expected bicyclolactone **5** (60–73%) as the only significant reaction product[5b] and thus represents an effective trap of the apparent, transient delocalized singlet vinylcarbene (Scheme II). The structure of the [3 + 4] cycloadduct **5** was clear from its spectroscopic properties[6] and was confirmed by conversion to deacetamidocolchiceine (**2b**) (Scheme II). Expectant efforts to promote decarboxylation of **5** to afford the cycloheptatrienone ketal **6** were successful, although the decarboxylation reaction required selected conditions for isolation and confirmation of the cycloheptatrienone ketal **6**.[7] Hydrolysis of **6**, which occurred upon attempted chromatographic purification of **6** or with mild aqueous acid treatment, provided **8**. More conveniently, warm aqueous acid treatment of **5**, which proceeds with initial ketal hydrolysis and is followed by a subsequent thermal decarboxylation,[8] provided tropone **8** in an excellent, direct conversion (70%). The intermediacy of the bicyclolactone **7** was demonstrated by its isolation[8] and subsequent thermal conversion to tropone **8**.

Introduction of the additional ring C hydroxyl required for the conversion of tropone **8** to **2a/b** was accomplished, as anticipated, by way of the deacetamidoisocolchiceinamide (**9**) by using existing protocols.[9,2d] Treatment of **8** with hydrazine afforded deacetamidoisocolchiceinamide (**9**),[9] which upon basic hydrolysis provided deacetamidocholchiceine (**2b**). Diazomethane methylation of **2b** provided deacetamidocolchicine (**2a**) and deacetamidoisocolchicine as previously described.[2b]

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Supplementary Material Available: Characterization and spectral information on **4–9** and **2b** are provided (4 pages). Ordering information is given on any current masthead page.

(6) Complete spectral information for **5** is provided in the supplementary material.

(7) Efforts to promote the thermal decarboxylation of **5** in solution (120 °C, toluene, 15 h, recovered **5**; 150–160 °C, mesitylene, recovered **5** and unidentified products; 200 °C, triisopropylbenzene, 1.5 h, unidentified products) were unsuccessful. Warming a solid sample of **5** at 210 °C (neat, 2–3 min) provided clean conversion of **5** to **6**.

(8) Treatment of **5** with mild aqueous acid [5% aqueous H_2SO_4–dioxane (1:1), 25 °C, 15 h] provided a mixture of recovered **5** (ca. 90%) and **7** (ca. 10%) with no detectable **8** (ca. 0%). Spectral characterization for **7** (^{1}H NMR) and **8** (full characterization) are provided in the supplementary material. Thermolysis of **7** (toluene, 110 °C, 1.5 h) provided complete conversion to tropone **8**. For related observations, see ref 4a.

(9) The reaction of tropone **8** with hydrazine under a variety of conditions afforded a 3:2 mixture of the 9-aminotropone **9** (deacetamidoisocolchiceinamide) and 11-aminotropone which were readily separated by chromatography and independently characterized. Deacetamidoisoamidoisocolchiceinamide (**9**) was identical in all respects with the properties reported for authentic material[2b] and upon hydrolysis provided deacetamidocolchiceine (**2b**) also identical in all respects with the properties reported for authentic material.[2b] Independent hydrolysis of the isomeric 11-aminotropone provided the corresponding 11-hydroxytropone (tropolone) displaying properties identical in all respects with that described for authentic material.[2b] In the Eschenmoser total synthesis of colchicine, on which most subsequent efforts have been based, this 11-hydroxytropone was converted to deacetamidoisocolchiceinamide (**9**) and subsequent hydrolysis provided deacetamidocolchiceine (**2b**).[2b]

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A Novel Synthetic Route to Heterocyclic Quinones

Summary: A new synthetic route to heterocyclic quinones is presented. This involves the addition of nucleophiles to the quinone methides generated from azidoquinones. The resulting azidohydroquinones proceed to aminoquinones which, in turn, lead to heterocyclic quinones via condensation of the amino substituent with proximal electrophilic sites.

Sir: Reported here are illustrative examples of transformations arising from an unusual and potentially general route to a large variety of heterocyclic quinones. As formally outlined in Scheme I, the method combines a number of reactions which alone have received little attention. Together, they constitute one mechanistic sequence which rationalizes the formation of the observed products and provides predictive insight to a variety of synthetic targets. The generalized sequence of steps include (1) equilibration of an appropriately substituted azidoquinone, **1**, to the quinone methide, **2**, and its in situ trapping (Michael addition) to give the unstable azidohydroquinone, **3**,[1] (2) spontaneous disproportionation of the azidohydroquinone to the aminoquinone,[2] **4**, and (3) in some cases subsequent ring closure or rearrangements induced by nucleophilic attack of the resulting amino group on a proximate electrophilic site.

The following represent illustrative examples of the above reaction sequence. Refluxing an aqueous THF solution of the azidoquinone **5** for 1.5 h resulted in the formation of the aminoquinone **6a** (79%) (Scheme II). When the reflux time was extended to 5 h the ring closed indoloquinone **7a** was isolated in 74% yield. In an analogous fashion, **6b** (77%) was obtained when **5** was decomposed in methanol. However, **7b** was not obtained by extending the reflux time (15 h) but was formed upon reduction of **6b** ($Na_2S_2O_4$) followed by subsequent air oxidation of the hydroquinone. Decomposition of **5** in acetic acid (90 °C) gave **7c** (65%). The structures of these products are based upon their spectral and analytical properties, and these data can be obtained as supplementary material. Structural data for **6a** and **7a** are provided here as representative examples. **6a**: mp 179–180 °C; IR (KBr, cm^{-1}) 3460 (s), 3400 (s), 3300, (s), 1740 (s), 1720 (s), 1680 (m); ^{1}H NMR ($CDCl_3$) δ 3.88 (s, 6 H), 4.46 (s, 1 H), 6.32 (br s, 2 H), 7.60–7.77 (m, 2 H), 8.03–8.11 (m, 2 H); MS (CI, M + 1), 320. Anal. Found: C, 56.46; H, 3.95. **7a**: mp 207–210 °C dec; IR (KBr, cm^{-1}) 3390 (m), 3250 (s), 1765 (s), 1730 (s), 1688 (m), 1680 (m); ^{1}H NMR ($CDCl_3$) δ 3.86 (s, 3 H), 4.48 (br s, 1 H), 7.73–7.86 (m, 3 H), 8.10–8.14 (m, 2 H); MS (M^+), calcd for $C_{14}H_9NO_6$ 287.04299, found 287.04269.

A number of unusual transformations were observed when the azidoquinones were treated with enolates of acidic ketones. For example, when **9** was slowly added to a THF solution of dimedone containing a catalytic amount of sodium hydride, **10** was isolated in 68% yield (Scheme III). Surprisingly, when the related azidoquinone **11** was subjected to the above reaction conditions, a different reaction pathway was followed. Here a 64% yield of the indoloquinone **12** was realized. Characteristic spectral data for **12** are as follows: mp 231–233 °C dec; IR (Nujol, cm^{-1}) 3220 (w), 1764 (m), 1750 (w), 1680 (m); ^{1}H NMR ($CDCl_3$) δ 1.8 (t, J = 7 Hz, 3 H), 1.23 (s, 3 H), 1.35 (s, 3 H), 2.28

(1) Equilibration of an azidoquinone to a quinonemethide has not previously been reported. However, precedent for such a transformation within the quinone field is well-known. See, for example: Smith, L. I.; Kaiser, E. W. *J. Am. Chem. Soc.* **1940**, *62*, 138. Jurd, L. *Aust. J. Chem.* **1978**, *31*, 347.

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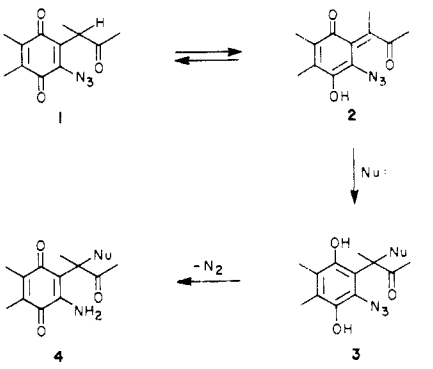
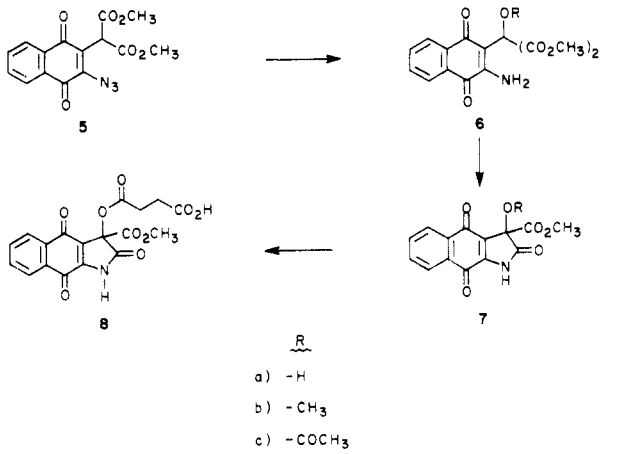
Scheme I

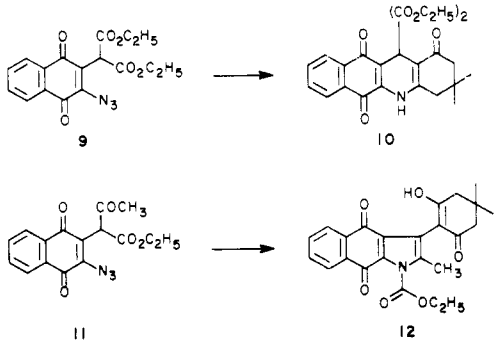


Scheme II



a) -H
b) -CH_3
c) -$COCH_3$

Scheme III



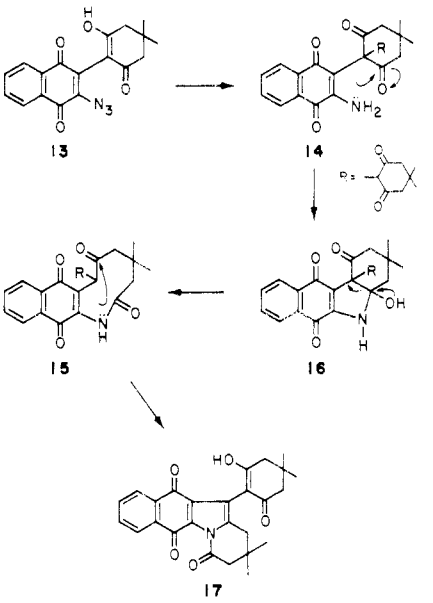
(s, 3 H), 2.46 (d, J = 16.0 Hz, 1 H), 2.68 (d, J = 16.0 Hz, 1 H), 2.75 (s, 2 H), 4.11 (q, J = 7.0 Hz, 2 H), 7.61-7.64 (m, 2 H), 8.06-8.10 (m, 2 H), 10.93 (s, 1 H); MS (CI, M + 1), 422.

The last and most unusual transformation described here was observed when the azidoquinone **13** was treated with dimedone and NaH in THF.[3] In this case, the tetracyclic indoloquinone **17** was realized in 63% yield (Scheme IV): mp 241-242 °C dec; IR (Nujol, cm^{-1}) 3432 (w), 1777 (s), 1666 (s), 1696 (s); ^1H NMR ($CDCl_3$) δ 1.18 (s, 3 H), 1.27 (s, 6 H), 1.43 (s, 3 H), 2.35 (dd, J = 13.5 Hz, 2 H), 2.47-2.72 (m, 6 H), 7.63-7.67 (m, 2 H), 8.05-8.10 (m, 2 H); MS (CI, M + 1), 432. Anal. Found: C, 72.20; H, 5.77.

A mechanistic rationale for the formation of **17** involves the conversion of **13** to **14** which is in analogy to the aminoquinone formation outlined in Scheme I. Subsequent

(3) The azidoquinone **13** is very unstable and could not be isolated in pure form. It was thus used directly without attempted purification.

Scheme IV



transformation of **14** to **17** is an example of "crisscross annelation".[4]

Finally, it is noted that the generalized reaction in Scheme I provides a facile entry to a variety of quinones that meet those structural requirements outlined for bioreductive alkylating agents.[5] For example, succinylation of **7a** gives **8**, a water-soluble (Na salt) quinone which undergoes an immediate conversion to the desuccinylated quinone upon treatment with sodium dithionite. This transformation most likely involves a quinonemethide intermediate which proceeds to the product upon proton transfer. The biological properties of **8** and related compounds is currently under investigation.

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Supplementary Material Available: Spectral data for **5-12** and **17** are available (2 pages). Ordering information is given on any current masthead page.

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Limatulone, a Potent Defensive Metabolite of the Intertidal Limpet *Collisella limatula*

Summary: The intertidal limpet *Collisella limatula* contains limatulone (**1**), a triterpene consisting of two identical C_{15} units, which inhibits fish and crab predation. Limatulone (**1**) is readily oxidized to a monohydroperoxide **2**.

Sir: Limpets are marine molluscs that are common to the intertidal zone. Their shells provide physical protection against the harsh environmental conditions that they experience. Among the five most abundant species of limpets along the coast of southern California, *Collisella limatula* is unique in having a chemical defense mechanism that

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