

# The Reaction of Azidoorganic Compounds with Acetylenes

JOHN A. DURDEN, Jr., HARRY A. STANSBURY, and WILLIAM H. CATLETTE  
Union Carbide Chemicals Co., South Charleston, W. Va.

Thirty-six novel 1,2,3-triazoles have been prepared by the reaction of alkyl- and aralkylazido compounds with various alkynes. Where unsymmetrical alkynes have been employed the products are most likely mixtures of isomers. A convenient method of synthesis for azidoalkanes involving reaction of the alkyl chloride and sodium azide in dimethylformamide is described. Five novel azido compounds are reported.

**T**HE PREPARATION of vicinal triazoles by the reaction of acetylenic compounds with organic azido compounds is well known (1, 2, 4, 5). In connection with certain work in these laboratories, this reaction has been extended to include some azides not previously employed (Table I).

Several of the azido compounds were prepared quite conveniently from the corresponding chlorides and sodium azide using DMF (dimethylformamide) as the solvent, where yields comparable to those reported previously could be obtained in somewhat shorter reaction time.

Certain of the azido compounds prepared in connection with this work are novel; their physical constants are reported in Table II. Of these, only bis(2-azidoethyl)ether has been employed in triazole syntheses. No difficulties were encountered in the synthesis of this or any of the other azides reported although controlled experiments have shown this ether to be a powerful explosive and moderately sensitive to shock and heat ( $\frac{1}{10}$  the shock sensitivity of nitroglycerin).

## EXPERIMENTAL

**Azide Synthesis.** The sodium azide used was the commercial product obtained from Matheson, Coleman, Bell. The DMF was commercial material used for the most part without further purification.

The azides listed in Table II were prepared as follows:

**Bis(2-AZIDOETHYL)ETHER.** A mixture of 650 grams of sodium azide (10.0 moles) in 1600 ml. of DMF was stirred at 100° C. To the mixture, 684.4 grams of bis(2-chloroethyl)ether (4.8 moles) were added over a period of two hours. After stirring at 100° C. for 17 more hours, it was chilled in an ice bath and filtered. The filtrate was diluted with 150 ml. of UCON (a polyalkyleneglycol of Union Carbide) which served as a distillation residue, and fractionated under reduced pressure to obtain 698 grams of product.

**Bis(2-AZIDO-1-METHYLETHYL)ETHER.** A slurry of 439.4 grams of sodium azide (6.76 moles) in 1000 ml. of DMF was stirred at 100° C. To this was added 550 grams of bis(2-chloro-1-methylethyl)ether (3.22 moles) over a period of 30 minutes. After being stirred at 100° C. for 67 hours, the mixture was cooled and filtered. The filtrate was diluted with 40 grams of UCON and fractionated under reduced pressure to obtain the product.

A mid-fraction having the following properties was identified as 2-chloro-1-methylethyl 1-methyl-2-azidoethyl ether with boiling point 65° C./3mm.,  $n_D^{30}$  1.4516. Mass spectrometric analysis indicated that this fraction was the pure monoazido ether.

**Bis 1,2-(2-AZIDOETHOXY)ETHANE.** A slurry of 144 grams of sodium azide (2.2 moles) in 300 ml. of DMF was stirred at 95° C. while 187 grams of 1,2-bis(2-chloroethoxy)ethane (1.0 mole) were added over a period of 2.25 hours. After stirring 48 hours at 95° C., the mixture was chilled and filtered to remove sodium chloride. The filtrate was

diluted with 50 ml. of UCON and fractionated under reduced pressure to obtain product.

**2-AZIDOMETHYL-5-HYDROXY-1,4-PYRONE.** To a suspension of 13 grams (0.2 mole) of sodium azide in 120 ml. of DMF was added 32 grams (0.2 mole) of 2-chloromethyl-5-hydroxy-1,4-pyrone (chlorokojic acid). Upon stirring the acid dissolved and heat was evolved. After 24 hours the reaction mixture was poured into water and the solid was collected on a filter to yield 25 grams of a golden brown solid, m.p. 131-132°. This material was crystallized from 300 ml. of ethyl acetate to yield 21 grams (63 per cent) of cream colored crystals.

**2-AZIDOETHYL AZIDOACETATE.** To a suspension of 78 grams (1.2 moles)  $\text{NaN}_3$  in 500 ml. DMF at 75 to 85° was added dropwise with stirring, over a period of 45 minutes, 157 grams (1.0 mole) of chloroethyl chloroacetate. The reaction was exothermic; no heat was required during the addition. After addition was completed the mixture was heated and stirred for five hours. After standing at room temperature overnight the mixture was chilled, filtered, 50 ml. UCON added, and distilled on a 14-inch  $\times$  24-inch mm. column packed with  $\frac{3}{16}$ -inch glass helices to give the product indicated in Table II.




The following azides were prepared by reaction of the corresponding chloride with  $\text{NaN}_3$  in DMF.

**1-AZIDOBUTANE.** To a suspension of 227.5 grams (3.5 moles) of sodium azide in 1000 ml. of DMF heated at 100° C. was added dropwise with stirring 227.5 grams (3.0 moles) of 1-chlorobutane over a period of 1.5 hours. The reaction mixture was heated at 100° C. for an additional 3.5 hours, cooled, and finally filtered to remove the fine precipitate of sodium chloride. At this point between 50 and 100 ml. of UCON was added to the reaction mixture. The product was distilled directly from the filtrate to yield 264 grams (89 per cent) of 1-azidobutane (*n*-butylazide) b.p. 71° C./225 mm. Hg,  $n_D^{27}$  1.4160 (lit. 71° C./225 mm.,  $n_D^{20}$  1.4192) (3).

**1,5-DIAZIDOPENTANE.** Using a procedure similar to that described above 42.3 grams (0.3 mole) of 1,5-dichloropentane reacted with 45.5 grams (0.67 mole) of sodium azide in 200 ml. of DMF at 100° C. with a 0.5 hour addition time and a 2.5 hour heating period. There was thus obtained after two distillations (on redistillation 50 ml. UCON was added to the crude azide in the kettle) 31 grams (68 per cent yield) of colorless liquid, b.p. 70° C./2.5 mm.,  $n_D^{26}$  1.4715, (lit. b.p. 100° C./9 mm.,  $n_D^{26}$  1.4729) (6). The infrared spectrum of this material was in agreement with the proposed structure.

**Triazole Syntheses.** For the most part a general procedure was followed in which stoichiometric proportions of azido compound and acetylenic material were reacted in the appropriate solvent at reflux for the indicated times (dictated more by convenience rather than by actual necessity) and then worked up either by crystallization, distillation or taking as a residue. This general procedure, supplemented by Table I describes the syntheses of most of the

Table I. Vicinal Triazoles Prepared in this Work

R	R'	Reaction <sup>a</sup> Solvent	Yield, %	M.P., °C. (B.P., °C./mm.)	Index of Refraction/°C.	Reaction Time, Hrs.	Analysis <sup>b</sup>					
							Carbon	Hydrogen	Nitrogen	Found		
$\text{—CH}_2\text{OH}$ $\text{OH}$	$\text{—H}$	T	64	(144-8/0.5)	1.4913-23/25	52	Calcd. 54.17	Calcd. 8.44	Calcd. 27.07	Found 53.95	Found 8.35	Found 27.18
$\text{—CHCH}_3$ $\text{OH}$	$\text{—H}$	T	74	(137-44/0.5-0.65)	1.4862/26	23	56.78	8.94	24.83	56.39	8.80	25.05
$\text{—C(CH}_3)_2$ $\text{OH}$	$\text{—H}$	T	92	(121-6/0.2-0.3)	1.4804/32	...	58.95	9.35	22.95	58.55	9.39	22.89
	$\text{—H}$	T	37	99-100	...	24	64.54	9.48	18.82	64.36	9.39	18.99
$\text{OH}$ $\text{—C(CH}_3)_2$ $\text{—CH}_3$ $\text{—C}_2\text{H}_5$	$\text{OH}$ $\text{—C(CH}_3)_2$ $\text{—H}$ $\text{—H}$	T A A	73 90 86	Res (102-6/2-2.5) (93-97/0.5-0.55)	1.4916/25 1.4664-90/30 1.4687- 1.4707/24.5	24 20.5 24	59.72 60.42 62.71	9.60 9.35 9.87	17.41 30.21 27.42	60.13 60.40 63.13	9.59 9.22 9.89	17.74 30.39 27.56
$\text{—CH}_2\text{OH}$ $\text{OH}$	$\text{—H}$	T	96	(209/0.8)	1.5253/25	3.5	41.95	6.33	29.35	41.85	6.29	29.43
$\text{—CHCH}_3$ $\text{OH}$	$\text{—H}$	T	22	(195-200/0.7)	1.5150/30	21	45.85	7.05	26.74	45.88	7.07	26.54
$\text{—C(CH}_3)_2$ $\text{OH}$	$\text{—H}$	T	18-20	(181/0.65)	1.5102/32	16	49.11	7.65	24.55	49.29	7.64	24.24
	$\text{—H}$	T	95	100-1	...	26	56.85	8.11	19.89	56.66	8.03	19.77
$\text{OH}$ $\text{—C(CH}_3)_2$ $\text{OH}$	$\text{OH}$ $\text{—C(CH}_3)_2$	T	...	169.5-170	...	21	52.38	8.35	18.33	52.78	8.17	18.47
$\text{—C}\equiv\text{C—C(CH}_3)_2$ $\text{—C}_2\text{H}_5$ $\text{—C}_2\text{H}_5$	$\text{—H}$ $\text{—H}$ $\text{—H}$	T T T	...	125-128 {34-39 (140/0.7)}	...	41	56.89	7.56	...	56.56	7.48	...
	$\text{—H}$	T	26	70-74	...	24	63.47	5.86	22.21	63.27	5.98	22.38
$\text{OH}$ $\text{—CH}_2\text{CH—}$	$\text{OH}$ $\text{—CH}_2\text{CH—}$	T	69	(175-180/0.4)	...	48	49.11	7.65	24.55	49.21	7.70	24.75

(Continued on page 230)

Table I. Vicinal Triazoles Prepared in this Work (Continued)

Triazole		Reaction <sup>a</sup> Solvent	Yield, %	M.P., °C. (B.P., °C./mm.)	Index of Refraction/ <sup>o</sup> C.	Reaction Time, Hrs.	Carbon		Hydrogen		Nitrogen	
R	R'						Calcd.	Found	Calcd.	Found	Calcd.	Found
$\begin{array}{c} \text{OH} \\   \\ \text{---CHCH}_3 \\   \\ \text{---CH}_3 \end{array}$	$\text{R}' = \text{---} \langle \text{C}_6\text{H}_4 \text{---} \text{CH}_2 \text{---} \rangle$	T	53	(175-85/0.5)	1.5592/30	72	65.27	65.10	6.23	6.45	20.47	20.68
		T	26	(200/0.6)	1.5583/30	72	...	...	...	...	...	...
		A	53	45-54 41-42	...	...	...	69.18	69.34	6.38	6.40	24.40
$\begin{array}{c} \text{OH} \\   \\ \text{---C}(\text{CH}_3)_2 \\   \\ \text{CH}_2 \\   \\ \text{---C---} \\   \\ \text{CH}_3 \end{array}$	$\text{R}' = \text{---} \langle \text{C}_6\text{H}_4 \text{---} \text{CH}_2 \text{---} \rangle$ $\text{X} = \text{---} \langle \text{C}_6\text{H}_4 \text{---} \rangle$	T	42	172-4	...	24	60.65	60.63	6.79	6.99	23.58	23.38
		T	...	188-91	...	3	67.47	66.91	6.29	6.31	...	...
$\begin{array}{c} \text{---CH}_2\text{OH} \\   \\ \text{OH} \\   \\ \text{---CHCH}_3 \\   \\ \text{OH} \\   \\ \text{---C}(\text{CH}_3)_2 \end{array}$	$\text{X} = \text{---} \text{CH}_2\text{CH}_2 \text{---}$	T	71	73-75	...	24	47.60	47.49	6.39	6.40	33.31	32.96
		T	19	110-120	...	24	...	...	...	...	29.98	30.23
		T	48	108-110	...	24	54.52	54.13	7.84	7.65	27.25	27.18
$\text{---CH}_2\text{OH}$	$\text{X} = \text{---} \text{CH}_2\text{CH}_2\text{CH}_2 \text{---}$	T	100	Res	1.5346/25.6	3.3	49.6	49.59	6.8	6.06	31.6	31.10
		T	86	Res	1.5370/26	24	44.76	44.48	6.01	6.02	31.32	31.20
$\begin{array}{c} \text{---CH}_2\text{OH} \\   \\ \text{OH} \\   \\ \text{---CHCH}_3 \end{array}$	$\text{X} = \text{---} \text{CH}_2\text{OCH}_2 \text{---}$	T	20	92-95	...	143	48.63	48.17	6.80	6.75	28.36	28.24
		T	38	73-75	...	27	59.38	59.25	7.97	7.93	...	...
$\begin{array}{c} \text{---CH}_2\text{OH} \\   \\ \text{H}_3\text{C---} \\   \\ \text{---CH---} \\   \\ \text{OH} \\   \\ \text{---} \langle \text{C}_6\text{H}_4 \text{---} \rangle \end{array}$	$\text{---CH}_2\text{OH}$	B	37	165-6.5	...	21	43.76	43.76	6.14	6.08	25.59	23.35
		T	91	Res	1.5277/26.5	40	58.99	58.87	7.42	7.64	...	...
$\text{---CH}_2\text{OH}$	$\text{X} = \text{---} \langle \text{C}_6\text{H}_4 \text{---} \rangle$	T	16	187-90	...	2	42.85	42.66	5.59	5.61	32.52	32.93

R'' = C <sub>2</sub> H <sub>5</sub> OCCH <sub>2</sub> -																				
-CH <sub>2</sub> OH	-H	T	85	Res	1.4982/26	18	45.39	45.40	5.98	5.99	22.69	22.93								
OH	-H	T	68	Res	1.4953/26.8	43	48.23	48.07	6.57	6.22	21.09	21.92								
-CHCH <sub>3</sub>	-H	T	80	Res	1.4853/25	72	50.69	50.47	7.09	7.16	19.70	20.05								
OH	-H	T	89	Res	1.5082/25	29	56.90	56.68	7.56	7.40	16.59	16.42								
-C(CH <sub>3</sub> ) <sub>2</sub>		T	16	192-6	...		59.10	58.96	4.47	4.59	20.68	20.65								
	-H	T	30	92-8.5	...	100	62.32	62.42	5.64	5.70	18.17	18.51								

<sup>a</sup>Solvent designations: T = toluene, E = ethanol, A = acetone, B = butanol.

<sup>b</sup>In all of these compounds the infrared spectrum was in agreement with proposed structure.

<sup>c</sup>This isomer was isolated as the free acid.

triazoles reported herein. Azides not described in the previous section were prepared by the methods in the literature.

When the acetylenic moiety was low boiling (propyne and butyne) the reaction was carried out in a stainless steel bomb.

The following examples illustrate the procedure.

**REACTION OF 1-AZIDOBUTANE WITH PROPYNE. 1-BUTYL-4(AND 5)-METHYL-1,2,3-TRIAZOLE.** A mixture of 200 grams (5.0 moles) of propyne and 396 grams (4.0 moles) 1-azidobutane in 600 ml. acetone in a 3-liter stainless steel bomb under an initial nitrogen pressure of 200 p.s.i.g. at 0° was heated at 90 to 98° for 20.5 hours. A maximum pressure of 320 p.s.i.g. at 85° was observed. As the reaction proceeded the pressure slowly fell to 240 p.s.i.g. at 98°. The bomb was cooled, vented, and the liquid contents (1987 grams) were discharged into a distillation flask. Volatile materials were removed under vacuum on a steam bath and the residue was distilled through a 31-inch × 45-mm. glass column packed with 3/16-inch triple turn glass helices to give 464 grams (83 per cent) yield of product, b.p. 110-196°/2 mm. Hg,  $n_D^{30}$  1.4664-1.4709. Samples collected throughout the distillation indicated, both by ultimate analyses and infrared studies, that the material was indeed the desired triazole (Table I).

The reaction product was chromatographed on a 6-foot Apiezon L on chromosorb W column at 220° to give two peaks, at 18 and 22 minutes. The isolated product was proved to be 55.4 per cent 1,4-isomer and 44.6 per cent 1,5-isomer assuming the two isomers have similar thermal properties during chromatography.

**REACTION BETWEEN ETHYL AZIDOACETATE AND PROPARGYL ALCOHOL. 1-CARBOETHOXY METHYL-4(AND 5)-HYDROXYMETHYL-1,2,3-TRIAZOLE.** A mixture of 14 grams (0.25 mole) propargyl alcohol and 32 grams (0.25 mole) ethyl azidoacetate in 100 ml. of ethanol was heated at reflux for about four days and the reaction mixture was then concentrated on a rotary evaporator at 1 to 2 mm. Hg at room temperature until the residue possessed a constant refractive index,  $n_D^{26}$  = 1.4916. Infrared studies indicated that no unreacted azide or alkyne was present. The carboethoxymethyl-hydroxyalkyl-triazoles were taken as residues since attempted distillation invariably resulted in polymerization and evolution of ethanol.

**REACTION BETWEEN PHENYLACETYLENE AND ETHYL AZIDOACETATE: 1-CARBOETHOXYMETHYL-4(AND 5)-PHENYL-1,2,3-TRIAZOLE.** A solution of 20.4 grams (0.2 mole) of phenylacetylene and 25.8 grams (0.2 mole) of ethyl azidoacetate in 50 ml. toluene was refluxed for three days at the end of which time the volatiles were removed under vacuum. The solid residue was dissolved in hot ethanol, the hot solution was filtered through charcoal, and, upon cooling, gave 14 grams (30 per cent) of an ester, m.p. 97-98.5°. The filtrate from this solid was concentrated to give a residue which would not crystallize (30 grams). This residue was heated in 75 ml. of 15 per cent sodium hydroxide solution at 100° until a clear solution was obtained which was filtered through charcoal and acidified to give 7 grams (16 per cent) of an acid crystallized from water. On the basis of the observation that 1,4-isomers are usually higher melting than the 1,5-isomer the solid ester is assumed to be the 1,4-isomer. It is probable that the liquid ester is predominately the 1,5-isomer although some of the other isomer may be present (Table I).

**REACTION BETWEEN BIS(2-AZIDOETHYL)ETHER AND 1,4-DIHYDROXYBUTYNE-2. BIS 2-[4,5-DI(HYDROXYMETHYL)-1,2,3-TRIAZOLYL-1 ETHYL]ETHER.** A mixture of 31.2 grams (0.2 mole) bis(2-triazoethyl)ether and 35.2 grams (0.2 mole) 1,4-butyne-2,3-diol in 80 ml. *n*-butyl alcohol was heated at reflux for 24 hours during which time solid material separated. The reaction mixture was cooled and the solid collected and air dried. The solid was purified by sus-

Table II. Novel Azido Compounds

Compound	Reaction Temp., ° C.	Reaction Time, Hrs.	Yield, %	B.P., ° C./mm. (M.P.)	Index of Refraction/ ° C.	Analysis <sup>a</sup>					
						Carbon		Hydrogen		Nitrogen	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
Bis(2-Azidoethyl)ether	100	19	92	73/3	1.4706/27	...	...	...	...	53.83	54.11
Bis(2-Azidoethoxy)ethane	95	36	85	83/0.3	1.4672/28.5	36.00	36.54	6.0	6.19	41.98	41.48
2-Azidomethyl-5-hydroxy- 1,4-pyrone	Ambient	24	63	(126-128)	...	43.12	43.14	2.99	3.02	25.15	25.15
Bis(2-Azido- 1-methylethyl)ether	100	67.5	44	78/2	1.4588/30	39.23	39.07	6.56	6.56	45.62	45.40
2-Azidoethyl Azidoacetate	80	3	41	90/1.1	1.4798/30	28.24	28.52	3.85	3.61	49.40	49.87

<sup>a</sup>The materials containing high percentages of nitrogen were difficult to analyze as they tended to explode at high temperatures.

pending it in boiling ethanol and adding water until solution occurred. Cooling gave 18 grams crystalline material, m.p. 165-166.5°. Evaporation of the filtrate with subsequent recrystallization as above gave an additional 8 grams material. Total yield 26 grams (37%) m.p. 165-166.5° (Table I).

REACTION BENZYL AZIDE AND 3-HYDROXYBUTYNE. 1-BENZYL-4(OR 5)-(1-HYDROXYETHYL)-1,2,3-TRIAZOLE. A mixture of 133 grams (1.0 mole) of benzylazide and 70 grams (1.0 mole) 3-hydroxybutyne in 150 ml. toluene was heated at 100° on the steam bath for about 3 days. The volume was then reduced under vacuum to a viscous residue which was subsequently distilled through short (1-2-inch) column. The product possessed the properties indicated in Table I.

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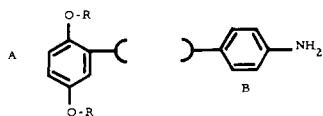
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## Anilino Hydroquinones: Precursors to Azo Dye-Developers

WARREN E. SOLODAR, SUSANNE LUKAS, and MILTON GREEN  
Polaroid Corporation, Cambridge, Mass.

Protected hydroquinones, joined by different groups to various anilines, are used in the preparation of photographic dye-developers. In this paper the preparation and properties of these developer functions are described.

THE PREPARATION of azo dye-developers, described in the patent literature (3, 4, 5, 12, 13), makes use of protected hydroquinone functions joined through various structures to an anilino group. These developer-connected anilines are diazotized, coupled into appropriate couplers, and the protecting groups then removed to give the dye-developers.



The structures of these compounds were dictated by the following considerations: The redox system had to be sufficiently insulated from the chromophore so that changes in the oxidation state of the developer would not change

the color of the dye. The hydroquinone had to be protected during the diazotization step from interaction with the diazonium salt (15) by a group that could be readily removed after coupling. Variations in the groups attached to ring A were made with a view toward modifying the photographic characteristics of the compound, or of changing some general property of the molecule, such as solubility. Substituents on ring B were generally chosen for the purpose of modifying the color of the azo dye.

In general, these compounds were synthesized by first assembling suitably chosen A and B fragments. This was frequently followed by demethylation of any methylated hydroxyl groups and replacing them with the readily removable acetate or carbethoxy functions. The amine precursor, a nitro group, was then reduced.

The reductions usually went readily at room temperature in a standard Parr apparatus. In many cases the free