Die UV-Spektren der $5 \cdot 10^{-5}$ M Lösungen von **1a–h** im jeweiligen Puffer wurden mit dem Spektrographen SPECORD UV-VIS, Carl Zeiss, Jena, registriert, wobei eine Pufferlösung mit dem jeweiligen pH-Wert, die die gleiche Menge Ethylalkohol wie die Probe enthielt, zum Ausgleich verwendet wurde. Die Messung der Extinktion erfolgte im Wellenlängenbereich von 200 nm bis 390 nm.
Die ^{1}H-NMR-Spektren wurden mit dem Spektrophotometer JEOL-JNM-PS-100 aufgenommen (8–10proz. Lösungen in $CDCl_3$, bezogen auf HMSO = 0).

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Synthesis and Central Nervous System Depression Properties of 3-[(1'-Pyrazolyl)phenyl]sydnones[1)]

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Some hitherto unknown 3-[*o*-(1-pyrazolyl)phenyl]sydnones were synthesized. Together with some 3-[*p*-(1-pyrazolyl)phenyl]sydnones they were studied for their CNS depression activity.

Synthese und ZNS-dämpfende Wirkung von 3-[(1-Pyrazolyl)phenyl]sydnonen

Mehrere bisher unbekannte 3-[o-(1-Pyrazolyl)phenyl]sydnone werden synthetisiert und zusammen mit einigen 3-[p-(1-Pyrazolyl)phenyl]sydnonen auf ihre ZNS-dämpfende Wirkung geprüft.

Sydnones, in particular the 3-arylsydnones, have been studied extensively for their biological properties. Of the various 3-arylsydnones, the 3-tolylsydnones have been found to show considerable CNS depression action[2)]. It has also been reported that the 3-tolylsydnones with an additional methyl group possess increased depression action and only the group in the phenyl ring at the 3-position is responsible for the enhanced CNS depression action[3)]. With this in view, a number of sydnones were synthesized by structural modification of the 3-aryl residue in order to study the biological variations. Instead of a methyl group in the phenyl ring of the 3-phenylsydnone, sydnones with a heteroaromatic moiety like pyrazole were synthesised. The synthesis of a number of derivatives of 3-[p-(1'-pyrazolyl)phenyl]sydnones has been already reported[4)].

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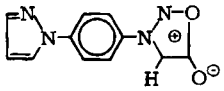
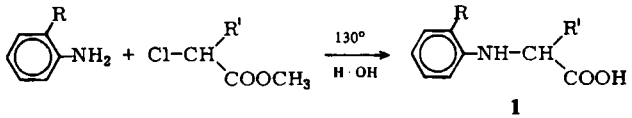


In continuation of the above work we now report the synthesis of 3-[o-(1′-pyrazolyl)phenyl]sydnone **(3a)** and its derivatives.



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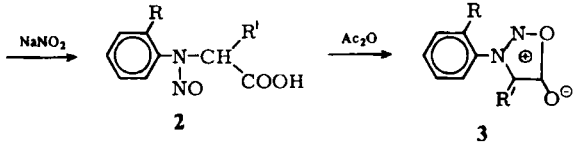
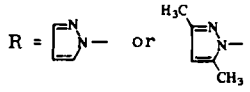


2 **3**



Pharmacology

All these compounds have been subjected for CNS depression action and it has been found that the compounds in the *o*-series are less active and more toxic than those in the *p*-series. Hence, the compounds in the p-series have been studied in detail.

For the preliminary screening, sydnones under test were dissolved in propylene glycol and injected intraperitonially to albino rats. Observation was focussed on the onset of action like sedation, sleep, muscle tone, movement. The effectiveness of the drug was evaluated on the basis of the duration of sleep or sedation.

The 3-[p-(1′-pyrazolyl)phenyl]sydnone possesses very mild depression action but the 3-[o-(1′-pyrazolyl)phenyl]sydnone **(3a)** shows a significant depression action together with considerable toxicity. The 3-[p-(3′,5′-dimethyl-1′-pyrazolyl)phenyl]sydnone shows marked CNS depression and the compound is highly toxic. Introduction of another methyl group at position 4 of the above sydnone, decreases the activity considerably. The 3-[p-(3′,4′,5′-trimethyl-1′-pyrazolyl)phenyl]sydnone is as active as the dimethyl pyrazolyl derivative but does not possess any toxicity.

Authors wish to thank Prof. *E.S. Jayadevappa* for encouragement and Mr. *V.A. Desai* for microanalysis. One of them (*S.B.H*) thanks UGC for the fellowship.

Experimental Section

M.P.: uncorr. *IR spectra*: (KBr) Beckman spectrophotometer. *NMR spectra*: 60 MHz, Varian A-60 spectrophotometer, TMS ref.

N-[o-(1-pyrazolyl)]phenylglycine **(1a)**

A mixture of 16.9 g (0.1 mole) of ethylbromoacetate, 15.9 g (0.1 mole) of 1-o-aminophenylpyrazole, 25 ml ethanol and 15.0 g of hydrated sodium acetate was refluxed at 130° for 40 h. The reaction mixture was then poured into 100 ml of water and the oily glycidester was hydrolysed with 80 ml of 10 perc. sodium hydroxide solution and little ethanol. It was cooled and extracted with ether to remove unreacted amine. The aqueous solution was acidified to obtain **1a**. Yield 9.0 g, m.p. 161–162°. $C_{11}H_{11}N_3O_2$ Calc.: C 58.1 H 4.85, Found: C. 58.3, H 4.68.

N-Nitroso-N-[o-(1-pyrazolyl)]phenylglycine **(2a)**

A solution of 1.8 g (0.025 mole) of sodium nitrite in 7.0 ml of water was added dropwise to a solution of 5.7 g (0.025 mole) of **1a** in 75 ml of 25 perc. hydrochloric acid at 0–5°. The reaction mixture was stirred further for 3 h. The separated solid was washed thoroughly with water, dried in air and crystallised from ethanol. Yield 5.0g, m.p. 121–122°. $C_{11}H_{10}N_4O_3$ Calc: C 53.7 H 4.07; Found: C 53.4 H 3.98.

N-Nitroso-N-[o-(3,5-dimethyl-1-pyrazolyl)]phenylglycine **(2b)**

16.9 g (0.1 mole) of ethylbromoacetate, 18.7 g (0.1 mole) of 1-o-aminophenyl-3,5-dimethylpyrazole, 25 ml ethanol and 15.0 g of hydrated sodium acetate were refluxed at 130° for 40 h and worked out in the usual manner and further nitrosated in 25 % hydrochloric acid without isolating the glycine. **2b** was isolated and crystallised from ethanol. Yield 12.0 g, m.p. 157–158°. $C_{13}H_{14}N_4O_3$ Calc: C 56.9 H 5.11; Found: C 56.9 H 5.05.

α-*Anilino-[o-(1-pyrazolyl)]propionic acid* **(1c)**

A mixture of 12.25 g (0.1 mole) of methyl-α-chloro-propionate, 15.9 g. (0.1 mole) of 1-o-amino-phenylpyrazole, 25 ml of ethanol and 15.0 g of hydrated sodium acetate was refluxed at 130° for 40 h. The glycidester was hydrolysed with 10 % sodium hydroxide solution. Acidified with hydrochloric acid to obtain **1c**. It was crystallised from ethanol. Yield 12.0 g, m.p. 83–84°. $C_{12}H_{13}N_3O_2$ Calc: C 62.3 H 5.63; Found: C 62.2 H 5.58.

N-Nitroso-α-anilino-[o-(1-pyrazolyl)]propionic acid **(2c)**

A solution of 3.45 g (0.05 mole) of sodium nitrite in 14 ml of water was added dropwise to a well stirred solution of 13.0 g (0.05 mole) of **1c** in 150 ml of 25 perc. hydrochloric acid at 0–5°. The reaction mixture was stirred further for 3 h. The separated sticky mass was estracted with ether, dried and directly used for cyclisation.

N-Nitroso-α-anilino-[o-(3,5-dimethyl-1-pyrazolyl)]propionic acid **(2d)**

18.7 g (0.1 mole) of 1-o-aminophenyl-3,5-dimethyl-pyrazole, 12.25 g (0.1 mole) of methyl-α-chloropropionate, 25 ml of ethanol and 15 g of hydrated sodium acetate were refluxed at 130° for 40 h. The resulting ester was hydrolysed with sodium hydroxide solution. The solution acidified and further nitrosated in 25 % hydrochloric acid solution without isolating the glycine. **2d** was washed thoroughly with water, dried in air and crystallised from ethanol. Yield 10.0 g, m.p. 104–105°. $C_{14}H_{16}N_4O_3$ Calc: C 58.3 H 5.56; Found: C 58.2 H 5.43.

N-Nitroso-α-anilino-[o-(1-pyrazolyl)]phenylacetic acid **(2e)**

8.0 g (0.05 mole) of 1-o-aminophenylpyrazole, 9.25 g. (0.05 mole) of methyl-α-chlorophenylacetate, 15 ml of ethanol and 7.5 g. of hydrated sodium acetate were refluxed at 130 for 40 h. The glycidester hydrolysed with 10 % sodium hydroxide solution and acidified to get the glycine. The glycine was further nitrosated in 25 % hydrochloric acid as usual, washed thoroughly with water, dried in air and crystallised from ethanol. Yield 9.0 g. m.p. 113–114°. $C_{17}H_{14}N_4O_3$ Calc: C 63.2 H 4.35; Found: C 63.3 H 4.28.

α-Anilino-[o-(3,5-dimethyl-1-pyrazolyl)]phenylacetic acid **(1f)**

A mixture of 9.0 g (0.05 mole) of 1-o-aminophenyl-3,5-dimethyl pyrazole, 9.3 g (0.05 mole) of methyl-α-chlorophenylacetate, 7.5 g. of hydrated sodium acetate and 15 ml of ethanol was refluxed at 130° for 40 h. The glycidester was further hydrolysed with 50 ml 10 perc. sodium hydroxide solution and acidified with hydrochloric acid to get **1f** and was crystallised from ethanol. Yield 9.0 g, m.p. 190–191°. $C_{18}H_{19}N_3O_2$ Calc: C 70.0 H 5.92; Found: C 69.9 H 5.88.

N-Nitroso-α-anilino-[o-(3,5-dimethyl-1-pyrazolyl)]phenylacetic acid **(2f)**

To a well stirred solution of 8.0 g (0.025 mole) of **1f** in 70 ml of 25 perc. hydrochloric acid a solution of 1.8 g of sodium nitrite in 7.0 ml of water was added at 0–5°. Stirring was continued further for 3 h. The solid was washed with water, dried and crystallised from ethanol. Yield 6.0 g, m.p. 115–116°. $C_{14}H_{18}N_4O_3$ Calc: C 65.1 H 5.14; Found: C 65.1 H 5.12.

Cyclisation to sydnones **3**

The N-nitrosoglycines **2** were dissolved in acetic anhydride (1 : 5 by weight) and heated on a water-bath for 3 h. The reaction mixture was poured into water and allowed to stand overnight. The solid was washed with water, 5 % $NaHCO_3$ solution, again with water and dried in air. All the sydnones **3** were crystallised from ethanol and are listed in table 1.

Spectral data

All the sydnones exhibit a strong IR band in the range of 1730–1760 cm^{-1} due to sydnone carbonyl stretching. The C-H stretchings of sydnone and pyrazole appear in the range of 3100–3200 cm^{-1}. Since these cannot be distinguished in the IR spectra, the sydnone and their derivatives are confirmed by NMR spectra. The data for the NMR signals of sydnone 4-proton and pyrazole 4-proton are given in table 1.

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Tab. 1: *3-[o-(1-Pyrazolyl)phenyl]sydnones* **3**

No. 3	R	R′	Yield %	m.p. °C	Calculated / Found C	Calculated / Found H	NMR δ (ppm) Sydnone H-4	NMR δ (ppm) Pyrazole H-4
a	Pyrazolyl	H	61	125–126	57.9 57.7	3.51 3.61	6.05	6.35 (t)
b	3,5-Dimethyl-pyrazolyl	H	64	155–156	60.9 61.0	4.68 4.59	6.0	5.85
c	Pyrazolyl	$-CH_3$	62	114–115	59.5 59.6	4.13 4.14	–	6.30 (t)
d	3,5-Dimethyl-pyrazolyl	$-CH_3$	65	153–154	63.1 63.2	5.30 5.24	–	5.90
e	Pyrazolyl	$-C_6H_5$	63	145–146	67.1 67.3	3.95 3.98	–	6.15 (t)
f	3,5-Dimethyl-pyrazolyl	$-C_6H_5$	60	166–167	68.5 68.5	5.11 5.01	–	6.00

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Trichlormethylquecksilber(II)chloro-18-krone-6

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Im Zusammenhang mit der Prüfung von Quecksilber(II)-kronenethern als Dehydrierungsreagenzien wurde bei der Aufarbeitung erstmals Trichlormethylquecksilber(II)chloro(1,4,7,10,13,16 hexaoxacyclooctadecan O^1, O^4, O^7, O^{10}, O^{13}, O^{16}) **(5)** isoliert. Die Struktur wurde durch Synthese bestätigt.

Trichloromethylmercurychloro-18-crown-6

In connection with the examination of mercury crown ethers as dehydrogenating reagents, trichloromethylmercurychloro(1,4,7,10,13,16-hexaoxacyclooctadecane-O^1, O^4, O^7, O^{10}, O^{13}, O^{16}) **(5)** was isolated for the first time. The structure was confirmed by synthesis.

Die bisherigen Dehydrierungen mit Quecksilber(II)-EDTA erforderten aufgrund der Löslichkeit des Komplexes praktisch immer ein weitgehend wäßriges Reaktionsmedium[1].

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