NOTES

Synthesis of 1,3-Diphenyl-1,2,4-triazole

By M. R. Atkinson[1] and J. B. Polya

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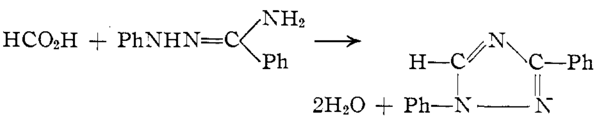
Einhorn, Bischkopff and Szelinski[2] reported the preparation of 1,3-diphenyl-1,2,4-triazole (I) from phenylhydrazine and N-formylbenzamide in 30% aqueous acetic acid. Thompson[3] showed that this reaction affords 1,5-diphenyl-1,2,4-triazole (II) identical with the preparations of Young[4] and Cleve.[5] We were able to confirm the work of Thompson and showed that II is obtained, although in inferior yield, when pyridine containing pyridinium hydrochloride is used instead of dilute acetic acid.[6]

It was necessary to synthesize I in order to assess the work of Einhorn and his collaborators as the physical data characterizing their triazole differ from those which apply to II by the agreement of other authors. The synthesis of I was accomplished by the method of Ponzio[7] which has been found useful in other triazole syntheses.[6,8] Benzamide phenylhydrazone heated with formic acid affords I in a yield of 36%. I, its hydrochloride and picrate differ from the corresponding products described by Einhorn and collaborators.



Experimental

Benzamide phenylhydrazone was prepared by the method of Voswinkel[9] and purified through its picrate, m.p. 196–198°. Benzamide phenylhydrazone (7.20 g.) was refluxed with 99% formic acid (8.0 ml.) on the water-bath for 90 minutes. The product was adjusted to *p*H 8 with aqueous 10% sodium carbonate and extracted with ether (3 × 50 ml.). Distillation of the dried ether extract between 160–220° (2 mm.) afforded oily crystals (4.5 g.) which were dissolved in dry ether (150 ml.) and treated with dry hydrogen chloride to precipitate the hydrochloride of I as a white, microcrystalline powder, m.p. 192–194° (Einhorn, *et al.*, 176°) in a yield of 5.73 g. *Anal.* Calcd. for $C_{14}H_{11}N_3 \cdot HCl$: Cl, 13.76. Found: Cl, 13.70.

The hydrochloride was decomposed with aqueous 10% sodium carbonate (100 ml.) and extracted with ether (3 × 50 ml.) to afford on removing the solvent colorless prismatic crystals of I, m.p. 79–81° (2.71 g., 36%). Purification through the picrate, yellow needles from ethanol, m.p. 161–161.5° (*Anal.* Calcd. for $C_{14}H_{11}N_3 . C_6H_3O_7N_3$: C, 53.33; H, 3.11; N, 18.67. Found: C, 53.35; H, 3.24; N, 17.67) (Einhorn, *et al.*, 148°) and two recrystallizations from petroleum ether (60–80°) raised the m.p. to 82.5–83° (Einhorn, *et al.*, 96–97°).

Anal.[10] Calcd. for $C_{14}H_{11}N_3$: C, 75.99; H, 5.01; N, 18.99. Found: C, 76.34; H, 5.33; N, 19.18.

The triazole and its picrate depress the m.p.'s of authentic II and its picrate,[3] respectively.

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[2] A. Einhorn, E. Bischkopff and B. Szelinski, *Ann.*, **343**, 227 (1905).

[3] Q. E. Thompson, This Journal, **73**, 5914 (1951).

[4] G. Young, *J. Chem. Soc.*, **67**, 1069 (1895).

[5] A. Cleve, *Ber.*, **29**, 2679 (1896).

[6] M. R. Atkinson and J. B. Polya, *J. Chem. Soc.*, in press, (1952).

[7] G. Ponzio, *Gazz. chim. ital.*, **40 i**, 85 (1910).

[8] D. Jerchel and R. Kuhn, *Ann.*, **568**, 185 (1950).

[9] H. Voswinkel, *Ber.*, **36**, 2484 (1903).

[10] Microanalyses by Dr. W. Zimmermann, Commonwealth Scientific and Industrial Research Organization, Melbourne.

The High Field Conductance of an Aqueous Solution of Cadmium Chloride at 25°[1]

By Frederick Eugene Bailey, Jr., and Andrew Patterson, Jr.

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The unusual behavior of cadmium halides in aqueous solution has been the basis for much discussion in the past.[2] Harned and Fitzgerald found that the behavior of aqueous solutions of cadmium chloride in electrolytic cells might be adequately explained[3] in terms of an equilibrium

$$\mathrm{CdCl^+} \rightleftharpoons \mathrm{Cd^{++}} + \mathrm{Cl^-};\ K(0) = 0.011 \text{ at } 25° \qquad (1)$$

it being assumed that the dissociation of $CdCl_2$ into $CdCl^+$ and Cl^- is complete. To investigate this electrolyte from another point of view, we have determined the high field conductance of an aqueous solution of cadmium chloride, 1.697×10^{-4} molar, at 25° relative to potassium chloride.

The procedure employed was identical with that of Gledhill and Patterson.[4] Baker and Adamson C.P. cadmium chloride was recrystallized once from conductivity water; the resulting hydrate was dried for four days in a vacuum oven at 70°, ground in an agate mortar, and again dried for four days in a vacuum oven at 70°. The resulting salt, assumed to be anhydrous, was then stored for use. Both the cadmium chloride and reference electrolyte, potassium chloride, were prepared by weighing in the form of strong stock solutions and then weight diluted to the desired concentrations in the conductance cells. The concentrations were: cadmium chloride, 1.697×10^{-4} molar; potassium chloride, 2.889×10^{-4} molar. The temperature was $25 \pm 0.015°$.

The results are shown in Fig. 1 for two determinations on the same solution. At 200 kv./cm. the fractional high field conductance quotient, $\Delta\lambda/\lambda_0$, has the value 1.07%; this value may be compared with those for potassium chloride, approximately 0.4%, and magnesium sulfate, approximately 3.3%, at the same field. No theory is currently available to permit computation of values for non-symmetrical valence-type electrolytes, although as a rough

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[1] Contribution No. 1133 from the Department of Chemistry, Yale University.

[2] N. V. Sidgwick, "The Chemical Elements and Their Compounds," Oxford University Press, New York, N. Y., 1950, p. 274.

[3] H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 2nd ed., Reinhold Publ. Corp., New York, N. Y., 1950 pp. 418–421.

[4] J. A. Gledhill and A. Patterson, *J. Phys. Chem.*, **56**, 999 (1952).

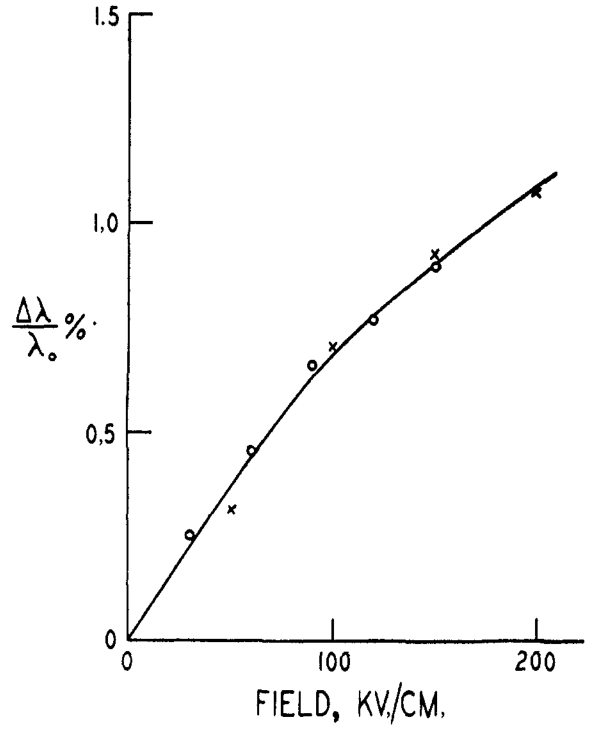

Fig. 1.—The high field conductance of an aqueous solution of cadmium chloride, 1.697×10^{-4} molar, relative to potassium chloride at 25°.

approximation the increase in equivalent conductance has been found[3] to be proportional to $(z_+z_-)^2$; thus, $(z_+z_-)^2 = 4$, and 4×0.4 (for potassium chloride) = 1.6%. The curve has a shape something like that of a strong electrolyte, but fails to bend over at so low a field or in so pronounced a manner as does magnesium sulfate, for example.

Determinations on similar valence-type, but stronger, electrolytes, *e.g.*, calcium chloride, are now under way. When completed, these will offer more information on the influence on the high field behavior of the weak ionization referred to in equation 1, above.

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Quaternary Salts of Halogenated Heterocyclic Nitrogen Compounds[1]

BY CARL TABB BAHNER, WILLIAM K. EASLEY, GEORGE E. BIGGERSTAFF, EMMA BROWN, MARGUERITE CLOSE, MARY MARGUERITE ISENBERG, HAROLD D. LYONS, LILBURN NORTON, EMOGENE STEPHEN, BILLY STUMP, BETTY GAY WALDEN BLANC AND MARY WATKINS

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A previous article[2] has reported the preparation of quaternary salts of halogenated pyridines and quinolines for screening against tumors in mice. The series have been extended by synthesis of the salts of 2-chloropyridine and 3-bromopyridine listed in Table I and the salts of 3-bromoquinoline, 6-chloroquinoline and 4,7-dichloroquinoline listed in Table II. Results of screening tests at the National Cancer Institute are to be published elsewhere.

4,7-Dichloroquinoline was particularly unreactive and was recovered unchanged from mixtures with several halogen compounds although a small quantity of quaternary salt was obtained in a few cases. Attempts to prepare quaternary salts of 8-chloroquinoline by reaction of the base with substituted phenacyl bromides at 45° produced the hydrobromide as the chief crystalline product instead of the expected quaternary salt.

TABLE I

SALTS OF SUBSTITUTED PYRIDINES

Salt from 2-Chloropyridine and:	Empirical formula	M.p., °C.	Ionic halogen, % Calcd.	Ionic halogen, % Found[a]
p-Methoxyphenacyl bromide	$C_{14}H_{13}BrClNO_2$	171	23.32	23.04
β-Naphthacyl bromide	$C_{17}H_{13}BrClNO$	175	22.04	22.00
5,6,7,8-Tetrahydro-β-naphthacyl bromide	$C_{17}H_{17}BrClNO$	190	21.79	21.69
4,4′-Bis-(bromoacetyl)-phenyl ether	$C_{26}H_{20}Br_2Cl_2N_2O_3$	210	25.01	24.79
3-Bromopyridine and:				
β-Phenylethyl iodide	$C_{13}H_{14}BrIN$	152–154	32.45	32.29
Iodoacetone	C_8H_9BrINO	180	37.10	37.29
Glycerol-α-monochlorohydrin	$C_8H_{11}BrClNO_2$	216	13.20	13.07
Iodoacetonitrile	C_7H_6BrIN	177–178	39.06	38.83
4,4′-Bis-(bromoacetyl)-phenyl ether	$C_{26}H_{20}Br_4N_2O_3$	220	21.95	21.52

[a] Average of two analyses.

TABLE II

QUATERNARY SALTS OF HALOGENATED QUINOLINES

Salt from	Empirical formula	M.p., °C.	Ionic halogen, % Calcd.	Ionic halogen, % Found[a]
3-Bromoquinoline and:				
Glycerol-α,γ-dibromohydrin	$C_{12}H_{12}Br_3NO$	251	18.76	18.91
3,4-Dihydroxyphenacyl chloride	$C_{17}H_{13}BrClNO_3$	245	[b]	
p-Methoxyphenacyl bromide	$C_{18}H_{15}Br_2NO_2$	241	18.28	18.30
p-Chlorophenacyl bromide	$C_{17}H_{12}Br_2ClNO_2$	240	18.10	18.15
p-Bromophenacyl bromide	$C_{17}H_{12}Br_3NO$	237	16.45	16.63
6-Bromoquinoline and:				
Glycerol-α,γ-dibromohydrin	$C_{12}H_{12}Br_3NO$	241	18.76	19.05
Allyl bromide	$C_{12}H_{11}Br_2N$	171	24.29	24.07
6-Chloroquinoline and:				
Iodoacetone	$C_{12}H_{11}ClINO$	186–187	36.50	36.54
p-Iodophenacyl bromide	$C_{17}H_{20}BrClINO$	230	16.36	16.32
4,7-Dichloroquinoline and:				
Phenacyl bromide	$C_{16}H_{12}BrCl_2NO$	163	20.12	19.93
p-*t*-Butylphenacyl bromide	$C_{12}H_{20}BrCl_2NO$	185–186	17.68	17.50

[a] Average of two analyses. [b] Calcd.: C, 51.73; H, 3.32. Found: C, 51.58; H, 3.49.

8-Chloroquinoline Hydrobromide.—Prepared by direct reaction of equimolecular quantities of the base and concentrated hydrobromic acid or as the principal crystalline prod-

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[2] C. T. Bahner, W. K. Easley, M. D. Pickens, H. D. Lyons, L. L. Norton, B. G. Walden and G. E. Biggerstaff, THIS JOURNAL, **73**, 3499 (1951).