Anal. Calcd. for $C_{17}H_{13}O_6N_3$: C, 57.4; H, 3.7; N, 11.8. Found: C, 57.0; H, 3.7; N, 12.1.

VII may also be prepared by the condensation of VI with PABA in methanol or aqueous alkali.

Methyl p-(2-formyl-2-nitroethylideneamino)benzoate (VIII). A solution of PABA methyl ester (5.1 g.) in aqueous methanol (80%, 50 ml.) containing piperidine (4 drops) was slowly added to a solution of NMA (4.7 g.) in aqueous methanol (60%, 75 ml.) with stirring, during 1.5 hr. After standing for 4 hr., the solution was concentrated under reduced pressure, during which the sodium salt of VIII crystallized. The mixture was acidified with 20 ml. of 2 *N* hydrochloric acid, filtered, and the product recrystallized from methanol. The yield of yellow crystals of *methyl p-(2-formyl-2-nitro-ethylideneamino)benzoate* was 6.26 g. (74%). It was purified by further crystallization from methanol, m.p. 186–188°.

Anal. Calcd. for $C_{11}H_{10}O_5N_2$: C, 52.8; H, 4.0; N, 11.2. Found: C, 52.7; H, 3.9; N, 11.3.

2-Amino-6-hydroxy-4-(2'-nitro-2'-formylethylideneamino)-pyrimidine (XIV). (a) *From NMA.* NMA (1.0 g.) and XII (1.0 g.) were heated together in water (10 ml.) for 1 hr. at 120° (oil bath). After cooling, the yellow sodium salt was filtered, giving 1.4 g. of the *sodium salt* of *2-amino-6-hydroxy-4-(2'-nitro-2'-formylethylideneamino)-pyrimidine.* The product was recrystallized from aqueous sodium hydroxide.

Anal. Calcd. for $C_7H_6O_4N_5Na \cdot {}^1/_2H_2O$: C, 32.8; H, 2.7; N, 27.4; Na, 8.9. Found: C, 32.5; H, 2.6; N, 27.3; Na, 9.1.

(b) *From VI.* VI (1.0 g.) and XII (0.58 g.) in water (25 ml.) containing sodium hydroxide (0.39 g.) were refluxed for 15 min., and again after standing overnight. After cooling, 1 g. of yellow solid was collected. Recrystallization from dilute aqueous sodium hydroxide gave the pure *sodium salt* of *XIV.*

Anal. Calcd. for $C_7H_6O_4N_5Na \cdot {}^1/_2H_2O$: C, 32.8; H, 2.7; N, 27.4. Found: C, 32.6; H, 2.8; N, 27.3.

Attempted nitrosation of XIV; isolation of free XIV. To a solution of the sodium salt of XIV sodium nitrite was added, and the solution was acidified with acetic acid. A solid separated from the yellow solution, but there appeared to be no nitrosation (no change in color). The solution was heated until gas was evolved, and hydrochloric acid was then added until most of the solid dissolved. After filtration and cooling, ammonia was added to *p*H 7. The solid which separated was filtered and dried, and was *2-amino-6-hydroxy-4-(2'-nitro-2'-formylethylideneamino)pyrimidine.*

Anal. Calcd. for $C_7H_7O_4N_5$: C, 37.4; H, 2.9; N, 30.4. Found: C, 37.3; H, 3.1; N, 30.6.

p-(2-Formylethylideneamino)benzoic acid (XIX). To a solution of ammonium chloride (10 g.) in water (50 ml.) MTA (6.3 g.) was added. After stirring at 60° for 15 min., a solution of PABA (5.0 g.) in aqueous methanol (50%, 100 ml.) was added in 5 min. to the yellow solution, the color changing to reddish brown. Heating and stirring at 60° were continued for 25 min., and stirring at room temperature for 5 hr. The product was filtered, giving 6.2 g. of *p-(2-formylethylideneamino)-benzoic acid.* After several recrystallizations it was obtained as orange-brown crystals, m.p. 247–248°, dec.

Anal. Calcd. for $C_{10}H_9O_3N$: C, 62.8; H, 4.7; N, 7.3. Found: C, 62.3; H, 5.0; N, 7.8.

When the condensation was carried out in 50% methanol at 50°, most of the PABA was recovered unchanged. When 10% hydrochloric acid was used in place of ammonium chloride, at 60°, the yield was 7.3 g., but the product was darker and much more difficult to purify.

PHILADELPHIA, PA.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY, DE PAUL AND PURDUE UNIVERSITIES]

Improved Method for the Synthesis of Alkyl Azides[1]

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An improved method has been devised for the preparation of alkyl azides involving the use of Carbitols as solvents for the interaction of an alkyl halide and sodium azide. The method eliminates the hazards and restrictions of sealed tubes and the formation of troublesome azeotropes. Utility of the procedure is demonstrated by the preparation of seven *n*-alkyl- and two cycloalkyl azides with yields from 64.4 to 99.6%, considerably higher than previously reported. Five new *n*-alkyl azides are described: propyl, pentyl, heptyl, octyl, and decyl azides.

Although 1-azido-2-methylbutane (one of the amyl azides) has been prepared by Levene and Rothen[3] using a sealed tube reaction, pure pentyl azide has not been hitherto prepared. Inasmuch as it was desired as an intermediate, a study of its preparation was carried out. The name 1-azido-pentane can be found in *Chemical Abstracts*.[4] An examination of the original literature[5] disclosed that the product was really a mixture of isomeric amyl azides since it was prepared from mixed amyl iodides (b.p. 140–148°) and silver azide. The boiling point given[5] for the isomeric amyl azides was 121–130°.

Pentyl azide was prepared from pentyl iodide and activated sodium azide.[6] Precaution was taken to wash the pentyl iodide with saturated sodium sulfite solution and to distil it under vacuum in the presence of deposited silver. In order to avoid the use of a sealed tube, the reaction was carried out in boiling propyl alcohol. In working up the product mixture, an effort was made to remove the propyl alcohol by diluting with water and then extracting the ether solution with saturated salt solutions. However, due to the incomplete removal of propyl alcohol, considerable difficulty was encountered in isolating the desired pentyl azide. Although the

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[2] De Paul University, to whom all requests for reprints and additional information should be addressed.

[3] Levene and Rothen, *J. Biol. Chem.*, **115**, 415 (1936).

[4] *Chem. Abstrs.*, **46**, 10440 (1952).

[5] Werle and Fries, *Biochem. Z.*, **322**, 511 (1952).

[6] Smith, *Org. Reactions*, III, 382 (1946).

TABLE I

NORMAL ALKYL AZIDES

Alkyl	Yield, %	B.P., °C./Mm.	n_D^{20}	Anal. Calcd.			Anal. Found		
				% C	% H	% N	% C	% H	% N
C_3H_7	64.4	58/357	1.4105	42.33	8.29	49.38	42.51	8.09	49.53
C_4H_9	78.3	71/225	1.4192	48.46	9.15	42.39	48.31	9.12	42.39
C_5H_{11}[a]	83.6	63.5/95	1.4266						
C_6H_{13}	86.6	85/63	1.4318						
C_7H_{15}	99.6	70/13	1.4343	59.53	10.71	29.76	59.49	10.47	29.53
C_8H_{17}	94.8	62/3.3	1.4368	61.89	11.04		61.64	10.87	
$C_{10}H_{21}$	89.2	67/0.65	1.4425	65.52	11.55	22.93	65.33	11.40	23.13
Cyclopentyl	82.0	72/77	1.4616	54.03	8.16	37.81	53.98	8.27	37.85
Cyclohexyl	75.2	72/30	1.4693	57.57	8.86		57.51	8.88	

[a] Anal. for pentyl azide using propyl alcohol as solvent: Calcd. for $C_5H_{11}N_3$: C, 53.06; H, 9.80; N, 37.20. Found: C, 53.04; H, 9.92; N, 37.20.

boiling point of pentyl azide is 76.5°/110 mm., or approximately 130–135° at atmospheric pressure, it forms a low boiling azeotrope with propyl alcohol at 51–52°/103 mm. A number of redistillations were required until this was located and the azeotrope broken by means of toluene. The yield was 52%, comparable to that obtained by Henkel and Weygand[7] for hexyl azide. Boyer and Hamer[8] reported the formation of an azeotrope of butyl azide and methanol and also pointed out that the combination of butyl bromide and sodium azide without the use of solvent did not lead to the formation of butyl azide.

Owing to the difficulties described above, the problem of choosing a different solvent for this reaction was studied. The simple aliphatic alcohols were eliminated because of their tendency to form azeotropes with both the alkyl halide and the alkyl azide. Furthermore, the aliphatic alcohols require the use of sealed tubes, while the higher members are insoluble in water and do not dissolve sodium azide. Glycols are good in dissolving sodium azide and many members are miscible in water. However, their solubility for alkyl bromides and iodides is quite low. Our final selection, based upon these solubility considerations, was the alkyl ethers of polyethylene glycols. They were found to be ideally suited for the purpose. They dissolve all of the reactants and products and are easily removed by dissolving in water. A choice of suitable boiling points, considerably higher than those of the reactants and products, is available.

A preparation of pentyl azide was thus carried out in Carbitol, as solvent, by heating at 100° for 20 hr. The reaction mixture was then poured into water, whereupon the pentyl azide separated as an upper layer. No difficulty of azeotrope formation was encountered during the distillation, and an improved yield of 81.4% was obtained. The method is much more convenient than the sealed tube processes reported[7,9] for the preparation of these hazardous alkyl azides. Further studies indicated that the use of activated sodium azide was not necessary, commercial sodium azide giving the same yield of pentyl azide as that of freshly activated sodium azide.

The versatility of this improved procedure was then tested with a series of alkyl and cycloalkyl halides. The data obtained are summarized in Table I. Of these, the butyl,[8] hexyl,[7] cyclopentyl,[10] and cyclohexyl[10] azides have been previously reported. The high yield reported in Table I for heptyl azide was readily duplicated.

No decrease in yield was observed when an alkyl bromide was used in place of an alkyl iodide. The yield of butyl azide from butyl bromide was 78.3% and that from butyl iodide was 78.1%. Similarly, the yield of cyclopentyl azide from cyclopentyl bromide was 82%, while the yield of cyclohexyl azide from cyclohexyl iodide was 75.2%. Boyer, Canter, Hamer, and Putney,[10] using the procedure of Henkel and Weygand,[7] obtained yields of cyclopentyl and cyclohexyl azides of 51 and 68%, respectively.

Three different monoalkyl ethers of diethylene glycol were used. No appreciable difference was found between methyl Carbitol and Carbitol. They are both completely miscible with water and much less soluble in diethyl ether. Their solubility of sodium azide, sodium iodide, and alkyl azide was about the same. The boiling point of butyl Carbitol is 231°. It is less soluble in water and much more soluble in ether than its methyl or ethyl homolog. Slightly more water had to be used with butyl Carbitol in order to dissolve completely the sodium azide. The choice among these three solvents was based solely on the ease of separation. Thus, methyl Carbitol or Carbitol was used for alkyl azides boiling below 156° (hexyl azide), Carbitol for heptyl azide, and butyl Carbitol for octyl azide. For decyl azide, whose estimated[11] atmospheric boiling point is 230°, methyl Carbitol was used, and the small

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[7] Henkel and Weygand, *Ber.*, **76**, 812 (1943).

[8] Boyer and Hamer, *J. Am. Chem. Soc.*, **77**, 951 (1955).

[9] Levene and Rothen, *J. Biol. Chem.*, **115**, 415 (1936); **120**, 759 (1937); **140**, 259 (1941).

[10] Boyer, Canter, Hamer, and Putney, *J. Am. Chem. Soc.* **78**, 325 (1956).

[11] *Vapor Pressure-Temperature Nomograph*, Nomo-Charts Company, P. O. Box 111, Roselle, New Jersey.

amount of it contained in the crude decyl azide was removed by distillation from the higher boiling azide.

Schard[12] has reported the preparation of isopropyl azide by the catalytic addition of hydrazoic acid to propylene. A number of C_4 to C_{10} secondary alkyl azides have been prepared by Levene and coworkers.[9] The latter invariably used sealed tubes to carry out the reaction between alkyl iodide and sodium azide. The yields obtained varied from 26.7% (for 2-ethylpentyl azide) to 81% (for 1-methylheptyl azide). When the sealed tube was not used, the yield of 2-methylhexyl azide was only 16.1% even after 60 hr. heating on a steam bath. The use of sealed tubes for alkyl azides is both hazardous and tedious. A violet explosion has been reported[13] on attempting to seal a tube containing methyl azide. The tediousness is due to the limited capacity of sealed tubes. The largest amount of azide reported[9] to be prepared was 17 grams of 2-ethylheptyl azide, for which seven sealed tubes had to be used. In another case,[9] nine tubes were used for the preparation of 13 grams of 2-ethylpentyl azide. The present method offers no such limitations and hazards. The capacity is limited only by safety considerations. The hazards of working with alkyl azides were considerably reduced by using water and by distillations under reduced pressure behind a safety barricade. No explosion or even noticeable decomposition of the azides was experienced.

EXPERIMENTAL[14]

Pentyl azide. Propyl alcohol as solvent. The pentyl iodide was purified by washing with three 50-ml. portions of a saturated Na_2SO_3 solution and two 50-ml. portions of water. The washed iodide was dried first with magnesium sulfate followed by Drierite. It was then vacuum distilled in the presence of metallic silver through a 13-in. column packed with glass helices. The fraction boiling 88–92°/100 mm., water white, n_D^{20} 1.4961 to 1.4970 was used. The sodium azide was activated by the method of Smith[11] and used at once, after drying under vacuum at water-bath temperature.

A mixture comprising 32.2 g. (0.5 mole) of activated sodium azide, 400 ml. of propyl alcohol, and 80 ml. water was introduced into a 1-l., three-necked flask equipped with a stirrer, thermometer, and reflux condenser. The mixture was rapidly stirred and 99 g. (0.50 mole) of pentyl iodide was added dropwise over a period of 20 min. The mixture was heated to reflux (86–90°) for 24 hr. Considerable solid was present during the entire heating period. After cooling, the reaction mixture was diluted with 200 ml. of ether and poured slowly into 1 l. of water. The lower aqueous layer was extracted with two 200-ml. portions of ether, and the ether extracts were combined with the original upper layer and shaken with four 100-ml. portions of saturated $CaCl_2$ solution and three 100-ml. portions of saturated NaCl solution. The final ether solution was dried, the ether removed, and the residue fractionated under vacuum through the 13-in. packed column. A fraction having a constant boiling point of 51°/92 mm., and weighing 26.6 g., n_D^{20} 1.3862 showed by nitrogen analysis an azide content of only 3.8%. Four successive vacuum fractional distillations were required in order to locate and break the pentyl azide–propyl alcohol azeotrope. This turned out to be the fraction boiling 51–52°/103 mm., obtained in the initial distillation, the azeotrope being broken by addition of toluene and refractionation. The final yield of pentyl azide, b.p. 76.5/110 mm., n_D^{20} 1.4263 was 29.4 g. (52%).

Pentyl azide. Carbitol as solvent. A mixture comprising 27 g. of activated sodium azide, 450 ml. Carbitol, and 75 ml. of water was stirred in the apparatus previously used. Sixty g. (0.30 mole) of purified pentyl iodide was added in one batch. After stirring a few minutes, all of the reactants were completely dissolved. With constant stirring, the solution was heated up to 95° in 3 hr. and maintained at this temperature for an additional 20 hr. After cooling to room temperature, the reaction mixture was added to two 800-ml. portions of ice water. The lower aqueous layer was extracted with two 200-ml. portions of ether. The ether extracts were combined with the original upper layer, and the ether was removed. The residue of 42 g. was vacuum fractionated. Yield, 27.8 g. (81.4%), b.p. 77–78°/112 mm., n_D^{20} 1.4266. These values agree with the boiling point and the n_D^{20} of the pentyl azide described above. Repetition of this experiment with commercial sodium azide (E.K., P2352) (0.26 mole), purified pentyl iodide, 0.20 mole, 300 ml. of Carbitol, and 50 ml. of water, gave 18.9 g. (83.6%) of pentyl azide having the same boiling point and n_D^{20}.

Propyl azide, butyl azide, hexyl azide, heptyl azide, octyl azide, decyl azide, cyclopentyl azide, and *cyclohexyl azide.* These were prepared as described above. The experimental conditions are summarized below:

Azide	Moles NaN_3[a]	Moles Halide	Solvent Type	Ml.	Ml. H_2O
Propyl	0.4	0.3[b]	Methyl Carbitol	450	75
Butyl	0.4	0.3[c]	Methyl Carbitol	450	75
Hexyl	0.4	0.3[b]	Carbitol	450	75
Heptyl	0.26	0.2[b]	Carbitol	300	50
Octyl	0.26	0.2[b]	Butyl Carbitol	300	60
Decyl	0.26	0.2[b]	Methyl Carbitol	300	60
Cyclopentyl	0.26	0.2[c]	Carbitol	300	50
Cyclohexyl	0.40	0.3[b]	Carbitol	150	50

[a] Not activated. [b] Iodide. [c] Bromide.

The experimental results are summarized in Table I.

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(12) Schard, U. S. **2,557,924**, June 26, 1951.

(13) Grundmann and Haldenwanger, *Angew. Chem.*, **62A**, 410 (1950).

(14) Microanalyses by Galbraith Microanalytical Laboratories.