromatography (petroleum ether : ethyl acetate, 4:1) to get a pure compound 3.

Table II — Physical data of compounds 4a-o and 7a-o

Compd	Yield (%)	m.p. (°C)	Mol. Formula (Mol. Wt)	Found (%) (Calcd)		
				C	H	N
4a	65	182-84	C ₂₇ H ₂₀ N ₂ O ₂ S (436.53)	74.07 (74.28)	4.73 4.61	6.53 6.42)
4b	67	135-36	C ₂₈ H ₂₂ N ₂ O ₃ S (466.56)	71.90 (72.08)	4.87 4.75	6.09 6.00)
4c	69	174-76	C ₂₇ H ₁₉ ClN ₂ O ₂ S (470.98)	69.05 (68.85)	3.94 4.06	6.07 5.95)
4d	65	168-69	C ₂₇ H ₁₉ BrN ₂ O ₂ S (515.43)	62.73 (62.91)	3.60 3.71	5.53 5.43)
4e	68	171-72	C ₂₈ H ₂₂ N ₂ O ₂ S (450.56)	74.44 (74.64)	4.81 4.92	6.36 6.22)
4f	70	162-63	C ₂₇ H ₁₈ Cl ₂ N ₂ O ₂ S (505.42)	64.01 (64.16)	3.65 3.58	5.45 5.54)
4g	66	147-48	C ₂₉ H ₂₄ N ₂ O ₃ S (480.60)	72.62 (72.47)	5.14 5.03	5.94 5.82)
4h	65	175-76	C ₂₈ H ₂₁ ClN ₂ O ₃ S (501.00)	67.34 (67.12)	4.31 4.22	5.68 5.59)
4i	68	155-56	C ₂₇ H ₁₈ BrClN ₂ O ₂ S (549.88)	59.12 (58.97)	3.36 3.29	5.00 5.09)
4j	70	178-80	C ₂₈ H ₂₀ Cl ₂ N ₂ O ₃ S (535.45)	62.99 (62.80)	3.86 3.76	5.11 5.23)
4k	64	184-86	C ₂₈ H ₂₀ ClN ₃ O ₃ (515.01)	65.18 (65.30)	4.00 4.11	8.03 8.15)
4l	64	168-70	C ₂₈ H ₂₀ Cl ₂ N ₂ O ₃ S (535.45)	62.64 (62.80)	3.70 3.76	5.15 5.23)
4m	69	165-66	C ₂₈ H ₂₁ ClN ₂ O ₂ S (485.00)	69.09 (69.34)	4.25 4.36	5.66 5.78)
4n	67	173-74	C ₂₈ H ₂₁ N ₃ O ₄ S (495.56)	68.08 (67.86)	4.38 4.27	8.63 8.47)
4o	72	154-55	C ₂₉ H ₂₃ N ₃ O ₅ S (525.58)	66.06 (66.27)	4.50 4.41	7.88 7.99)
7a	67	135-36	C ₂₁ H ₁₅ NO ₃ S (361.42)	69.59 (69.78)	4.33 4.18	3.95 3.87)
7b	70	134-55	C ₂₂ H ₁₇ NO ₄ S (391.44)	67.38 (67.50)	4.22 4.37	3.69 3.57)
7c	70	142-44	C ₂₁ H ₁₄ ClNO ₃ S (395.86)	63.86 (63.71)	3.67 3.56	3.60 3.53)
7d	66	154-55	C ₂₁ H ₁₄ BrNO ₃ S (440.32)	57.14 (57.28)	3.29 3.20	3.09 3.18)
7e	64	120-21	C ₂₂ H ₁₇ NO ₃ S (375.44)	70.56 (70.38)	4.45 4.56	3.81 3.73)
7f	70	147-48	C ₂₁ H ₁₃ Cl ₂ NO ₃ S (430.31)	58.77 (58.61)	2.97 3.04	3.36 3.25)
7g	64	175-76	C ₂₃ H ₁₉ NO ₄ S (405.47)	68.35 (68.13)	4.63 4.72	3.57 3.45)
7h	66	127-28	C ₂₂ H ₁₆ ClNO ₄ S (425.89)	61.90 (62.04)	3.91 3.78	3.38 3.28)
7i	65	163-64	C ₂₁ H ₁₃ BrClNO ₃ S (474.76)	53.00 (53.12)	2.84 2.75	3.02 2.95)
7j	69	147-48	C ₂₂ H ₁₅ Cl ₂ NO ₄ S (460.33)	57.58 (57.40)	3.20 3.28	2.97 3.04)
7k	66	128-29	C ₂₂ H ₁₆ ClNO ₄ S (425.89)	62.20 (62.04)	3.64 3.78	3.38 3.28)
7l	65	135-36	C ₂₂ H ₁₅ Cl ₂ NO ₄ S (460.33)	57.55 (57.40)	3.16 3.28	3.11 3.04)
7m	67	149-50	C ₂₂ H ₁₆ ClNO ₃ S (409.89)	64.29 (64.46)	4.05 3.93	3.49 3.41)
7n	66	135-36	C ₂₂ H ₁₆ N ₂ O ₅ S (420.44)	62.64 (62.84)	3.94 3.83	6.54 6.66)
7o	68	152-53	C ₂₃ H ₁₈ N ₂ O ₆ S (450.47)	61.53 (61.32)	4.14 4.02	6.11 6.21)

Table III			
H NMR spectral data of compounds 3' and 6			
Compd	C ₄ -H	C ₅ -H	Substituents
3a	5.74	5.31	-
3b	5.72	5.34	3.80 (Ar-OCH ₃)
3c	5.78	5.35	-
3e	5.72	5.30	2.34 (Ar-CH ₃)
3g	5.74	5.28	2.33 (Ar-CH ₃); 3.76 (Ar-OCH ₃)
3h	5.79	5.32	3.76 (Ar-OCH ₃)
3k	5.75	5.30	3.78 (Ar-OCH ₃)
3l	5.80	5.34	3.80 (Ar-OCH ₃)
3m	5.73	5.35	2.34 (Ar-CH ₃)
3o	5.76	5.34	2.32 (Ar-CH ₃); 3.78 (Ar-OCH ₃)
6a	5.73	5.28	-
6b	5.70	5.25	3.78 (Ar-OCH ₃)
6d	5.72	5.30	-
6e	5.74	5.26	2.32 (Ar-CH ₃)
6h	5.80	5.26	3.80 (Ar-OCH ₃)
6i	5.78	5.32	-
6j	5.80	5.31	3.77 (Ar-OCH ₃)
6l	5.76	5.29	3.78 (Ar-OCH ₃)
6m	5.74	5.31	2.35 (Ar-CH ₃)
6n	5.77	5.30	2.32 (Ar-CH ₃)

3,5-Diaryl-4-arylsulfonyl-4,5-dihydro-2-isoxazolines 6: General procedure. A mixture of aryl styryl sulfone (0.001 mole), araldoxime (0.001 mole), chloramine-T (0.0015 mole) in ethanol (20 mL) was heated to reflux for 3 hr. The salt formed during the course of the reaction was filtered off and washed with ethanol. The filtrate and washings were concentrated under reduced pressure and the residue was extracted with dichloromethane, washed with water and with 1N NaOH and dried. The solvent was evaporated and the remaining solid was recrystallized from chloroform: petroleum ether (2:3) to get pale yellow crystals.

Dehydrogenation of pyrazolines and isoxazolines 3 and 6: General Procedure. A solution of appropriate 3 or 6 (0.005 mole) and chloranil (0.0052 mole) in xylene (15 mL) was

refluxed for 24-32 hr. It was washed with 5% NaOH solution. The organic layer was repeatedly washed with water, dried and distilled under reduced pressure. The solid left was purified by recrystallization from ethanol or glacial acetic acid to furnish 4 or 7.

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References

- Sayed G H, *Indian J Chem*, 19B, 1980, 364.
- Bheemasankara Rao Ch, Subba Raju G V & Narasimha Raju P V, *Indian J Chem*, 25B, 1986, 400.
- Bhaskar Reddy D, Radhakrishna Murthy K, Seshamma T, Seenaiah B & Padmaja A, *Sulfur Lett*, 12, 1990, 73.
- Bhaskar Reddy D, Seshamma T & Ramana Reddy B V, *Acta Chim Hungarica*, 122, 1986, 119.
- Bhaskar Reddy D, Bhaskara Reddy D, Subba Reddy N & Balaji T, *Indian J Chem*, 23B, 1984, 983.
- Mukaiyama T & Hoshino T, *J Am Chem Soc*, 82, 1960, 5339.
- Stuart J Barrow & Christopher J Easton, *Tetrahedron Lett*, 38(12), 1997, 2175.
- Christl M & Heisgen R, *Chem Ber*, 106, 1973, 3345.
- Fusw R, Garanti L & Zecehi G, *Chem Ind. (Milan)* 16, 1975, 57.
- Bast K, Christl M, Huisgen R & Mack W, *Chem Ber*, 105, 1972, 2825.
- Bhaskar Reddy D, Ramachandra Reddy K & Padmaja A, *Indian J Chem*, 36B, 1997, 608.
- Padmaja A, Ramachandra Reddy K, Padmavathi V & Bhaskar Reddy D, *Collect Czech Chem Commun*, (in press).
- Padmaja A, Ramachandra Reddy K & Bhaskar Reddy D, ¹³C_H—Models in Chemistry (communicated).
- Hameli M Hassaneen, Rifaat H Halal, Nehal M Elwan Abdelhamid Harhash & Ahmad S Shawali, *J Heterocycl Chem*, 21, 1984, 1013.
- Stothers J B, *Carbon-13 NMR Spectroscopy* (Academic Press, New York), 1972, p 254.