CHEMISTRY OF AZIDOQUINONES. SYNTHESIS AND THERMOLYSIS OF THE AZIDO-o-QUINONE, 3-AZIDO-4-(4-METHYLCYCLOHEXA-3,6-DIONE-1,4-DIENYL)-1,2-NAPHTHOQUINONE

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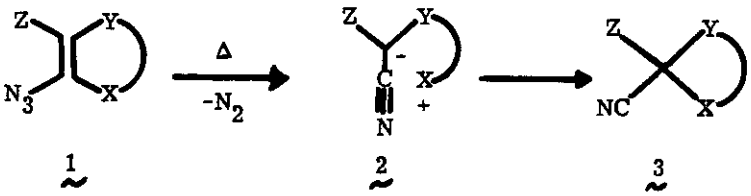
Abstract - The synthesis and thermal decomposition of 3-azido-4-(4-methylcyclohexa-3,6-dione-1,4-dienyl)1,2-naphthoquinone (7) is reported. This is the first example of the thermal chemistry of an azido-o-quinone and is shown to undergo facile ring closure to the carbazolebisquinone 9. Analogous ring closures were observed for the hydroquinone derivatives of 7, i.e., 10a and 10b.

We have shown that appropriately substituted cyclic vinyl azides cleave to zwitterionic intermediates under relatively mild thermolytic conditions (Zwittazido Cleavage).[1] In its most general form this transformation is viewed as outlined in Scheme 1. Specifically, cyclic vinyl azides of structure 1 can ionize to 2 provided X is a group capable of existing as a stabilized carbocation. It is possible that the facility of this ionization may be enhanced as a function of the anion stabilizing influence of the Z and Y groups; however, no such data currently exists. Depending upon the specific substitution pattern, the zwitterion, 2, can proceed to a variety of products, one of which is 3, the ring-contracted nitrile.

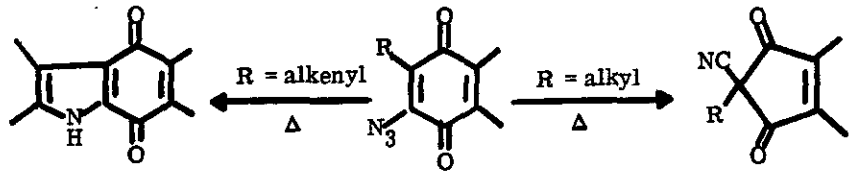
Scheme 1



1 2 3

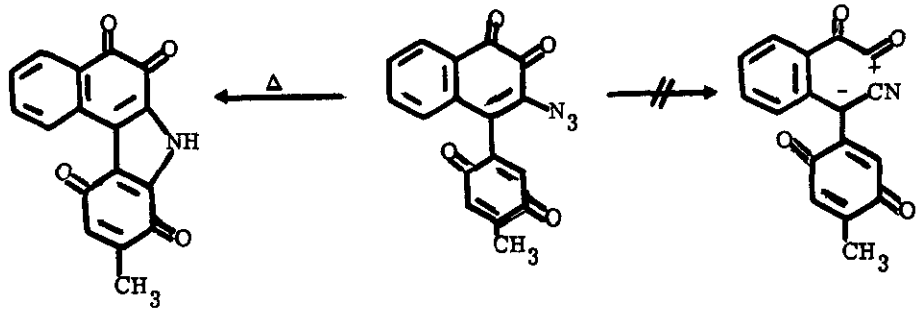
A limitation of this ring-contraction was observed when the Z-substituent is an alkenyl.[2] Here electrocyclic ring closure occurs to give indoles. These two transformations are specifically illustrated for the azido-1,4-

benzoquinone 4. When R is an alkyl group, the cyclopentenedione 5 is formed, and when R is an alkenyl group, the indolequinone 6 results.



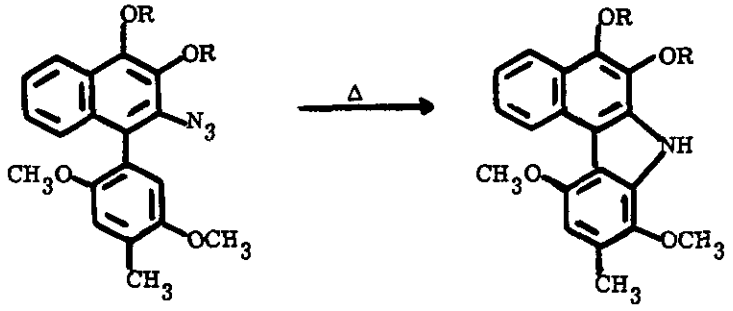
6 4 5

Reported in this manuscript is the synthesis and thermolysis of 3-azido-4-(4-methylcyclohexa-3,6-dione-1,4-dienyl)-1,2-naphthoquinone 7. Such a study was of interest since no previous examples of the thermolysis of an azido-1,2-quinone have been reported.[3] As a result, the primary interest concerned the course of the thermolysis reaction. That is, zwittazido cleavage would proceed to the zwitterionic intermediate 8. This ion would have an exceptionally stabilized anionic center, but the cation would be an α-keto-acylium ion and would probably suffer a destabilizing influence of the α-keto group. On the other hand, the 1,4-benzoquinone group at C-4 provides a conjugated double bond, and as a result the indolequinone pathway is also available. This would result in 9 and thus provide a synthetic route to a previously unknown class of bisquinones. The observed reaction proceeds exclusively by the ring closure mode to give 9. The product was obtained in 88% yield when 7 was subjected to thermolysis in refluxing benzene. It is noteworthy that this result suggests a potentially general route to indolequinones which compliments the previously reported 4 → 6 transformation[2].



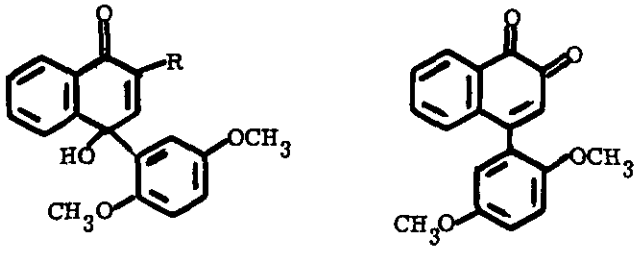
9 7 8

It has previously been reported that 2-azido-1,4-diacetoxybenzenes undergo thermolysis to give N-acyl-o-quinoneimines.[4] As a result it was of interest to also investigate the thermolysis of 10a since an analogous transformation would give an unusual 3,4-naphthoquinoneimine. However, compound 10a also underwent facile ring closure in refluxing o-dichlorobenzene to give the carbazole 11a in 90% yield.[5] A similar transformation was observed for the tetramethoxy derivative 10b which gave 11b in 66% yield.



10 a) R = $COCH_3$ b) R = CH_3 11

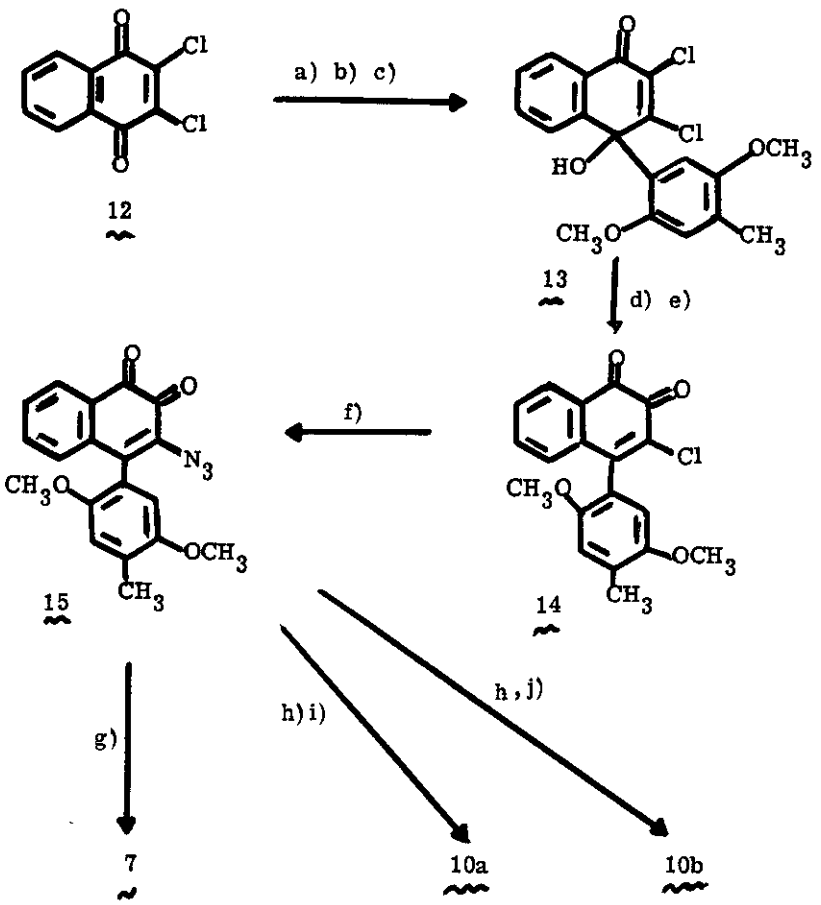
The starting organic azides, 7, 10a, 10b, were conveniently prepared starting with 2,3-dichloro-1,4-naphthoquinone as outlined in Scheme 2. The most unusual reaction in this sequence is the hydrolysis of 13 to give the o-quinone 14 rather than a product of a dienone-phenol rearrangement. This reaction appears to be quite general as illustrated by the fact that the quinols 16a and 16b behaved analogously.[6] Both of these gave the o-quinone 17; the former gave 17 directly and the latter gave the hydroquinone when treated with HCl/CH_3CO_2H.



16 a) R = Cl b) R = H 17

The structure of 17 was unambiguously established by converting 16b to 17 by an independent route. Specifically, the enone double bond was reduced to give 18. Dehydration of 18 gave the phenol 19 and subsequent

Scheme 2



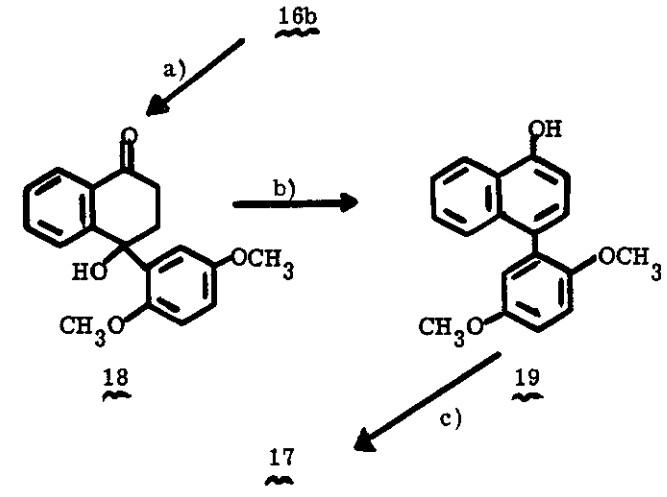
a) $(CH_3)_3SiCN$ b) 1-lithio-2,5-dimethoxy-4-methylbenzene

c) NaF d) H^+, $(CF_3CO)_2O$ e) $NaHCO_3/H_2O/C_2H_5OH$

f) NaN_3 g) AgO/H^+ h) $Na_2S_2O_4$ i) Ac_2O, py j) CH_3I, K_2CO_3

Fremy salt oxidation gave 17 (Scheme 3).

Scheme 3



Finally, it is noted that some carbazolequinones which are somewhat structurally analogous to 9 have been reported to show biological activity.[7] For example, 20 expresses tranquilizing activity in mice, dogs, and rabbits at nontoxic doses.

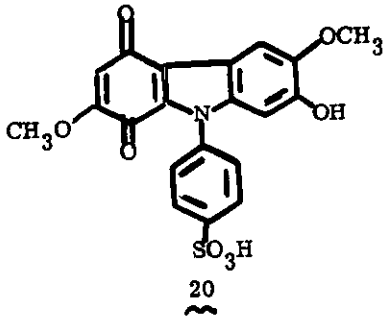


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Table 1

Spectral and Physical Properties

Compound	Yield	mp	ir (nujol, cm^{-1})	^1H nmr ($CDCl_3$, δ)
7	68	dec.	2120,1682,1670;1665	8.30-6.98, m, 4H; 6.89, q, J, 2 Hz, 1H; 6.82, s, 1H; 2.13, d, J, 2 Hz, 3H
9	88	320 dec.	3422,1675,1670,1660	9.20, d, J, 6.7 Hz, 1H; 8.00-7.35, m, 3H; 6.76, q, J, 1.6 Hz, 1H; 2.03, d, J, 1.6 Hz, 3H
11a	89	228-230	3490, 1760	9.71, d, J, 7 Hz, 1H; 8.00-7.20, m, 5H; 8.80, b, s, 1H; 4.02, s, 3H; 3.90, s, 3H; 2.47, s, 3H; 2.40, s, 3H
11b	66	144-146	3470	9.88, d, J, 7.5 Hz, 1H; 8.45-7.25, m, 4H; 4.07, 3.96, 3.94, 3.83, s, 3H; 2.38, s, 3H
13	70	232-233	3455,1650	8.20-6.68, m, 6H; 6.00, bs, 1H; 3.80, 3.10, s, 3H
14	72	213-215	1680	8.30-6.60, m, 6H; 3.67,3.60, s, 3H; 3.25, s, 3H
15	58	dec.	2120, 1675, 1672	8.30-6.54, m, 6H; 3.68, 3.63, s, 3H; 2.25, s, 3H
10a	89	37-38	2130, 1770, 1750	7.90-6.67, m, 7H; 3,72, 3.60, s, 3H, 2.42, 2.34, s, 3H
10b	31	dec.	2120	8.32-7.82, m, 4H; 6.93, 6.68, s, 1H; 3.94, s, 3H; 3.60, 3.52, s, 3H; 2.22, s, 3H
16a	57	162-164	3300, 1660	8.15-6.70, m, 7H; 7.02, s, 1H; 3.77, 3.12, s, 3H
16b	81	170-171	3230, 1660	8.10-6.50, m, 7H; 6.78, d, J, 10 Hz, 1H; 6.28, d, J, 10 Hz, 1H; 3.80, 3.12, s, 3H
17	85	165-167	1660, 1670	8.30-6.70, m, 7H; 6.31, s, 1H; 3.72, 3.82, s, 3H

Compound	Yield	mp	ir (nujol, cm^{-1})	^1H nmr ($CDCl_3$, δ)
18	90	--	3520, 1690	8.20-6.00, m, 7H; 4.50, bs, 1H; 3.67, 3.45, s, 3H; 3.00-2.00, m, 4H
19	92	--	3600	8.60-6.50, m, 9H; 3.70, 3.52, s, 3H

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4. D.S. Pearce, M.S. Lee, and H.W. Moore, J. Org. Chem., 1974, 39, 1362.
5. Carbazole ring formation from o-azidobiphenyls has previously been established. See: S. Patai, Ed., "The Chemistry of the Azide Group," J. Wiley and Sons, 1971.
6. Compounds 16a and 16b were prepared as outlined in Scheme 2 except the starting quinones were respectively 2-chloro-1,4-naphthoquinone and 1.4-naphthoquinone.
7. A.S. Hammam, Egypt J. Chem., 1972, 5, 391

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