was continued until the red color was completely discharged (*ca.* 20 min.). The alcoholic solution was separated by filtration and on concentration and cooling, it deposited colorless crystals (*ca.* 0.82 g.).

Anal. Calcd. for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.04; H, 5.26; N, 8.46.

They were identified as 1-phenyl-4-diphenylmethyl-3,5-pyrazolidinedione (VIa). Determination of the melting point and mixed m.p. with a sample of VIa, obtained as above, gave no depression; similarly the infrared spectra of both samples were found to be identical.

Action of triphenylchloromethane on 1-phenyl-3,5-pyrazolidinedione. To a solution of 0.23 g. of metallic sodium in 10 ml. of absolute ethyl alcohol was added a solution of 1.78 g. of 1-phenyl-3,5-pyrazolidinedione[8] in 15 ml. of absolute ethyl alcohol. The stirred reaction mixture was treated, at room temperature, with a solution of 2.28 g. of triphenylchloromethane in 15 ml. of absolute ethyl alcohol. It was left overnight and then refluxed (steam bath) for 1 hr. to effect completion of the reaction. The cooled reaction mixture was poured into ice cold water and the solid that separated was filtered off, washed with water, and crystallized from a chloroform–ethyl alcohol mixture (*ca.* 1.9 g.), m.p. 234° (dec.).

Anal. Calcd. for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.32; H, 5.84; N, 7.24.

The reaction product proved to be identical with VIb; (melting point and mixed melting point determination with a sample of VIb obtained as above).

Action of phenylmagnesium bromide on VII. One gram of VII was treated with phenylmagnesium bromide as described in the case of V. The reaction product (VIII) was obtained from ethyl alcohol and/or from acetone in colorless crystals (*ca.* 0.78 g.), m.p. 285°.

Anal. Calcd. for $C_{28}H_{24}N_2O_2$: C, 79.97; H, 5.75. Found: C, 79.92; H, 5.93.

Action of aniline on ethyl diphenylmethylmalonate. Ethyl diphenylmethylmalonate was prepared after the procedure described for the preparation of ethyl *n*-butylmalonate,[10] and was obtained as colorless crystals from petroleum ether (b.p. 50–80°) (52% yield), m.p. 55°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.44; H, 6.15. Found: C, 73.53; H, 6.45.

A mixture of 2 g. of ethyl diphenylmethylmalonate and 6 g. of freshly distilled aniline was refluxed (oil bath) for 7 hr. The cooled reaction mixture was treated with ether and the separated solid was filtered off, washed with ether, and crystallized from ethyl alcohol. Colorless needles (*ca.* 1.9 g.), m.p. 285°.

Anal. Calcd. for $C_{28}H_{24}N_2O_2$: C, 79.97; H, 5.75. Found: C, 80.26; H, 5.58.

It proved to be identical with VIII (m.p. and mixed m.p. determinations).

GIZA, CAIRO
U. A. R.

(10) *Cf. Org. Syntheses*, I, 250 (1948).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF ABERDEEN]

Studies in the Juglone Series. IV. The Addition of Aniline and Toluene-*p*-thiol to 5-Substituted 1,4-Naphthoquinones

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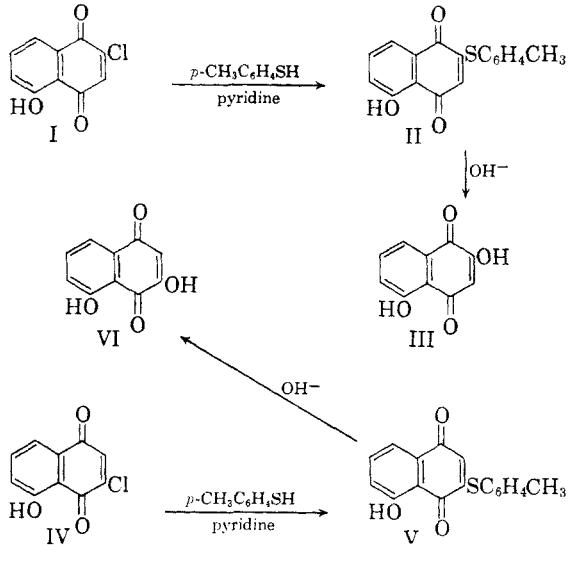
The structures previously assigned to the products of addition of toluene-*p*-thiol to juglone and juglone acetate have been confirmed. Addition of both aniline and toluene-*p*-thiol to 5-methoxy-, 5-methyl-, 5-acetamido- and 5-chloro-1,4-naphthoquinones takes place predominantly at position 3.

In Part III[1] of this series it was reported that addition of toluene-*p*-thiol and thioglycolic acid to juglone occurred predominantly at position 3, whereas addition to juglone acetate occurred mainly at position 2. The 3-substituted juglones were also prepared by reaction of 3-chlorojuglone with the appropriate thiol in the presence of pyridine; in addition 2-*p*-tolythiojuglone was obtained, in small yield [together with a second product, now identified as 2,3-di(*p*-tolythio)juglone] by reaction of 2-chlorojuglone with toluene-*p*-thiol in the presence of pyridine. These reactions were considered to establish the structures of the addition products. However, the thioglycolic acid reactions were recently reexamined by Rothman[2] who concluded that addition to juglone occurred predominantly at position 2, while addition to juglone acetate occurred mainly at position 3. These results are opposite to those found earlier by one of us,[1] and, at first sight appear to be very satisfactory insofar as they bring thioglycolic acid and, by implication, toluene-*p*-thiol, into line with other nucleophilic additions in the juglone series, and the radical addition mechanism proposed[1] becomes unnecessary. Unfortunately, Rothman's experimental evidence is not entirely convincing. His method of orientation consisted in catalytic reduction of each juglone-thioglycolic acid, followed by condensation of the carboxyl group with the neighboring quinol hydroxyl group. This gave two isomeric lactones (which can be regarded as substituted naphthalene-1,5- and 4,5- diols) which were distinguished by their relative abilities to increase the acidity of a boric acid solution. As one of the lactones was amorphous (and no analysis was reported) the results are in some doubt, and further verification is therefore desirable. We have confirmed (by comparison of their ethyl esters) that the compound obtained by addition of thioglycolic acid to juglone is identical with that formed by reaction

(1) R. H. Thomson, *J. Org. Chem.*, 16, 1082 (1951).
(2) F. G. Rothman, *J. Org. Chem.*, 23, 1049 (1958).

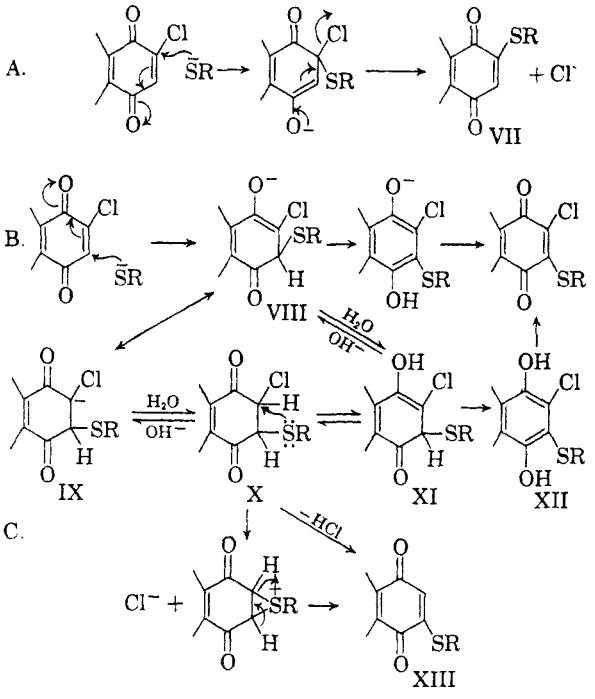
of 3-chlorojuglone with thioglycolic acid, but in view of Rothman's findings the structures of these juglone-thioglycolic acids may be regarded as an open question. We hope to obtain independent evidence establishing their structure in due course.

In this communication we are concerned with the addition of toluene-*p*-thiol to juglone and other 5-substituted-1,4-naphthoquinones. Rothman's results imply that the structures originally proposed[1] for the *p*-tolylthiojuglones are incorrect, and consequently that the method used to determine these structures is ambiguous. Attention is drawn to "the unreliability of assuming that in stoichiometric replacements of halogen in haloquinones the replacing substituent will occupy the same position as the halogen."[2] We have now confirmed the original structures by converting the tolylthio compounds into the corresponding hydroxyjuglones by alkaline hydrolysis.[3] The structures of 2-chlorojuglone I (obtained *via* chromic acid oxidation of 5 - acetoxy - 2,4 - dichloronaphthalene[4]) and 2-hydroxyjuglone III (prepared *via* condensation of *p*-nitrosodimethylaniline with 5-methoxytetralone-1[5]) cannot be doubted. Hence the conversion of I into III must either proceed as shown, or *via* the sequence, 2-chlorojuglone → 3-*p*-tolylthiojuglone → 2-hydroxyjuglone. The last step, in particular, seems highly improbable. 3-Chlorojuglone is made



by elimination of hydrochloric acid from juglone dichloride[6] and, by difference, must be the 3-isomer. The structure of 3-hydroxyjuglone is established independently through the alternative syntheses of droserone[6,7] (3-hydroxy-2-methyljuglone). Here again, we believe that the conversion of IV into VI proceeds *via* V, and not *via* its isomer. Admittedly, it may not be wise to extrapolate from these results to all halogenoquinones and all thiols, and thioglycolic acid, which is particularly reactive,[8] may be exceptional. The use of pyridine is a possible complicating factor, and in the replacement reactions described below, this has been avoided by converting the thiol into its anion by addition of aqueous sodium hydroxide, before reaction with the halogenoquinone.

We consider that the normal nucleophilic replacement reaction proceeds according to reaction Scheme *A*, and the normal addition reaction according to Scheme *B*. If an "abnormal" replacement reaction occurs (Scheme *C*), this must also proceed *via* the intermediate anion VIII (mesomeric with structure IX). Abstraction of a proton (*e.g.*, from a water molecule) will give rise to the



tautomers X and XI. Assuming that X is formed (*i.e.*, 1,2-addition of the thiol to the quinone), it is then possible that a neighboring group displacement reaction could lead to the formation of XIII, as indicated (and/or VII), but enolization of XI to form the aromatic tautomer XII would be energetically much more favorable. Alternatively, XIII might arise from structure X by direct dehydrochlorination, but this implies initial removal of the proton from position 3 whereas the proton at position 2 should be more readily detached (since chlorine has a much more powerful inductive

(3) The juglone-thioglycolic acids also hydrolyze under these conditions but working up invariably leads to tar formation.

(4) R. H. Thomson, *J. Org. Chem.*, **13**, 371 (1948).

(5) R. G. Cooke and W. Segal, *Australian J. Sci. Research*, **3A**, 628 (1950).

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

(7) R. H. Thomson, *J. Chem. Soc.*, 1277 (1949); M. Asano and J. Hase, *J. Pharm. Soc. Japan*, **63**, 90 (1943); M. Asano, Y. Miyashita, and J. Hase, *J. Pharm. Soc. Japan*, **63**, 109 (1943).

(8) A. Blackhall and R. H. Thomson, *J. Chem. Soc.*, 1138 (1953).

effect than the tolythio group). Thus elimination of halogen by direct replacement (*e.g.*, reaction of 5-acetamido-3-bromo-1,4-naphthoquinone with toluene-*p*-thiol), or addition without replacement (*e.g.*, reaction of 2,5-dichloro-1,4-naphthoquinone with toluene-*p*-thiol, in the cold), or both (*e.g.*, reaction of 2-chlorojuglone with toluene-*p*-thiol), seem more probable than the reactions depicted in Scheme *C*.

The addition of toluene-*p*-thiol to juglone acetate is peculiar. As reported some years ago,[1] it leads to the formation of 2-*p*-tolylthiojuglone acetate. This has been successfully repeated, but recently this reaction has given predominantly the 3-isomer on several occasions! The implication is that the expected nucleophilic addition is taking place at position 3 while radical addition[1] is occurring under different, but as yet undefined, conditions at position 2. The problem is under investigation. Our present purpose is to demonstrate that toluene-*p*-thiol usually undergoes addition to 5-substituted-1,4-naphthoquinones to give products having the same orientation as the corresponding aniline addition products, although this, of itself, does not prove that the toluene-*p*-thiol additions proceed by an ionic mechanism. In some cases the more reactive thiols attack both positions 2 and 3, and appreciable quantities of two isomers can be isolated. In the case of 6-substituted-1,4-naphthoquinones, it has been shown[9] that addition of aniline affords one isomer in good yield (*ca.* 80%) whereas toluene-*p*-thiol gives a mixture of approximately equal amounts of both isomers. As can be seen from Table I, in the corresponding reactions with 5-substituted-1,4-naphthoquinones,[10] both reagents give predominantly one isomer, nucleophilic additions taking place mainly at position 3,[11] in agreement with predictions.[1] It is also noteworthy that both aniline and toluene-*p*-thiol react with 2,5-dichloro-1,4-naphthoquinone, in the cold, by addition at position 3, and 2-chlorojuglone reacts with toluene-*p*-thiol in the hot, in the presence of pyridine, to give both 2-*p*-tolylthio- and 2,3-di(*p*-tolylthio)juglones.

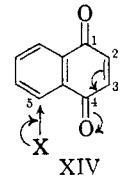
Two results call for comment: (a). It was considered[1] that an electron-releasing group situated at position 5 and hence conjugated with the carbonyl group at position 4, would diminish the electronic displacement from the C_2—C_3 double bond shown in XIV, leading to preferential nucleophilic attack at position 3. It is therefore surprising

TABLE I

ADDITION OF ANILINE AND TOLUENE-*p*-THIOL TO 5-SUBSTITUTED 1,4-NAPHTHOQUINONES

Quinone[a]	Orientation and Yields (%)[b] of Compound(s) produced by	
	Aniline	Toluene-*p*-thiol
5-Hydroxy-1,4-NQ[c]	—	3(90%)
5-Acetoxy-1,4-NQ[c]	3(66%)[d]	3 or 2[e] (75–80%)
5-Methoxy-1,4-NQ	3(86%)	3(73%)
5-Methyl-1,4-NQ	3(72%)	3(75%); 2(10%)
5-Acetamido-1,4-NQ	—	3(72%)
5-Chloro-1,4-NQ	3(86%)	3(49%); 2(12%)

[a] NQ-naphthoquinone. [b] The yields given are for the quinones obtained by oxidation of the initial adducts. [c] See ref. 1. [d] Given, in error, as 56% in ref. 1. [e] See Discussion, p. 38.



XIV

to find that a chlorine atom at position 5 has the same orientating influence as the other substituents listed in Table 1.[12] This may be due to the direct field effect of the chlorine atom on the neighboring carbonyl group, or possibly to a steric effect, the rather large chlorine atom tending to displace the 4-carbonyl group out of the plane of the rings. Both effects would hinder conjugative activation at position 2, and hence nucleophilic addition at position 3 would predominate.

(b). Juglones undergo nucleophilic attack at position 2, in a few instances; namely, the addition of dimethylamine to juglone,[1] and the reaction of various 2,3-dihalogenojuglones with aniline and *p*-toluidine.[6,13] In the first case the yield is poor. To account for these reactions it was suggested that a hydroxyl group at position 5 (in contrast to other electron-releasing groups) could assist the electronic displacement shown in XIV, by virtue of the intramolecular hydrogen bond which enhances the electronegativity of the carbonyl oxygen at position 4. If the addition of toluene-*p*-thiol to juglone at position 3 *is* a nucleophilic reaction (which has yet to be established) it is clear that the hydrogen bond has no significant effect in this case. It was hoped that the reactions of 5-acetamido-1,4-naphthoquinone (which also has an intramolecular hydrogen bond) would clarify the situation but unfortunately this quinone, like juglone, only gives black amorphous material, on reaction with aniline.

Orientation of the products. 5-Methoxy-1,4-naphthoquinone. Acid hydrolysis of the aniline deriva-

(9) J. M. Lyons and R. H. Thomson, *J. Chem. Soc.*, 2910 (1953).

(10) This work was done concurrently with that reported in ref. 9.

(11) R. G. Cooke, H. Dowd, and W. Segal, *Australian J. Chem.*, **6**, 38 (1953), have shown that reaction of 5-methoxy-1,4-naphthoquinone with excess dimethylamine gives (in 42% yield) a mixture of two isomers. Similar treatment of 5-methyl-1,4-naphthoquinone gave mainly the 3-isomer, with indications of the presence of the other.

(12) In the corresponding 6-substituted naphthoquinones the orientating effect of a chlorine atom is opposite to that of electron-releasing groups.[9]

(13) R. H. Thomson, *J. Org. Chem.*, **13**, 870 (1948).

tive, followed by demethylation, gave the known 3,5-dihydroxy-1,4-naphthoquinone. The intermediate 3-hydroxy-5-methoxy-1,4-naphthoquinone was also obtained by alkaline hydrolysis of the toluene-*p*-thiol addition product which is therefore also the 3-isomer.

5-Methyl-1,4-naphthoquinone. This compound is most conveniently prepared *via* Diels-Alder addition of piperylene to benzoquinone.[11] Herzenberg and Ruhemann[14] obtained a yellow quinone, $C_{11}H_8O_2$, m.p. 102–103°, by chromic acid oxidation of 1-methylnaphthalene, which they claimed was 5-methyl-1,4-naphthoquinone. On repeating this work we obtained a small yield of the same product which proved to be 2-methyl-1,4-naphthoquinone.[15] Evidently our sample of 1-methylnaphthalene, like theirs, contained some of the 2-isomer, and the alleged hemimellitic acid, m.p. 190°, which they obtained by permanganate oxidation of the quinone, must have been phthalic acid.

Addition of toluene-*p*-thiol to 5-methyl-1,4-naphthoquinone yielded two isomers. Alkaline hydrolysis of the major product afforded the known 3-hydroxy-5-methyl-1,4-naphthoquinone which was also obtained by acid hydrolysis of the anilino-5-methyl-1,4-naphthoquinone. 2-Hydroxy-5-methyl-1,4-naphthoquinone was prepared by acid hydrolysis of 5-methyl-1,4-naphthoquinone-2,3-epoxide.

5-Acetamido-1,4-naphthoquinone. Two monobromo derivatives were obtained from this quinone by addition of bromine followed by elimination of hydrogen bromide from the dibromide. One of these (the 2-isomer) was identical with that prepared by chromic acid oxidation of 5-acetamido-2,4-dibromo-1-naphthol. Reaction of the other product (5-acetamido-3-bromo-1,4-naphthoquinone) with sodium *p*-tolylthiolate gave the same quinone as that obtained by addition of toluene-*p*-thiol to the acetamidonaphthoquinone, *i.e.*, 5-acetamido-3-*p*-tolylthiol-1,4-naphthoquinone.

5-Chloro-1,4-naphthoquinone. Hydrolysis of the anilino derivative gave a hydroxyquinone different from that derived from 5-chloro-1,4-naphthoquinone-2,3-epoxide. The latter was shown to be the 2-isomer by (a) an unambiguous synthesis from 5-chloro-1-naphthol (*via* its 2,4-dinitro and diamino derivatives) and (b), reductive acetylation to give 1,2,4-triacetoxy-5-chloronaphthalene which was also obtained by Thiele acetylation of 5-chloro-1,2-naphthoquinone. Thus the addition of aniline to 5-chloro-1,4-naphthoquinone gives the 3-anilino derivative. Aniline also reacts with 2,5-dichloro-1,4-naphthoquinone at position 3: hydrolysis of the resulting anilinodichloroquinone gave a dichlorohydroxyquinone identical with that obtained by chlorination of 5-chloro-3-hydroxy-1,4-naphthoquinone. Reaction of 2,5-dichloro-1,4-naphthoquinone with toluene-*p*-thiol in the cold gave 2,5-dichloro-3-*p*-tolylthio-1,4-naphthoquinone, but when the sodium salt of the thiol was used in boiling alcohol, the reactive chlorine was replaced forming 5-chloro-2-*p*-tolylthio-1,4-naphthoquinone. This enabled the products obtained by addition of toluene-*p*-thiol to 5-chloro-1,4-naphthoquinone to be orientated.

(14) J. Herzenberg and S. Ruhemann, *Ber.*, **60**, 897 (1927).

(15) *Cf.* Elsevier's *Encyclopaedia of Organic Chemistry*, **12B**, 2837 (1952).

EXPERIMENTAL

Light petroleum refers to the fraction b.p. 100–120° unless otherwise stated.

2,5-Dihydroxy-1,4-naphthoquinone. A solution of 0.4 g. of 2-*p*-tolylthiojuglone (obtained by addition of toluene-*p*-thiol to juglone acetate and subsequent hydrolysis[1]) in 16 ml. of ethanol was shaken for 30 min. with 1.35 ml. of 2*N* sodium hydroxide. After addition of water (8 ml.), the mixture was refluxed for 15 min. The red solution was then cooled and poured onto ice containing 8 ml. of 4*N* sulfuric acid. The sticky precipitate formed was taken into ether, extracted with 2% aqueous sodium acetate, and acidified. The resulting orange precipitate was crystallized from a small volume of glacial acetic acid forming orange-brown needles, m.p. 216–219° (dec.) not depressed by an authentic sample of 2-hydroxyjuglone. (Mixed m.p. with 3-hydroxyjuglone, 190°). Yield 59%. It formed a diacetate which crystallized from light petroleum in yellow needles, m.p. and mixed m.p. 152°.

3,5-Dihydroxy-1,4-naphthoquinone. A mixture of 0.3 g. of 3-*p*-tolylthiojuglone (obtained by addition of toluene-*p*-thiol to juglone[1]), 24 ml. of ethanol, and 12 ml. of 2*N* sodium hydroxide was refluxed on the steam bath for 1 hr., diluted with water (30 ml.), cooled in ice, and acidified with 4*N* sulfuric acid. The resulting brown crystalline precipitate was recrystallized from a small volume of glacial acetic acid forming brown needles, m.p. 215° (blackening from 210°), not depressed by authentic 3-hydroxyjuglone. The diacetate crystallized from methanol in yellow needles, m.p. and mixed m.p. 137°.

2,3-Di(p-tolylthio)juglone. A solution of 80 mg. of toluene-*p*-thiol in 4 ml. of ethanol was added to a suspension of 80 mg. of 2,3-dichlorojuglone in 10 ml. of the same solvent. The mixture was heated to boiling, dark red crystals separating almost at once. Recrystallization from light petroleum yielded dark red needles, m.p. 188°, not depressed by material obtained by the reaction of 2-chlorojuglone with toluene-*p*-thiol.[1] Yield 87%.

Anal. Calcd. for $C_{24}H_{18}O_3S_2$: C, 68.9; H, 4.3; S, 15.3. Found: C, 69.0; H, 4.3; S, 15.3.

3-Anilino-5-methoxy-1,4-naphthoquinone. Aniline in excess (20 ml.) was added to a suspension of 2 g. of 5-methoxy-1,4-naphthoquinone in 40 ml. of cold ethanol. After 5 days the mixture was poured into dilute sulfuric acid. The precipitate which formed was crystallized from light petroleum in deep red needles, m.p. 152°. Yield 86.5%.

Anal. Calcd. for $C_{17}H_{13}NO_3$: C, 73.1; H, 4.7; N, 5.0. Found: C, 73.35; H, 4.6; N, 4.7.

3-Hydroxy-5-methoxy-1,4-naphthoquinone. (*a*) A solution of 0.5 g. of the above anilinoquinone in 20 ml. of concentrated sulfuric acid was cautiously diluted with 40 ml. of water, and the suspension gently boiled under reflux for 5 min. After cooling and dilution with 60 ml. of water, the yellow hydroxyquinone was collected, washed, and dried. It crystallized from light petroleum in yellow plates, m.p. 211° (dec.). Yield 82%.

(*b*) A fine suspension of 0.3 g. of 5-methoxy-3-*p*-tolylthio-1,4-naphthoquinone in 12 ml. of ethanol was shaken for 10 min. with 2 ml. of cold 2*N* sodium hydroxide. The resulting dark red solution was poured onto a mixture of ice and excess 2*N* sulfuric acid. The precipitate obtained was crys-

tallized first from ethanol, and then from light petroleum (charcoal) in glistening yellow plates, m.p. 209–211° (dec.), identical with those obtained in (*a*). Yield 50%. [The m.p. taken in a Pyrex tube sharpened to 210.5–211° (dec.)]

Anal. Calcd. for $C_{11}H_8O_4$: C, 64.65; H, 3.95. Found: C, 64.45; H, 4.1.

Demethylation was effected by refluxing a solution of the quinone (0.5 g.) in 50 ml. of benzene with 1.5 g. of anhydrous aluminium chloride for 35 min. The mixture was then cooled, poured onto ice and hydrochloric acid, and extracted with ether, from which the dihydroxyquinone was removed by shaking with 2% aqueous sodium acetate. After treatment with charcoal, the alkaline solution was acidified with 2*N* sulfuric and extracted with ether. Evaporation of the dried extract gave a residue which was sublimed *in vacuo* and then crystallized from light petroleum. It formed orange needles, m.p. 216° (dec.) not depressed by an authentic sample of 3,5-dihydroxy-1,4-naphthoquinone. The diacetate had m.p. and mixed m.p. 135–136°.

5-Methoxy-3-p-tolylthio-1,4-naphthoquinone. A solution of 0.34 g. of toluene-*p*-thiol in 4 ml. of ethanol was added to a cold suspension of 0.5 g. of 5-methoxy-1,4-naphthoquinone in 20 ml. of ethanol. Next day the mixture was warmed to complete solution, cooled, and then oxidized by pouring into a mixture of 0.6 g. of potassium dichromate, 0.3 ml. of concentrated sulfuric acid, and 3 ml. of ice water. Crystallization of the precipitate from ethanol gave 5-methoxy-3-*p*-tolylthio-1,4-naphthoquinone as long yellow needles, m.p. 162–162.5°. Yield 73%.

Anal. Calcd. for $C_{18}H_{14}O_3S$: C, 69.65; H, 4.55; S, 10.3. Found: C, 69.45; H, 4.45; S, 10.3.

3-Anilino-5-methyl-1,4-naphthoquinone. On addition of 8 ml. of aniline to a suspension of 1.5 g. of 5-methyl-1,4-naphthoquinone in 15 ml. of ethanol the quinone rapidly dissolved forming a red solution. The crystals which separated on keeping were collected after 3 days, and recrystallized from benzene forming fine scarlet needles, m.p. 179–180°. Yield 72%.

Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.55; H, 5.0; N, 5.3. Found: C, 77.6; H, 5.2; N, 5.15.

3-Hydroxy-5-methyl-1,4-naphthoquinone. (*a*) 3-Anilino-5-methoxy-1,4-naphthoquinone (0.65 g.) was hydrolyzed, as above, by boiling for 5 min. with 75 ml. of 33% (v./v.) sulfuric acid. The hydroxyquinone, which separated on cooling, followed by dilution with 75 ml. of water, crystallized from light petroleum (b.p. 80–100°) in yellow plates, m.p. 176–177°. Yield 79.5%.

(*b*) A fine suspension of 0.5 g. of 5-methyl-3-*p*-tolylthio-1,4-naphthoquinone in 20 ml. of ethanol, was shaken with 4 ml. of 2*N* sodium hydroxide for 20 min. in the cold. The mixture was then brought to the boil, diluted with water until dissolution was complete, and refluxed for 5 min. After cooling, acidification with 4*N* sulfuric acid precipitated the hydroxyquinone. It was taken into ether and extracted with 2% aqueous sodium acetate. After treatment with charcoal the hydroxyquinone was reprecipitated, and then crystallized from methanol forming yellow plates, m.p. 175–176°, not depressed by material obtained in (*a*). (Lit.[11] 175–176°). Yield 50%. Reductive acetylation using zinc dust, acetic anhydride, and a drop of pyridine afforded 1,3,4-triacetoxy-5-methylnaphthalene which separated from light petroleum, (b.p. 80–100°) in colorless needles, m.p. 132–133.5°.

Anal. Calcd. for $C_{17}H_{16}O_6$: C, 64.55; H, 5.1. Found: C, 64.45; H, 5.3.

5-Methyl-1,4-naphthoquinone-2,3-epoxide.[16] A solution of 1 g. of 5-methyl-1,4-naphthoquinone in 10 ml. of hot ethanol was cooled to the crystallizing point when 0.2 g. of sodium carbonate, dissolved in 5 ml. of water containing 1 ml. of 30% hydrogen peroxide, was added with continued cooling. An initial deep purple coloration was followed by a copious precipitate. After dilution with water, this was collected, dried, and crystallized from light petroleum (b.p. 80–100°) forming long needles, m.p. 111°. Yield 31%.

Anal. Calcd. for $C_{11}H_8O_3$: C, 70.2; H, 4.3. Found: C, 70.2; H, 4.05.

2-Hydroxy-5-methyl-1,4-naphthoquinone. The above oxide (0.34 g.) was stirred with 1.5 ml. of concentrated sulfuric acid until it dissolved. After 10 min., 6 ml. of water were carefully added, with cooling. The resulting precipitate was dissolved in warm 2% aqueous sodium acetate, and filtered. Acidification of the red filtrate with 5*N* sulfuric acid yielded the hydroxyquinone which was crystallized from aqueous methanol in yellow needles, m.p. 146°. (Lit.[11] 145–146°). Yield 59%. Reductive acetylation afforded 1,2,4-triacetoxy-5-methylnaphthalene, which separated from ethanol in needles, m.p. 144°.

Anal. Calcd. for $C_{17}H_{16}O_6$: C, 64.55; H, 5.1. Found: C, 64.3; H. 5.2.

2-Bromo-5-methyl-1,4-naphthoquinone. A solution of bromine in glacial acetic acid (10 ml. of 5% v./v.) was added to a solution of 1.7 g. of 5-methyl-1,4-naphthoquinone in 10 ml. of the same solvent. After 10 min., the dibromide was precipitated with water. (Crystallized from light petroleum (b.p. 60–80°) it had m.p. 98–100°). To this (2.55 g.) in 10 ml. of glacial acetic acid, 0.8 g. of anhydrous sodium acetate was added, and the mixture was boiled for 3 min. Dilution with water afforded the bromoquinone which crystallized from light petroleum (b.p. 60–80°) in yellow needles, m.p. 90.5–92°. Yield 62.5% (from the dibromide).

Anal. Calcd. for $C_{11}H_7O_2Br$: C, 52.6; H, 2.8. Found: C, 52.65; H, 2.55.

5-Methyl-2- and 3-p-tolylthio-1,4-naphthoquinones. A solution of 0.72 g. of toluene-*p*-thiol in 10 ml. of ethanol was added to a suspension of 2 g. of 5-methyl-1,4-naphthoquinone in 20 ml. of the same solvent, and boiled for 2 min. Nearly pure 5-methyl-3-*p*-tolylthio-1,4-naphthoquinone separated on cooling. After recrystallization from ethanol it formed deep yellow diamond-shaped plates, m.p. 186°. Yield 75%.

Anal. Calcd. for $C_{18}H_{14}O_2S$: C, 73.45; H, 4.8; S, 10.9. Found: C, 73.4; H, 4.8; S, 10.8.

After keeping for 2 days the initial mother liquor deposited 5-methyl-2-*p*-tolylthio-1,4-naphthoquinone. It separated from light petroleum (b.p. 60–80°) in orange needles, m.p. 123°. Yield 10%.

Anal. Calcd. for $C_{18}H_{14}O_2S$: C, 73.45; H, 4.8; S, 10.9. Found: C, 73.45; H, 4.75; S, 10.75.

This compound was also obtained by mixing boiling solutions of 0.5 g. of 2-bromo-5-methyl-1,4-naphthoquinone in 10 ml. of ethanol, and 0.25 g. of toluene-*p*-thiol in a little ethanol containing 1 ml. of 2*N* sodium hydroxide. The product, obtained on cooling, formed orange needles, m.p. and mixed m.p. 122–123° (from light petroleum). Yield 76%.

5-Acetamido-1,4-naphthoquinone. A solution of 4 g. of 5-acetamido-1-naphthol in 200 ml. of methanol was oxidized[17] by addition of 12.7 g. of potassium nitrosodisulfonate dissolved in 700 ml. of water and 200 ml. of 0.16*M* potassium dihydrogen phosphate. Almost pure 5-acetamido-1,4-naphthoquinone separated on standing overnight. When recrystallized from acetone it formed orange needles, m.p. 173–174° (Pyrex). Yield 63%. The infrared spectrum (Nujol), showed bands at 1702 and 1695 (amide carbonyl), 1665 (free quinone carbonyl) and 1644 cm.$^{-1}$ (chelated quinone carbonyl). (*Cf.* 5-hydroxy-1,4-naphthoquinone[18] which also shows 2 quinonoid carbonyl frequencies at 1667 and 1643 cm.$^{-1}$) The chelated NH band appeared at 3219 cm.$^{-1}$ (KBr disk).

5-Acetamido-2,4-dibromo-1-naphthol. To a solution of 2 g. of 5-acetamido-1-naphthol in 20 ml. of glacial acetic

(16) Following the procedure of L. F. Fieser, *Experiments in Organic Chemistry*, 2nd ed., D. C. Heath & Co., 1941, p. 235.

(17) Oxidation by the method of H.-J. Teuber and N. Götz, *Ber.*, **87**, 1236 (1954).

(18) R. H. Thomson, *J. Chem. Soc.*, 1737 (1950).

acid, an equal volume of a 5% (v./v.) solution of bromine in the same solvent was added slowly, keeping the temperature at 18–20°. A precipitate soon appeared and was collected after 30 min. Crystallization from acetone afforded 5-acetamido-2,4-dibromo-1-naphthol in needles, m.p. 185°. Yield 42%.

Anal. Calcd. for $C_{12}H_9Br_2NO_2$: N, 3.9; Br, 44.5. Found: N, 3.9; Br, 44.0.

The acetone mother liquor yielded a small amount (0.35 g.) of a second compound,[19] m.p. 188–190° (mixed m.p. with the previous compound 177–180°).

5-Acetamido-2- and 3-bromo-1,4-naphthoquinone. A suspension of 2.5 g. of 5-acetamido-1,4-naphthoquinone in 12.5 ml. of glacial acetic acid was treated with 11.6 ml. of a 5% (v./v.) solution of bromine in the same solvent. After 15 min. the mixture was poured onto ice water forming a slightly sticky, yellow-orange precipitate of the dibromide. When dried (4.1 g.), this was refluxed for 2 min. in 25 ml. of glacial acetic acid containing 1.35 g. of anhydrous sodium acetate, and then poured onto ice. Crystallization of the product from glacial acetic acid gave 5-acetamido-3-bromo-1,4-naphthoquinone, m.p. 169–170°. After further crystallization from light petroleum it formed orange needles, m.p. 181°. (Yield, 9% from the dibromide).

Anal. Calcd. for $C_{12}H_8BrNO_3$: C, 49.0; H, 2.75; N, 4.75. Found: C, 48.9; H, 2.65; N, 4.8.

The acetic acid mother liquor was poured onto ice forming a precipitate which crystallized from methanol in orange-brown needles, m.p. 171–172.5°. (Yield, 26% from the dibromide.) The same compound, 5-acetamido-2-bromo-1,4-naphthoquinone, was obtained by treating a suspension of 0.5 g. of 5-acetamido-2,4-dibromo-1-naphthol in 2 ml. of glacial acetic acid with 0.5 g. of chromium trioxide dissolved in 1 ml. of water. The temperature rose spontaneously to 35° and was raised to 50° by warming. The bromoquinone separated on cooling, and recrystallized from methanol in dark red needles, m.p. 171–172.5°, not depressed by the material prepared above. Yield 54%.

Anal. Calcd. for $C_{12}H_8BrNO_3$: C, 49.0; H, 2.75; N, 4.75; Br, 27.2. Found: C, 49.05; H, 2.85; N, 4.65; Br, 27.0.

5-Acetamido-2-p-tolylthio-1,4-naphthoquinone. A solution of 85 mg. of toluene-*p*-thiol in 4 ml. of ethanol was neutralized with aqueous sodium hydroxide, brought to the boil, and added all at once to a boiling solution of 200 mg. of 5-acetamido-2-bromo-1,4-naphthoquinone in 12 ml. of ethanol. The tolylthioquinone separated on cooling, and was recrystallized from methanol in orange-red needles, m.p. 201°. Yield 57%.

Anal. Calcd. for $C_{19}H_{15}NO_3S$: C, 67.6; H, 4.5; S, 4.15. Found: C, 67.4; H, 4.45; N, 4.3.

5-Acetamido-3-p-tolylthio-1,4-naphthoquinone. (*a*) A suspension of 0.5 g. of 5-acetamido-1,4-naphthoquinone in 10 ml. of ethanol was treated with 0.15 g. of toluene-*p*-thiol dissolved in 2 ml. of ethanol, raised to the boil, and left to crystallize. The new quinone formed orange needles, m.p. 231° (from methanol). Yield 72%.

(*b*) Reaction of 5-acetamido-3-bromo-1,4-naphthoquinone (50 mg.) with neutralized toluene-*p*-thiol (20 mg.) in boiling ethanol, as above, gave the same product, m.p. and mixed m.p. 231°. Yield 52%.

Anal. Calcd. for $C_{19}H_{15}NO_3S$: C, 67.6; H, 4.5; N, 4.15; S, 9.5. Found: C, 67.65; H, 4.3; N, 4.0; S, 9.6.

3-Anilino-5-chloro-1,4-naphthoquinone. Five ml. of aniline were added to a suspension of 0.5 g. of 5-chloro-1,4-naphthoquinone in 60 ml. of ethanol. Dissolution occurred rapidly and the anilinoquinone began to crystallize almost at once. It recrystallized from benzene in dark red plates, with a bronze sheen, m.p. 221° (Lit.[20] m.p. 219°). Yield 86%.

(19) This compound is 5-acetamido-2-bromo-1-naphthol: a small amount of 5-acetamido-2-bromo-1,4-naphthoquinone is also formed (K. M. Dargie and J. W. MacLeod, unpublished).

(20) K. Fries and E. Köhler, *Ber.*, **57**, 496 (1924).

Similarly, the product Fries and Köhler[20] obtained by addition of aniline to 5-bromo-1,4-naphthoquinone must be 3-anilino-5-bromo-1,4-naphthoquinone.

5-Chloro-1,4-naphthoquinone-2,3-epoxide. This was prepared, as above, by treating 5-chloro-1,4-naphthoquinone (1 g.) in ethanol with alkaline hydrogen peroxide (1.78 ml., 30%). After 5 min. the oxide was precipitated by dilution with water. It crystallized from light petroleum in needles, m.p. 152–153°. Yield 74%.

Anal. Calcd. for $C_{10}H_5ClO_3$: C, 57.55; H, 2.4; Cl, 17.0. Found: C, 57.5; H, 2.7; Cl, 16.7.

5-Chloro-2-hydroxy-1,4-naphthoquinone. (*a*) The above oxide (0.8 g.) was warmed on a water bath with 3 ml. of concentrated sulfuric acid until it had all dissolved, the color changing from green to red. Ten minutes later the solution was cooled in ice and diluted cautiously with water (20 ml.). The hydroxyquinone which precipitated, crystallized from light petroleum in stout red needles, m.p. 199–200° (dec.). Yield 69%.

(*b*) The same compound was prepared from 5-chloro-1-naphthol following the method of Fieser and Brown[21] (which they used to obtain 7-chloro-2-hydroxy-1,4-naphthoquinone); intermediates were not purified. The product had m.p. 199–200°, not depressed by the above. Yield 25%.

Anal. Calcd. for $C_{10}H_5ClO_3$: C, 57.55; H, 2.4; Cl, 17.0. Found: C, 57.6; H, 2.1; Cl, 16.7.

5-Chloro-1,2-naphthoquinone. To an ice-cold solution of 3.3 g. of 5-chloro-1-naphthol and 1.27 g. of sodium nitrite in 31 ml. of 0.6*N* sodium hydroxide, 2.4 g. of concentrated sulfuric acid in 3.3 ml. of water, was added, dropwise. After stirring for 30 min., the nitroso compound was collected, washed, and dissolved in 9.5 ml. of 2*N* sodium hydroxide and 13 ml. of water. Fifteen ml. of 5*N* sodium hydroxide were then added, followed, at 35°, by 7.6 g. of sodium dithionite, in portions. On cooling, concentrated hydrochloric acid was added to precipitate the amine hydrochloride. This was recrystallized quickly from dilute hydrochloric acid (1:10), and then dissolved in 180 ml. of water containing 0.3 ml. of concentrated hydrochloric acid, at 35°, and oxidized by adding a solution of 4.3 g. of ferric chloride in 12 ml. of water and 1.3 ml. of concentrated hydrochloric acid. The crude quinone was collected, and repeatedly crystallized from ether (charcoal) in clusters of red needles, m.p. 150°. Yield 21%.

Anal. Calcd. for $C_{10}H_5ClO_2$: C, 62.35; H, 2.65. Found: C, 62.35; H, 2.7.

The *o*-quinone formed a quinoxaline with *o*-phenylene diamine, crystallizing from light petroleum in cream needles, m.p. 188°.

Anal. Calcd. for $C_{16}H_9ClN_2$: C, 72.6; H, 3.45. Found: C, 72.9; H, 3.6.

5-Chloro-3-hydroxy-1,4-naphthoquinone. The deep violet solution of 0.3 g. of 3-anilino-5-chloro-1,4-naphthoquinone in 7 ml. of concentrated sulfuric acid, was carefully diluted with 7 ml. of water, and refluxed for 10 min. After cooling and further dilution to complete precipitation of the hydroxyquinone, it was dissolved in ether (charcoal). The residue, after drying and evaporation, crystallized from light petroleum in long orange needles, m.p. 212–213°. Yield 86%.

Anal. Calcd. for $C_{10}H_5ClO_3$: C, 57.55; H, 2.4. Found: C, 57.4; H, 2.3.

Reductive acetylation afforded 1,3,4-triacetoxy-5-chloronaphthalene, crystallizing from light petroleum in needles, m.p. 137°.

Anal. Calcd. for $C_{16}H_{13}ClO_6$: C, 57.1; H, 3.9. Found: C, 57.3; H, 3.9%.

1,2,4-Triacetoxy-5-chloronaphthalene. (*a*) 5-Chloro-2-hydroxy-1,4-naphthoquinone was reduced with zinc dust, acetic anhydride, and a drop of triethylamine, in the usual

(21) L. F. Fieser and R. H. Brown, *J. Am. Chem. Soc.*, 71, 3615 (1949).

way. The triacetate crystallized from light petroleum in needles, m.p. 152–153°.

(*b*) An ice-cooled suspension of 0.75 g. of 5-chloro-1,2-naphthoquinone in 1.5 ml. of acetic anhydride was treated with 2 drops of concentrated sulfuric acid. The quinone dissolved rapidly and the triacetate began to separate after 10 min. It formed needles, m.p. 153° (from light petroleum), identical with those obtained in (*a*).

Anal. Calcd. for $C_{16}H_{13}ClO_6$: C, 57.1; H, 3.9; Cl, 10.55. Found: C, 57.3; H, 4.05; Cl, 10.45.

2,5-Dichloro-1,4-naphthoquinone. Three grams of chlorine were passed into a suspension of 4 g. of 5-chloro-1,4-naphthoquinone in 80 ml. of glacial acetic acid. The quinone dissolved, the dichloride soon began to separate, and was collected after 1 hr. (5.1 g., m.p. 164–165°). This was refluxed for 10 min. in 100 ml. of glacial acetic acid containing 2.55 g. of anhydrous sodium acetate, and diluted with water. Crystallization of the precipitate from aqueous methanol afforded 2,5-dichloro-1,4-naphthoquinone in yellow plates, m.p. 98–100°. (Yield 70% from the dichloride.)

Anal. Calcd. for $C_{10}H_4Cl_2O_2$: C, 52.9; H, 1.8. Found: C, 53.0; H, 1.8. Reductive acetylation afforded 1,4-diacetoxy-2,5-dichloronaphthalene in needles, m.p. 160° (from ethanol).

Anal. Calcd. for $C_{14}H_{10}Cl_2O_4$: C, 53.7; H, 3.2. Found: C, 54.0; H, 3.2.

3-Anilino-2,5-dichloro-1,4-naphthoquinone. Aniline (1 ml.) was added to a suspension of 0.25 g. of 2,5-dichloro-1,4-naphthoquinone in 3.5 ml. of ethanol, and left overnight. The crystalline product was collected, and recrystallized from benzene in dark red needles, m.p. 220–221°. (Mixed m.p. with 3-anilino-5-chloro-1,4-naphthoquinone, 192–196°). Yield 57%.

Anal. Calcd. for $C_{16}H_9Cl_2NO_2$: C, 60.4; H, 2.85; N, 4.4. Found: C, 60.7; H, 2.29; N, 4.8.

2,5-Dichloro-3-hydroxy-1,4-naphthoquinone. (*a*) The above anilinodichloroquinone was hydrolyzed by boiling in 50% (v./v.) sulfuric acid for 10–15 min., as before. Crystallization from light petroleum, followed by sublimation *in vacuo* gave orange needles, m.p. 180–181°. Yield 33%.

(*b*) A solution of 0.18 g. of chlorine in 5 ml. of glacial acetic acid was added to 0.35 g. of finely powdered 5-chloro-3-hydroxy-1,4-naphthoquinone. The mixture was warmed for 3 hr. on the water bath and the product then isolated by pouring into water (50 ml.). Purification as above gave orange crystals, m.p. and mixed m.p. 180–181°. Yield 27%.

Anal. Calcd. for $C_{10}H_4Cl_2O_3$: C, 49.4; H, 1.65. Found: C, 49.6; H, 1.75.

5-Chloro-2 and 3-p-tolylthio-1,4-naphthoquinone. A solution of 0.33 g. of toluene-*p*-thiol in 2 ml. of methanol was added to a suspension of 0.5 g. of 5-chloro-1,4-naphthoquinone in 5 ml. of the same solvent. Next day the dark red solution was poured into an oxidizing solution of 0.6 g. of potassium dichromate, 0.3 ml. of concentrated sulfuric acid, and 5 ml. of ice water. The resulting precipitate was crystallized from methanol to give (*a*) orange-red needles and plates, m.p. 158° (49%), and (*b*) more soluble, pale orange needles, m.p. 175–176° (12%).

Anal. Calcd. for $C_{17}H_{11}ClO_2S$: C, 64.9; H, 3.5; Cl, 11.3; S, 10.2. Found: (a), C, 64.7; H, 3.25; Cl, 11.2; S, 9.7. (b), C, 64.6; H, 3.8; Cl, 10.85; S, 9.9.

Compound (*b*) was shown to be 5-chloro-2-*p*-tolylthio-1,4-naphthoquinone as follows: Solutions of 140 mg. of toluene-*p*-thiol in 1 ml. of ethanol, and 45 mg. of sodium hydroxide in 1 ml. of water, were mixed, brought to the boil, and added, all at once, to a boiling solution of 250 mg. of 2,5-dichloro-1,4-naphthoquinone in 4 ml. of ethanol, boiled for 1 min. and cooled. The product separated on cooling, and recrystallized from ethanol in pale orange needles, m.p. 175–176°, not depressed by admixture with material (*b*) obtained above. Yield 58%.

2,5-Dichloro-3-p-tolylthio-1,4-naphthoquinone. Solutions of 250 mg. of 2,5-dichloro-1,4-naphthoquinone in 4 ml. of ethanol, and 70 mg. of toluene-*p*-thiol in 1 ml. of ethanol, were mixed in the cold. After 4 hr. the red precipitate was collected and crystallized from light petroleum in lustrous, dark red needles, m.p. 148–149°. Yield 62%.

Anal. Calcd. for $C_{17}H_{10}Cl_2O_2S$: C, 58.45; H, 2.9. Found: C, 58.6; H, 3.1.

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ABERDEEN, SCOTLAND

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Synthesis of Two Atom-Bridged Tetracyclic Ketones

H. K. HALL, JR.

August 31, 1959

Addition of acrylonitrile to bicycloheptadiene gave 6-cyano-tetracyclo[3:2:1:$1^{3,8}$:$0^{2,4}$]nonane, I, which was converted by standard reactions to tetracyclo[3:2:1:$1^{3,8}$:$0^{2,4}$]nonan-6-one, IV, and tetracyclo[3:3:1:$1^{3,9}$:$0^{2,4}$]decan-6-one, VII.

In connection with the synthesis of various atom-bridged lactams,[1] polycyclic ketones were required as intermediates. Dr. D. C. England of the Central Research Department[2] had found that acrylonitrile adds to bicycloheptadiene in a homoconjugate manner to give nitrile I (for analogous reactions see ref. 3 and 4). In the present work, this nitrile was converted to the interesting tetracyclo[3:2:1:$1^{3,8}$:$0^{2,4}$]nonan-6-one, IV, and tetracyclo[3:3:1:$1^{3,8}$:$0^{2,4}$]decane-6-one, VII, as shown in the reaction sequences diagram. Yields were mediocre, however, and no conversions to lactams were carried out.

(1) H. K. Hall, Jr., *J. Am. Chem. Soc.*, in press.
(2) Unpublished work.
(3) E. F. Ullman, *Chem. and Ind.*, 1173 (1958).
(4) A. T. Blomquist and Y. C. Meinwald, *J. Am. Chem. Soc.*, **81**, 667 (1959).

EXPERIMENTAL

6-Cyano-tetracyclo[3:2:1:$1^{3,8}$:$0^{2,4}$]nonane (I). A mixture of 500 g. (5.44 mol.) of bicycloheptadiene, 300 g. (5.66 mol.) of acrylonitrile, and 3 g. of cupric acetate was heated at 200° for 12 hr. The product was poured into 4 l. of hexane