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Dimethylvinylethoxysilane and Methylvinyldiethoxysilane

BY M. COHEN AND J. R. LADD

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A mixture of magnesium (2.63 moles) and absolute ether (800 ml.) was placed in a two-liter, three-necked, round-bottom flask equipped with a mercury-sealed stirrer, Dry Ice condenser and a gas inlet tube. A stopcock had been previously sealed to the bottom of the reaction flask. Methyl bromide was bubbled into the stirred mixture until all the magnesium had dissolved.

After excess methyl bromide had been allowed to evaporate from the solution, the methylmagnesium bromide solution was added to a stirred solution of 500 g. (2.63 moles) of vinyltriethoxysilane[1] and 960 ml. of ether in a three-liter, three-necked, round-bottom flask equipped with a mercury-sealed stirrer and a water condenser. All outlets were protected with calcium chloride tubes. The rate of addition was such that the ether refluxed gently.

The mixture was stirred under reflux one hour, and the ether distilled off. The distillation was continued at atmospheric pressure until the temperature of the distillate reached 100°. The remainder of the silanes was separated from the residue of magnesium salts at reduced pressure (40 mm.). On fractionation of the combined silanes there was obtained 19 g. (5.6% yield) of vinyldimethylethoxysilane, b.p. 99°, $n^{20}D$ 1.3983, d^{20}_4 0.790; *MR* calcd.[2] 39.8, obsd. 39.8; and 241 g. (57.4% yield) of vinylmethyldiethoxysilane, b.p. 133 to 134°, $n^{20}D$ 1.4000, d^{20}_4 0.858; *MR* calcd.[2] 45.2, obsd. 45.3.

Anal. Calcd. for $C_6H_{14}OSi$: C, 55.3; H, 10.8; Si, 21.5. Found: C, 55.4; H, 11.1; Si, 21.0. Calcd. for $C_7H_{16}O_2Si$: C, 52.5; H, 10.1; Si, 17.5. Found: C, 52.5; H, 10.2; Si, 17.2.

(1) Linde Air Products, New York, N. Y.

(2) E. L. Warrick, THIS JOURNAL, **68**, 2455 (1946).

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Thiosemicarbazones of Thiophene Derivatives[1]

BY E. CAMPAIGNE, P. A. MONROE, B. ARNWINE AND W. L. ARCHER

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Due to the effectiveness of *p*-acetaminobenzaldehyde thiosemicarbazone (Tibione)[2] as an antituberculous agent, a number of thiosemicarbazones have been prepared for biological testing. Among these have been a number of heterocyclic derivatives, including several of the thiophene series. 2-Thenaldehyde thiosemicarbazone has been reported to have a relatively high order of activity against the tubercle bacillus *in vitro*.[3,4] In addition, Anderson, *et al.*,[4] reported *in vitro* tests on the thiosemicarbazones of 2-acetothienone, 2-propiothienone, 2-butyrothienone and 2,5-dimethyl-3-acetothienone. Of these, 2-propiothienone thiosemicarbazone afforded the best protection. A later report[5] indicated that 2-thenaldehyde thiosemicarbazone gave weak protection to mice infected with tuberculosis.

In recent papers[6,7] Hamre, *et al.*, reported that *p*-aminobenzaldehyde thiosemicarbazone caused a significant delay in death of chick embryos and mice infected with vaccinia virus. This observation was confirmed by Thompson, Price and Minton[8] who reported that benzaldehyde thiosemicarbazone prevents multiplication of vaccinia virus in check embryonic tissue, but that substitution in the *p*-position of the benzene nucleus reduced virostatic activity.

In pursuing a program of virus chemotherapy, we have synthesized a number of heterocyclic thiosemicarbazones, and report here a group of thiophene derivatives. All of the carbonyl compounds used in preparing the thiosemicarbazones have been reported previously, either from these laboratories, or from other sources. The compounds prepared, their melting points and analyses are presented in the table. The biological testing data have been reported elsewhere by Dr. R. L. Thompson.[9]

TABLE I

THIOSEMICARBAZONES OF THIOPHENE DERIVATIVES

Cmpd. No.		M.p., °C.[a]	Formula	Nitrogen, % Calcd.	Found
	3-Thenaldehydes				
1	Unsubstituted	151–152	$C_6H_7N_3S_2$	22.78	22.70
2	2-Chloro-	196–198 dec.	$C_6H_6N_3S_2Cl$	19.15	19.06
3	2-Bromo-	192–194 dec.	$C_6H_6N_3S_2Br$	15.91	15.64
4	2,5-Dichloro-	232–233 dec.	$C_6H_5N_3S_2Cl_2$	...[b]	...[b]
	2-Thenaldehydes				
5	5-Chloro-	164–165	$C_6H_6N_3S_2Cl$[c]	19.15	19.27
6	5-Bromo-	182–184	$C_6H_6N_3S_2Br$	15.91	15.97
7	5-Nitro-	252–255 dec.	$C_6H_6N_4O_2S_2$	24.36	24.05[d]
8	5-Acetamido-	231–233	$C_8H_{10}N_4OS_2$	23.15	23.05[d]
9	5-Methyl-	160–161	$C_7H_9N_3S_2$	21.08	21.02[d]
10	3-Methyl-	185–187	$C_7H_9N_3S_2$	21.08	21.40[d]
11	5-*t*-Butyl-	182–183	$C_{10}H_{15}N_3S_2$	17.42	17.40
	2-Acetothienones				
12	Unsubstituted[e]	147–148	$C_7H_9N_3S_2$	21.08	21.12[d]
13	5-Bromo-	200–201	$C_7H_8N_3S_2Br$	15.11	14.99[d]
14	5-Methyl-	161–163	$C_8H_{11}N_3S_2$	19.73	19.72[d]
15	4-Nitro-5-methyl-	232–235 dec.	$C_8H_{10}N_4O_2S_2$	21.72	21.48[d]

[a] All melting points uncorrected. [b] Calcd.: S, 25.2; Cl, 28.0. Found: S, 25.2; Cl, 27.9. [c] Calcd.: S, 29.16. Found: 29.06. [d] Analyses by H. L. Clark, Urbana, Ill. [e] Previously reported by F. E. Anderson, C. J. Duca and J. V. Scudi, THIS JOURNAL, **73**, 4967 (1951), m.p. 148–149° uncor.

(1) Contribution No. 571 from the Chemistry Laboratory of Indiana University. This work was supported by a contract between the Office of Naval Research, Department of the Navy, and Indiana University.

(2) R. Behnisch, F. Mietzsch and H. Schmidt, *Am. Rev. Tuberc.*, **61**, 1 (1950).

(3) R. Donovick, F. Pansy, G. Stryker and J. Bernstein, *J. Bact.*, **59**, 667 (1950).

(4) F. E. Anderson, C. J. Duca and J. V. Scudi, THIS JOURNAL, **73**, 4967 (1951).

(5) C. J. Duca, M. V. Rothlauf and J. V. Scudi, *Antibiotics and Chemo.*, **2**, 16 (1952).

(6) D. Hamre, J. Bernstein and R. Donovick, *Proc. Soc. Exp. Biol. Med.*, **73**, 275 (1950).

(7) K. A. Brownlee and D. Hamre, *J. Bact.*, **61**, 127 (1951).

(8) R. L. Thompson, M. L. Price and S. A. Minton, Jr., *Proc. Soc. Exp. Biol. Med.*, **78**, 11 (1951).

(9) R. L. Thompson, S. A. Minton, Jr., and J. E. Officer, *J. Immunology*, in press.

The following points about the chemical work are worthy of comment. 1. The addition of a small amount of acetic acid facilitated the reaction of thiosemicarbazide with the carbonyl compounds; so that it was essentially complete in one-half to one hour. Anderson, *et al.*,[4] reported the reaction time to vary from 8 to 80 hours when no acetic acid was added. 2. The synthesis of 5-chloro-2-thenaldehyde in 50–55% yield by formylation of thiophene with N-methylformanilide was recently reported.[10] It was therefore interesting to carry out the synthesis of this compound by the Sommelet procedure, in order to compare the yields by the two methods. When 5-chloro-2-methylthiophene was converted to the thenyl bromide with N-bromosuccinimide, and thence to the aldehyde, a 33% yield was obtained. When 2-chlorothiophene was chloromethylated by the procedure of Cairns and McKusick[11] and the thenyl chloride converted to the aldehyde, a 25% yield was obtained. Thus neither process is as efficient as the formylation procedure.[10]

Experimental

Thiosemicarbazones.—The general procedure for the preparation of all the thiosemicarbazones was as follows: 0.1 mole of the carbonyl compound was dissolved in 100 ml. of 50% ethanol (95% ethanol was used for the less soluble compounds) and approximately 2 ml. of glacial acetic acid and 9.1 g. (0.10 mole) of thiosemicarbazide added. The solution was warmed with occasional swirling until the thiosemicarbazide dissolved and then refluxed for approximately one hour. After cooling, the crystalline thiosemicarbazone was collected and recrystallized from 50% ethanol or methanol. The crude yields ranged from 90–96%. The thiosemicarbazones are all yellow crystalline compounds, but occasionally on fresh crystallization, some of them appear almost white. After drying and exposure to air, however, they assume a yellow tinge.

Intermediate Carbonyl Compounds.—Although all of the thenaldehydes and acetothienones have been previously reported, some of them were prepared by methods not previously applied to these compounds and these are briefly described. 3-Thenaldehyde was prepared by the Sommelet procedure, as previously described,[12] as were 2-chloro-, 2-bromo-, and 2,5-dichloro-3-thenaldehyde.[13] In the latter case, 54 g. (59%) of crude 2,5-dichloro-3-thenaldehyde was obtained from 108 g. (0.65 mole) of 2,5-dichloro-3-methylthiophene and 0.6 mole of N-bromosuccinimide, which is a considerable improvement over the yield previously reported, although no changes were made in the procedure.

5-Nitro-2-thenaldehyde was prepared by the method of Patrick and Emerson.[14] The observation of Dullaghan, *et al.*,[15] that this compound could not be obtained by application of the Sommelet procedure to the product obtained on treatment of 5-nitro-2-methylthiophene with N-bromosuccinimide was confirmed.

5-Methyl-, 3-methyl-, 5-*t*-butyl- and 5-acetamido-2-thenaldehyde were obtained by the dimethylformamide formylation procedure described by Campaigne and Archer.[16] The various 2-acetothienones were samples previously prepared in this Laboratory.[17]

5-Chloro-2-thenaldehyde.—A mixture of 125 g. (0.94 mole) of 5-chloro-2-methylthiophene[18] and 1 g. of benzoyl peroxide was refluxed in 250 ml. of dry benzene, and 160 g. (0.9 mole) of N-bromosuccinimide mixed with 1 g. of benzoyl peroxide was added portionwise at such a rate as to maintain vigorous refluxing of the benzene. When addition was complete, the mixture was refluxed vigorously for about 5 minutes, then cooled and filtered with suction. Most of the benzene was removed by distillation at water-pump vacuum, and the crude 5-chloro-2-thenyl bromide was added dropwise to a refluxing stirred solution of 132 g. (0.94 mole) of hexamethylenetetramine in 200 ml. of chloroform. The heavy crystalline precipitate was collected, washed repeatedly with chloroform and dried *in vacuo*, yielding 220 g. (0.62 mole) of hexamine salt of 5-chloro-2-thenyl bromide. Without further purification, this salt was dissolved in 1 l. of 50% acetic acid and the solution rapidly steam distilled. Extraction of the distillate with ether yielded 43.9 g. (33.4% over-all yield) of 5-chloro-2-thenaldehyde, b.p. 85–88° (5–6 mm.). Oxidation of a small sample with silver oxide gave an acid melting at 147–148°.[19]

5-Bromo-2-thenaldehyde.—5-Bromo-2-thenyl chloride[20] was converted to the hexamine salt by refluxing with hexamine in chloroform and the crude salt steam-distilled in 1 l. of 50% acetic acid. After working up by the usual procedure, a 32% yield of 5-bromo-2-thenaldehyde, b.p. 81–84° (4 mm.), was obtained. Oxidation gave an acid which melted at 141–142°.[21] This process does not afford as good yields of this aldehyde as the phosphorus oxybromide formylation reported by King and Nord.[22]

(10) W. J. King and F. F. Nord, *J. Org. Chem.*, **13**, 635 (1948).
(11) T. L. Cairns and B. C. McKusick, *ibid.*, **15**, 790 (1950).
(12) E. Campaigne and W. M. LeSuer, THIS JOURNAL, **70**, 1555 (1948).
(13) E. Campaigne and W. M. LeSuer, *ibid.*, **71**, 333 (1949).
(14) T. M. Patrick and W. S. Emerson, *ibid.*, **74**, 1356 (1952).
(15) M. E. Dullaghan, L. J. Owen and F. F. Nord, *ibid.*, **74**, 2676 (1952).
(16) E. Campaigne and W. L. Archer, *ibid.*, **75**, 989 (1953).
(17) E. Campaigne and J. L. Diedrich, *ibid.*, **73**, 5240 (1951).
(18) E. Campaigne and W. M. LeSuer, *ibid.*, **70**, 415 (1948).
(19) J. F. Bunnett, D. M. Bachman, L. P. Snipper and J. H. Maloney, *ibid.*, **71**, 1493 (1949).
(20) R. C. Clapp, *et al.*, *ibid.*, **69**, 1549 (1947).
(21) H. D. Hartough and L. G. Conley, *ibid.*, **69**, 3096 (1947).
(22) W. J. King and F. F. Nord, *J. Org. Chem.*, **14**, 405 (1949).

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The Use of Dimethylformamide as a Formylation Reagent[1]

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The direct formylation of the thiophene nucleus by N-methylformanilide and phosphorus oxychloride has been recently reported.[3,4] Dimethylformamide has been reported in the patent literature as an effective substitute for N-methylformanilide in formylation of aromatic tertiary amines.[5] Tyson and Shaw[6] obtained a 72% yield of 3-indolecarboxaldehyde upon formylation of indole with dimethylformamide, and the application of this formylating agent to thiophenes has been patented.[7]

This formylation agent has two strong advantages despite the somewhat lower yields of aldehydes as compared to the N-methylformanilide procedure. Firstly, dimethylformamide is commercially an inexpensive reagent as compared to N-methylformanilide and therefore can be used in liberal excess as solvent, and secondly the weight of formyl group per mole of dimethylformamide is approximately twice the available formyl weight afforded by N-methylformanilide.

(1) Contribution No. 570 from the Chemistry Laboratory of Indiana University. This work was supported by a Contract between the Office of Naval Research, Department of the Navy, and Indiana University.
(2) Abstracted from the thesis of Wesley L. Archer, to be submitted to Indiana University in partial fulfillment for the Degree of Doctor of Philosophy.
(3) W. J. King and F. F. Nord, *J. Org. Chem.*, **13**, 635 (1948).
(4) A. W. Weston and R. J. Michaels, Jr., THIS JOURNAL, **72**, 1422 (1950).
(5) C. D. Wilson, U. S. Patents 2,437,370 (1948), 2,558,285 (1951).
(6) F. T. Tyson and J. T. Shaw, THIS JOURNAL, **74**, 2273 (1952).
(7) W. S. Emerson and T. M. Patrick, U. S. Patent 2,581,009 (1952).