## Rearrangements of Azidoquinones. XI. Acid-Catalyzed Rearrangements of 2,5-Diazido-1,4-benzoquinones

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The acid-catalyzed decomposition of 2,5-diazido-1,4-benzoquinones (1) provides a convenient route to  $\beta$ -azido- $\gamma$ -cyanoalkylidene- $\Delta^{\alpha,\beta}$ -butenolides (4). Bulky substituents (*tert*-butyl or *tert*-pentyl) on the butenolide ring cause a subsequent cycloaddition of the  $\beta$ -azido group to the cyano moiety giving the tetrazoles (5). Synthetic uses of these products are also discussed, *e.g.*, the conversion of  $\alpha$ -phenyl- $\beta$ -azido- $\gamma$ -cyanomethylidene- $\Delta^{\alpha,\beta}$ -butenolide (4c) to the indole 10 and the formation of the lactone-lactams (12) from the tetrazoles (5).

Azidoquinones constitute a synthetically versatile class of reagents which can be specifically converted to a large variety of other compounds.<sup>2</sup> Of particular importance regarding the present manuscript is the previously reported stereospecific acid-catalyzed rearrangements of azidoquinones to  $\gamma$ -cyanoalkylidene- $\Delta^{\alpha,\beta}$ -butenolides.<sup>2a</sup> This rearrangement is very general, usually proceeding in high yields, and does not seem to depend upon the substitution pattern of the quinone. Even the diazidoquinone, 2,5-diazido-3,6dimethyl-1,4-benzoquinone (1b), was shown to rearrange in 87% isolated yield to  $\alpha$ -methyl- $\beta$ -azido- $\gamma$ cvanoethylidene- $\Delta^{\alpha,\beta}$ -butenolide (4b) in cold concentrated sulfuric acid.<sup>2a</sup> Recently, we have observed that 2,5-diazido-3,6-di-tert-butyl-1,4-benzoquinone rearranges under the same conditions to the unique tetrazole lactone 5a. This anomalous tetrazole formation, along with the fact that the  $\beta$ -azido- $\gamma$ -cyanoalkylidene- $\Delta^{\tilde{\alpha}, \beta}$ -butenolides provide a most interesting system in their own right, has prompted a more detailed investigation of the acid-catalyzed rearrangements of 2.5-diazido-1.4-benzoquinones. Reported here are the results of such a study.

Synthetic Scope.—The synthetic utility of this reaction is summarized in Scheme I. In general,  $\beta$ -azido- $\gamma$ -cyanoalkylidene- $\Delta^{\alpha,\beta}$ -butenolides were formed from all of the 2,5-diazido-1,4-benzoquinones investigated except those having bulky substituents in the 3,6 orientation. Such compounds, 2,5-diazido-2,6-di-tertbutyl- and 2,5-diazido-3,6-di-tert-pentyl-1,4-benzoquinone, rearranged to the tetrazoles (5a and 5b) which are envisaged as arising via an intramolecular 1,3dipolar cycloaddition of the azido group to the cyano moiety in the intermediate butenolides. Cycloadditions of this kind are well known,<sup>3</sup> and the present case would be expected to be facilitated by the release of steric strain between the bulky  $\alpha$  substituent and the  $\beta$ -azido group in 4 [R<sub>1</sub> = R<sub>2</sub> = C(CH<sub>3</sub>)<sub>3</sub> or C(CH<sub>3</sub>)<sub>2</sub>- $C_2H_5$ ].

The transformation of the 2,5-diazido-1,4-benzoquinones (1) to the  $\beta$ -azido- $\gamma$ -cyanoalkylidene- $\Delta^{\alpha,\beta}$ butenolides (4) provides a facile route to  $\gamma$ -lactones which are substituted with the highly reactive azido group in the  $\beta$  position. A number of synthetic pos-



sibilities can be envisaged for such compounds, and their subsequent study should be fruitful.

The rearrangements reported here were all accomplished by the same general procedure, which constitutes the slow addition of the diazide to cold  $(0-5^{\circ})$ , vigorously stirred, concentrated sulfuric acid. After nitrogen evolution ceased, the reaction solution was poured into ice-water and the product was collected by filtration.

The diazides were conveniently prepared from the corresponding 2,5-dichloro-1,4-benzoquinones by reaction with aqueous ethanolic sodium azide. These azidoquinones are generally obtained in high yield from this reaction as beautifully colored crystalline compounds which decompose (sometimes violently) at their melting points.

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<sup>(2) (</sup>a) H. W. Moore, H. R. Shelden, D. W. Deters, and R. J. Wikholm,
J. Amer. Chem. Soc., 92, 1675 (1970); (b) W. Weyler, Jr., D. S. Pearce,
and H. W. Moore, 95, 2603 (1973); (c) W. Weyler, Jr., and H. W. Moore, *ibid.*, 93, 2812 (1971); (d) H. W. Moore and W. Weyler, Jr., *ibid.*, 92, 4132 (1970); (e) H. W. Moore and H. R. Shelden, J. Org. Chem., 33, 4019 (1968).

<sup>(3)</sup> A. I. Meyer and J. C. Sircar in "The Chemistry of the Cyano Group," Z. Rappoport, Ed., Interscience, New York, N. Y., 1970, p 351.

Structures.—The structures of the butenolides (4af) and the tetrazoles (5a and 5b) are based primarily upon spectral properties (Table I). However, for

TABLE I

Spectral Properties of Butenolides (4), Tetrazoles (5), AND LACTONE-LACTAMS (12) Compd Ir (Nujol), cm-1 Nmr (CDCl<sub>3</sub>),  $\delta$ 2230, 2160, 1780, 5.31 (d, 1, J = 1.3 Hz), 6.004a 1650(d, 1, J = 1.3 Hz)2200, 2130, 1785 4c 5.93 (s, 1), 7.08-7.88 (m, 5) 4d 2210, 2120, 1780, 1.13 (d, 6, J = 6 Hz), 2.11 1640 (s, 3), 3.08 (h, 1, J =6 Hz) 2210, 2140, 1785, 4e 1.25 (d, 6, J = 6 Hz), 2.03(s, 3), 3.08 (h, 1, J =16406 Hz) 4f 2210, 2120, 1780, 1.13 (d, 6, J = 6 Hz), 1.30 (d, 6, J = 6 Hz), 3.061640(h, 2, J = 6 Hz)1785, 1685, 1650 5a 1.41 (s, 9), 1.51 (s, 9) 5b1780, 1685, 1650 0.90 (m, 6), 1.36 (s, 6), 1.46 (s, 6), 1.74 (m, 4) 12a 3150, 1800, 1725, 1.30 (s, 9), 1.33 (s, 9), 9.16 1680, 1650 (s, 1) 12b 3200, 1800, 1720, 0.83 (m, 6), 1.28 (m, 12), 1680, 1655 1.71 (m, 4), 9.50 (s, 1)

some, chemical data are also provided. The butenolides all show characteristic<sup>2s</sup> azido, nitrile, alkene, and lactone carbonyl absorptions in their infrared spectra. Their nmr spectra all show absorptions with consistent chemical shifts and proton counts for the proposed structures (Table I).

Two quinones studied were unsymmetrically substituted, namely 2,5-diazido-3-methyl-6-isopropyl-1,4benzoquinone (1d) and 2,5-diazido-3-phenyl-1,4-benzoquinone (1c). The former gave 4d and 4e in a ratio of 2.6:1.0; the latter gave only 4c isolated in 90% yield. In both instances the major or exclusive products arise via an initial protonation on the least hindered carbonyl of the quinone (Scheme I). The orientation of the methyl and isopropyl groups in 4d was unambiguously established by its borohydride reduction to the known amino derivative,  $\alpha$ -isopropyl- $\beta$ -amino- $\gamma$ -cyanoethylidene- $\Delta^{\alpha,\beta}$ -butenolide.<sup>1e</sup> In an analogous fashion, using catalytic reduction, 4a was reduced to  $\beta$ amino- $\gamma$ -cyanomethylidene- $\Delta^{\alpha,\beta}$ -butenolide, а compound of known constitution.<sup>4</sup>

The structure of **4c** did.not lend itself to elucidation by such a direct approach. However, on the basis of the spectral data presented below, along with chemical data to be presented later, its structure is firmly documented. The vinyl proton in **4c** absorbs at  $\delta$  5.93 in its nmr spectrum. This chemical shift is best in agreement with a structure having a vinyl proton on the exocyclic methylene group. This is based upon a comparison with other butenolides<sup>2a</sup> having analogous vinyl protons as well as vinyl protons at the  $\alpha$  position, which appear respectively at  $\delta$  6.00–6.40 and 5.10– 5.67.

Synthetic Utility. A. Indole Formation. —The availability<sup>5</sup> of  $\alpha$ -aryl- $\beta$ -azido- $\gamma$ -cyanoalkylidene- $\Delta^{\alpha,\beta}$ -butenolides, e.g., **4c**, by the method reported here suggests a possible new and general route to  $\alpha,\beta$ -diacyl substituted indoles. That is, thermal decomposition of such azides could give the indoles (8) via a nitrenoid insertion reaction.<sup>6</sup> Subsequent hydrolysis would give the diacyl derivatives (9), which would be most useful



compounds for the synthesis of a variety of natural products.

In order to test this possible route to indoles, the thermal decomposition of **4c** in refluxing *o*-dichlorobenzene was studied. The indole **10** was formed, but



in low isolated yield (5-10%). In spite of the yield, which was not maximized, these results are encouraging and this reaction is currently being actively pursued.

The structure of **10** is in complete accord with its spectral and analytical properties, which are recorded in the Experimental Section.

B. Tetrazole Hydrolysis.-The tetrazoles (5a and 5b) show a most interesting hydrolytic transformation to the respective lactone-lactams 12a and 12b. Simply refluxing 5a in aqueous ethanol causes its conversion to 12a in 76% isolated yield. On the other hand, it is necessary to reflux the more hindered tert-pentyl homolog in acidic aqueous ethanol in order to accomplish its analogous transformation to 12b in 53% isolated yield. These reactions are envisaged as arising via addition of water to the tetrazoles to give the adducts 11a and 11b, which then suffer loss of hydrazoic acid. Subsequent tautomerization would then give the observed products. To our knowledge, the only other example of such compounds in the literature is the corresponding diphenyl analog, generated from 2amino-5-hydroxy-3,6-diphenyl-1,4-benzoquinone upon dimethyl sulfoxide-acetic anhydride oxidation.7

<sup>(4)</sup> H. W. Moore, H. R. Shelden, and D. F. Shellhamer, J. Org. Chem., 34, 1999 (1969).

<sup>(5)</sup> Variously aryl-substituted quinones are available by a number of routes. See, for example, C. S. Rondestvedt, Jr., Org. React., **11**, 189 (1960).

<sup>(6)</sup> Such insertion reactions are very well documented in the literature. See, for example, P. A. S. Smith in "Nitrenes," W. Lwowski, Ed., Interscience, New York, N. Y., 1970, and references cited therein.

<sup>(7)</sup> R. J. Wikholm and H. W. Moore, J. Amer. Chem. Soc., 94, 6152 (1972).



## **Experimental Section**

β-Azido-γ-cyanomethylidene-Δα,β-butenolide (4a).—2,5-Diazido-1,4-benzoquinone<sup>4</sup> (1a, 1.5 g, 7.8 mmol) was slowly added to 20 ml of vigorously stirred concentrated sulfuric acid (0-5°) over a period of 45 min. After gas evolution ceased (5 min after addition of the azide) the reaction solution was poured into icewater. The resulting homogeneous solution was extracted twice with methylene chloride and twice with diethyl ether. The combined organic layers were dried and concentrated *in vacuo*. Upon cooling, 600 mg (47%) of the butenolide 4a precipitated, mp 116-118°.

 $\beta$ -Amino- $\gamma$ -cyanomethylidene- $\Delta^{\alpha,\beta}$ -butenolide.—Reduction of the butenolide 4a with hydrogen and PtO at 40 psi in methanol solvent gave a quantitative yield of  $\beta$ -amino- $\gamma$ -cyanomethylidene- $\Delta^{\alpha,\beta}$ -butenolide.<sup>4</sup>

 $\alpha$ -Phenyl- $\beta$ -azido- $\gamma$ -cyanomethylidene- $\Delta^{\alpha,\beta}$ -butenolide (4c). 2,5-Diazido-3-phenyl-1,4-benzoquinone (1c, 3.9 g, 14 mmol) was slowly added to 50 ml of vigorously stirred concentrated sulfuric acid at 0.5°. After gas evolution had ceased, the yellow-brown reaction mixture was poured into 300 ml of ice-water. The resulting light yellow precipitate was collected, dried, and recrystallized from 95% ethanol, giving 2.7 g (90%) of the butenolide 4c, mp 152-154°. Three more recrystallizations gave the analytical sample.

Anal. Caled for  $C_{12}H_6N_4O_2$ : C, 60.50; H, 2.52; N, 23.52. Found: C, 60.42; H, 2.39; N, 23.48.

α-Isopropyl-β-azido-γ-cyanoethylidene- $\Delta^{\alpha,\beta}$ -butenolide (4d) and α-Methyl-β-azido-γ-(1-cyano-2-methylpropylidene)- $\Delta^{\alpha,\beta}$ -butenolide (4e).—2,5-Diazido-3-methyl-6-isopropyl-1,4-benzoquinone<sup>2e</sup> (1d, 4.3 g, 17 mmol) was slowly added (40 min) to 60 ml of vigorously stirred concentrated sulfuric acid at 0°. Five minutes subsequent to the addition of the azide, nitrogen evolution ceased and the reaction mixture was poured into 300 ml of water. The resulting mixture was extracted four times with methylene chloride. The combined organic layers were dried and the solvent was removed *in vacuo* to give 3.7 g which by nmr analysis was shown to be a mixture of the butenolides 4d and 4e in a ratio of 2.6:1.0, respectively. Three recrystallizations from ethanol gave the major isomer 4d in pure form, mp 79-81°. *Anal.* Caled for C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>: C, 55.04; H, 4.58; N, 25.68.

Anal. Caled for  $C_{10}H_{10}N_4O_2$ : C, 55.04; H, 4.58; N, 25.68. Found: C, 55.13; H, 4.59; N, 25.75.

α-Isopropyl-β-azido-γ-(1-cyano-2-methylpropylidene)- $\Delta^{\alpha,\beta}$ -butenolide (4f).—2,5-Diazido-3,6-diisopropyl-1,4-benzoquinone<sup>2b</sup> (1f, 200 mg, 0.7 mmol) was slowly added to 15 ml of vigorously stirred concentrated sulfuric acid at 0°. After gas evolution ceased, the reaction was worked up in the standard way (above), giving 172 mg (95%) of the butenolide 4f, mp 62-66°. Recrystallization from ethanol gave the analytical sample, mp 66-68°. Anal. Caled for  $C_{12}H_{14}N_4O_2$ : C, 58.53; H, 5.69; N, 22.79. Found: C, 58.48; H, 5.68; N, 22.83.

Acid-Catalyzed Decomposition of 2,5-Diazido-3,6-di-tert-butyl-1,4-benzoquinone. Formation of the Tetrazole 5a.—2,5-Diazido-3,6-di-tert-butyl-1,4-benzoquinone<sup>2d</sup> (4 g, 14 mmol) was slowly added (15 min) to 100 ml of vigorously stirred concentrated sulfuric acid at 0-10°. The reaction solution was stirred for an additional 1 hr, during which time gas evolved. It was then poured into water and the resulting bright yellow, crystalline solid was collected by filtration, yielding 2.9 g (76%) of the tetrazole 5a. The sample was recrystallized from benzene to give the analytical sample, mp 134-136°.

the analytical sample, mp 134–136°. *Anal.* Calcd for  $C_{14}H_{18}N_4O_2$ : C, 63.60; H, 7.28; N, 18.54. Found: C, 63.56; H, 7.32; N, 18.23.

Acid-Catalyzed Decomposition of 2,5-Diazido-3,6-di-tert-pentyl-1,4-benzoquinone. Formation of the Tetrazole 5b.—2,5-Diazido-3,6-di-tert-pentyl-1,4-benzoquinone<sup>2d</sup> (3.30 g, 10 mmol) was slowly added (15 min) to 70 ml of vigorously stirred, cold (5°) concentrated sulfuric acid. After 1 hr of stirring no more gas evolution could be detected. The solution was then poured into 300 ml of ice-water and the resulting yellow tetrazole 5b (2.3 g, 80%) was collected, mp 85-90°. Recrystallization from ethanol gave an analytical sample, mp 92-94°.

Anal. Calcd for  $C_{16}H_{22}N_4O_2$ : C, 63.60; H, 7.28; N, 18.54. Found: C, 63.56; H, 7.32; N, 18.23.

Reaction of the Tetrazole 5a with Aqueous Ethanol. Formation of the Lactone-Lactam 12a.—A solution of 1.0 g (3.6 mmol) of the tetrazole 5a in 30 ml of 95% ethanol was refluxed for 5 min. The reaction solution was then cooled and allowed to stand at room temperature for 12 hr. The solution was then heated to  $60^{\circ}$  and water was added until the solution became turbid. It was then cooled to  $0^{\circ}$  and filtered, giving 650 mg (76%) of the white crystalline lactone-lactam 12a, mp 192-193°.

Anal. Caled for  $C_{14}H_{19}NO_3$ : C, 67.44; H, 7.62; N, 5.62. Found: C, 67.57; H, 7.66; N, 5.62.

Reaction of the Tetrazole 5b with Acidic Aqueous Ethanol. Formation of the Lactone-Lactam 12b.—A solution of 0.5 g (1.7 mmol) of the tetrazole 5b in 30 ml of 80% ethanol and 1 drop of cencentrated sulfuric acid was refluxed for 15 min and then allowed to stand at ambient temperature for 12 hr. At the end of this time a light yellow precipitate had formed which was collected and recrystallized from 95% ethanol to give 250 mg (53%) of the white crystalline lactone-lactam 12b, mp 180-181°. Anal. Calcd for  $\dot{C}_{16}H_{28}NO_3$ : C, 69.31; H, 8.30; N, 5.05.

*Anal.* Calcd for  $C_{16}H_{22}NO_3$ : C, 69.31; H, 8.30; N, 5.05. Found: C, 69.39; H, 8.24; N, 5.13.

 $\alpha$ -Isopropyl- $\beta$ -amino- $\gamma$ -cyanoethylidene- $\Delta^{\alpha,\beta}$ -butenolide.—A solution of 200 mg (9 mmol) of the butenolide 4d in 50 ml of methanol was treated with excess sodium borohydride. After 30 min, 10 ml of water was added and the reaction solution was cooled to 0° and left for 48 hr. At the end of this time a white, crystalline precipitate had formed which was collected giving 75 mg of the known 2-isopropyl- $\beta$ -amino- $\gamma$ -cyanomethylidene- $\Delta^{\alpha,\beta}$ butenolide (1e).

Thermolysis of  $\alpha$ -Phenyl- $\beta$ -azido- $\gamma$ -cyanomethylidene- $\Delta^{\alpha,\beta}$ butenolide (4c). Formation of the Indole 10.— $\alpha$ -Phenyl- $\beta$ azido- $\gamma$ -cyanomethylidene- $\Delta^{\alpha,\beta}$ -butenolide (4c, 650 mg, 2.7 mmol) was suspended in 1 ml of dry *o*-dichlorobenzene. This suspension was added dropwise over a period of 1 min to 15 ml of refluxing *o*-dichlorobenzene. After the addition was complete, the solution was refluxed for an additional 5 min. Carbon tetrachloride was then added until the solution became turbid and the precipitate which formed upon cooling to 0° was collected. This crude solid was purified by column chromatography over silica gel (eluting with 10% acetone in CH<sub>2</sub>Cl<sub>2</sub>). The second compound which was collected was the colorless crude indole. Recrystallization from *n*-butyl alcohol gave 30 mg (5.2%) of an analytical sample: mp 248–250°; ir (Nujol) 3300 (NH), 2220 (CN), and 1800 cm<sup>-1</sup> (CO); nmr (DMSO)  $\delta$  6.14 (s, 1, CH==C), 7.32–7.96 (m, 4, ArH).

Anal. Caled for  $C_{12}H_6N_2O_2$ : C, 68.57; H, 2.86; N, 13.33. Found: C, 68.37; H, 3.06; N, 13.03.

Registry No.—1a, 19462-78-3; 1c, 41675-57-4; 1d, 17448-05-4; 1f, 41675-59-6; 1 ( $R_1 = R_3 = t$ -Bu), 29342-21-0; 1 ( $R_1 = R_3 = t$ ert-pentyl), 41675-60-9; 4a, 41675-61-0; 4c, 41675-62-1; 4d, 41675-63-2; 4e, 41675-64-3; 4f, 41753-76-8; 5a, 41675-65-4; 5b, 41675-66-5; 10, 41675-67-6; 12a, 41675-68-7; 12b, 41675-69-8.