References

**Part II: Arch. Pharm. (Weinheim) *313,* 108 (1980).

1 A. K. Mansour, S. B. Awad and S. Antoun, Z. Naturforsch., *29b,* 792 (1974).

2 M. M. M. Sallam, Y. A. Ibrahim and S. Abdel-Latif Abdel Hady, Helv. Chim. Acta *59,* 1093 (1976).

3 V. J. Ram, Arch. Pharm. (Weinheim) *312,* 147 (1979).

4 I. Saikawa, T. Maeda, S. Takano, Japan Pat. 6824, 424 22 Oct. 1968; C. A. *70,* 57909c (1969).

5 a) H. Biltz, Justus Liebigs Ann. Chem. *339,* 143 (1905).
b) M. Giantueo, Gazz. Chim. Ital. *82,* 595 (1952).
c) A. Mustafa, a. K. Mansour and H. A. A. Zaher, Justus Liebigs Ann. Chem. *733,* 177 (1970).

6 P. v. Laakso, R. Rovinson and H. P. Vanderwals, Tetrahedron *1,* 103 (1957).

[Ph 159]

Arch. Pharm. (Weinheim) *313,* 471–476 (1980)

Organosulfur Compounds as Potential Pesticides

Vishnu Ji Ram

Department of Chemistry, S. C. College, Ballia (U. P.) India

Eingegangen am 21. August 1979

Condensation of 1-nitro-2,2-bis(methylmercapto)ethylene with aralkylamines gave the 1-nitro-2,2-bis-(aralkylamino)ethylenes **1** while its reaction with aromatic amines gave the 1-nitro-2-arylamino-2-methylmercaptoethylenes **2** under similar conditions. Reactions of methyl 1-cyano-2,2-bis(methylmercapto)acrylate with aromatic amines and hydrazine gave the methyl 1-cyano-2-arylamino-2--methylmercaptoacrylate **3** and the 1-substituted 3-methylmercapto-4-methoxycarbonyl-5-aminopyrazoles **4**, respectively. All the compounds except **4** were screened for their pesticidal activities but only five of them were found to be active.

Organo-Schwefelverbindungen als potentielle Pestizide

Die Kondensation von 1-Nitro-2,2-dimethylmercapto-ethylen mit Aralkylaminen gab die 1-Nitro-2,2-diaralkylamino-ethylene **1**, während die Reaktion mit aromatischen Aminen unter ähnlichen Bedingungen die 1-Nitro-2-arylamino-2-methyl-mercapto-ethylene **2** ergab. Die Reaktion von 1-Cyan-2,2-dimethylmercapto-acrylsäuremethylester mit aromatischen Aminen und Hydrazin gab die 1-Cyan-2-arylamino-2-methylmercapto-acrylsäuremethylester **3** und die 1-substituierten 3-Methyl-mercapto-4-carbmethoxy-5-aminopyrazole **4**. Alle Verbindungen außer **4** wurden auf ihre pestizide Aktivität untersucht, aber nur fünf davon waren wirksam.

0365–6233/80/0505–0471 $ 02.50/0

Since long organo-sulphur compounds have been known as effective pesticides. The avid interest of studying organo-sulphur compounds as bio-active substances engendered a number of publications on dithiophosphates, dithioxanthates, dithiocarboxylates and their metal chelates[1] during recent years. Recent investigations in the field of pesticidal compounds have led to the development of highly active organo-sulfur compounds such as thioureas[2], dithiocarbamates[3] and their derivatives. As later substances are in general neither poisonous to higher plants nor to men or cattle, their applicability is not restricted to special objects. So it was thought worthwhile to study the pesticidal activities of compounds which possess the essential structural feature (RNCS) responsible for bio-responses.

The broad spectrum pesticidal properties of sulphur compounds led to the synthesis of various derivatives of 1-nitro-2,2-dimethyl-mercaptoethylene and methyl-1-cyano-2,2-dimethylmercaptoacrylate in order to find out the structural feature responsible for biological activities by varying the substituents without alteration of net structural frame. 1-Nitro-2,2-diaralkylaminoethylene was prepared by the condensation of 1-nitro-2,2-dimethylmercaptoethylene **(1)** with aralkyl amines in 1 : 2 ratio while aromatic amines under similar condition gave only 1-nitro-2-arylamino-2-methylmercaptoethylene **(2)**. Similar condensation products are also derived from the reaction of methyl-1-cyano-2,2-dimethylmercaptoacrylate with aromatic amines while with substituted hydrazine such as 4-hydrazino-5,6,7,8-tetrahydrobenzothieno[2,3-d]-pyrimidine,4-(3′-methylmercapto-4′-carbomethoxy-5′-amino-pyrazol-1′-yl)-5,6,7,8--tetrahydrobenzothieno[2,3-d]pyrimidine **4** was yielded. The structures of the compounds were proved by elemental analyses and spectroscopic studies. The NMR spectrum of 1-nitro-2-m-fluoro-anilino-2-methylmercaptoethylene showed three singlets at 2.48, 6.74 and 11.46 ppm due to CH_3, CH, and NH protons respectively. The CH proton resonated in very low field due to the presence of electron withdrawing group (NO_2) in its vicinity. The aromatic protons resonated as multiplet at 7.16–7.76 ppm.

Scheme of the reaction

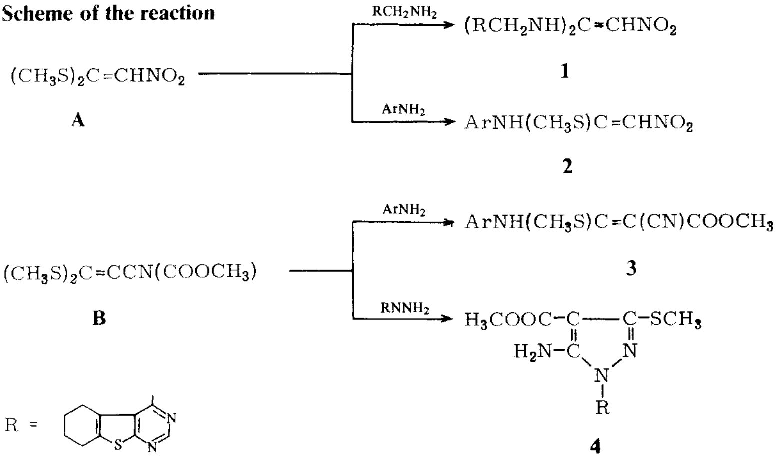
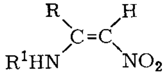


Table 1: *Compounds* **1** *and* **2**



$R(H)C{=}C$ with R^1HN and NO_2

S.No.$^+$	R	R^1	M.P. °C	Molecular formula	M^+
1a	$2\text{-Cl-}C_6H_4CH_2NH$	$2\text{-Cl-}C_6H_4CH_2NH$	178–182	$C_{16}H_{15}Cl_2N_3O_2$	352
b	$3\text{-Cl-}C_6H_4CH_2NH$	$3\text{-Cl-}C_6H_4CH_2NH$	185	$C_{16}H_{15}Cl_2N_3O_2$	352
c	$4\text{-Cl-}C_6H_4CH_2NH$	$4\text{-Cl-}C_6H_4CH_2NH$	245	$C_{16}H_{15}Cl_2N_3O_2$	352
d	$2,4\text{-}Cl_2C_6H_3CH_2NH$	$2,4\text{-}Cl_2C_6H_3CH_2NH$	193–195	$C_{16}H_{13}Cl_4N_3O_2$	421
e	β-N-Pyrrolidino-ethylamino	β-N-Pyrrolidino-ethylamino	122	$C_{14}H_{27}N_5O_2$	297
2a	SCH_3	$2\text{-F-}C_6H_4$	105	$C_9H_9F\,N_2O_2S$	228
b	SCH_3	$4\text{-}C_6H_5N{=}NC_6H_4$	118	$C_{15}H_{14}N_4O_2S$	314
c	SCH_3	$4\text{-Cl-}C_6H_4$	130–135	$C_9H_9ClN_2O_2S$	244.5
d	SCH_3	$4\text{-I-}C_6H_4$	115	$C_9H_9IN_2O_2S$	336
e	SCH_3	$3\text{-I-}C_6H_4$	106	$C_9H_9IN_2O_2S$	336
f	SCH_3	$4\text{-}C_2H_5O\text{-}C_6H_4$	160	$C_{11}H_{14}N_2O_3S$	254

$^+$ All the compounds were analysed for C, H and N satisfactorily.

Pesticidal activity

All the compounds reported here were screened for their insecticidal fungicidal, bactricidal and herbicidal activities by standard procedure reported earlier$^{4)}$ but only five compounds were found to be active and their pesticidal activities are presented in the table 2.

It has been assumed that toxic action of these derivatives might be due to its enzymatic decomposition to methylmercaptan or amine. The decomposition of parent molecule to methylmercaptan seems to be unlikely because only the methyl 1-cyano-2-(p-)fluoroanilino-2-methylmercapto analogue exhibited 100 % bactericidal at 64 ppm concentration and is completely inactive at lower concentrations while 98 % fungicidal activity was noted against *Botrytis cinerea* at 600 and 300 ppm concentrations.

In contrast to above compound only 1-nitro-2(o-)fluoro-anilino-2-methylmercapto-ethylene demonstrated 90 % activity against *Botrytis cinerea* and phytotoxicity of 11 against *Pythium* and *Rhizoctonia solani* while its meta and para fluoro analogues were completely inactive. The significant fungicidal activity of o-fluoro analogue might be due to the ortho effect.

It is evident from the table 2 that only the compounds **2b–2d** exhibited marginal herbicidal activity in post-emergence tests. The toxic action may be due to the molecule as whole by deactivating metal enzymes or precipitating the metal ions in the cell or deactivating the SH group of enzyme by the formation of disulphide linkages.

Table 2: *Pesticidal Activity*

Species$^+$	Compounds X	 2a	 **2b**	 2c	 **2d**
Fungicidal screening					
Pythium (64 kg/acre)	0	PH 11	0	0	0
Rhizoctonia solani (64 kg/acre)	0	PH 11	0	0	0
Botrytis cinerea (1200, 600, 300 ppm)	0,98,98	90	33	0	0
Bactericidal screening (64 ppm conc.)					
Escherichia coli	100	–	–	–	–
Streptococcus faecalis	100	–	–	–	–
Salmonella cholerasuis	100	–	–	–	–
Salmonella gallinarum	100	–	–	–	–
Herbicidal screening					
Post-emergence test at 8lb/acre					
Pig weed	0	0	0	0	0
Wild mustard	0	0	0	0	0
Velvet leaf	0	0	10	0	0
Red millet	0	0	10	0	0
Green foxtail	0	0	20	10	10

X = Methyl-1-cyano-2-(p-)fluoroanilino-2-methylmercaptoacrylate. PH = Phytotoxicity

$^+$ Activity is expressed in % control.

Non of the mechanism may be generalised for the compounds of the type **X, 2a** and **2b** but tentatively it can be concluded that it is the fluoro substituent which is responsible for higher bioresponses.

Experimental

All the m. ps. are uncorrected.

1-Nitro-2,2-dimethylmercaptoethylene **(A)**

It was prepared from nitromethane and CS_2 by the procedure reported by *Gompper* and *Schaefer*[5] in 70 % yield, m. p. 125°C.

Methyl-1-cyano-2,2-dimethylmercaptoacrylate **(B)**

It was synthesised from CS_2 and methylcyanoacetate in alkaline medium in 84 % yield, m. p. 84°C (Rep.[6] 87°C).

1-Nitro-2-(p-)fluoroanilino-2-methylmercaptoethylene

A mixture of 2.2 g p-fluoroaniline and 1.65 g 1-nitro-2,2-dimethylmercaptoethylene in 10 ml ethanol was refluxed for 10 h and cooled. The crystalline solid which separated was washed with little ethanol and finally crystallised from ethanol, yield 84 % (1.92 g), m. p. 154°C, M^+ 228; 181 ($-SCH_3$), 135 ($-NO_2$). NMR (DMSO d^6) δ (ppm) = 2.46 (CH_3, s); 6.76 (CH, s); 7.18–7.5 (C_6H_4, m); 11.34 (NH, s). $C_9H_9FN_2O_2S$ (228) Calcd.: C 47.4 H 3.9 N 12.3 Found: C 47.6 H 4.1 N 12.1.

1-Nitro-2-(m-)fluoroanilino-2-methylmercaptoethylene

It was synthesised by the reaction of 1.65 g m-fluoroaniline and 1.1 g **A** as described in the preceding experiment in 70 % yield, m. p. 114°C, M^+ 228; 181 ($-SCH_3$); 135 ($-NO_2$); 95 ($-CH_2CN$). $C_9H_9F N_2O_2S$ (228) Calcd.: C 47.4 H 3.9 N 12.3 Found: C 47.8 H 3.6 N 12.1.
Other compounds in this series are prepared similarly and are presented along with their relevant data in table 1.

1-Nitro-2,2-bis(β-N-morpholinoethylamino)ethylene

A solution of 1.65 g **A** in ethanol was refluxed with 3.0 g β-N-morpholino-ethylamine overnight. At the end, excess of solvent was removed under reduced pressure and the oil on scratching gave a crystalline solid which was finally crystallised from methanol (2.75 g), m. p. 103–105°C, M^+ 329; 282 ($-NO_2$). $C_{14}H_{27}N_5O_4$ (329) Calcd.: C 51.1 H 8.2 N 21.3 Found: C 51.5 H 8.5 N 21.1.
Other similar compounds reported in table 1 are prepared similarly.

Methyl-1-cyano-2-(p-)fluoroanilino-2-methylmercaptoacrylate

A mixture of 1.0 g methyl-1-cyano-2,2-dimethylmercaptoacrylate and 1.1 g p-fluoroaniline was refluxed for 3 h and cooled overnight in refrigerator. The light yellow precipitate thus separated was washed with water and crystallised from water-ethanol mixture, yield 1.26 g, m. p. 125°C, M^+ 266. $C_{12}H_{11}FN_2O_2S$ (266) Calcd.: C 54.1 H 4.1 N 10.5 Found: C 54.2 H 4.3 N 10.3.

Methyl-1-cyano-2-(p-)chloroanilino-2-methylmercaptoacrylate

A solution of 1.0 g **B** and 0.65 g p-chloroaniline in ethanol was refluxed for 4 h and cooled. The resulting precipitate was crystallised from ethanol, yield 80 %, m. p. 130°C, M^+ 282.5. $C_{12}H_{11}ClN_2O_2S$ (282.5) Calcd.: C 51.0 H 3.9 N 9.9 Found: C 51.3 H 3.6 N 10.3.

Methyl-1-cyano-2-(p-)bromoanilino-2-methylmercaptoacrylate

It was prepared from 1.0 g **B** and 0.9 g p-bromoaniline as described in the preceding experiment in 85 % yield, m. p. 132°C, M^+ 327. $C_{12}H_{11}BrN_2O_2S$ (327) Calcd.: C 44.0 H 3.4 N 8.6 Found: C 44.2 H 3.1 N 8.3.

Methyl-1-cyano-2-(p-)iodoanilino-2-methylmercaptoacrylate

An ethanolic solution of 1.0 g **B** was refluxed with 1.09 g p-iodoaniline for 3 h and the product isolated in 80 % yield, m. p. 125°C, M^+ 374. $C_{12}H_{11}IN_2O_2S$ (374) Calcd.: C 38.5 H 2.9 N 7.5 Found: C 38.3 H 3.1 N 7.3.

4-(3'-Methylmercapto-4'-carbmethoxy-5'-aminopyrazol-1'-yl)-5,6,7,8-tetrahydrobenzothieno-(2,3-d)pyrimidine **(4)**

A mixture of 0.22 g 4-hydrazino-5,6,7,8-tetrahydrobenzothieno(2,3-d)pyrimidine and 0.2 g **B** in ethanol was refluxed for 3 h and cooled. The precipitate thus obtained was washed with little ethanol and finally crystallised from ethanol, m. p. 163°C, M^+ 375. $C_{16}H_{17}N_5O_2S_2$ (375) Calcd.: C 51.2 H 4.5 N 18.7 Found: C 51.5 H 4.2 N 18.6.

References

1 K. Nag and S. Joardar, Inorg. Chim. Acta *14,* 133 (1975).
2 D. J. Beaver, D. P. Roman and P. J. Stoffel, J. Am. Chem. Soc. *79,* 1236 (1957).
3 A. Goth and F. J. Robinson, J. Pharmacol. Exp. Ther. *93,* 430 (1948).
4 V. J. Ram, H. N. Pandey and L. Mishra, Arch. Pharm. (Weinheim) *312,* 586 (1979).
5 R. Gompper and H. Schaefer, Chem. Ber. *100,* 591 (1967).
6 R. Gompper and W. Töpel, Chem. Ber. *95,* 2861 (1962).

[Ph 160]

Kurzmitteilung

Neue Benzodioxinderivate****)

Piroska Kertész*)**) und Johannes Reisch***)

Institut für Pharmazeutische Chemie**) Semmelweis Medizinische Universität, H 1088 Budapest, Puskin u. 11–13, Ungarn und
Institut für Pharmazeutische Chemie***) Westfälische Wilhelms-Universität, Hittorfstr. 58–62, D 4400 Münster

Eingegangen am 15. Februar 1980

Eine Reihe biologisch wertvoller Naturstoffe wie bestimmte Cumarine, Neolignane und Flavanolignane enthalten als Partialstruktur ein 2,3-Dihydro-benzo[1,4]dioxin. Die vorliegende Mitt. befaßt sich mit der Frage, ob derartige Naturstoffe mit Hilfe der *Schönberg*-Reaktion[1] zugänglich sind. Dies wäre ein weiterer Ansatzpunkt zur Klärung der Frage, ob sekundäre Pflanzeninhaltsstoffe bzw. deren Synthesezwischenprodukte in

---

****) 40. Mitt.: Photo- und Strahlenchemische Studien, zugl. 77. Mitt.: Studien auf dem Gebiet der Naturstoffchemie. 39. bzw. 76. Mitt.: G. Reisch und J. Reisch, Pharmazie, im Druck bzw. J. Reisch, I. Mester und E. A. Sofowora, Planta Med., im Druck.

0365–6233/80/0505–0476 $ 02.50/0