Molecular weight: calcd. for $C_6H_8N_2O$, 124. Found: (micro-isopiestic) 150 ± 15.

Acknowledgment. The authors are indebted to Miss E. C. Eberlin for the execution, interpretation, and reproduction of the infrared curves presented herein.

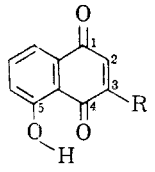
STAMFORD RESEARCH LABORATORIES
AMERICAN CYANAMID CO.
STAMFORD, CONN.

Reaction of Juglone with Thioglycolic Acid

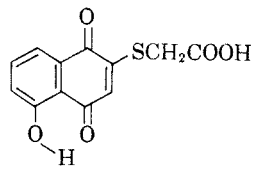
FRANK G. ROTHMAN[1]

Received November 26, 1957

The reaction of excess juglone (Ia) with thioglycolic acid affords only one of the two possible isomeric products, Ib and II, isolated in 73% yield.[2]



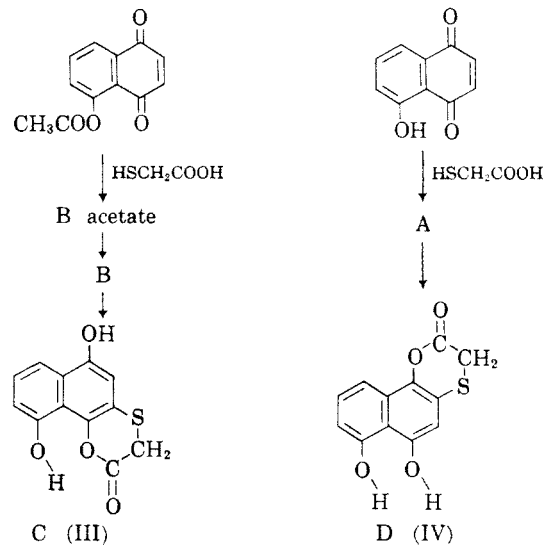
I (a) R = H
(b) R = SCH_2COOH
(c) R = Cl



II

Structure Ib was assigned to this product (A) since it is also formed (in 39% yield) in the reaction of 3-chlorojuglone (Ic) with thioglycolic acid in the presence of pyridine. The reaction of juglone acetate with thiogylcolic acid is reported to form only the acetate of the other isomer (B, isolated in 70% yield) to which structure II was assigned by exclusion. Since these results are opposite to those expected for nucleophilic addition,[2,3] and observed for several other reactions, *e.g.* the reaction of 2,3-dibromojuglone and its acetate with aniline,[4] a free-radical mechanism was suggested for the reactions with thiolgycolic acid, and with *p*-thiocresol and *p*-toluenesulfinic acid for which similar results were obtained.[2] No independent evidence was advanced in support of this hypothesis, which does not readily account for the observed orientations. The reaction of thioglycolic acid with 3-chlorojuglone may proceed by attack at either position 2 or 3 (each of which is the β position of an α,β unsaturated carbonyl system) followed by loss of HCl, leading to the formation of either Ib or II or a mixture of both. An unequivocal assignment of structures to the two isomers A and B was therefore desirable. This has been achieved by the reactions summarized in Scheme 1.

Scheme 1



C (III)

D (IV)

Catalytic hydrogenation of isomer B,[5] followed by treatment of the crude reaction mixture with *N,N'*-dicyclohexylcarbodiimide[6] afforded compound C, $C_{12}H_8O_4S$, m.p. 193–203° (dec.), which could be identified as III and not IV on the basis of its effect in increasing the acidity of a boric acid solution. While naphthalene derivatives with free hydroxyl groups in the *peri*-positions (*e.g.*, IV) show an effect of unique magnitude in this test,[7] compound C gave only a slight increase (Table I), attributable to the acidity of the phenolic hydroxyl groups. Since compound C is III, structure IV can be assigned to D.

Isomer A on hydrogenation and treatment with *N,N'*-dicyclohexylcarbodiimide was converted into a tan amorphous solid D. The behavior of D in the boric acid test (Table I) is in accord with its formulation as IV.

(1) Present Address: Department of Biology, Massachusetts Institute of Technology, Cambridge 39, Mass. A portion of this work was performed at the Department of Chemistry, University of Wisconsin, Madison, Wis.

(2) R. H. Thomson, *J. Org. Chem.*, **16**, 1082 (1951).

(3) In additions to juglone acetate, conjugation of the unshared electrons of the phenolic oxygen at position 5 with the carbonyl group at position 4 opposes addition to the α,β unsaturated carbonyl system terminating at position 4 and hence 3-substituted derivatives are formed preferentially. This effect is also expected in additions to juglone, but is opposed by the effect of the intramolecular hydrogen bond between the hydroxyl group and the oxygen at position 4, which is expected to favor the accumulation of negative charge in the transition state at O-4 rather than O-2. In the nucleophilic reactions previously reported[2,4] the latter effect predominates.

(4) R. H. Thomson, *J. Org. Chem.*, **13**, 377 (1948).

(5) The infrared spectrum of the residue from the mother liquor of crystallization of B acetate showed the presence of a few per cent of A acetate in the reaction mixture.

(6) *Cf.* R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey, and R. W. Kierstead, *J. Am. Chem. Soc.*, **78**, 2023 (1956).

(7) J. Boeseken, J. A. de Bruin, and W. E. van Rijswijk de Jong, *Rec. trav. chim.*, **58**, 3 (1939), *cf.* F. A. Hochstein, C. R. Stephens, L. H. Conover, P. P. Regna, R. Pasternack, P. N. Gordon, F. J. Pilgrim, K. J. Brunings, and R. B. Woodward, *J. Am. Chem. Soc.*, **75**, 5455 (1953).

TABLE I

EFFECTS ON THE ACIDITY OF BORIC ACID[a]

Compound	ΔpH
1,5-Dihydroxynaphthalene	−0.3
1,4,5-Trihydroxynaphthalene	−2.7
C	−0.2[b]
D	*ca.* −2.7[c]

[a] One part (by volume) of a 0.05*M* solution of compound in tetrahydrofuran mixed with one part of 0.5*M* aqueous boric acid. [b] Value extrapolated to zero time (see text). [c] A small portion of compound not in solution.

After aqueous boric acid was added to a solution of C in tetrahydrofuran, the *p*H of the solution decreased gradually (from *ca.* 4.8 to 3.5 in an hour[8]). This change was accompanied by the appearance of a yellow color. These observations are readily explained by hydrolysis of the lactone ring and oxidation to form quinone Ib whose carboxyl group accounts for the decrease in *p*H.[9] After several hours, bronze crystals, m.p. 190–193° (dec.), separated from the solution. The ultraviolet spectrum of this material suggests that it is the quinhydrone of Ib.

The preferential attack of thioglycolic acid at position 2 of juglone and position 3 of juglone acetate are in agreement with predictions for nucleophilic addition[2] and render unnecessary the postulation of a free radical mechanism for these reactions. The directive effect of chlorine substitution in the quinone ring on the course of addition reactions remains to be determined. Preliminary experiments on the reaction of 3-chlorojuglone and its acetate with thioglycolic acid in the absence of pyridine (whose presence permits the possibility of reaction mechanisms involving initial addition of pyridine to the quinone) show that the preponderance of products from reactions other than addition followed by elimination of HCl (*e.g.*, oxidation-reduction) makes these reactions unsuitable for studying this effect. The results of this investigation demonstrate the unreliability of assuming that in stoichiometric replacements of halogen in haloquinones the replacing substituent will occupy the same position as the halogen.

EXPERIMENTAL[10]

Thioglycolic acid (Fisher Scientific Co.) was freshly distilled prior to use.

Ultraviolet spectra were determined in 90% ethanol, 0.01*N* in HCl.

Juglone-2-thioglycolic acid (II). The reaction of juglone with thioglycolic acid was carried out according to the procedure of Thomson[2] who regarded the product as the 3-isomer. The crude product (53%) showed a strong band in the infrared region (in dioxane solution) at 13.05μ which was also found to be present in the spectrum of the recrystallized product, but absent in the spectrum of the 3-isomer. Since no distinctive bands were found in the spectrum of the 3-isomer which are absent in that of the 2-isomer, small amounts of the latter may have escaped detection in the crude material. Recrystallization from ethanol afforded orange-red needles, m.p. 202–205° (dec.) (reported[2] 218°, dec.), λ_{max} 239 mμ (log ϵ 4.17), 251 mμ (log ϵ 4.16), 308 mμ (log ϵ 3.83), and 438 mμ (log ϵ 3.78).

Juglone-2-thioglycolic acid acetate was prepared by acetylation of juglone-2-thioglycolic acid according to the procedure of Thomson[2] who regarded the product as the 3-isomer. Two recrystallizations from benzene afforded fine yellow needles, m.p. 158–161° (reported[2] 174°), $\lambda_{max}^{CHCl_3}$ 5.67, 5.80, 6.00, 6.07, 6.27, 6.33, 6.40, 7.34, 7.51, 7.90, 8.90, 9.08, 11.33, and 11.76μ.

Juglone-3-thioglycolic acid acetate. The reaction of juglone acetate with thioglycolic acid was carried out by adding thioglycolic acid to a solution of juglone acetate in hot ethanol, and allowing the solution to stand overnight. The amounts used and workup was according to the directions of Thomson[2] who regarded the product as the 2-isomer. Three recrystallizations of the crude product (67%) from 60% ethanol gave fine yellow needles, decomposing at 202–203° (reported[2] 217–218°, dec.), $\lambda_{max}^{CHCl_3}$ 5.66, 5.78, 5.99, 6.25, 6.30, 6.38, 6.84, 7.32, 7.50, 7.72, 8.77, 9.13, and 10.40μ. In the infrared spectrum of the residue obtained on evaporation of the mother liquor of the first recrystallization, the intensities of the bands at 7.72μ and 8.78μ were diminished and shoulders at 6.04μ and 7.90μ and a band at 9.08μ appeared.

Juglone-3-thioglycolic acid (Ib). Hydrolysis of juglone-3-thioglycolic acid acetate according to the directions of Thomson,[2] who regarded this as the 2-isomer, gave, after two recrystallizations from 24% aqueous ethanol, fine orange needles, m.p. 202–203° (dec.) (reported[2] 217–218°, dec.), λ_{max} 238 mμ (log ϵ 4.15), 249 mμ (log ϵ 4.11), 308 mμ (log ϵ 3.85), and 414 mμ (log ϵ 3.82).

Reduction of juglone-3-thioglycolic acid and lactonization of the product. Six hundred mg. (2.28 mmoles) of juglone-3-thioglycolic acid (m.p. 202–203°, dec.) was added to a prereduced suspension of 0.1 g. precipitated palladium (Palladium Black, Fisher Scientific Co.) in 120 ml. of dioxane. On hydrogenation at room temperature and atmospheric pressure *ca.* 2.7 mmoles (1.2 equiv.) of hydrogen was consumed. The hydrogen was replaced by a nitrogen atmosphere and a solution of 492 mg. (2.28 mmoles) of *N,N'*-dicyclohexylcarbodiimide in 25 ml. of dioxane was added rapidly in order to minimize exposure of the reaction mixture to the atmosphere. The flask was flushed with nitrogen and allowed to stand at room temperature. Colorless crystals (of *N,N'*-dicyclohexylurea) separated after a few minutes. After *ca.* 18 hr. the precipitate was removed by filtration. Lyophilization of the filtrate afforded 693 mg. of a light tan powder. Five hundred and fifty mg. of this product was suspended in 200 ml. of anhydrous ether, the bulk of it dissolving. The mixture was partly decolorized by treatment with 0.3 g. of Norit for 0.5 hr., and after filtration, the yellow solution was brought to dryness at the aspirator. Addition of *ca.* 20 ml. of chloroform to the yellow-tan residue induced crystallization. The yellow crystalline mass was boiled with 250 ml. of chloroform, and after filtration of the hot solution, the residue was boiled with 50 ml. of chloroform. The combined chloroform extracts were evaporated to 100 ml., and fine crystals began to separate: 157 mg. (crop 1) almost colorless needles, m.p. 192–201° (dec.); 30 mg. (crop 2) tan crystals. Recrystallization of crop 1 from chloroform by a similar procedure gave colorless needles, m.p. 193–203° (dec.), λ_{max}^{KBr} 2.8, 3.04, 5.75, 6.13, 6.24, 6.55, 6.77, 6.92, 7.16, 7.33, 7.65, 8.10, 8.62, 8.73, 9.05, 9.46, 10.60, 10.92, 11.18, 11.95, 12.37, 12.50, 13.37, and 13.84μ.

(8) The *p*H of a solvent blank decreased from 4.7 to 4.4 during an equal time interval, presumably due to evaporation of tetrahydrofuran.

(9) No decrease of *p*H with time was observed with D. suggesting that participation of the hydroxyl group at position 5 in C accelerates the hydrolysis of the lactone ring,

(10) Melting points are not corrected. Analyses by Dr. W. C. Alford and associates, National Institute of Arthritis and Metabolic Diseases, Bethesda, Md.

Anal. Calcd. for $C_{12}H_8O_4S$: C, 58.06; H, 3.22; S, 12.91. Found: C, 58.02; H, 3.30; S, 12.97.

Reduction of juglone-2-thioglycolic acid and lactonization of the product. The reduction of juglone-2-thioglycolic acid was carried out in the same manner as reduction of the 3-isomer, using 87 mg. of catalyst and a solution of 355 mg. of the quinone, in *ca.* 125 ml. of dioxane. Lactonization was effected by adding a solution of 288 mg. of *N,N'*-dicyclohexylcarbodiimide in 15 ml. of dioxane to the hydrogenated product under nitrogen. The reaction mixture was worked up in the same way as the 3-isomer, yielding 0.35 g. of a brown powder as the crude product. No crystalline material was obtained on attempted crystallizations from various solvents or chromatography on silicic acid. On sublimation at 160° (*ca.* 0.1 mm.) for a week, about 15% of the crude material was obtained as a very light tan amorphous solid, λ_{max}^{KBr} 5.80, 6.22, 6.35, 6.93, 7.21, 7.30, 7.58, 8.08, 8.20, 8.75, 8.92, 9.07, 9.50, 10.16, 11.06, 11.24, 12.10, 12.20, 12.35, 13.20μ. A second sublimation did not change the infrared spectrum.

Determination of the effect of compounds on the acidity of boric acid. One part (volume) of a 0.05*M* solution of the compound to be tested in tetrahydrofuran was added to one part of 0.5*M* aqueous boric acid solution, and the *p*H was measured on a Beckman *p*H meter, Model G. The *p*H of a blank consisting of one part tetrahydrofuran and one part 0.5*M* boric acid was 4.8–5.2 depending on the sample of tetrahydrofuran used.

A solution of 12.5 mg. (0.05 mmoles) of analytically pure compound D in 1 ml. of tetrahydrofuran was added to 1 ml. of 0.5*M* boric acid. The *p*H decreased from 4.8 to 3.5 in an hour. After the mixture had stood in an open cup for 2.5 hr., bronze crystals, m.p. 190–193° (dec.), λ_{max} 235 mμ ($E_{1\,cm.}^{1\%}$ 71), 252 mμ ($E_{1\,cm.}^{1\%}$ 36), 322 mμ ($E_{1\,cm.}^{1\%}$ 14), 334 mμ ($E_{1\,cm.}^{1\%}$ 15), 350 mμ ($E_{1\,cm.}^{1\%}$ 14), 410 mμ ($E_{1\,cm.}^{1\%}$ 3.6) had separated.

Acknowledgment. The author is grateful to Professor W. S. Johnson of the University of Wisconsin for his suggestions concerning the manuscript.

DEPARTMENT OF DERMATOLOGY
WALTER REED ARMY INSTITUTE OF RESEARCH
WALTER REED ARMY MEDICAL CENTER
WASHINGTON, D. C.

Reactions of Sodium Phenylacetylide and Sodium Alkoxide with Tosyl and Mesyl Azides[1]

J. H. BOYER, C. H. MACK, N. GOEBEL, AND L. R. MORGAN, JR.

Received December 2, 1957

Six examples of nitrogen singly bound to *sp* carbon have been described in the literature.[2] Current interest in the azidoacetylene unit recognized the possibility for further demonstration of this single bond and for making observations on the properties of this unknown unit.

Initial attempts to prepare phenylazidoacetylene from either phenyliodo- or phenylbromo acetylene and sodium azide were unsuccessful. Attention was then directed to adducts obtained from sulfonyl azides and sodium phenylacetylide since aryl azides had resulted from hydroylsis of triazene salts obtained from aromatic organometallic reagents and tosyl azide.[3] The adduct (I) from sodium phenylacetylide and tosyl azide apparently underwent ring-closure isomerization with the formation of a sodium salt (II) of 1-tosyl-5-phenyltriazole (no triple bond absorption near 4.6 to 4.8μ). Upon hydrolysis linear compounds were not isolated. With equimolar amounts of sodium phenylacetylide and tosyl azide or with an excess of sodium phenylacetylide, a product was obtained to which the structure of 1-tosyl-5-phenyltriazole (III) was assigned,[4] whereas an excess of tosyl

(1) This research was supported by the Office of Ordnance Research, U. S. Army, under Contract No. DA-01-009-ORD-428, a National Institutes of Health Grant No. H-2295, and by a grant from Eli Lilly & Co. Presented at the 131st National Meeting of the American Chemical Society, Miami, April 7–12, 1957.

(2) The observation that 1-aminoacetylenes are probable intermediates in the transformation of substituted propiolic acid amides into fatty acid nitriles by the action of alkaline hypohalite [I. J. Rinkes, *Rec. trav. Chim.*, **46**, 268 (1927)] renders unlikely the claim that a 1-aminoacetylene was isolated upon reduction of a 1-nitroacetylene [F. Krafft and G. Heizmann, *Ber.*, **33**, 3586 (1900)]. Trimethylethynylammonium hydroxide [(J. Bode, *Ann.*, **267**, 268 (1890)] and cyanogen azide [A. Angelli, *Atti accad. Lincei*, [6], **5**, 732 (1927); *Chem. Abstr.*, **21**, 3603 (1927)] have been reported and nitroxylnitrile oxide has been considered as an intermediate [R. A. Barnes, "Isoxazoles" in R. C. Elderfield, *Heterocyclic Compounds*, John Wiley, New York, 1957, Vol. **5**, p. 459]. An adduct, [Ar—N=N—N=N—C≡C—N=N—N=N—Ar]$^{=}$(MgX)$_2^{++}$, obtained from the acetylenic Grignard reagent and aryl azide [H. Kleinfeller and G. Bonig, *J. prakt. Chem.*, **132**, 175 (1932)] contained an eight atom system in conjugation with two aromatic rings over which the π electron density of the doubly charged anion could be spread. Ring closure isomerization also occurred and upon hydrolysis a substituted triazole was obtained along with a bis-acetylenic triazene or its tautomer, Ar—N=N—N=CH—CH=N—N=N—Ar.

(3) P. A. S. Smith, private communication. See J. H. Boyer and F. C. Canter, *Chem. Revs.*, **54**, 40 (1954). In contrast hydrolysis of the triazene salt obtained from a sulfonyl azide and the lithium salt of cyclopentadiene led to the formation of diazocyclopentadiene and a sulfonamide [W. von E. Doering and C. H. Depuy, *J. Am. Chem. Soc.*, **75**, 5955 (1953)], a reversal of earlier observations that diazonium salts and sulfonamides reacted with the formation of the expected triazene salt [P. K. Dutt, H. R. Whitehead, and A. Wormall, *J. Chem. Soc.*, **119**, 2088 (1921); P. K. Dutt, *J. Chem. Soc.*, **125**, 1463 (1924); A. Key and P. K. Dutt, *J. Chem. Soc.*, 2035 (1928)].

(4) In 1937 it was claimed [S. G. Fridman and N. N. Lisovskaja, *Zapiski Inst. Khim., Akad. Nauk Ukr. R.S.R., Inst. Khim.*, **6**, 353 (1940); *Chem. Abstr.*, **35**, 2470 (1941)] that sodium phenylacetylide reacted with β-chloroethyl azide with the formation of 4-vinyl-5-phenyltriazole. This required initial attack by the acetylide anion upon carbon, elimination of hydrazoic acid and then recombination presumably by a Diels-Alder reaction to form the disubstituted triazole. The structure proof consisted in oxidation with facile decarboxylation to the known 4-phenyltriazole. Since triazole-4-carboxylic acid did not decarboxylate at temperatures under 210° [O. Baltzer and H. v. Pechmann, *Ann.*, **262**, 317 (1891); O. Dimroth, *Ber.*, **35**, 1044 (1902)], the assignment of the above product as 1-vinyl-5-phenyltriazole is now suggested. Its formation would require initial attack by acetylide ion upon the terminal azido nitrogen, ring-closure isomerization, and hydrolysis. Now, oxidation