known of spontaneous dilactonization of keto diacids at room temperature.[16]

Experimental Section[17]

Ketalization of Keto Dinitrile II.—Keto dinitrile II (8.30 g, 40.7 mmoles) was dissolved in 125 ml of ethylene glycol and to this was added, over a 15-min period with stirring and cooling, 25.0 ml (28.1 g, 198 mmoles) of freshly distilled boron trifluoride etherate. After standing for 8 days at room temperature, the mixture was worked up by pouring into excess aqueous potassium hydroxide. Extraction with ether gave a solution which, when dried and concentrated, yielded 6.95 g (68%) of white nuggets, mp 67–69°. Recrystallization from methyl acetate–hexane narrowed the melting range to 68–69°; $\nu_{max}^{CCl_4}$ 2245 cm^{-1}; nmr 4 H singlet at τ 6.07, 16 H complex at 7.4–8.6.

Anal. Calcd for $C_{14}H_{20}N_2O_2$: C, 67.71; H, 8.12. Found: C, 67.78; H, 8.22.

Basic Hydrolysis of Ketal Dinitrile III.—A mixture of 3.00 g of ketal dinitrile III (12.1 mmoles), 10 ml of ethanol, 50 ml of water, and 7.50 g (114 mmoles) of potassium hydroxide was refluxed under nitrogen for 24 hr and worked up by addition of excess aqueous oxalic acid and extraction with ether. Concentration of the dried extracts yielded a white solid which was recrystallized from xylene to give 3.19 g (92%) of diacid IV, as a white powder: mp 156–158.5°; $\nu_{max}^{CHCl_3}$ 3510, 3400–2200, 1710 cm^{-1}.

Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.74. Found: C, 58.78; H, 7.74.

Reduction of IV with Lithium Aluminum Hydride.—A solution of 700 mg (2.45 mmoles) of ketal diacid IV in 14 ml of tetrahydrofuran was added under nitrogen over a 2-min period to a stirred suspension of 350 mg (9.25 mmoles) of lithium aluminum hydride in 10 ml of tetrahydrofuran. The mixture was refluxed under nitrogen for 6 hr and worked up by addition of saturated aqueous sodium sulfate, addition of ether, and decantation of the organic solution. Concentration of the dried extracts gave a colorless oil, distilled in a Hickman still at 170° (0.03 mm) to yield 570 mg (90%) of viscous liquid: $n^{25}D$ 1.5050; $\nu_{max}^{CHCl_3}$ 3630, 3430 cm^{-1}; nmr 4 H singlet at τ 6.13, 6 H double peak at 6.2–6.7, 16 H peak at 8.2–9.1 centered at 8.57.

Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.08; H, 10.14. Found: C, 64.58; H, 10.11.

Acid Hydrolysis of Ketal Diol VII.—The distilled ketal diol VII (249 mg, 0.97 mmole) as a solution in a mixture of 5 ml of tetrahydrofuran and 13 ml of water was treated with 1 ml of concentrated hydrochloric acid and stirred for 1 hr at room temperature. The mixture was neutralized by addition of aqueous sodium bicarbonate and then saturated with potassium chloride. Extraction with pentane and concentration of the extracts gave crystalline material which was sublimed at *ca.* 50° (1 mm) to give 179 mg (95%) of white solid, mp 51.5–52°. Some crystals, formed by evaporation of a solution, melted at 53–53.5°. The infrared spectrum of this material lacks absorption in the 3- or 6-μ regions attributable to hydroxyl or carbonyl; nmr 4 H complex at τ 5.8–6.7, 16 H peak at 8.0–8.9 centered at 8.45.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.43; H, 10.34.

Acid Hydrolysis of Ketal Diacid IV.—Ketal diacid IV (350 mg, 1.22 mmoles), dissolved in a mixture of 5 ml of tetrahydrofuran and 15 ml of water, was treated with 2 ml of concentrated hydrochloric acid and was allowed to stand for 2 hr. The mixture was worked up by neutralization of excess acidity, saturation with potassium chloride, and extraction with ether–methylene chloride. Concentration of the dried extracts gave a solid which, on recrystallization from toluene, yielded 270 mg (91%) of white platelets, mp 132–133° (lit.[11] mp 136°).

Preparation of Keto Diester Vb.—A solution of 500 mg (2.06 mmoles) of keto diacid Va in 15 ml of absolute ethanol containing 7 drops of concentrated sulfuric acid was refluxed under nitrogen for 1 hr and worked up by addition of excess solid sodium bicarbonate followed by water and extraction with ether–pentane. Concentration of the dried extracts gave a colorless oil distilled in a Hickman still at 145° (0.05 mm) to yield 593 mg (96%) of mobile liquid: $n^{25}D$ 1.4695; $\nu_{max}^{CCl_4}$ 1728, 1708 cm^{-1}; nmr 4 H quartet at τ 3.96 (J = 7 cps), 16 H complex at 7.5–8.4, 6 H triplet at 8.79 (J = 7 cps).

Anal. Calcd for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78. Found: C, 64.21; H, 8.61.

Dilactonization of Keto Diacid Va.—A mixture of 250 mg (1.03 mmoles) of keto diacid Va, 2 ml of acetyl chloride, and 5 ml of acetic anhydride was refluxed under nitrogen for 40 hr and worked up by removal of solvent under reduced pressure. Addition of ether to the residue produced 52 mg (22%) of crystals which were washed with ether and with aqueous sodium bicarbonate and sublimed at 130° (0.05 mm). Recrystallization from cyclohexane–ethyl acetate produced needles, mp 143.5–144.5°. The infrared spectrum of this material shows a single intense carbonyl band at 1750 cm^{-1} and absence of the usual carboxylic acid absorption in the 3–4-μ region; nmr 4 H triplet at τ 7.38 (J = 7.5 cps), 12 H complex at 7.8–8.7.

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.26; H, 6.97.

Registry No.—III, 7641-49-8; IV, 7641-50-1; Va, 7641-52-3; Vb, 7677-62-5; VII, 7641-51-2; IX, 7666-49-1.

(16) M. D. Soffer, R. A. Stewart, J. C. Cavagnol, H. E. Gellerson, and E. A. Bowler, *J. Am. Chem. Soc.*, **72**, 3704 (1950), and the references cited therein.

(17) Melting points were determined with a Mel-Temp apparatus and are uncorrected; infrared spectra were taken using a Beckman IR-10 spectrometer; nmr spectra were determined with a Varian A-60 spectrometer and utilizing an internal standard; microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill.

Synthesis of Arylidene-2-methyl-2H-tetrazol-5-ylhydrazones *via* 1,3-Bis(2-methyl-2H-tetrazol-5-yl)triazene

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In our recent investigation[2] of the methylation reactions of arylidenetetrazol-5-ylhydrazones in basic medium we have found that, while direct methylation affords a satisfactory route to a number of methylated derivatives, it is not effective for the 2-alkylated derivatives (**4**) which are formed in very low yields and not at all in some instances depending on the arylidene substituent X. Because of these complications we were unable to present conclusive evidence for our proposed structure of these materials at that time. We now report data which confirm these earlier structural proposals and open a new route to workable yields of these hydrazones (**4**).

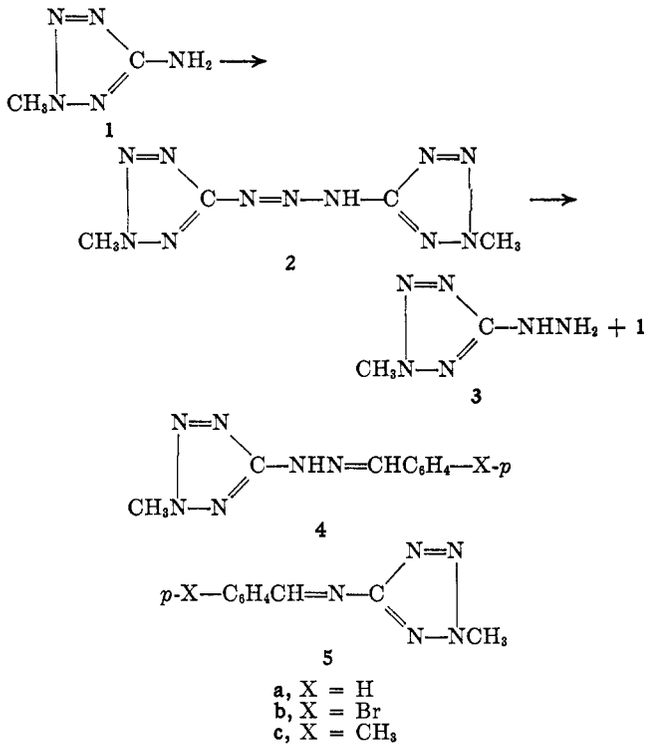
When 2-methyl-5-aminotetrazole (**1**) is treated with amyl nitrite in aqueous acetic acid solution at 0–5° the triazene (**2**)[3a] is formed along with some decomposition gums. This material, a stable, white, crystalline solid, does not show the deflagration and extreme hygroscopic properties of its unmethylated analog,[3b] which was formed by the reaction of aminoguanidine[4] with sodium nitrite in acetic acid. Mild reduction of

(1) This author acknowledges a State Maintenance Grant for Research.

(2) R. N. Butler and F. L. Scott, *J. Org. Chem.*, **31**, 3182 (1966).

(3) (a) See K. Hattori, E. Lieber, and J. P. Horwitz, *J. Am. Chem. Soc.*, **78**, 411 (1956). (b) K. A. Hofmann and H. Koch, *Ber.*, **43**, 1866 (1910); K. A. Hofmann, H. Koch, and R. Roth, *ibid.*, **43**, 1087 (1910).

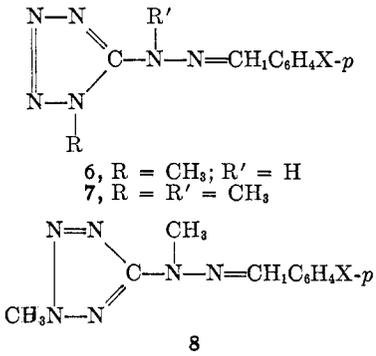
(4) J. Reilly, J. P. Teegan, and M. F. Carey, *Sci. Proc. Roy. Dublin Soc.*, **24**, 349 (1948); J. Reilly, J. P. Teegan, and M. F. Carey, *Nature*, **159**, 643, (1947). For a review of the synthesis of tetrazole derivatives from aminoguanidines, see F. Kurzer, *Angew. Chem. Intern. Ed. Engl.*, **2**, 468 (1963).



compound **2** with zinc[5] in aqueous acetic acid results in the degradation of the triazene (**2**) to the hydrazine (**3**) and the parent amine. These materials were isolated as their *p*-bromobenzaldehyde derivatives (**4b** and **5b**).

This degradation reaction is useful for the synthesis of the tetrazolylhydrazones (**4**) which are not accessible by ordinary routes.[6] The hydrazones are prepared most efficiently when the over-all reaction is carried out *in situ* without the isolation of the intermediates as described below for materials **4a**, **4b**, and **4c**.

A comparison of the nmr spectra[7] (Table I) of the hydrazones (**4**) with their 1-methylated isomers (**6**)[2] and the dimethylated hydrazones (**7**)[2] demonstrates that methyl groups at the 1- or 2-tetrazole positions[8] of tetrazolylhydrazones absorb at the same frequency while at the 6 position[9] the exocyclic methyl group absorbs at higher fields. Insertion of the exocyclic methyl group also results in an upfield shift in the frequency of the H_1 proton.[2] These data conclusively establish the structure (**8**) for the products obtained



from the methylation of the hydrazones (**4**) in our earlier studies[2] since the nmr spectra of these materials exhibit the definite characteristics of the exocyclic 6-N-methyl group (upfield shift of the N-methyl and H_1 frequencies). This confirms our former structural proposals for these materials.

Further studies on the reactions of the arylidene-2-methyl-2H-tetrazol-5-ylhydrazones (**4**) are currently in progress.

TABLE I

NMR DATA ON METHYLATED TETRAZOLYLHYDRAZONES

Compd	Chemical shift, τ			
	1-NCH_3	2-NCH_3	H_1	6-NCH_3
6a	5.75	...	1.86	...
6c[a]	5.70	...	1.92	...
7b[b]	5.74	...	2.38	6.28
7c[a,b]	5.80	...	2.33	6.37
4a[b]	...	5.70	1.97	...
4b	...	5.72	2.12	...
4c[c]	...	5.77	2.08	...
8b[b]	...	5.75	2.37	6.37
8c[a,b]	...	5.74	2.33	6.37

[a] The *p*-CH_3 protons appeared at τ 7.62. [b] The spectra of these materials were measured on a Varian A-60 instrument. [c] The *p*-CH_3 protons appeared at τ 7.68.

Experimental Section

Melting points are corrected and were measured on an Electrothermal apparatus. Microanalytical determinations were carried out by Mrs. K. Duggan of the Analytical Section of this Department and by Pascher Microanalytical Laboratories, Bonn, Germany. Nmr spectra were recorded on a Varian HA-100 spectrometer with tetramethylsilane as internal reference and deuteriochloroform as solvent except where otherwise stated.

2-Methyl-5-aminotetrazole was prepared by direct methylation of 5-aminotetrazole in the manner described by Henry and Finnegan.[10] The material had mp 103° and the yield was 21% (lit.[10] mp 104.5–105.5°; yield 24%).

1,3-Bis(2-methyl-2H-tetrazol-5-yl)triazene (2).—Amyl nitrite (2.6 ml) was added to a solution of 2-methyl-5-aminotetrazole (1 g) in 20 ml of glacial acetic acid and 10 ml of water at 0°. After the solution was stirred for 1 hr at 0–5°, its volume was brought to 200 ml by careful addition of water with stirring. Further cooling of the mixture in ice yielded white crystals of compound **2** (229 mg; mp 203–204° from 95% alcohol; filtrate A, lit.[3a] mp 208°).

Anal. Calcd for $C_4H_7N_{11}$: C, 22.96; H, 3.34; N, 73.68. Found: C, 23.30; H, 3.37; N, 73.49.

The filtrate (A) was thoroughly extracted with ether (five 150-ml portions). Evaporation of the ethereal solution to 10 ml under a current of warm air yielded a further crop (210 mg mp 203–204°) of compound **2**. The remaining ethereal acetic acid solution was evaporated. The residue which consisted of the triazene (**2**, 209 mg, mp 202°) mingled with a yellow gum, was swirled in ether (20 ml) to remove the gum. Total yield of compound **2** was 648 mg (51%).

Degradation of 1,3-Bis(2-methyl-2H-tetrazol-5-yl)triazene (2).—A suspension of the triazene (**2**, 630 mg) and zinc dust (2 g)

(5) (a) E. Nolting and F. Binder, *Ber.*, **20**, 3004, 3014 (1887); K. Clusius and H. R. Weisser, *Helv. Chim. Acta.*, **35**, 1548 (1952). (b) For recent reviews of the chemistry of triazenes, see P. A. Smith, "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. II, W. A. Benjamin Inc., New York, N. Y., 1966, p 333; C. Suling, Houben-Weyl-Muller, "Methoden Der Organischen Chemie," Band X/3, Georg Thieme, Verlag, Stuttgart, 1965, p 726.

(6) F. L. Scott, W. N. Morrish, and J. Reilly, *J. Org. Chem.*, **22**, 692 (1957).

(7) For sources of assignments in the nmr data, see J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall Inc., Englewood Cliffs, N. J., 1965; L. M. Jackson, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959.

(8) See J. H. Markgraf, W. T. Bachmann, and D. P. Hollis, *J. Org. Chem.*, **30**, 3472 (1965).

(9) For the numbering system which we have suggested for tetrazolylhydrazones, see ref 2.

(10) R. A. Henry and W. G. Finnegan, *J. Am. Chem. Soc.*, **76**, 923 (1954); for further alkylation studies on 5-aminotetrazoles, see K. R. Wilson, R. M. Herbst, and W. J. Haak, *J. Org. Chem.*, **24**, 1046 (1959); D. F. Percival and R. M. Herbst, *ibid.*, **22**, 925 (1957); R. A. Henry, W. G. Finnegan, and E. Lieber, *J. Am. Chem. Soc.*, **76**, 2894 (1954).

in 15 ml of acetic acid and 75 ml of water was stirred for 90 min at 0–5°, followed by 90 min at ambient temperatures. Undissolved zinc was removed and the solution was added slowly with stirring to a solution of *p*-bromobenzaldehyde (567 mg, 1.1 moles) in absolute alcohol (18 ml). White crystals separated immediately. The mixture after its being heated briefly at 60°, was stirred at ambient temperatures for 15 min and cooled in ice. White crystals of compound **4b** (filtrate A, 750 mg, 89%, mp 211° from 95% alcohol) which separated were washed with water. This material was identical (mixture melting point and infrared spectrum) with a sample obtained from the methylation reactions previously described.[2]

Anal. Calcd for $C_9H_9BrN_6$: C, 38.43; H, 3.20. Found: C, 38.15; H, 3.04.

The filtrate (A) was extracted with ether (four 100-ml portions). Evaporation of the ethereal solution under a current of warm air yielded a solid mingled with a brownish gum. This residue was stirred in ether (30 ml) and the ethereal solution, after its being filtered to remove some intractable material, yielded a white solid (210 mg, 87–95°) on evaporation of the ether. Recrystallization of this solid from benzene (5 ml) gave white crystals (140 mg) of 2-methyl-5-aminotetrazole (mixture melting point and infrared spectrum) of mp 102°. Addition of pentane (40–60°) to the benzene filtrate yielded a second crop (44 mg, mp 94–98°) of this material (188 mg, 63%). The yields are based on 100% yields of both degradation products.

When 1.5 g (2.5 moles) of *p*-bromobenzaldehyde was used in the above experiment, the ethereal extract on evaporation deposited white flakes (60 mg, mp 163–167°) mingled with a yellow oil. The oil was removed in cold ether (15 ml). Some of the white solid which dissolved was recovered by fractional evaporation of the ether. This material, compound **5b** (mp 166–167° from 95% alcohol), was also prepared as follows.

A solution of 2-methyl-5-aminotetrazole (105 mg) and *p*-bromobenzaldehyde (196 mg) in 95% alcohol (20 ml) was boiled for 10 min and allowed to stand at ambient temperatures for 36 hr with periodic stirring. On cooling the solution in ice white crystals (50 mg, mp 166–167°) of compound **5b** separated.

Anal. Calcd for $C_9H_8BrN_5$: C, 40.60; H, 3.01; Br, 30.07; N, 26.32. Found: C, 40.61; H, 3.40; Br, 30.10; N, 26.90.

Addition of water to the alcoholic filtrate resulted in the precipitation of a further crop (95 mg, mp 165–167°) of this material along with some unreacted aldehyde which was removed by stirring the precipitate in cold ether (10 ml). Yield of compound **5b** was 145 mg (50%).

Arylidene-2-methyl-2H-tetrazol-5-ylhydrazones (4).—Amyl nitrite (2.6 ml) was added to a solution of 2-methyl-5-aminotetrazole (1 g) in 20 ml of acetic acid and 10 ml of water at 0°, and the resulting mixture was stirred for 1 hr at 0–5°. Water (80 ml) was then added to the solution followed by zinc dust (2.65 g) and the mixture was stirred for 1 hr further at 0–5° and for 3 hr at ambient temperatures. Residual zinc was removed and the solution was added to benzaldehyde (1 ml) in 95% alcohol (20 ml), stirred for 45 min at ambient temperatures, and cooled in ice. The glistening, white crystals of compound **4a** (840 mg, 81%) were washed with water and had mp 136–137° (from aqueous alcohol).

Anal. Calcd for $C_9H_{10}N_6$: C, 53.46; H, 4.95; N, 41.58. Found: C, 53.72; H, 5.15; N, 41.84.

By a similar procedure using the appropriate aldehydes, compounds **4b** and **4c** (mp 164–166° from 95% alcohol. *Anal.* Calcd for $C_{10}H_{12}N_6$: C, 55.65; H, 5.35. Found: C, 55.74; H, 5.29) were obtained in 72.5 and 99% yields, respectively.

Efforts to prepare these hydrazones by the established procedure[6] of diazotization of the amine followed by reduction were unsuccessful. The attempted reduction of an acidic solution of the amine (1) and sodium nitrite with stannous chloride resulted in the evolution of a gas from the reaction mixture and the only materials encountered on work-up were decomposition gums.

Registry No.—2, 7593-32-0; **6c**, 4314-09-4; **7b**, 7593-34-2; **7c**, 7593-35-3; **4a**, 7593-36-4; **4b**, 7593-37-5; **4c**, 7593-38-6; **8b**, 7593-39-7; **8c**, 7593-40-0; 2-methyl-5-aminotetrazole, 6154-04-7; **5b**, 7593-42-2.

Acknowledgment.—We are deeply indebted to Dr. J. Feeney and Miss A. Heinrich, Varian Associates, Walton-on-Thames, for assistance with measuring and interpreting the nmr data.

The Use of 2,5-Dichlorothiophene in the Synthesis of 3,4-Disubstituted Thiophenes

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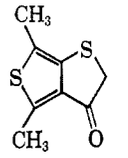
The facile electrophilic substitution of the 2 and 5 positions of the thiophene ring has rendered the direct synthesis of 3-substituted and 3,4-disubstituted thiophene derivatives somewhat difficult. The ready availability of 3-thenyl bromide[2] and 3-bromothiophene[3] has somewhat reduced this difficulty. However, ring closure from a 3-substituted thiophene with both the 2 and 4 positions unsubstituted, results in exclusive substitution in the 2 position.[4] Only when the 2 position is blocked may ring closure take place at the 4 position.[5]

The use of 2,5-dichlorothiophene to introduce useful substituents into the 3 position of the thiophene ring has been reported by several workers.[6] By virtue of the facile removal of the 2,5-chlorine atoms from certain substituted 2,5-dichlorothiophenes, the method becomes useful for the synthesis of 3,4-disubstituted thiophenes. In the present work, 2,5-dichlorothiophene is utilized as starting material in the synthesis of a number of cyclopenta[*c*]thiophene derivatives.

The literature records a small number of thiophenes possessing a five-membered ring fused across the 3,4 positions of the thiophene ring. The compounds I[5b] and II to V[7] have been reported. As far as we have been able to ascertain, neither the parent compound, cyclopenta[*c*]thiophene, nor any of its derivatives have been reported in the literature.



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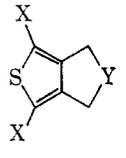

II, X = CO_2CH_3; Y = S
III, X = CO_2CH_3; Y = SO_2
IV, X = CO_2H; Y = S
V, X = H; Y = S

Treatment of 2,5-dichloro-3-thenyl chloride (VI) according to the method of Lawesson and Busch[8] afforded the malonic ester (VII) in 60% yield. Saponi-

(1) (a) National Science Foundation Undergraduate Research Participant 1965–1966; (b) National Science Foundation Undergraduate Research Participant 1966–1967.

(2) E. Campaigne and B. F. Tullar, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 921.

(3) S. Gronowitz and T. Raznikiewicz, *Org. Syn.*, **44**, 9 (1964).

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(6) (a) J. A. Blanchette and E. V. Brown, *J. Am. Chem. Soc.*, **73**, 2779 (1951); (b) S. Gronowitz, *Arkiv Kemi*, **8**, 441 (1955); (c) E. Profft and G. Solf, *J. Prakt. Chem.*, **24**, 38 (1964).

(7) H. Wynberg and D. J. Zwanenburg, *J. Org. Chem.*, **29**, 1919 (1964).

(8) S. O. Lawesson and T. Busch, *Acta. Chem. Scand.*, **13**, 1717 (1959).