(composite 25) and concentrated to about 3 ml. under vacuum. After storage at 5° a pale yellow crystalline product formed which was filtered off (0.027 g.). The material recrystallized from ethanol melted at 119 to 123° and had an $[\alpha]^{25}D$ of 25.61 in pyridine. A negative Molisch test for sugars and glycosides was obtained. In alcoholic solution the compound gave no coloration when warmed with a chip of magnesium turnings and concentrated hydrochloric acid (a negative test for flavones). The mixed melting point of VII with an authentic sample of byakangelicin[15] was not depressed, and a comparison of the infrared spectra of the two compounds indicated they were identical.

Anal. Calcd. for $C_{17}H_{18}O_7$: C, 61.1; H, 5.43; 1 MeO–, 9.3. Found: C, 61.6; H, 5.59; MeO–, 8.9.

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[CONTRIBUTION FROM THE RESEARCH DIVISION OF ABBOTT LABORATORIES]

The Preparation of Some Organic Diazides

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The polymethylene diazides containing five to ten carbon atoms and examples of other classes of organic diazides have been prepared through displacement of halogen or arenesulfonoxy groups by the azide ion.

A recent review[1] of the literature on organic azides lists no diazidoalkanes other than 1,2-diazidoethane.[2] We have prepared a series of eight aliphatic diazides containing five to ten carbon atoms for pharmacologic testing as hypotensive agents. Examples of the oxa and aza analogs of these diazides were also synthesized, as was α,α'-diazido-*p*-xylene. Pharmacologic studies in these laboratories have shown that some of these diazides possess marked hypotensive action in normal animals.[3]

The treatment of polymethylene dibromides with sodium azide in aqueous methanol[4] generally gave the corresponding diazides in good yield.

$$Br—(CH_2)_n—Br + 2NaN_3 \rightarrow N_3—(CH_2)_n—N_3 + 2NaBr$$

Replacing one or both primary alkyl bromide groups in the reactant by secondary groups gave progressively lower yields of product. Table I summarizes the data obtained from these diazidoalkanes. α,α'-Diazido-*p*-xylene, in which an aromatic ring joins two azidoalkyl groups, was obtained in the same manner from α,α'-dichloro-*p*-xylene and sodium azide.

The displacement of an arenesulfonoxy group by azide ion, a method recently applied to the preparation of cyclohexyl azide,[5] is an effective alternate method of synthesis. The benzenesulfonic acid or *p*-toluenesulfonic acid esters of 1,6-hexanediol and 1,7-heptanediol were thus converted to the corresponding diazidoalkanes.

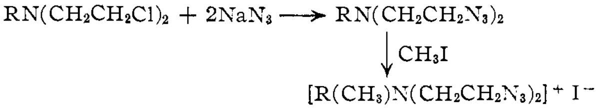
$$Ar—SO_3—(CH_2)_n—O_3S—Ar + 2NaN_3 \longrightarrow N_3—(CH_2)_n—N_3 + 2ArSO_3Na$$

Because 1,7-diazidoheptane possesses greater hypotensive potency than its homologs,[3] an isoster, di-3-azidopropyl ether, was prepared by the following reactions.

$$(ClCH_2CH_2CH_2)_2O + 2NaI \longrightarrow (ICH_2CH_2CH_2)_2O$$

$$(ICH_2CH_2CH_2)_2O + 2NaN_3 \longrightarrow (N_3CH_2CH_2CH_2)_2O$$

Treatment of N-methyl- and N-phenyl-N,N-bis-(β-chloroethyl)-amines with sodium azide gave the corresponding amino diazides, one of which was converted to a diazide quaternary ammonium salt.



$$\begin{tikzcd} RN(CH_2CH_2Cl)_2 + 2NaN_3 \arrow[r] & RN(CH_2CH_2N_3)_2 \arrow[d, "CH_3I"] \\ & {[R(CH_3)N(CH_2CH_2N_3)_2]^+ I^-} \end{tikzcd}$$

No fires or explosions were experienced in working with these diazides. However, because of the reported sensitivity to heat of diazidoethane they were regarded as potentially explosive materials and handled accordingly.

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Experimental

Dibromoalkanes.—With two exceptions these were commercially available. 1,7-Dibromoheptane and 1,8-dibromoöctane were made by the action of anhydrous hydrogen bromide[6] upon the corresponding glycols. The latter compounds were obtained by reduction of methyl or ethyl esters of pimelic and suberic acids with lithium aluminum hydride.[7] In the synthesis of diethyl pimelate from pimelonitrile using alcoholic hydrogen chloride there was obtained, along with the desired ester (75%), **ethyl pimelamate**, m.p. 76–77°, in 4% yield.

Anal. Calcd. for $C_9H_{17}NO_3$: C, 57.73; H, 9.15; N, 7.48; O, 25.64. Found: C, 58.29; H, 9.16; N, 7.47; O, 25.43.

Arenesulfonic Esters.—**1,6-Dibenzenesulfonoxyhexane**, prepared by a procedure described for alkyl esters,[8] decomposed upon attempted distillation and was purified by crystallization from alcohol which gave crystals melting at 58–60°.

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TABLE I

DIAZIDOALKANES $N_3—CHR—(CH_2)_n—CHR_1—N_3$

			Yield,	B.p.				Carbon, %		Hydrogen, %		Nitrogen, %	
n	R	R_1	%	°C.	Mm.	$n^{25}D$	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found
3	H	H	81	100	9	1.4729	$C_5H_{10}N_6$	38.95	39.43	6.54	6.34	54.51	54.80
4	H	H	80	119	12	1.4707	$C_6H_{12}N_6$	42.84	43.20	7.19	7.16	49.97	49.42
5	H	H	73	116	5	1.4700	$C_7H_{14}N_6$	46.14	46.36	7.74	7.75	46.12	45.77
6	H	H	75	129	5	1.4698	$C_8H_{16}N_6$	48.96	49.36	8.22	7.96	42.83	43.46
7	H	H	89	142	6	1.4685	$C_9H_{18}N_6$	51.40	51.59	8.63	8.68	39.97	39.91
8	H	H	72	105	0.2	1.4693	$C_{10}H_{20}N_6$	53.54	53.72	8.99	8.90	37.47	37.41
2	CH_3	H	66	88	8	1.4690	$C_5H_{10}N_6$	38.95	38.89	6.54	6.44	54.51	54.58
2	CH_3	CH_3	37	116	26	1.4642	$C_6H_{12}N_6$	42.84	43.31	7.19	6.86	49.97	50.04

Anal. Calcd. for $C_{18}H_{22}O_6S_2$: S, 16.09. Found: S, 16.29.

1,6-Di-*p*-toluenesulfonoxyhexane[9] and **1,7-di-*p*-toluenesulfonoxyheptane** were obtained in yields of 87 and 71%, respectively, by Tipson's method.[10] The latter compound melted at 77–78° after crystallization from ethanol.

Anal. Calcd. for $C_{21}H_{28}O_6S_2$: C, 57.25; H, 6.41. Found: C, 57.54; H, 6.34.

Diazidoalkanes. From Dibromoalkanes.—To a solution of 0.1 mole of the dibromoalkane in 225 ml. of methanol, there was added a slurry of 16.3 g. (0.25 mole) of sodium azide in 15 ml. of water. The mixture was refluxed for 24 hr., the methanol removed and the residue diluted with 50 ml. of water. The resultant oil was extracted by 200 ml. of ether, dried over calcium chloride and distilled. Table I describes the diazidoalkanes obtained by this procedure.

1,7-Diazidoheptane was prepared also by the following method.[11] A solution containing 78 g. (1.2 moles) of sodium azide and 27 g. of sodium acetate in 270 ml. of water was added to a warm solution of 129 g. (0.5 mole) of 1,7-dibromoheptane in 460 ml. of absolute ethanol. The mixture was refluxed for 24 hr. on a steam-bath, and 375 ml. of alcohol was then distilled from the mixture. The residue was poured into 0.5 l. of water and shaken with three 200-ml. portions of benzene. Distillation of the extract gave 83 g. (95%) of the product, b.p. 80–81° at 0.3 mm., $n^{25}D$ 1.4698.

From Arenesulfonic Esters. 1,7-Diazidoheptane.—A mixture of 22 g. (0.05 mole) of 1,7-di-*p*-toluenesulfonoxyheptane, 9.8 g. (0.15 mole) of sodium azide, 150 ml. of acetone and 20 ml. of water was refluxed on a steam-bath for 24 hr. The condenser was removed and acetone was allowed to evaporate during 15 minutes. Water (100 ml.) was added and the oil which formed was extracted into benzene and distilled. There was obtained 8.5 g. (93%) of product, b.p. 72° at 0.2 mm., $n^{25}D$ 1.4701.

By this method the benzene- and *p*-toluenesulfonic acid diesters of 1,6-hexanediol were converted to 1,6-diazidohexane in yields of 74 and 83%.

α,α′-Diazido-*p*-xylene.—The general method described for the preparation of diazidoalkanes was applied to α,α′-dichloro-*p*-xylene. The product, a colorless oil, b.p. 82–83° at 0.1 mm., $n^{25}D$ 1.5590, was obtained in 90% yield.

Anal. Calcd. for $C_8H_8N_6$: N, 44.66. Found: N, 44.10.

Di-3-azidopropyl Ether. Di-3-iodopropyl Ether.—To a solution of 45 g. (0.3 mole) of sodium iodide in 250 ml. of acetone was added 20 g. (0.12 mole) of di-3-chloropropyl ether, and the mixture was refluxed for 19 hr. The salt was removed by filtering and the filtrate was concentrated and distilled. Redistillation of material (25 g.), b.p. 141–154° (10 mm.), gave 15 g. (36%) as a center cut, b.p. 134–142° (7 mm.), $n^{25}D$ 1.5638. This material was used for the next reaction without further purification.

Anal. Calcd. for $C_6H_{12}I_2O$: I, 71.70. Found: I, 69.10.

Di-3-azidopropyl Ether.—A mixture of 14.5 g. (0.04 mole) of di-3-iodopropyl ether, 6.5 g. (0.1 mole) of sodium azide, 75 ml. of ethanol and 15 ml. of water was heated to reflux for 25 hr. After the mixture had been diluted with 200 ml. of water, the oil which separated was extracted by benzene. Two distillations of the oil remaining after concentration of the extract gave 5 g. (68%) of product, b.p. 116–117° at 8 mm., $n^{25}D$ 1.4661.

Anal. Calcd. for $C_6H_{12}N_6O$: C, 39.12; H, 6.57; N, 45.63. Found: C, 38.99; H, 6.59; N, 45.47.

Diazido Amines. N,N-Bis-(β-azidoethyl)-aniline.—A mixture of 21.8 g. (0.1 mole) of N,N-bis-(β-chloroethyl)-aniline, 16.3 g. (0.25 mole) of sodium azide, 225 ml. of methanol and 15 ml. of water was refluxed for 24 hr. on the steam-bath. The methanol was removed under reduced pressure, and the residue was diluted with 225 ml. of water and shaken with 200 ml. of ether. The extract was dried over sodium sulfate and distilled to obtain 18 g. (79%) of product, b.p. 132–134° at 0.2 mm., $n^{25}D$ 1.5748. A redistilled sample was analyzed.

Anal. Calcd. for $C_{10}H_{13}N_7$: C, 51.93; H, 5.67; N, 42.40. Found: C, 52.66; H, 5.86; N, 41.09.

N,N-Bis-(β-azidoethyl)-methylamine.—A solution of 16.3 g. (0.25 mole) of sodium azide in 100 ml. of water was added to 39 g. (0.2 mole) of N,N-bis-(β-chloroethyl)-methylamine hydrochloride. After the mixture had stood 6 hr., it was warmed on the steam-bath and an additional 26 g. (0.4 mole) of sodium azide was added. The mixture was heated another hour, cooled and treated with 60 ml. of aqueous 25% sodium hydroxide. The oil was extracted by three 100-ml. portions of ether, dried over potassium hydroxide pellets and distilled. By redistillation of the material boiling at 97–100° at 5 mm., there was obtained 15 g. (44%) of product, b.p. 98–99° at 5 mm., $n^{25}D$ 1.4824.

Anal. Calcd. for $C_5H_{11}N_7$: C, 35.49; H, 6.55; N, 57.95. Found: C, 35.77; H, 6.65; N, 57.51.

Its oxalate, prepared in ether and recrystallized in isopropyl alcohol, melted at 95–97°.

Anal. Calcd. for $C_7H_{13}N_7O_4$: N, 37.83. Found: N, 37.17.

N,N-Bis-(β-azidoethyl)-dimethylammonium Iodide.—A solution of N,N-bis-(β-azidoethyl)-methylamine and methyl iodide in absolute ethanol was allowed to stand several days. Dilution with dry ether gave a small amount of white crystalline solid, m.p. 72–74°.

Anal. Calcd. for $C_6H_{14}IN_7$: C, 23.16; H, 4.54; N, 31.51. Found: C, 23.52; H, 4.58; N, 31.76.

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