rimido(4,5-*d*)pyrimidines, or a mixture of both, depending on the aldehyde substituent.

Experimental Section

The melting points were taken on a Thomas–Hoover melting point apparatus and are corrected. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. The nmr spectra were obtained with a Varian A-60 spectrometer. A Beckman IR-8 spectrophotometer was used to determine the ir spectra. Glass plates coated with silica gel G were used for tlc in ethanol–water.

General Procedure for the Reaction of 4-Amino-5-(aminomethyl)-2-methylpyrimidine (1)[7] and 4-Amino-5-(aminomethyl)-2-phenylpyrimidine (10) with Substituted Benzaldehydes.—To a solution of 0.075 mol of the benzaldehyde in 150 ml of benzene was added 0.075 mol of the pyrimidine with stirring. The mixture was heated under reflux for 8–12 hr in the presence of a Dean–Stark trap. The reaction mixture was filtered while hot to remove any unreacted pyrimidine. The product, the Schiff base or the tetrahydropyrimido(4,5-*d*)pyrimidine, was obtained in 70–90% yield by either cooling the filtrate or by evaporating it to dryness and triturating the residue with petroleum ether (bp 30–60°). The analytical samples were obtained by three or four recrystallizations from benzene or ethanol. The analyses as well as the nmr data are summarized in Table I.

Hydrolysis of 4-Amino-5-(*p*-chlorobenzylideneaminomethyl)-2-methylpyrimidine (6).—A solution of 2.06 g (0.008 mol) of **6** in 50 ml of 1 *N* hydrochloric acid was kept at room temperature for 15–20 min. Colorless crystals, mp 45–48°, of *p*-chlorobenzaldehyde were obtained by filtration of the reaction mixture. Extraction of the mother liquors with ether furnished an additional yield of *p*-chlorobenzaldehyde, mp 45–48°. The *p*-chlorobenzaldehyde thus obtained was dissolved in ether and treated with a solution of 2,4-dinitrophenylhydrazine in ether. Filtration afforded 2.3 g (93%) crystals of *p*-chlorobenzaldehyde-2,4-dinitrophenylhydrazone, mp 264–267° (lit.[8] mp 266°).

4-Amino-5-(*p*-chlorobenzylaminomethyl)-2-methylpyrimidine (13).—To a solution of 2.0 g (0.008 mol) of **2** in 40 ml of absolute MeOH at −5° was added slowly and with stirring 0.43 g (0.012 mol) of sodium borohydride. The reaction mixture was heated under reflux for 20 min and then made basic by the addition of 45 ml of 1.0 *N* sodium hydroxide with vigorous stirring. Extraction with six 25-ml portions of ether and evaporation of the ether extract to dryness afforded 1.7 g (84%) of crystals of **13**, mp 97–100°. Three recrystallizations from benzene furnished the analytical sample: mp 101.5–102.5°; nmr ($CHCl_3$-*d*) δ 1.50 (m, 1, **NH**), 2.43 (s, 3, CH_3), 3.64 (s, 2, 5 CH_2), 3.75 (m, 2, benzylic CH_2), 6.23 (s, 2, NH_2), 7.30 (m, 4, aromatics), and 7.92 (s, 1, 6 H); ir ν_{max}^{Nujol} 3400 and 3300 cm^{-1} (NH_2).

Anal. Calcd for $C_{13}H_{15}ClN_4$: C, 59.42; H, 5.75; N, 21.33. Found: C, 59.36; H, 5.82; N, 21.48.

3-(*p*-Chlorobenzyl)-2,7-dimethyl-1,2,3,4-tetrahydropyrimido(4,5-*d*)pyrimidine (14).—Two drops of concentrated HCl was added to a solution of 2.0 g (0.008 mol) of **13** and 2.5 g (0.06 mol) of acetaldehyde in 75 ml of benzene. The reaction mixture was heated under reflux for 6 hr. Evaporation to dryness afforded 1.6 g (73%) of crystals of **14**, mp 144–146°. Recrystallization from benzene gave the analytical sample: mp 146–147°; nmr ($CHCl_3$-*d*) δ 1.40 (d, 3, J = 7.0, 2 CH_3), 2.47 (s, 3, 7 CH_3), 3.57 (d, 2, J = 2.0, 3 CH_2), 3.73 (d, 2, J = 7.0, 4 CH_2), 5.71 (m, 1, 1 NH), 7.31 (m, 4, aromatics), and 7.85 (s, 1, 5 H); ir ν_{max}^{Nujol} 3230 cm^{-1} (NH).

Anal. Calcd for $C_{15}H_{17}ClN_4$: C, 62.92; H, 5.88; N, 19.40. Found: C, 63.25; H, 6.10; N, 19.23.

Registry No.—**2**, 20352-37-8; **3**, 20352-38-9; **4**, 20352-39-0; **5**, 20352-40-3; **6**, 20352-46-9; **7**, 20352-47-0; **8**, 20352-48-1; **9**, 20352-41-4; **11**, 20352-42-5; **12**, 20352-43-6; **13**, 20352-44-7; **14**, 20352-45-8.

Acknowledgment.—This work was supported by a grant from the Michigan Cancer Foundation.

---

[7] W. H. Huber, *J. Amer. Chem. Soc.*, **66**, 876 (1944).

[8] G. Harris, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1966, p 599.

Preparation of Substituted 5,6-Dihydro-1,4-dithiins

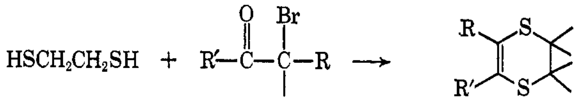
Harry Rubinstein and Michael Wuerthele

Department of Chemistry, Lowell Technological Institute, Lowell, Massachusetts 01854

Received January 29, 1969

There is a great deal of interest in the chemistry of 1,4-dithiins and 1,4 dithianes.[1] Unsubstituted dithiins and dithianes can be prepared by relatively straightforward procedures.[2,3] There are, however, few good methods for the preparation of simple alkyl or aryl dithianes or dithiins. Of the existing methods, the usual procedures give 2,5-disubstituted or 2,3,5,6-tetrasubstituted derivatives.[4-9] The reported methods for the preparation of monoalkyl and aryl substituted dithiins usually involve multistep syntheses and proceed with poor yields.[10,11] There are no reports in the literature of simple procedures for the preparation of 2,3-disubstituted dithianes or dithiins except for benz-1,4-dithianes.[12]

We report here a novel synthesis of 2- and 2,3-mono- and disubstituted 5,6-dihydro-1,4-dithiins (**1**). These compounds can readily be prepared by treating ethanedithiol with an α-bromo ketone.



1a, R = H; R′ = CH_3
b, R = R′ = C_6H_5

When α-bromoacetone is treated with ethanedithiol, the resulting 2-methyl-5,6-dihydro-1,4-dithiin (**1a**) is obtained in 60% yield. This compound has previously been reported in a multistep synthesis which resulted in 10% yields[10] of **1a**. As an example of the formation of 2,3-disubstituted dithiins, 2-bromo-2-phenylacetophenone gives the corresponding 2,3-diphenyl-5,6-dihydro-1,4-dithiin (**1b**) in 50% yield.

The dihydrodithiins resulting from these reactions may be reduced to the dithianes[12] or oxidized to the dithiins[13] by established procedures.

Experimental Section

Micro analyses were carried out by Werby Laboratories, Boston, Massachusetts. Melting points are corrected. Nuclear

---

[1] W. E. Parham in "The Chemistry of Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press Ltd., London, 1966, p 248.

[2] R. G. Gillis and A. B. Lacey in "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., John Wiley & Sons, New York, N. Y., 1963, p 396.

[3] W. Schroth and J. Peschel, *Z. Chem.*, **4** (7), 27 (1964).

[4] W. Draher, *Chem. Ber.*, **100** (5), 1559 (1967).

[5] Y. Hiroyoshi, *Chem. Pharm. Bull.* (Tokyo), **16** (3), 148 (1968); *Chem. Abstr.*, **69**, 20399 (1968).

[6] K. D. Gundermann and C. Burba, *Chem. Ber.*, **94**, 2157 (1961).

[7] B. Hirsch and H. Fink, *Angew. Chem.*, **74**, 28 (1962).

[8] R. H. Baker and C. Barkenbus, *J. Amer. Chem. Soc.*, **58**, 262 (1936).

[9] H. Szmant and L. M. Alfonso, *ibid.*, **79**, 205 (1957).

[10] A. Bottini and E. F. Böttner, *J. Org. Chem.*, **31**, 586 (1966).

[11] W. Schroth, B. Strekenbach, and B. Werner, *Z. Chem.*, **7** (4), 152 (1967).

[12] W. E. Parham, T. M. Roder, and W. R. Hasek, *J. Amer. Chem. Soc.*, **75**, 1647 (1953).

[13] S. Landa and A. Mrnkova, *Collection Czech. Chem. Commun.*, **31** (5), 2202 (1966); *Chem. Abstr.*, **65**, 545*h* (1966).

magnetic resonance spectra were determined on a Varian Model A-60 nmr spectrometer using tetramethylsilane as a standard.

Preparation of 5-Methyl-2,3-dihydro-1,4-dithiin (1a).—A 250-ml single neck flask fitted with a Dean–Stark trap and a magnetic stirrer was charged with 120 ml of benzene (sodium dried), 26.6 g (0.196 mol) of α-bromoacetone,[14] 18.3 g (0.195 mol) of 1,2-ethanedithiol and 0.044 g of purified *p*-toluenesulfonic acid. The resulting solution was stirred and refluxed for 3 hr, and 4.22 ml of water was collected in the trap. The reaction mixture was cooled and washed twice with 100 ml of 2 *N* sodium hydroxide and twice with 100 ml of water. The organic layer was concentrated and distilled, giving 13.7 g, bp 44–52° (0.5–0.7 mm), and 2.6 g, bp 70–94° (0.7–0.9 mm). The purity of these fractions was checked by glpc using a 6 ft Carbowax column; the first fraction was 98% **1a** and the second fraction 72% **1a**. A total yield of 60% **1a** was obtained in this reaction (by glpc assay); this product showed the correct microanalysis, nmr, and infrared spectra for **1a** as previously reported.[10]

Preparation of 4,5-Diphenyl-2,3-dihydro-1,4-dithiin (1b).—The above described apparatus was charged with 5.31 g (0.0194 mol) of 2-bromo-2-phenylacetophenone (Eastman), 2.48 g (0.0265 mol) of 1,2-ethanedithiol, 0.02 g of *p*-toluenesulfonic acid, and 120 ml of benzene (sodium dried). The resulting solution was refluxed for 54 hr, and 0.4 ml of water was collected. The reaction mixture was washed and concentrated as above, leaving a solid residue. This was recrystallized three times from methanol, giving a white solid: 2.66 g (50.6%), mp 101.9–102.2°. Examination of the nmr spectrum (CCl_4) showed a singlet at δ 7.05 (aromatic) and a singlet at δ 3.31 (aliphatic); the ratio of aliphatic to aromatic protons was 2:5.

Anal. Calcd for $C_{16}H_{14}S_2$: C, 71.1; H, 5.18; S, 23.7. Found: C, 71.30; H, 5.22; S, 23.73.

Registry No.—1a, 5769-49-3; 1b, 20273-71-6.

---

(14) P. A. Levene in "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., John Wiley & Sons, New York, N. Y., 1963, p 88.

Synthesis of 2,5-Dihydrothiophenonium 2,4,6-Trinitrobenzenesulfonates from Butadienes and Methanesulfenyl 2,4,6-Trinitrobenzenesulfonates[1]

George K. Helmkamp, Dennis C. Owsley,[2]
and Bruce R. Harris[3]

Department of Chemistry, University of California at Riverside, Riverside, California 92502

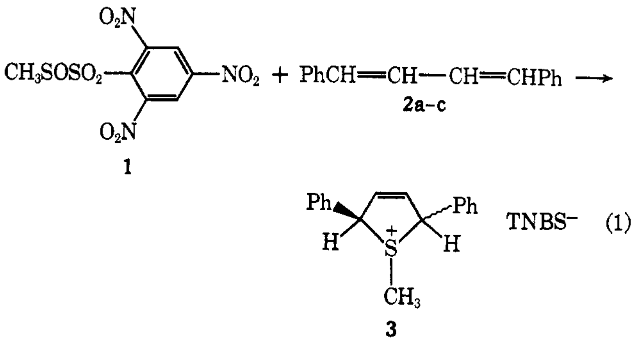
Received January 24, 1969

The reaction of a very limited variety of sulfenyl compounds with conjugated dienes has received recent attention, but the process has the potential of providing interesting results related to the problem of concerted cycloaddition. Mueller and Butler[4,5] studied the reaction of methanesulfenyl or benzenesulfenyl chloride with a number of conjugated dienes. Their findings showed that the additions occurred predominantly in a 1,2 manner. This was in contrast to the report of earlier workers[6] in which 1,4 addition was tentatively proposed to occur in the reaction of sulfenyl chlorides with cyclopentadiene or cyclooctatetraene.

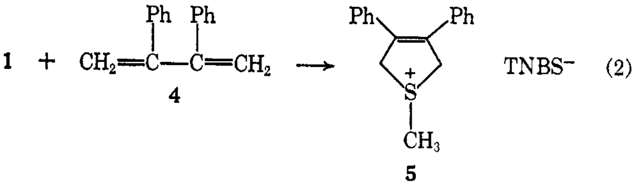
An alkanesulfenium ion (RS^+, or its alkanesulfenyl 2,4,6-trinitrobenzenesulfonate progenitor) can be compared to nitrenes and carbenes with regard to formation of three-membered rings from alkenes. With one exception, all of the reported examples of the reaction of conjugated dienes with carbenes[7] and nitrenes[8] proceed by formation of 1,2 adducts as primary reaction products. In that exceptional case[9] a concerted 1,4 cycloaddition of cyanonitrene to cyclooctatetraene was proposed on the basis of a time- and temperature-dependency study of the stability of the 1,2 adduct in the system.

As part of our continuing studies on the synthetic utility of methanesulfenyl 2,4,6-trinitrobenzenesulfonate[10,11] (**1**), some of the isomeric diphenylbutadienes have been used as substrates for this reagent. It was of interest to determine whether the products isolated from these reactions arose from a 1,4 cycloaddition in a concerted manner, a 1,2 addition, or a 1,2 addition followed by rearrangement to the 1,4 product.

The reaction of **1** with *trans,trans*- (**2a**), *cis,trans*- (**2b**), or *cis,cis*-1,4-diphenylbutadiene (**2c**) was found to yield the same product, namely 2,5-dihydro-2,5-diphenyl-S-methylthiophenonium 2,4,6-trinitrobenzenesulfonate (**3**) as shown in eq 1. The structure of **3** was assigned on the basis of its nmr spectrum and molecular weight (data are provided in the Experimental Section). The structural equivalence of **3** originating from the three different dienes was based on comparison of infrared and nmr spectra, on mixture melting points, and on constancy of these physical characteristics on repeated purification procedures.



(1)



(2)

$TNBS^-$ = 2,4,6-trinitrobenzenesulfonate anion

The reaction of the same reagent (**1**) with 2,3-diphenylbutadiene (**4**, eq 2) yielded 2,5-dihydro-3,4-diphenyl-S-methylthiophenonium 2,4,6-trinitrobenzenesulfonate (**5**).

The stereochemistry of **3** has not been established unequivocally, although nmr data suggest that the

---

[1] This investigation was supported by the National Science Foundation under Grant No. GP-8594.

[2] Environmental Sciences Trainee, United States Public Health Service, 1967–1969.

[3] NSF-URP Summer Fellow, 1968 (Grant No. GY-3041).

[4] W. H. Mueller and P. E. Butler, *Chem. Commun.*, 646 (1966).

[5] W. H. Mueller and P. E. Butler, *J. Org. Chem.*, **33**, 2642 (1968).

[6] H. Brintzinger and H. Eilwanger, *Chem. Ber.*, **87**, 300 (1954).

[7] See, for example, W. Kirmse, "Carbene Chemistry," Academic Press, New York, N. Y., 1964.

[8] For example of isolable, stable 1,2-adducts see: S. Masamune and N. T. Castellucci, *Angew. Chem.*, **76**, 569 (1964); K. Hafner, W. Kaiser, and R. Puttner, *Tetrahedron Lett.*, 3953 (1964).

[9] A. G. Anastassiou, *J. Amer. Chem. Soc.*, **90**, 1527 (1968).

[10] D. J. Pettitt and G. K. Helmkamp, *J. Org. Chem.*, **29**, 2702 (1964).

[11] G. K. Helmkamp, D. C. Owsley, W. M. Barnes, and H. N. Cassey, *J. Amer. Chem. Soc.*, **90**, 1635 (1968).