5-Methyl-5H-indolo[2,3-f]piaselenole.—To a stirred solution of 0.21 g. of 2,3-diamino-9-methylcarbazole in 4 ml. of hot alcohol was added 0.12 g. of selenium dioxide. The mixture was refluxed for 5 minutes and allowed to cool. The red crystals were crystallized from xylene to give 0.25 g. (88%) of red needles, m.p. 243–244°. The compound dissolved in concentrated sulfuric acid with a dark yellow color which turned green on heating and dark violet on the addition of a little water.

Anal. Calcd. for $C_{13}H_9N_3Se$: N, 14.7. Found: N, 14.5.

3-Nitro-9-methylcarbazole.—Two and a half grams of nitric acid (d. 1.49) in 5 ml. of acetic acid was added dropwise to a stirred mixture of 6.1 g. of N-methylcarbazole[23] in 100 ml. of acetic acid at 0–10°. After standing one hour at 0–10° the reaction mixture was poured into excess water. Crystallization from aqueous methyl cellosolve and then alcohol gave 6.1 g. (80%) of long glossy yellow needles, m.p. 171–172°, lit. m.p. 170–172°.[24]

3-Amino-9-methylcarbazole.—This compound was prepared in a 70–80% yield by the procedure used for the 2-amino isomer. Crystallization from methanol or heptane gave colorless needles, m.p. 173–174°, lit. m.p. 171–173°.[24]

3-Acetylamino-9-methylcarbazole.—The amine in benzene solution was acetylated with acetic anhydride by standard procedure. Crystallization from aqueous methanol gave a 95% yield of colorless needles, m.p. 210°.

Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.63; H, 5.89; N, 11.8. Found: C, 75.52; H, 5.67; N, 11.8.

3-Trifluoroacetylamino-9-methylcarbazole.—The amine in benzene solution was acylated with trifluoroacetic anhydride by standard procedure. Crystallization from heptane gave a 92% yield of colorless needles, m.p. 184–185°.

Anal. Calcd. for $C_{15}H_{11}F_3N_2O$: N, 9.59. Found: N, 9.77.

3-Carbethoxyamino-9-methylcarbazole.—The amine in ice-cold pyridine solution was treated with ethyl chlorocarbonate by standard procedure. Crystallization from heptane gave an 86% yield of colorless needles, m.p. 110.0–110.5°.

(23) T. S. Stevens and S. H. Tucker, *J. Chem. Soc.*, **123**, 2140 (1923).

(24) D. H. Hey and R. D. Mulley, *ibid.*, 2276 (1952).

Anal. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.64; H, 5.97; N, 10.4. Found: C, 71.80; H, 6.06; N, 10.4.

3-Carbethoxyamino-4-nitro-9-methylcarbazole.—To a stirred solution of 1.88 g. of 3-carbethoxyamino-9-methylcarbazole in 10 ml. of acetic acid at room temperature was added 3.5 ml. of dilute nitric acid (d. 1.5 diluted, 1:10 with acetic acid). The mixture was allowed to stand an hour. The red crystalline precipitate was crystallized from heptane to give 1.25 g. (57%) of long orange needles, m.p. 184–185°.

Anal. Calcd. for $C_{16}H_{15}N_3O_4$: N, 13.4. Found: N, 13.1.

3-Amino-4-nitro-9-methylcarbazole.—A suspension of 1 g. of 3-carbethoxyamino-4-nitro-9-methylcarbazole in 12 ml. of methyl cellosolve and 9 ml. of 15% aqueous sodium hydroxide was refluxed for 1 hour. Excess water was added. The precipitate was crystallized from heptane to give 0.68 g. (88%) of red crystals, m.p. 145–146°.

Anal. Calcd. for $C_{13}H_{11}N_3O_2$: N, 17.4. Found: N, 17.1.

3,4-Diamino-9-methylcarbazole.—Reduction of 3-amino-4-nitro-9-methylcarbazole was achieved by the procedure used for the 2,3-isomer. Crystallization from heptane gave a 78% yield of colorless needles, m.p. 127–128°.

Anal. Calcd. for $C_{13}H_{13}N_3$: N, 19.9. Found: N, 19.9.

6-Methyl-6H-indolo[3,2-e]piaselenole.—A solution of 0.12 g. of selenium dioxide in 2 ml. of alcohol was added to a hot solution of 0.20 g. of 3,4-diamino-9-methylcarbazole in 5 ml. of alcohol. The solution was refluxed 0.5 hour and then allowed to cool. The yellow-brown crystals were crystallized from benzene–heptane to give 0.22 g. (81%) of yellow crystals, m.p. 180–181°.

Anal. Calcd. for $C_{13}H_9N_3Se$: N, 14.7. Found: N, 14.7.

5H-Indolo[2,3-f]piaselenole.—This compound was prepared from 2-nitro-3-aminocarbazole by the same methods used for the preparation of the other piaselenoles. As only a small amount of starting product was available, only a minute amount of alcohol-soluble red powdery piaselenole was obtained. This compound, m.p. 243–245°, gave a red-yellow color in concentrated sulfuric acid.

Anal. Calcd. for $C_{12}H_7N_3Se$: N, 15.4. Found: N, 14.6.

GAINESVILLE, FLA.

[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION, LABORATORY OF ADVANCED RESEARCH, REMINGTON RAND, INC.]

Synthesis of 4-Alkyl-v-triazoles from Acetylenic Compounds and Hydrogen Azide[1]

BY L. W. HARTZEL AND F. R. BENSON

RECEIVED AUGUST 28, 1953

Members of the hitherto undescribed class of 4-alkyl-v-triazoles have been synthesized by reaction of substituted acetylenes with hydrogen azide. Absorption spectra and molar refractions for some of these v-triazoles have been obtained.

The synthesis of v-triazoles which involves the combination of hydrogen azide with acetylenic compounds was originated by Dimroth and Fester.[2] These investigators prepared the parent compound by heating an alcoholic solution of hydrazoic acid with an acetone solution of acetylene at 100° for 70 hours. The same reaction has been used to obtain 4-carboxy-, 4-carboxy-5-phenyl-, and 4,5-dicarboxy-v-triazole[3] as well as 4-formyl-v-triazole[4a] and its acetal.[4b] These v-triazole syntheses are similar to those used for the preparation of tetrazoles by the reaction of nitriles with hydrazoic acid.[5] The present article describes the extension of this reaction to monoalkyl acetylenes.

It was found that these ethynyl compounds combine readily with hydrazoic acid in benzene solution by heating in closed vessels at temperatures ranging from 90 to 135° for 29 to 48 hours. In all cases, during the course of the reaction a white solid appeared at the top of the reaction vessels which was identified as ammonium azide. The formation of this material by the decomposition of hydrazoic acid has been described previously.[6] The physical properties, yields and chemical analyses of the 4-alkyl-v-triazoles thus formed are listed in Table I. The members of

(1) This work was performed under a subcontract from Arthur D. Little, Inc., by Remington Rand, Inc., in connection with an Army Ordnance Corps project. Publication of this article has been approved by the Public Information Division, National Military Establishment. Presented before the Division of Organic Chemistry, American Chemical Society, Chicago, September 8, 1953.

(2) O. Dimroth and G. Fester, *Ber.*, **43**, 2219 (1910).

(3) E. Oliveri-Mandala and A. Coppola, *Gazz. chim. ital.*, **40II**, 436 (1910).

(4) (a) R. Huttel, *Ber.*, **74B**, 1680 (1941); (b) J. C. Sheehan and C. A. Robinson, THIS JOURNAL, **71**, 1436 (1949).

(5) A. Hantzsch and A. Vagt, *Ann.*, **314**, 339 (1901); J. S. Mihina and R. M. Herbst, *J. Org. Chem.*, **15**, 1082 (1950).

(6) L. P. Audrieth, *Chem. Revs.*, **15**, 169 (1934).

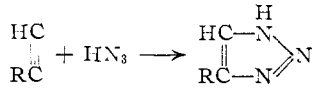
TABLE I

4-ALKYL-V-TRIAZOLES

R	B.p. °C.	Mm.	M.p., °C.	Yield, %	Reacn. temp., °C.	Reacn. time, hr.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
H[a]	203	752	23.5				$C_2H_3N_3$	34.78	34.6	4.38	4.28	60.84	60.4
CH_3	108–109	25	35–36	14	100	40	$C_3H_5N_3$	43.36	43.2	6.06	6.26	50.58	49.7
C_2H_5[b]	114	14		24	95–100	40	$C_4H_7N_3$	49.46	49.4	7.27	7.00	43.27	43.2
n-C_3H_7[c]	122–124	13		31	95–100	48	$C_5H_9N_3$	54.03	53.7	8.16	7.40	37.81	37.4
n-C_4H_9[d]	83–85	1		56	132–135	29	$C_6H_{11}N_3$	57.57	57.0	8.86	8.60	33.57	33.2
n-C_5H_{11}[e]	103–105	1		41	95–100	40	$C_7H_{13}N_3$	60.40	60.6	9.41	9.16	30.19	30.2
Iso-C_5H_{11}[f]	102–103	0.8		56	100–120	40	$C_7H_{13}N_3$	60.40	60.3	9.41	9.30	30.19	30.0
n-C_6H_{13}	120–122	2	27.0–27.2	63	95–100	40	$C_8H_{15}N_3$	62.71	62.9	9.89	9.81	27.42	27.6
n-C_7H_{15}[g]	126–128	1.5	10.7–11.1	66	120	40	$C_9H_{17}N_3$	64.63	64.4	10.25	10.7	25.12	24.7
n-C_8H_{17}	126–127	0.6	49.0	36	95–100	40	$C_{10}H_{19}N_3$	66.25	66.0	10.56	10.2	23.18	23.6
n-C_9H_{19}	139–140	0.8	47.0	72	120	40	$C_{11}H_{21}N_3$	67.64	67.8	10.84	10.7	21.51	21.8
n-$C_{10}H_{21}$	148–149	0.6	58.5–59.0	29	107–115	40	$C_{12}H_{23}N_3$	68.85	68.5	11.08	10.9	20.08	20.3

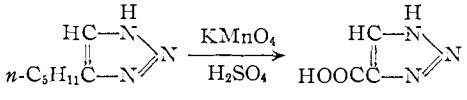
[a] $n^{23}D$ 1.4937, d^{23}_4 1.1925. [b] $n^{22}D$ 1.4826, d^{22}_4 1.0600. [c] $n^{22}D$ 1.4760, d^{22}_4 1.0270. [d] $n^{22}D$ 1.4805, d^{21}_{21} 1.0046. [e] $n^{23}D$ 1.4763. d^{23}_4 0.9784. [f] $n^{23}D$ 1.4735, d^{23}_4 0.9752. [g] $n^{29}D$ 1.4727. d^{29}_4 0.9532.

this series reported at this time include the n-alkyl derivatives from methyl through n-decyl as well as 4-isoamyl-v-triazole.



In addition 4-phenyl-v-triazole and v-triazole were synthesized in the course of this study to provide reference material for spectral studies. Preparation of 4-phenyl-v-triazole was effected by reaction of hydrogen azide with phenylacetylene; previously this compound has been obtained only by decarboxylation of 4-carboxy-5-phenyl-v-triazole.[3] Decarboxylation of 4-carboxy-v-triazole was used to obtain v-triazole.

To prove the identity of these compounds as 4-alkyl-v-triazoles the 4-n-amyl derivative was oxidized by means of potassium permanganate in acid solution to yield a compound identified as 4-carboxy-v-triazole.



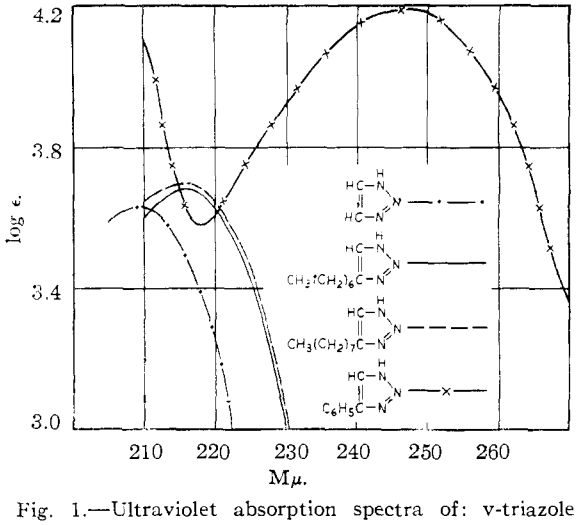


Fig. 1.—Ultraviolet absorption spectra of: v-triazole; 4-n-heptyl-v-triazole; 4-n-octyl-v-triazole; 4-phenyl-v-triazole (all in 95% ethanol).

Certain physico-chemical properties of the 4-alkyl-v-triazoles as well as those of v-triazole and 4-phenyl-v-triazole have been studied. From the refractive indices and densities of the liquid members of the series, molar refractions were calculated. Utilizing accepted data for the C–C and C–H bond refractions[7] the value for the refraction due to the v-triazole skeleton as shown, was calculated (Table II) to be 13.11 ± 0.16.

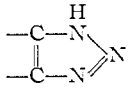


TABLE II

EXPERIMENTAL MOLAR REFRACTION OF 4-ALKYL-V-TRIAZOLES AND CALCULATED MOLAR REFRACTION OF THE V-TRIAZOLE SKELETON

Alkyl in 4-position	Exp. molar refraction	Bond refraction of substituents on carbon atoms of triazole ring	Calcd. molar refraction for v-triazole skeleton
C_2H_5	26.16	12.95	13.20
n-C_3H_7	30.52	17.60	12.92
n-C_4H_9	35.43	22.25	13.18
n-C_5H_{11}	40.15	26.90	13.25
n-C_7H_{15}	49.19	36.19	13.00

Ultraviolet spectra of v-triazole, 4-n-heptyl-, 4-n-octyl- and 4-phenyl-v-triazoles have been determined and are shown in Fig. 1. The spectrum of v-triazole shows a maximum at 210 mμ which compares favorably with the presence of a maximum in the spectrum of pyrrole at about 210 mμ[8] and an absence of a maximum in the spectrum of tetrazole[9] above 210 mμ. Substitution of an alkyl group in the 4-position results in a slight bathochromic shift to 215–216 mμ as would be expected.[10]

(7) A. I. Vogel, W. T. Cresswell, G. H. Jeffery and J. Leicester, *J. Chem. Soc.*, 514 (1952).

(8) "International Critical Tables," Vol. V, McGraw-Hill Book Co., Inc., New York, N. Y., p. 373.

(9) F. W. Schueler, S. C. Wang, R. M. Featherstone and E. G. Gross, *J. Pharm. Exp. Ther.*, **97**, 266 (1949); B. Elpern and F. C. Nachod, THIS JOURNAL, **72**, 3379 (1950).

(10) R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., p. 17.

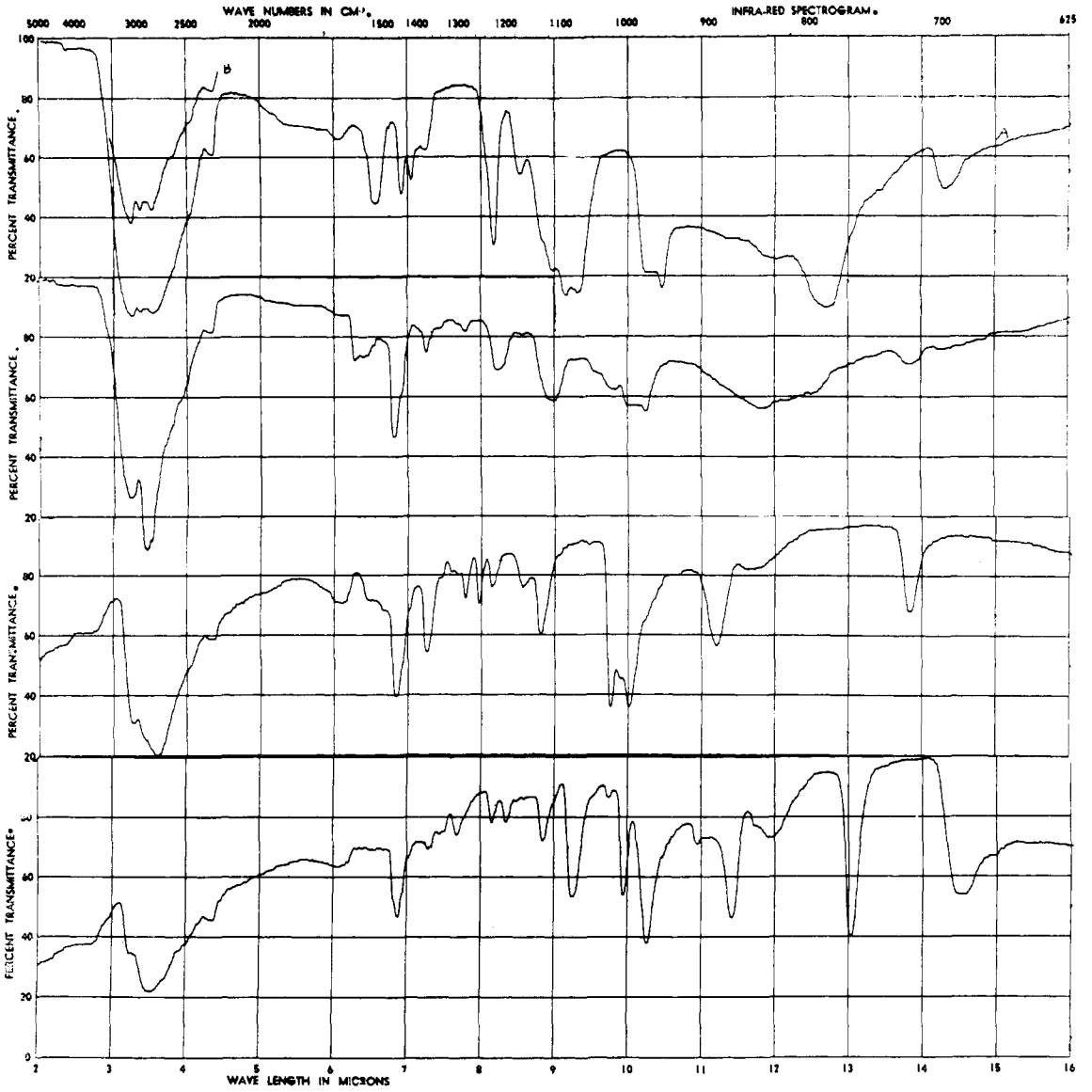


Fig. 2.—Infrared absorption spectra of (from top to bottom): v-triazole: 4-*n*-heptyl-v-triazole; 4-*n*-octyl-v-triazole; 4-phenyl-v-triazole.

It is of interest that both biphenyl[11] and 4-phenyl-v-triazole have a maximum at 245 mμ and a minimum in the range of 216–220 mμ, a similarity which emphasizes the aromatic character of the v-triazole grouping.

Some infrared spectra[12] of the v-triazoles have been determined and are found in Fig. 2. Examination of these data suggests that characteristic absorption bands of the v-triazole ring may lie between 8.8 and 9.2 μ and between 9.8 and 10.3 μ. It is of interest that the absorption bands for the tetrazole ring have been estimated to be 9.3 to 9.6 μ and 9.9 to 10.1 μ.[13]

Bacteriological tests of these compounds showed that growth of *Micrococcus Pyogenes Aureus*, *E. Coli*, *Klebsiella Pneumoniae* and *Serratia Marcescens* are slightly inhibited by 4-*n*-amyl-, *n*-hexyl-. *n*-heptyl-, *n*-octyl- and *n*-nonyl-v-triazole.

Anti-tumor and toxicity tests on this series were carried out at Sloan-Kettering Institute.[14] None of the compounds effected inhibition of the growth of Sarcoma 180 in mice. The maximum tolerated dose estimations showed the toxicity of the 4-alkyl derivatives to increase roughly with molecular weight to the 4-*n*-heptyl derivative which was the most toxic, then to decrease rapidly with increase in chain length.

Experimental

All melting points are corrected for stem exposure.

The acetylenes used as intermediates in this work were purchased from the Farchan Research Laboratories, Cleveland, Ohio.

v-Triazole was prepared by the method of Baltzer and v. Pechmann.[15]

(11) Reference 8, p. 375.

(12) Infrared spectra determinations were carried out by Samuel P. Sadtler and Sons, Philadelphia, Pa.

(13) E. Lieber, D. R. Levering and L. J. Patterson, *Anal. Chem.*, **23**, 1594 (1951).

(14) Anti-tumor and toxicity tests were conducted by courtesy of Dr. C. Chester Stock.

(15) O. Baltzer and H. v. Pechmann, *Ann.*, **262**, 320 (1891).

The following preparations are typical of the general procedure used to prepare the alkyl v-triazoles.

4-*n*-Propyl-v-triazole.—Four soda type bottles (capacity about 180 ml.) each containing 16 ml. (0.16 mole) of pentyne-1 and 50 ml. of benzene solution containing 18.5 g. of hydrazoic acid per 100 ml. (0.22 mole) were capped and heated at 95–100° for 48 hours. The bottles were cooled, opened, the contents filtered and the filter washed with benzene. The filtrate was evaporated to low volume on a steam-bath, then distilled under vacuum to yield 22.5 g. (31%) of crude 4-*n*-propyl-v-triazole, boiling at 120–130° (14 mm.). The crude triazole was purified by extracting with two 5-ml. portions of water followed by drying the non-aqueous phase over magnesium sulfate and finally redistillation under vacuum, boiling point 122–124° (13 mm.).

4-*n*-Butyl-v-triazole.—Two tubes each containing 10 g. of hexyne-1 (0.12 mole) and 50 ml. of benzene containing 14.7 g. of hydrazoic acid per 100 ml. (0.16 mole) were sealed and heated at 132–135° for 29 hours. The tubes were cooled, opened, the contents filtered, and the filter washed with benzene. The filtrate was evaporated to low volume on a steam-bath and distilled under vacuum to yield 17 g. of crude 4-*n*-butyl-v-triazole (56%) boiling at 83–85° at 1 mm. The crude material was purified by redistillation, boiling at 96–97° (12 mm.). On cooling to −40° the substance formed a glass, but did not crystallize.

The neutralization equivalent was determined according to the procedure of Fritz and Lisicki[16] which involves titration with sodium methylate in benzene–methanol using thymol blue as an indicator. The triazole was dissolved in pyridine. Neutralization equivalent: calcd. 125.2, found 127.

In the preparation of 4-*n*-butyl-v-triazole, as well as in all other reactions in which hydrazoic acid was heated at temperatures above 90° for prolonged periods, a small amount of white crystals formed at the top of the sealed tubes during the course of the reaction. The tubes were held in an upright position during heating; the crystals appeared to have sublimed from the reaction mixture, the level of which was about 25 cm. below the top of the tube. Crystals were isolated from one experiment and were found to be soluble in water and insoluble in ethyl acetate. The crystals melted at 150–155° with sublimation. With sodium hydroxide solution, ammonia was liberated. Addition of silver nitrate to a solution of the crystals produced a white precipitate, insoluble in dilute nitric acid. These properties indicated the material to be ammonium azide.

4-*n*-Decyl-v-triazole.—Four tubes each charged with 20 g. (0.12 mole) of dodecyne-1 and 50 ml. of benzene containing 14 g. of hydrazoic acid per 100 ml. were sealed and heated at 107–115° for 40 hours. The tubes were cooled and opened; the contents were filtered and the filter washed with ethanol. The filtrate was reduced to low volume by evaporation on a steam-bath, then distilled under vacuum to yield 30 g. of crude 4-*n*-decyl-v-triazole (29%) boiling at 148–149° at 0.6 mm. pressure, as well as 30 g. of unchanged dodecyne-1. The crude triazole which solidified in the condensing flask was recrystallized twice from heptane, washed with a small amount of petroleum ether, and dried under vacuum at 40–50° overnight. The pure triazole melted at 58.5–59°.

4-Phenyl-v-triazole.—Three combustion tubes, each containing 14.7 g. of phenylacetylene (0.144 mole) and 50 ml. of 14.2% hydrazoic acid in benzene (0.165 mole HN_3) were sealed and heated in a bath for 40 hours at 110–115°. Some crystals were present in the tubes on first removing them from the heating bath. After cooling to room temperature nearly the entire contents appeared to crystallize. The solid was collected on a filter and washed with benzene. After twice recrystallizing from benzene using decoloring charcoal during the first crystallization 30 g. of product melting at 148.4° was obtained. The yield was 48% of the theoretical amount.

Oxidation of 4-*n*-Amyl-v-triazole.—To a mixture of 1.9 g. of 4-*n*-amyl-v-triazole in 20 ml. of water and 5.6 ml. of concentrated sulfuric acid was added portionwise 7 g. of potassium permanganate keeping the temperature at 60–70°. After all the permanganate had been added, the mixture was heated 30 minutes on a steam-bath, and allowed to stand at room temperature for 48 hours. The mixture was cooled in ice and the white solid which had precipitated was filtered and recrystallized from a small amount of water. The 4-carboxy-v-triazole so obtained melted at 213°. The melting point recorded in the literature[3] for this compound is 213–215°.

Anal. Calcd. for $C_3H_3N_3O_2$: C, 31.83; H, 2.67. Found: C, 31.7; H, 2.3.

The absorption spectra were determined in 95% ethanol solution with a Model DU Beckman quartz spectrophotometer.

The authors wish to express their appreciation to Dr. Paul D. Sternglanz and staff for the analytical and ultraviolet absorption spectra data and to Mr. D. James Kay for the bacteriological tests reported here.

SOUTH NORWALK, CONN.

(16) J. S. Fritz and N. M. Lisicki, *Anal. Chem.*, **23**, 589 (1951).

[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORIES, THE LUBRIZOL CORPORATION]

Chemistry of the Aliphatic Esters of Phosphorothioic Acids.[1] III. Alkoxide Cleavage of O,O,S-Trialkyl Phosphorodithioates[2]

BY W. E. BACON AND W. M. LESUER

RECEIVED JULY 21, 1953

A convenient sulfide synthesis based on the alkoxide cleavage of O,O,S-trialkyl phosphorodithioates is described. The addition of O,O-dialkyl hydrogen phosphorodithioates to unsymmetrical olefins exhibits a peroxide effect. The structures of the O,O,S-trialkyl phosphorodithioates formed in this addition reaction were proven by alkoxide cleavage and subsequent identification of the sulfides obtained.

The alkoxide cleavage reaction of O,O-diethyl-S-(2-octyl) phosphorodithioate with sodium ethoxide and ethanol to yield ethyl 2-octyl sulfide and sodium O,O-diethyl phosphorothioate has been reported.[2] The present work has extended this reaction to similar phosphorodithioates as a method for the determination of the structure of O,O,S-trialkyl phosphorodithioates, and as a convenient method for the preparation of certain sulfides. Table I lists the starting triesters and the sulfides obtained. The sulfides were identified by conversion to sulfones or sulfilimines for comparison with synthetic samples. In all cases we have compared the infrared absorption spectra of the sulfides with authentic samples.

$$(RO)_2P(=S)-SR'' + NaOR' \longrightarrow \begin{cases} (RO)_2PSONa + R'SR'' \\ \text{or} \\ RO(R'O)PSONa + RSR'' \end{cases} \quad (1)$$

The O,O,S-trialkyl phosphorodithioates were

(1) The nomenclature of organic phosphorus compounds used throughout this paper has been outlined in *Chem. Eng. News*, **30**, 4515 (1952).

(2) For preceding article in this series see G. R. Norman, W. M. LeSuer and T. W. Mastin, THIS JOURNAL, **74**, 161 (1952).