Incorporation of Nicotinamide-4-*d* into DPN.—One hundred and ten mg. of DPN (Pabst) was incubated at 37° for 3 hours in the presence of 100 mg. of nicotinamide-4-*d* with 5 ml. of beef spleen DPNase (*ca.* 750 units). After inactivation of the enzyme by heating the reaction mixture for 10 minutes in a water-bath at 70°, the mixture was cooled and centrifuged. The precipitate was washed with 5 ml. of H_2O and the combined supernatants were added to a Dowex-1 formate exchange column (20 × 1 cm.). The column was washed with 200 ml. of H_2O followed by 0.1 *M* formic acid which eluted the DPN. Seventy-seven mg. of material containing 68% DPN by enzymatic assay was recovered by lyophilization from the DPN-containing fractions. A portion of this DPN was analyzed for excess deuterium with glycine as a diluent.[7]

Reduction of DPN Containing Nicotinamide-4-*d*.—Forty mg. of the above material containing 27 mg. of pure DPN was reduced in 5 ml. of 1.3% $NaHCO_3$ solution with 30 mg. of $Na_2S_2O_4$.[11] After the reaction was complete, the mixture was pipetted into 15 ml. of absolute ethanol together with 0.5 ml. of wash water. After 20 minutes at −20°, the mixture was centrifuged free of precipitated salts. The latter were dissolved in 1 ml. of H_2O and the salts were reprecipitated with 3 ml. of absolute ethanol. The supernatants were combined, poured into 90 ml. of absolute ethanol and stored at −15° overnight. The resulting precipitate was centrifuged, washed with ether and dried *in vacuo*. The dried powder weighed 42 mg. and contained 18 mg. of reduced DPN by enzymatic assay.

Enzymatic Oxidation of Reduced DPN Containing Nicotinamide-4-*d*.—Thirty-one mg. of the reduced DPN (containing 13.2 mg. of reduced DPN by enzymatic assay) was oxidized with 0.18 ml. of 0.1 *M* sodium pyruvate in the presence of crystalline muscle lactic dehydrogenase in 5.0 ml. of 0.1 *M* phosphate buffer, *p*H 7.4. When the reaction was complete as indicated by the disappearance of the absorption band at 340 mμ, the enzyme was destroyed by heating for 1 minute in a boiling water-bath. The reaction mixture was cooled, adjusted to *p*H 1–2 with 6 *N* H_2SO_4 and 50.0 mg. of unlabeled lithium-L-lactate was added (26.9-fold dilution). The solution was centrifuged to remove denatured protein and the lactic acid was recovered by ether extraction and converted to its phenacyl ester which was analyzed for D, all as previously described.[8]

(11) P. Ohlmeyer, *Biochem. Z.*, **297**, 66 (1938).

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Azabenzazulenes. II. Attempted Preparation of Three Azatribenzazulenes and One Diazatribenzazulene

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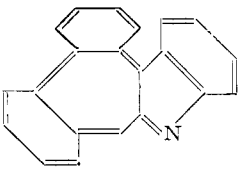
Studies on the preparation of 1-azatribenzazulenes are of interest because the additional benzene ring adds two double bonds for conjugation but is likely to make the tribenzo derivatives slightly more strained and much less nearly coplanar than the dibenzo derivatives.

The method used for the preparation of 1-azadibenzazulenes[2] was not successful for the preparation of either 1-azatribenz[b,e,g]azulene (I) or 1-azatribenz[b,f,h]azulene (II). The ketones used in the attempted preparations were, respectively, dibenzo[a,c][1,3]cycloheptadien-6-one (III) and dibenzo[a,c][1,3]cycloheptadien-5-one (IV). Ketone III was prepared with some improvements by a



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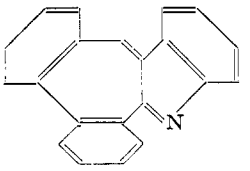


II

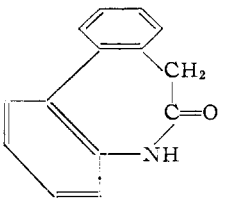
combination of the best reported methods[3a,b,c] in 5 steps in an over-all yield of 61%. Ketone IV was prepared in 14.5% over-all yield in ten steps by the method of Rapoport and Williams[4] except that 2′-cyanodiphenyl-2-carboxylyl chloride was obtained by the method of Bell.[5]

Ketone III was converted readily to 1,8-dihydro-1-azatribenz[b,e,g]azulene (V) by the method of Rogers and Corson.[6] However, ketone IV did not yield the expected indole, 1,8-dihydro-1-azatribenz[b,f,h]azulene (VI), when the foregoing method was tried. This failure was quite unexpected because 5H-6,7,8,9-tetrahydrocycloheptabenzen-5-one[2] did yield an indole with the foregoing method.

The dehydrogenation of V was unsuccessfully attempted by using (1) the chloranil[7] and (2) the palladium-on-charcoal[8] methods both of which had been used successfully for the preparation of 1-azadibenzazulenes.[2] Also unsuccessful for the dehydrogenation of V were (3) iodine and nitrobenzene,[9] (4) selenium in sealed tube[10] and (5) palladium-on-charcoal in sealed tube methods.

It should be noted that no benzazulene with a quinonoid structure has been reported and that 1-azatribenz[b,e,g]azaulene (I) would have an ortho-quinonoid structure in at least one benzene nucleus in each of the resonance forms.

Oxindole[11] and homophthalimide[12] both have a methylene group which will condense with benzaldehyde. However, it was found that the methylene group of the lactam of 2-amino-2′-biphenylacetic acid (VII) would not condense with benz-



VII

aldehyde, nitrosobenzene[13] or *p*-N,N-dimethylaminonitrosobenzene.[13] If the condensation reaction with VII had been successful, cyclization attempts to prepare azazulenes would have been made.

(1) From the M.S. thesis of W. L. S., 1952, and Ph.D. Dissertation of Z. B. P., 1954, both from West Virginia University.

(2) C. W. Muth, D. O. Steiniger and Z. B. Papanastassiou, THIS JOURNAL, **77**, 1006 (1955).

(3) (a) D. M. Hall, M. S. Laeslie and E. E. Turner, *J. Chem. Soc.*, 711 (1950); (b) T. Sakan and M. Nakazaki, *C.A.*, **46**, 5036 (1952); (c) C. W. Moore and J. F. Thorpe, *J. Chem. Soc.*, **93**, 165 (1908).

(4) H. Rapoport and A. Williams, THIS JOURNAL, **71**, 1774 (1949).

(5) F. Bell, *J. Chem. Soc.*, 3247 (1928).

(6) C. U. Rogers and B. B. Corson, THIS JOURNAL, **69**, 2910 (1947).

(7) W. Treibs, R. Steinert and W. Kirchoff, *Ann.*, **581**, 54 (1953).

(8) A. G. Anderson, J. A. Nelson and J. J. Tazuma, THIS JOURNAL, **75**, 4980 (1953).

(9) W. Treibs, *Ann.*, **576**, 110 (1952).

(10) V. Prelog and K. Balenovic, *Ber.*, **74**, 1508 (1941).

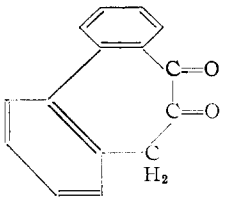
(11) A. Wahl and P. Bagard, *Bull. soc. chim.*, [4] **5**, 1033 (1909).

(12) A. Meyer, *C.A.*, **30**, 2962 (1936).

(13) P. W. Neber and H. Kappler, *Ber.*, **57**, 778 (1924).

Lactam VII was synthesized by the catalytic reduction of methyl 2-nitro-2′-biphenylacetate which was obtained by the Arndt–Eistert synthesis on 2-nitro-2′-biphenylcarboxylic acid.

Benzo[d]tropolone exhibits ketonic properties[14] whereas tropolone does not.[15] Ketone VIII does not enolize to form dibenzo[c,e]tropolone which



VIII

would have a cycloheptatriene nucleus as also would the azatribenzazulenes. Therefore, one benzene ring decreases the aromatic character of the tropolone nucleus and two benzene rings prevent the formation of the tropolone nucleus. Similar considerations indicate that the azatribenzazulenes are not likely to be stable if their synthesis is at all possible.

Experimental[16]

2,2′-Di-(bromomethyl)-diphenyl.—The temperature always was maintained below 2° as 200 ml. of concentrated sulfuric acid and 217.0 g. (1.01 moles) of finely powdered 2,2′-di-(hydroxymethyl)-diphenyl[3a] was added slowly to 1500 ml. of 48% hydrogen bromide solution. The mixture was brought to reflux temperature during *ca.* one hour and maintained at this temperature for an additional hour. After cooling the reaction mixture, a solid was formed which was separated by decanting the supernatant liquid. The liquid was extracted with benzene, and the benzene extract was used to dissolve the solid which had been separated previously. The benzene solution then was washed with water, 10% sodium bisulfite solution, water and dried. On concentrating this solution, 336.7 g. (98%) of large white crystals, m.p. 91–93° (lit.[17] 91–93°), separated.

Dibenzo[a,c][1,3]cycloheptadien-6-one (III).—5-Cyanodibenzo[a,c][1,3]cycloheptadien-6-imine was prepared independently in 96% yield by the method of Sakan and Nakazaki the publication of which was abstracted later.[3b] We were not able to prepare ketone III from the imino cyano compound by the reported method.[18] The following successful method is a modification of the method of Moore and Thorpe.[3c]

A solution of 7.0 g. (0.03 mole) of the foregoing imino cyano compound in 90 ml. of concentrated sulfuric acid was left for *ca.* 24 hours at room temperature. At the end of that period it was poured slowly into the distilling flask of a steam distillation apparatus which already contained 60 ml. of concentrated sulfuric acid diluted with 460 ml. of water. The mixture was heated to *ca.* 100° and a fast current of steam was introduced. Approximately 8–10 liters of cloudy distillate was collected and cooled for two days. The yield was 4.6 g. (74%) of white crystals, m.p. 78–80° (lit.[18] 78–79°).

The oxime of ketone III had m.p. 191–193° (lit.[18] 189°). A phenylhydrazone could not be prepared.

1,8-Dihydro-1-azatribenz[b,e,g]azulene (V).—From 11.0 g. (0.053 mole) of ketone III and 10.5 g. (0.06 mole) of phenylhydrazine in 60 ml. of glacial acetic acid,[6] 12.4 g. (83%) of a white powder, m.p. 257–260°, was obtained after recrystallization from benzene.

The infrared absorption spectrum of the foregoing product in chloroform or benzene solutions had a definite absorption peak at 3.6 μ which is attributed to the N–H group.

Anal. Calcd. for $C_{21}H_{15}N$: C, 89.65; H, 5.37; N, 4.98. Found: C, 89.93; H, 5.56; N, 4.53.

Dibenzo[a,c][1,3]cycloheptadien-5-one (IV).—2′-Cyanodiphenyl-2-carboxylyl chloride was prepared by the method of Bell.[5] The subsequent steps for the preparation of IV were the same as reported[4] except for the hydrolysis of 6-cyanodibenzo[a,c][1,3]cycloheptadien-5-imine to IV which was carried out as described for III.

6-Cyanodibenzo[a,c][1,3]cycloheptadien-5-imine had m.p. 176–178° (lit.[4] 160–161°,[19] 177–178°).

The 2,4-dinitrophenylhydrazone of ketone IV was prepared in the usual way, m.p. 240° dec. (lit.[4] 240°).

Attempted Preparation of 1,4-Dihydro-1-azatribenz[b,f,h]azulene (VI).—A solution of 4.0 g. (0.0193 mole) of ketone IV and 2.1 g. (0.0194 mole) of phenylhydrazine in 50 ml. of glacial acetic acid[6] was heated on a steam-bath for 2 hours. After concentrating and cooling the reaction mixture, 2.2 g. of material, m.p. 146–166°, was obtained. Addition of water to the filtrate yielded 2.0 g. of solid, m.p. 170–180°. Repeated crystallizations of the combined solids from methanol–benzene mixture produced 1.2 g. of yellow crystals, m.p. 169–170°.

Anal. Calcd. for $C_{21}H_{18}N_2$ (phenylhydrazone of IV): C, 84.52; H, 6.07; N, 9.39. Found: C, 84.24; H, 6.39; N, 9.07.

The aqueous hydrochloric acid method[6] yielded, after recrystallizations from methanol and ethanol, material m.p. 160–165°; from the method of Armit and Robinson[20] material with m.p. 163–166° was obtained; the phenylhydrazone with zinc chloride yielded resinous material.

2-Nitro-2′-biphenylcarboxylyl Chloride.—Approximately 70 ml. of purified thionyl chloride[21] was added to 31.33 g. (0.129 mole) of 2-nitro-2′-biphenylcarboxylic acid in a distilling flask fitted with a receiver protected with a drying tube. After standing overnight the reaction mixture was concentrated by distillation under reduced pressure. The resulting residue was diluted repeatedly with benzene or ether and concentrated. The yellow crystalline mass after standing over anhydrous sodium hydroxide in a vacuum desiccator weighed 33.1 g. (98%), m.p. 58–61°. Crystallization was accomplished from benzene–ether mixture by cooling with Dry Ice. The acid chloride reacted with concentrated ammonium hydroxide to give the amide which after crystallization from methanol had m.p. 140–141°.

Anal. Calcd. for $C_{12}H_{10}O_3N_2$: C, 64.46; H, 4.16. Found: C, 64.65; H, 3.89.

Methyl 2-Nitro-2′-biphenylacetate.—During 75 minutes 25.87 g. (0.099 mole) of 2-nitro-2′-biphenylcarboxylyl chloride in 225 ml. of anhydrous ether was added to approximately 0.43 mole of diazomethane[22] in 800 ml. of ether with constant stirring and protection from moisture. The reaction temperature was kept between −10 and −15° during the addition of the acid chloride and then at about 0° for 12 hours.

The ethereal reaction mixture was concentrated under reduced pressure. The residue was dissolved nearly completely in 100 ml. of ether plus a little benzene and then the mixture was cooled with Dry Ice. As the mixture was stirred and allowed to warm to room temperature, 15.6 g. of a yellow powder formed, m.p. 74–77° dec.

The foregoing yellow solid and the oily residue obtained from its mother liquor were subjected separately to the Wolff rearrangement according to the improved method of Newman and Beal[23] to give 16.10 g. of light orange oil, b.p. 165–170° (1 mm.), m.p. 41–46°. Crystallization from methanol gave dense, pale yellow crystals, m.p. 46–48°. The overall yield of methyl 2-nitro-2′-biphenylacetate from 2-nitro-2′-biphenylcarboxylyl chloride was 60%. When 2-nitro-2′-biphenylcarboxylic acid was converted to methyl 2-nitro-2′-biphenylacetate without isolating any of the intermediates,

(14) D. S. Tarbell and J. C. Bill, THIS JOURNAL, **74**, 1234 (1952).

(15) J. W. Cook, A. R. Gibb, R. A. Raphael and A. R. Somerville, *J. Chem. Soc.*, 503 (1951).

(16) All temperatures are uncorrected; all elemental analyses were made by Galbraith Laboratories, Knoxville, Tenn.

(17) D. M. Hall and E. E. Turner, private communication.

(18) J. Kenner and E. G. Turner, *J. Chem. Soc.*, **99**, 2101 (1911).

(19) Professor H. Rapoport reports, in a private communication, that his sample of imino cyano compound, after standing 4 years, has this higher melting point.

(20) J. W. Armit and R. Robinson, *J. Chem. Soc.*, 3199 (1951).

(21) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 381.

(22) F. Arndt, "Diazomethane" in C. R. Noller (Ed.), "Organic Syntheses," Vol. XV, John Wiley and Sons, Inc., New York, N. Y., 1938, p. 3.

(23) M. S. Newman and P. F. Beal III, THIS JOURNAL, **72**, 5163 (1950).

the over-all yield was about the same as in the foregoing experiments and there was a great saving of time.

Anal. Calcd. for $C_{15}H_{13}O_4N$: C, 66.41; H, 4.64; N, 5.16. Found: C, 66.39; H, 4.83; N, 5.15.

Lactam of 2-Amino-2'-biphenylacetic Acid (VII).—In a low pressure Parr apparatus methyl 2-nitro-2'-biphenylacetate in the presence of platinum was reacted with hydrogen at room temperature. The amount of hydrogen needed to reduce the nitro group to an amino group was used in the course of one hour. Approximately 75 ml. of absolute ethanol was used for 10.56 g. (0.039 mole) of the nitro compound. After the filtered reaction mixture had stood at room temperature for 15 hours, 4.15 g. of long white needles, m.p. 231–234°, had separated. Concentration of the filtrate yielded an additional 1.66 g. of white crystals, m.p. 230–233°, to make the total yield 72%. Attempts to diazotize and acetylate this product were unsuccessful. Three crystallizations of the white needles from ethanol gave material with m.p. 231–233°.

Anal. Calcd. for $C_{14}H_{11}ON$: C, 80.36; H, 5.30; N, 6.70. Found: C, 80.21; H, 5.21; N, 6.69.

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Action of Alkali on Allyl Alcohol Chloroiodides. "β-Epichlorohydrin" (2-Chloroallyl Alcohol)

BY WAYLAND E. NOLAND AND BRUCE N. BASTIAN[1]

RECEIVED FEBRUARY 5, 1955

In 1891 Bigot[2] reported that action of powdered sodium hydroxide on allyl alcohol chloroiodides in ether solution yielded, as distillable products, allyl alcohol (19%), epichlorohydrin (12%), "β-epichlorohydrin" (10%), epiiodohydrin (1.8%) and "β-epiiodohydrin" (1.2%). The only evidence given for identification of allyl alcohol (b.p. 96°), epichlorohydrin (b.p. 115–116°) and epiiodohydrin (b.p. 160–162°) was their boiling points. "β-Epichlorohydrin" (b.p. 132–134°) was shown by elemental analysis and vapor density to be an isomer of epichlorohydrin. The choice between the unknown 2-chlorotrimethylene oxide (3-chlorocycloöxabutane) structure and 2-chloroallyl alcohol was based on an extensive study of the chemical properties of "β-epichlorohydrin." Bigot was unaware that 2-chloroallyl alcohol had been prepared nine years before, in 1882, by Henry[3] and van Romburgh.[4] "β-Epiiodohydrin" (b.p. 172–174°) had the correct iodine analysis for an isomer of epiiodohydrin, but the only chemical property reported was inertness to concentrated potassium hydroxide solution at 100°. The 2-iodotrimethylene oxide (3-iodocycloöxabutane) structure was assigned to "β-epiiodohydrin" by analogy with "β-epichlorohydrin."

In 1944 Nilsson and Smith[5] repeated Bigot's procedure in order to determine the heat of combustion of "β-epichlorohydrin." Epichlorohydrin (11.5%) and "β-epichlorohydrin" (6.3%) were obtained, but the other fractions were not investigated. The identity of epichlorohydrin was proved by comparison of physical properties with authentic samples. The measured heat of combustion of "β-epichlorohydrin" was 404.0 ± 0.2 kcal. per mole at 19.3°, where "β-epichlorohydrin" is a liquid and hydrogen chloride is in aqueous solution.[5,6] The structure of "β-epichlorohydrin" proposed by Bigot[2] was accepted although the molar refractivity (21.76) did not agree well with that calculated for 2-chlorotrimethylene oxide (20.85).[7] Nilsson and Smith did not notice the remarkable similarity of the physical properties which they reported for "β-epichlorohydrin" to those of 2-chloroallyl alcohol (see Table I).

TABLE I

COMPARISON OF PHYSICAL PROPERTIES OF "β-EPICHLOROHYDRIN" AND 2-CHLOROALLYL ALCOHOL

	Cl, %	B.p., °C.	n_D	d_4	Molar refractivity
"β-Epichlorohydrin"[a]	38.24 (found)	133.0–133.8 (atm.)	$1.4588^{20°}$	$1.1618^{20°}$	21.76 (found)
2-Chloroallyl alcohol[b]	38.32 (calcd.)	135–135.5 (752 mm.)	$1.4573^{19°}$	$1.1601^{19°}$	21.99[c] (calcd.)

[a] Reference 5. [b] A. N. Nesmeyanov and K. K. Kochetkov, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 76 (1949) [*C.A.*, **43**, 7412 (1949)]. [c] Reference 7.

Formation of a four-membered oxide ring is difficult. For example, the rate of propylene oxide formation from 1-chloro-2-propanol (propylene chlorohydrin) with base is 10,000 times faster than the rate of trimethylene oxide formation from the isomeric 3-chloro-1-propanol (trimethylene chlorohydrin).[8] The expected difficulty in closing a trimethylene oxide ring, and the existence of a plausible alternative involving elimination of hydrogen iodide from 2-chloro-3-iodo-1-propanol to give 2-chloroallyl alcohol, cast doubt upon the 2-chlorotrimethylene oxide structure for "β-epichlorohydrin." This, together with our belief that the reported reactions and physical properties of "β-epichlorohydrin" could better be interpreted as those of 2-chloroallyl alcohol caused us to reinvestigate the structure of "β-epichlorohydrin."

Since Bigot[2] did not state the amount of powdered sodium hydroxide used, the molar ratio of sodium hydroxide to allyl alcohol chloroiodides was varied from 1.15 to 3.19. Increasing the amount of alkali reduced the yield of distillable products and changed the nature of the higher boiling fractions. In contrast to the report of Bigot, allyl alcohol was obtained only in small amount. The presence of epichlorohydrin was confirmed. The fraction corresponding in physical properties to the "β-epichlorohydrin" of Bigot[2] and Nilsson and Smith[5] had an infrared spectrum identical with that

(1) From the M.S. Thesis of Bruce N. Bastian, University of Minnesota, 1954. On training assignment from the U. S. Air Force Institute of Technology.

(2) A. Bigot, *Ann. chim. et phys.*, [6] **22**, 433 (1891).

(3) L. Henry, *Compt. rend.*, **95**, 849 (1882).

(4) P. van Romburgh, *Rec. trav. chim.*, **1**, 233 (1882).

(5) T. Nilsson and L. Smith, *Svensk Kem. Tidskr.*, **56**, 156 (1944).

(6) L. Smith and E. Schjånberg, *ibid.*, **43**, 218, 221 (1931).

(7) Calculated from the atomic refractivities and the correction for a 4-membered ring given in S. M. McElvain, "The Characterization of Organic Compounds," revised ed., The Macmillan Co., New York, N. Y., 1953, p. 35. (Nilsson and Smith[5] used the calculated value of 20.36.)

(8) W. P. Evans, *Z. physik. Chem.*, **7**, 337 (1891).