explained reaction pathway. Since, at the reaction conditions used, considerable 2-furaldehyde is evolved from uronic acids, it must also contribute to product formation in this reaction. Assuming that all of the reductic acid labeled at C-1–C-3 formed during uronic acid decomposition is 2-furaldehyde derived and using the radioisotopic label distribution figures obtained herein, it can be concluded that, of the reductic acid-^{14}C formed from D-galacturonic acid-1-^{14}C, all of the C-1–C-3-labeled product and 15% of the C-2-labeled product are derived from 2-furaldehyde. The remaining 75%, labeled exclusively at C-2, must be formed by a mechanism unique to hexuronic acids.

Experimental Section

Materials and Methods.—Specific activities of labeled compounds were determined on a Model No. 3003 Packard Tricarb spectrometer using an internal toluene-^{14}C standard. D-Xylose-1-^{14}C was obtained from CalBiochem, Los Angeles, Calif. Radiochemically inert reductic acid was prepared from pectin as described in a previous report[9] and had mp 211–212°, λ_{max} 267 mμ (ϵ 13,300) (95% ethanol). Thin layer chromatography was performed on silica gel GF coated glass plates and spots were detected with either aniline hydrogen phthalate spray reagent or uv irradiation.

Reductic Acid-^{14}C From D-Xylose-1-^{14}C.—To an 8-mm pyrex glass tube was added 25 μCi of D-xylose-1-^{14}C (200 mg) and 1.0 ml of 5% sulfuric acid. The tube was sealed and heated at 150° for 2 hr and the contents were then transferred to a beaker and neutralized with barium carbonate. The resulting solution, after filtration through Celite, was passed through a column of Dowex 50 (hydrogen form) and evaporated to dryness. Thin layer chromatograms of the residue using chloroform–acetic acid (9:1) as irrigant indicated that reductic acid was the major product. To the residue was added 1.50 g of radiochemically inert reductic acid and the sample was recrystallized from N,N-dimethylformamide: yield 1.37 g. The resulting crystals were sublimed five times at 140° (0.1 mm), whereupon a constant specific activity of 4.20 × 10^{-3} μCi/mmol was attained.

Reductic Acid-^{14}C from 2-Furaldehyde-α-^{14}C.—The 2-furaldehyde-α-^{14}C used in this experiment was prepared essentially by the method described by Hughs and Acree.[10] To 750 ml of 5.0 *N* sulfuric acid was added 75 μCi (3.0 g) of D-xylose-1-^{14}C and the solution was slowly distilled. At the end of 6 hr, 250 ml of distillate (containing the 2-furaldehyde-α-^{14}C) was collected. This solution was made 5% in sulfuric acid and was heated 1.5 hr at 150° in a glass-lined Parr bomb. Reductic acid was qualitatively detected, isolated, and purified as described above with 3.0 g of inert reductic acid being used as diluent. The pure product (2.0 g) had a specific activity of 1.98 × 10^{-3} μCi/mmol.

Chemical Degradation of the Reductic Acids-^{14}C.—A 1.2-g sample of reductic acid-^{14}C (specific activity 4.20 × 10^{-3} μCi/mmol) derived from D-xylose-1-^{14}C was converted into succinic acid by permanganate oxidation as described in a previous report.[9] After recrystallization from water, the succinic acid (mp and mmp 182°) had a specific activity of 1.74 × 10^{-3} μCi/mmol. This material (500 mg) was subjected to a Curtius degradation as described by Benson and Bassham[11] to give crystalline ethylenediamine dihydrochloride (mp and mmp 203°) having a specific activity of 1.40 × 10^{-5} μCi/mmol. Repetition of the above experiments using 2-furaldehyde-α-^{14}C derived reductic acid-^{14}C (specific activity 1.90 × 10^{-3} μCi/mmol) gave succinic acid having a specific activity of 0.82 × 10^{-3} μCi/mmol and subsequently, ethylenediamine dihydrochloride having a specific activity of 2.2 × 10^{-5} μCi/mmol.

Registry No.—2,3-Dihydroxy-2-cyclopenten-1-one-2-^{14}C, 19214-81-4; D-xylose-1-^{14}C, 19588-10-4; 2-furaldehyde-α-^{14}C, 19238-30-3.

(10) E. E. Hughes and S. F. Acree, *J. Res. Natl. Bur. Std.*, **21**, 327 (1938); **23**, 293 (1939).

(11) A. A. Benson and J. A. Bassham, *J. Amer. Chem. Soc.*, **70**, 3939 (1948).

Rearrangement of Azidoquinones. III. Reaction of 1,4-Benzoquinone with Sodium Azide

HAROLD W. MOORE, H. RAYMOND SHELDEN,
AND DALE F. SHELLHAMER

Department of Chemistry, University of California at Irvine, Irvine, California 92664

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In 1915, Oliveri-Mandalá and Calderao[1,2] showed that 1,4-benzoquinone reacts with hydrazoic acid in benzene to give 2-azido-1,4-benzohydroquinone (**1**). Twenty years later Fieser and Hartwell[3] obtained an azidohydroquinone, believed to be the same as that reported in the earlier work,[1,2] when an acetic acid solution of 1,4-benzoquinone was treated with sodium azide. We have reinvestigated this latter reaction and find the product to be 2,5-diazido-1,4-benzohydroquinone (**2**). The structure of **2** is based upon its spectral properties and upon its conversion into a diacetate (**3**), 2-amino-5-azido-1,4-benzoquinone (**4**), 2,5-diamino-1,4-benzoquinone (**5**), and the γ-cyanomethylene-$\Delta^{\alpha,\beta}$-butenolide (**6**).

Addition of excess sodium azide to an acetic acid solution of 1,4-benzoquinone resulted in a mildly exothermic reaction followed by the precipitation of diazide **2** in 33% isolated yield. The nmr spectrum of this *highly explosive* compound is consistent for the diazide structure, showing only one sharp singlet at δ 6.53 for the two equivalent aromatic protons. The ir spectrum of **2** shows characteristic absorptions for the phenolic hydroxyl and azide groups at 3300 and 2120 cm^{-1}, respectively. The hydroquinone structure was confirmed by the formation of a diacetate derivative, **3**, in 92% yield when **2** was treated with acetic anhydride. The spectral (nmr, ir, and mass spectrum) properties and combustion analysis of **3** are in agreement with its formulation. This diacetate is a relatively stable compound, melting with decomposition at 160–161°. The diacetate reported by Oliveri-Mandalá and Calderao[2] for monoazidehydroquinone **1** melted from 115 to 120° and decomposed at 140°.

These data, although consistent for **2** as the structure of the diazidohydroquinone, do not rule out other possible formulations, particularly with regard to the orientation of the two azide substituents. In order to establish this relationship, diazide **2** was converted into a known compound, 2,5-diamino-1,4-benzoquinone[4] (**5**) and to γ-lactone **6** (Scheme I). The key intermediate in both of these transformations is 2-amino-5-azide-1,4-benzoquinone (**4**). We have previously shown[5] that azidohydroquinones readily disproportionate to give aminoquinones and, when this reaction was applied to the azidohydroquinone, **2**, the required 2-amino-5-azido-1,4-benzoquinone (**4**) was obtained in 75% yield. The nmr spectrum of **4** strongly indicates that the azido and amino groups are in the 2 and 5 positions since the

(1) E. Oliveri-Mandalá and E. Calderao, *Gazz. Chim. Ital.*, **45**, 307 (1915).

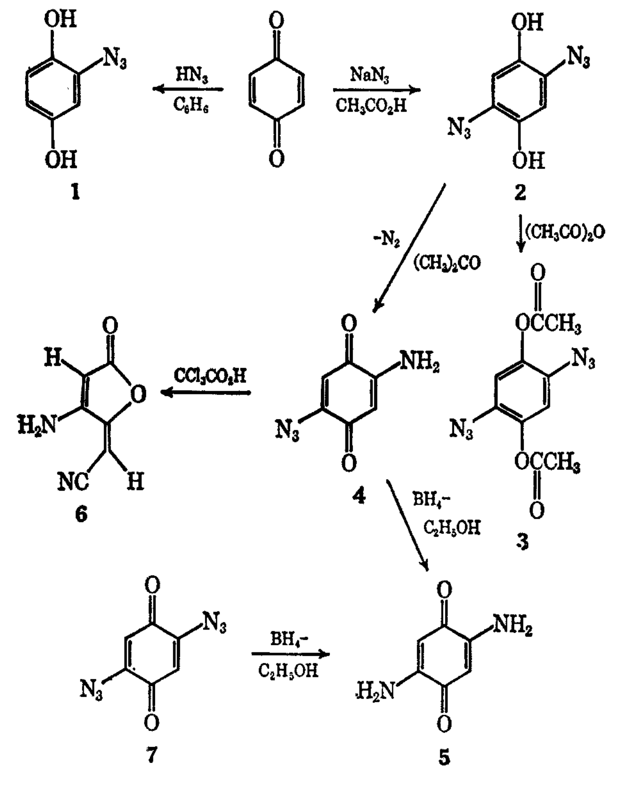
(2) E. Oliveri-Mandalá and E. Calderao, *ibid.*, **45**, 120 (1915).

(3) L. F. Fieser and J. L. Hartwell, *J. Amer. Chem. Soc.*, **57**, 1482 (1935).

(4) F. Kehrman and G. Betsch, *Ber.*, **30**, 2095 (1897).

(5) H. W. Moore and H. R. Shelden, *J. Org. Chem.*, **33**, 4019 (1968).

Scheme I



vinyl protons appear as sharp singlets at δ 6.00 and 5.68.[6] The ir spectrum of **4** also gives critical structural data for the azidoaminoquinone, showing absorptions for the primary amino group at 3310 and 3110 cm^{-1}, an azide group at 2140 cm^{-1} and quinone carbonyl at 1660 cm^{-1}.

Sodium borohydride reduction of **4** gives 2,5-diamino-1,4-benzoquinone[4] (**5**). However, this compound did not melt under 360° even though the reported melting point is 325-330°.[4] Only a color change from deep purple to black was observed at the latter temperature. The spectral properties of **5** are in complete agreement with its structure. The nmr spectrum of **5** shows singlet absorptions for the four amino protons and for the two equivalent vinyl protons at δ 7.35 and 5.32, respectively. The ir spectrum shows characteristic absorptions for the amino group at 3410 and 3315 cm^{-1} and for the quinone carbonyl at 1560 cm^{-1}. The mass spectrum of **5** shows a molecular ion at *m/e* 138, consistent with the formulation $C_6H_6N_2O_2$. 2,5-Diamino-1,4-benzoquinone was prepared by an independent pathway involving borohydride reduction of 2,5-diazido-1,4-benzoquinone (**7**), and was shown to be identical in all respects with compound **5** described above.

Azidoquinones undergo a highly stereoselective rearrangement in acidic medium to give γ-cyanoalkylidene-$\Delta^{\alpha,\beta}$-butenolides.[7] The isomer obtained is the one in which the nitrile group is *trans* to the lactone oxygen. The other substituent on the exocyclic double bond is the one which was originally adjacent to the azide group in the starting quinone. In order to confirm the structure of **4** and, therefore, also of **2** and **5**, this reaction was carried out with **4** in trichloroacetic acid, and γ-lactone **6** was obtained in 44% yield. The oreintation of the protons in **6** and thus of the azido and amino groups in **4** are assigned from the nmr spectrum of the lactone. These vinyl protons in **6** give rise to an AB pattern centered at δ 5.62 showing a coupling constant of 1.6 cps. This observed coupling is characteristic of protons in a 1,4-*trans-trans* relationship on the butadiene moiety of the γ-alkylidene-$\Delta^{\alpha,\beta}$-butenolide ring system.[7] This is in complete agreement with the work of Bothner-By, *et al.*,[8-12] who have investigated long-range coupling in a large number of butadienes and found that 1,4-vinyl protons in the *trans-trans* configuration to show coupling constants ranging between 1.3 and 1.9 cps. All other long-range couplings were found to be appreciably smaller. The ir and mass spectra and C and H analyses of **6** are also in agreement with its structure.

Experimental Section

2,5-Diazido-1,4-benzohydroquinone (**2**).—A solution of 10 g (0.093 mol) of 1,4-benzoquinone in 100 ml of glacial acetic acid was cooled to 10°, and 20 ml of an aqueous solution containing 13.5 g (0.208 mol) of sodium azide was then added in one portion. After a few minutes the reaction solution was filtered to remove any unreacted sodium azide and the mother liquor cooled. 2,5-Diazido-1,4-benzohydroquinone (**2**) precipitated as white crystalline needles. An additional fraction of the product was obtained by pouring the mother liquor into water. The combined fractions were dried to give 5.9 g (33% yield) of diazide **2**. This compound is quite thermally and photolytically unstable which prevented satisfactory combustion analysis. It violently *explodes* at 100° and rapidly turns red upon exposure to laboratory light.

1,4-Diacetoxy-2,5-diazidobenzene (**3**).—2,5-Diazido-1,4-benzohydroquinone (**2**, 1 g, 0.0052 mol) was dissolved in 80 ml of warm acetic anhydride and the solution was allowed to stand at room temperature for 6 hr. The resulting white precipitate was collected and dried to give 1.3 g (91% yield) of diacetate **3**, mp 160-161° dec.

The nmr spectrum ($CDCl_3$) of **3** shows two absorptions in the ratio of 2:6 at, respectively, δ 6.89 and 2.28. The ir spectrum (Nujol) shows absorptions for acetate carbonyl at 1760 cm^{-1} and for azide at 2120 cm^{-1}. The mass spectrum of **3** shows a molecular ion at *m/e* 276 in accord with the formulation $C_{10}H_8N_6O_4$.

Anal. Calcd for $C_{10}H_8N_6O_4$:, C, 43.47; H, 2.90; N, 30.43. Found: C, 43.27; H, 2.92; N, 30.39.

2-Amino-5-azido-1,4-benzoquinone (**4**).—2,5-Diazido-1,4-benzohydroquinone (**2**, 5.8 g, 0.03 mol), was dissolved in 500 ml of spectrograde acetone. The solution immediately became purple with the simultaneous evolution of nitrogen. After nitrogen evolution ceased, the solution was filtered to remove a small amount of 2,5-diamino-1,4-benzoquinone (**5**) which had formed. The solution was then concentrated *in vacuo* at 40° to the point where azide **4** began to precipitate. The solution was then cooled and the precipitate collected to give 3.7 g (75% yield) of the purple crystalline 2-amino-5-azido-1,4-benzoquinone (**4**). It was impossible to obtain a melting point on this product. The compound did not melt when it was slowly heated to 360° and it *violently decomposed* when placed in a bath at 200°. The spectral data (ir, nmr) *vida infra* for **4** are in complete agreement with its formulation. The mass spectrum of **4** does not show a molecular ion peak, but the second most intense (47%) peak is at *m/e* 136, corresponding to the loss of nitrogen from azidoaminoquinone **4**.

2,5-Diamino-1,4-benzoquinone (**5**).—2,5-Diazido-1,4-benzoquinone (**7**, 1 g, 0.005 mol) was dissolved in 50 ml of 95% ethanol. Excess sodium borohydride was added and the reaction solution

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[6] R. K. Norris and S. Sternhell [*Aust. J. Chem.*, **19**, 617 (1966)] have investigated long-range coupling quinones and found no observable coupling between protons in positions 2 and 5.

[7] H. W. Moore and H. R. Shelden, *Tetrahedron Lett.*, 5431 (1968).

[8] A. A. Bothner-By and R. K. Harris, *J. Amer. Chem. Soc.*, **87**, 3455 (1965).

[9] A. A. Bothner-By and R. K. Harris, *ibid.*, **87**, 3445 (1965).

[10] A. A. Bothner-By and D. Jung, *ibid.*, **90**, 2342 (1968).

[11] A. A. Bothner-By and E. Moser, *ibid.*, **90**, 2347 (1968).

[12] A. A. Bothner-By and D. F. Koster, *ibid.*, **90**, 2351 (1968).

was maintained at 20° by means of an external ice bath. The purple product precipitated from the solution and was collected to give 426 mg (62% yield) of 2,5-diamino-1,4-benzoquinone (**5**), mp >360° (lit.[4] mp 325–330°). The spectral data (ir, nmr, and mass spectra), *vida infra*, are in complete agreement with structure **5**.

Anal. Calcd for $C_6H_6N_2O_2$: C, 52.17; H, 4.35. Found: C, 51.94; H, 4.53.

2,5-Diamino-1,4-benzoquinone (**5**) was also prepared in 31% yield from 2-amino-5-azido-1,4-benzoquinone (**4**) according to the above procedure. The compounds prepared by both methods were shown to be identical in all respects.

2,5-Diazido-1,4-benzoquinone (**7**).—A solution of 5 g (0.028 mol) of 2,5-dichloro-1,4-benzoquinone in 60 ml of dimethylformamide and 20 ml of acetone was cooled to 15°. An aqueous solution of 4 g (0.061 mol) of sodium azide in 20 ml of water was slowly added keeping the temperature below 18°. The bright orange diazide, **7**, precipitated from the reaction solution in 94% yield. Recrystallization from warm ethanol gave pure 2,5-diazido-1,4-benzoquinone (**7**), mp 93–94° dec. The nmr spectrum of **7** ($CDCl_3$) shows only one peak at δ 6.20. The ir spectrum (Nujol) shows characteristic absorptions at 2150 and 2110 (azide) and 1660 cm^{-1} (quinone carbonyl). The mass spectrum of **7** showed a molecular ion at *m/e* 190 in accord with the molecular formula $C_6H_2N_6O_2$. Reliable combustion analysis could not be obtained owing to the instability of the diazide.

β-Amino-γ-cyanomethylene-$\Delta^{\alpha,\beta}$-butenolide (**6**).—2-Amino-5-azido-1,4-benzoquinone (**4**, 0.02 g, 0.0013 mol) was added in small portions to 3 g of trichloroacetic acid at 65° over a period of 30 min. During this time the solution became dark and nitrogen was evolved. The reaction solution was then poured into 10 ml of ice–water and cooled; the product was collected by filtration giving 0.08 g (44% yield) of β-amino-γ-cyanomethylene-$\Delta^{\alpha,\beta}$-butenolide (**6**), mp 201–204°. Recrystallization from aqueous ethanol gave an analytical sample of **6** as a white crystalline solid, mp 204°.

Anal. Calcd for $C_6H_4N_2O_2$: C, 52.94; H, 2.94; N, 20.59. Found: C, 52.93; H, 2.99; N, 20.68.

The ir spectrum of **6** shows characteristic absorptions at 3490, 3200 and 3300 (NH_2), 2250 (CN), and 1780 and 1760 cm^{-1} (C=O). The mass spectrum of **6** shows a molecular ion at *m/e* 136 (59%) in accord with the formulation $C_6H_4N_2O_2$.

Registry No.—1,4-Benzoquinone, 106-51-4; sodium azide, 12136-89-9; **2**, 19462-75-0; **3**, 19462-76-1; **4**, 19462-77-2; **6**, 19459-07-5; **7**, 19462-78-3.

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Synthesis of Isoquinolines. IX. 1,2,3,4-Tetrahydroisoquinolines *via* the Mannich Condensation[1]

J. M. BOBBITT AND C. P. DUTTA[2]

Department of Chemistry, the University of Connecticut, Storrs, Connecticut 06268

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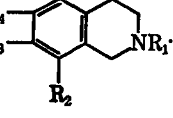
In recent years, we have developed and explored a facile synthesis of simple oxygenated isoquinolines, based upon modifications of the Pomeranz–Fritsch reactions.[3] These modifications have involved the

TABLE I

1,2,3,4-TETRAHYDROISOQUINOLINE HYDROCHLORIDES



Compd	R_1	R_2	R_3	R_4	R_5	Yields,[a] %	Mp, °C	Lit. mp, °C	Calcd, % C	Calcd, % H	Calcd, % N	Calcd, % Cl	Found, % C	Found, % H	Found, % N	Found, % Cl
5	CH_3	OH	OCH_3	H	H	68	212–214	*b*	57.47	7.02	6.09	15.43	57.03	6.74	6.22	15.36
6	CH_3	H	OCH_3	OH	H	26	286–288	285–290[c]								
7	CH_3	OH	OCH_3	OCH_3	H	63	236–238	*d*	55.49	6.96	5.39	13.68	55.37	6.71	5.83	13.83
8	CH_3	OH	OH	H	H	30	228–230		60.11	7.06	7.01	17.75	59.78	7.09	6.64	17.25
9	H	OH	OCH_3	H	H	42	281–283	282–283[e]								
10	H	OH	OCH_3	OCH_3	H	63	257–258	258[f]								
11	CH_3	OH	OCH_3	H	CH_3	50	282–284		59.14	7.45	5.74	14.55	59.13	7.44	5.90	14.94

[a] Yields are calculated on the basis of the starting phenols. [b] Compound **5** was prepared in 70% over-all yield by our published procedure[5] and was identical with this sample. [c] J. M. Bobbitt, D. N. Roy, A. Marchand, and C. W. Allen, *J. Org. Chem.*, **32,** 2225 (1967). [d] Free base prepared by neutralization, mp 130–132° [E. Späth and A. Becke, *Ber.*, **68,** 944 (1935)] reported mp 131–133°). [e] See ref 3. [f] E. Kauder, *Arch. Pharm.*, **237,** 190 (1899); A. Heffter, *Ber.* **34,** 3004 (1901) (as cited in ref 9 of the former).

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[1] Paper VIII: J. M. Bobbitt and T. E. Moore, *J. Org. Chem.*, **33,** 2958 (1968). This work was sponsored, in part, by Contract DA-49-193-MD-2948 from the U. S. Army Medical Research and Development Command, Publication 513 from the Army Research Program on Malaria.

[2] Recipient of a Fullbright Travel Grant, 1966.

[3] J. M. Bobbitt, J. M. Kiely, K. L. Khanna, and R. Ebermann, *J. Org. Chem.*, **30,** 2247 (1965). See also preceeding papers in this series.