(5, 11 mg or ca. 0.02 mmol) in water (0.05 ml) was kept at 40° with 0.5 ml of acid-form cation exchange resin [Rexyn 101 (H$^+$)]. The resin was removed by filtration, and a stream of nitrogen was passed through the combined filtrate and washings (1.35 ml), for 15 min, in order to deoxygenate the solution. To this solution was added a similarily deoxygenated solution of 1.0 N sodium hydroxide (0.15 ml), therefore making the reaction mixture 0.1 N in sodium hydroxide. The reaction mixture was immediately agitated to ensure adequate mixing and after 2 min was neutralized with an acid-form resin (1 ml). During the course of the reaction, the color of the solution went from colorless, to light yellow, to light green. Neutralization with the resin rendered the solution colorless once again.

Reduction of the Products from Alkali Treatment of 2. Sodium borohydride (12 mg) was added to the neutralized aqueous reaction mixture (2.5 ml) and the resulting solution kept at room temperature for 6 hr. This solution was treated with acid-form resin until hydrogen evolution ceased, the resin was removed by filtration, and the filtrate was freeze-dried to give a white fluffy mass. Boric acid was removed from the mixture as trimethyl borate in vacuo at 35°. A solution of the residue in water (0.5 ml) was transferred to a 3-ml centrifuge tube and the water removed by freeze-drying. The amorphous product from the reduction, after being treated with 300 μl of trimethylsilylating reagent,[11,12] gave a mixture that was gently warmed for several minutes and then kept at room temperature for an additional 2 hr before subjecting it to GC.

Preparative GC of the Reduction Products from 2. For preparative GC, 20-μl aliquots of the trimethylsilylation mixture were injected into the gas chromatograph. Two semisolid fractions were collected, fraction I corresponding to peaks 1 and 2, and fraction II, to peaks 3–5 (Figure 1). The fractions were eluted from the collection tubes with methanol, and then an aliquot of each was concentrated to dryness under a stream of nitrogen, trimethylsilylated, and analyzed by GC. Although fractions I and II were somewhat cross-contaminated, neither of the fractions contained any component other than those corresponding to peaks 1–5.

Dephosphorylation and GC of Fractions I and II. Fractions I and II were dissolved in deionized water (0.3 ml), and tris(hydroxymethyl)aminomethane-Mg^{2+} buffer (1 ml) was added. The buffer was prepared by the addition of MgCl$_2$·0.6 H$_2$O (406 mg) to 50 ml of 1 M tris(hydroxymethyl)aminomethane hydrochloride (pH 7.4). The solutions were then incubated with alkaline phosphatase (Miles Laboratories, Inc., Kankakee, Ill.) (50 μl) for 2.5 hr at 40°

and subsequently deionized with a mixed-bed resin (1:1, v/v, Amberlite IR 120 H$^+$:IRA 400 OH$^-$). The resin was filtered off and the combined filtrate and washings (ca. 10 ml) freeze-dried. The residues were then treated with the trimethylsilylating reagent (25 μl) and gas chromatographed at 170° on the 3% SE-30 column.

Gas Chromatography–Mass Spectrometry. An LKB-9000 gas chromatograph-mass spectrometer—PDP-12 computer system[13] was used to obtain all spectra. The GC conditions were: 0.25 in. o.d. × 4 ft glass column (3% SE-30 on 80–100 mesh Gas Chrom Q) operated at 30 ml of He/min and temperatures appropriate to the experiment. The MS was operated with 70-eV electron beam ionization energy, while the source and separator temperatures were 270 and 240°, respectively.

References and Notes

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Melochinone, a Novel Quinolinone from *Melochia tomentosa* L.[1a,b]

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Abstract: Melochinone (C$_{22}$H$_{21}$NO$_2$) from the tumorogenic plant *Melochia tomentosa* has been found to have the quinolinone structure II containing a fused seven-membered ring. The structure was obtained by X-ray crystallography using direct methods.

Decoctions of certain plants used as folk remedies by natives of Curacao have been implicated in their relatively high local rate of esophageal cancer.[3] *Melochia tomentosa*[4] is one such plant, roots of which have been used to relieve throat inflammation; in earlier studies, an extract of roots

of this plant was indeed reported[7] to be tumorogenic. A benzene extract, obtained while fractionating the root constituents in search of this principal, gave a positive Dragendorff test and subsequent chromatography on silicic acid afforded a small amount of crystalline product, mp 316–318°,
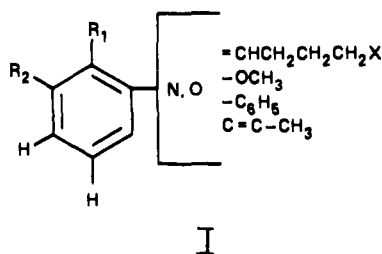
which we have designated melochinone.

Melochinone was found to be a neutral compound insoluble in aqueous acid and alkali, inert to the action of boiling 10% alcoholic hydrochloric acid and 5% boiling alcoholic potassium hydroxide. It was recovered unchanged from lithium aluminum hydride in tetrahydrofuran and was recovered unchanged from attempts at dehydrogenation with Pd on charcoal at 350°C. A molecular formula $C_{22}H_{21}NO_2$ was suggested from elemental analysis but mass spectral scans in the electron ionization mode showed an apparent molecular ion at m/e 322 inconsistent with the above, along with an equally intense peak at m/e 321. However, chemical ionization with isobutane showed only an intense MH^+ ion at m/e 322 proving that ion–molecule reactions were responsible for this peak even under electron impact conditions. The uv spectrum (Figure 1) suggested an extended aromatic system, while the ir showed bands at 1620, 1538, and 1493 cm^{-1}. The band at 1620 cm^{-1} did not appear to be intense enough to represent a carbonyl group. The proton NMR in CDCl$_3$ suggested several structural features: (1) a quartet δ 1.94 (2 H) which simplified to a triplet, when decoupling was applied at δ 6.60 (1 H), thus suggesting an allylic methylene–methine configuration; (2) a multiplet δ 2.45 (2 H) coupled to both δ 1.94 (2 H) and to a triplet at δ 3.56 (2 H); these data allowed postulation of an X—CH$_2$CH$_2$CH$_2$CH=C< fragment as part of the molecule; (3) two three-proton singlets δ 2.45 and 3.96 assignable to an olefinic C methyl (confirmed by the ^{13}C chemical shift δ 14.05) and a methoxyl, respectively; (4) an AB pattern in the aromatic region δ 7.03 and 7.17 (2 H) together with five additional protons suggesting a phenyl group, later confirmed by hydrogenation experiments.

The proton spectrum in trifluoroacetic acid showed all aliphatic protons to be shifted downfield with the δ 2.45 singlet moving away from the previously partially obscured multiplet in the same region which could now be easily recognized as a quintet. In the aromatic region, the AB pattern was no longer visible, having shifted into the five-proton aromatic pattern showing that these protons were strongly affected by the charge.

Since solubility limitations precluded CDCl$_3$, Me$_2$SO-d_6 was used for the ^{13}C spectra. The ^{13}C chemical shift with multiplicities from off-resonance decoupling are listed in Table I. Peaks for 20 carbons were resolved with an overlap of 2 carbons in the peaks δ 127.5 and 128.4, giving a total of 22 carbons. The δ 175.8 peak was of such low intensity due to its long relaxation time that it was at first disregarded as an artifact.

At this point the partial structure was represented by I, but the available data failed to suggest to us a suitable envi-

ronment for the nitrogen-containing moiety. The unexplained lack of basicity in the absence of carbonyl absorption in the ir was of particular concern.

Since degradation experiments were unsuccessful and because only small quantities of the compound were available, an X-ray crystallographic analysis was undertaken.
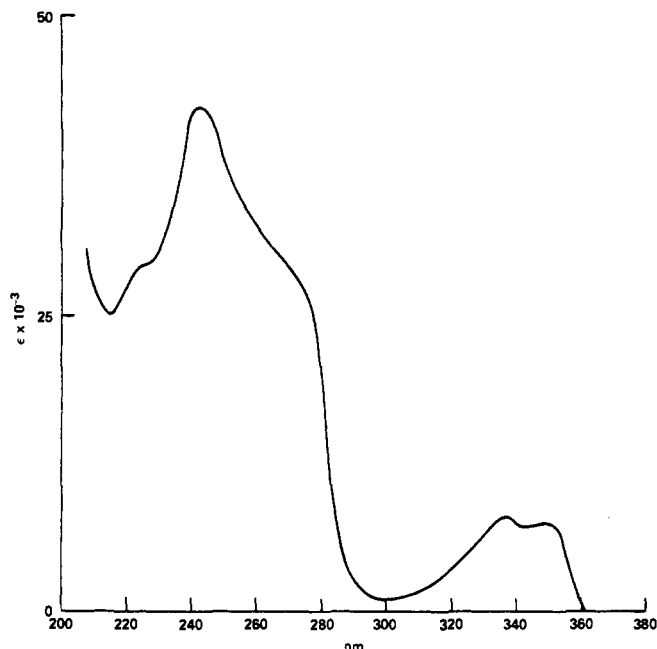
Figure 1. Uv spectrum of melochinone.

Table I^a

δ^{13}C	δ^{13}C
14.1 (Q)	130.7 (D)
25.4 (T)	134.8 (S)
27.4 (T)	138.9 (S)
36.9 (T)	139.6 (S)
58.8 (Q)	140.9 (S)
115.5 (D)	141.0 (S)
123.0 (S)	142.0 (S)
127.1 (D)	142.7 (S)
127.5 (2 carbons) (D)	175.8 (S)
128.4 (2 carbons) (D)	
129.2 (D)	

^{a} In Me$_2$SO, relative to Me$_4$Si 0.00. Q = quartet, T = triplet, D = doublet, S = singlet.

Discussion

(a) **Crystal Structure.** Direct methods, using procedures previously reported,[8] gave the structure II (2-methoxy-3-methyl-7-phenyl-9,10,11-trihydro(4H)cyclohepta[f]quinol-

I

II
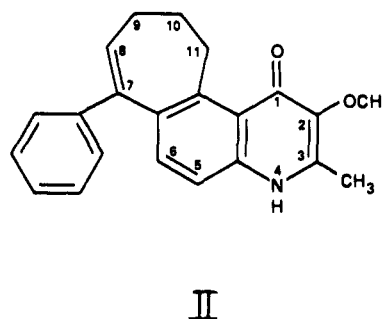
inone) whose molecular conformation and thermal ellipsoids are shown in Figure 2. The bond lengths and angles are given in Figure 3.

The phenyl ring appears to be quite normal although some of the observed bond lengths are probably shortened by thermal motion. The relatively large thermal parameters of the atoms may be caused by the lack of close contacts (Figure 4), and the benzene ring seems to be undergoing

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Figure 2. ORTEP drawing of molecular conformation and thermal ellipsoids (50% probability for heavier atoms) ORTEP is described by C. K. Johnson, Oak Ridge National Laboratories Technical Report, 1965, p 3794.

Figure 3. Bond lengths and angles.

torsional vibration about the connecting bond. The angles of the phenyl ring are not significantly different from 120° except at C(1p) and C(2p). The distortions may result from the close contacts C(8)-C(2p), C(8)-C(1), C(6)-C(1), and C(6a)-C(1p) with lengths of 2.992, 2.472, 3.033, and 2.559 Å, respectively.

In the seven-membered ring, all C-C bonds, except for C(9)-C(10) and C(10-C(11), involve sp² hybridized carbon atoms and the average values, 1.491 Å for unconjugated sp²-sp² single bonds and 1.499 Å for sp²-sp³ are as expected. The two sp³-sp³ bonds are a little shorter than the standard value of 1.54 Å, but the difference appears to be real since the thermal parameters of the appropriate atoms are not excessively large. The ring angles are all greater than the tetrahedral angle, but internal angles in rings with six or more members usually show a similar expansion which is likely to be reinforced by the two double bonds in the present structure.

There is little information in the literature on crystal structures of compounds containing the 4-quinolinone moiety; in fact the only compound which we have been able to find is the alkaloid bromodihydroacronycine which contains

not a 4-quinolinone but an acridone nucleus.[9] This compound is not strictly comparable since there is considerable distortion of the pyridinone ring with the two triangles containing the carbonyl carbon and nitrogen atoms as apices being bent away from the plane of the other four atoms at angles of 7 and 11° so as to give the whole ring a distinctly boat conformation. The pattern of long and short formally equivalent bonds present in the 4-quinolinone nucleus of melochinone is not seen in the structure of bromodihydroacronycine, although differences in bond lengths may be obscured by the higher esd of the latter structure. The present pattern is consistent with a considerable admixture of ionized canonical forms in the valence bond description of the nucleus (N^+, O^-). Such an admixture of ionized forms has been invoked by Calleri and Speakman to explain the bond lengths in bis(1-methyl-2-quinolinone)·HAsF$_6$[10] and is consistent with results for 1-methyl-2-quinolinone dihydrogen arsenate[11] and for phenanthridone.[12] Other compounds whose structures may be of some relevance are 2-pyridinone[13] (structure from projections), 5-chloro-2-pyridinone,[14] l-mimosine (a 4-pyridinone whose structure is complicated by further resonance possibilities),[15] 3,5-dichloro-2,6-dimethyl-2-pyridinone,[16] and the complex of 2-pyridinone with 6-chloro-2-hydroxypyridine.[17] Except for bromodihydroacronycine and the 2-quinolinone complex, there is usually considerable asymmetry in the reported pyridinone C-N bond lengths with one bond often being as short as the comparable bond in pyridine [1.340 (1) Å][18] and the other being significantly longer. An average C-N length, weighted by the esd in the above structures, is 1.365 Å which is close to the mean of the two lengths in the present structure, 1.361 Å. The internal angle at the nitrogen atom in the present structure is 122.8° which may be compared with a weighted average value of 123.7° for comparable molecules with a hydrogen-substituted nitrogen atom. If one also includes the 5-quinolinone reported by Sax, Desiderato, and Dakin,[19] weighted averages for all the pyridinone and quinolinone structures give values of 1.258 Å and 115.6° for the C-O bond length and the internal angle at the carbonyl atom, respectively. These values can be compared with the present values of 1.256 Å and 116.3°. There is a close approach (2.22 Å) between O(1) and a hydrogen atom attached to C(11) which may explain the inequality of the two exterior angles at C(1). Other substituent exterior angles are also probably distorted by close approaches.

In 1,3-cycloheptadiene, a C_2 conformation similar to that present in melochinone has been calculated[20] to be 4.3 kcal/mol more stable than the C_s conformation found by vapor phase electron diffraction.[21]

The major influence controlling the crystal packing (Figure 4) is the relatively strong N(4)-O(1) hydrogen bond (2.749 Å) between molecules related by the glide plane. The hydrogen bond, with a calculated O-H-N angle of

Figure 4. Packing diagram. The projection is down b.

171° can be considered linear since the deviation of the hydrogen atom from the line O–N is less than 3σ. The presence of strings of molecules extending through the crystal probably explains the relatively high melting point. All other intermolecular contacts are greater than or equal to van der Waals distances.

(b) Chemical Structure and Spectra. In retrospect, our failure to recognize the presence of a 4-quinolinone moiety was a severe handicap. The 4-quinolinone system is indeed unique in failing to show distinctive carbonyl bands. While several weak bands are observed at 1500–1600 cm^{-1}, Price and Willis[22] have shown that the bond regarded as characteristic of 4-quinolinones at 1620–1625 cm^{-1} is present also in 2- and 4-methoxyquinolines. Furthermore, these authors show that distinction between 2- and 4-quinolines by ir, as had been proposed earlier, is unreliable. McCorkindale has noted[23] that the "carbonyl" bands of 4-quinolinones have only one-fourth of the integrated intensity of 2-quinolinones, but no comparisons were made with the corresponding methoxyquinolines, etc., and Rapaport has proposed[24] the use of the characteristic shift in the ultraviolet on acidification shown by simple 4-quinolinones in contrast to their 2-isomers.

Clearly, a general spectral technique for identification of the pyridinone (or quinolinone) system as well as distinction between its 2- and 4-isomers is still very much in need.

A further point of confusion in the preliminary chemical work was based on the hypothetical electronegative group X in partial structure I. This assumption was derived from the NMR signal at δ 3.56 which is seen to be shifted downfield ~1 ppm from its expected location due to the paramagnetic influence of the carbonyl group. As mentioned previously, the latter is in close proximity to at least one of the CH$_2$ hydrogens in the crystal state.

The ultraviolet spectrum of II (Figure 1) is only superficially similar to that of other known quinolinones[25] due in part to the influence of the 3-methoxy group although, in the crystal (and probably in solution), this group is canted from the plane of the ring. Furthermore, as Figure 2 shows, there is little overlap in the crystal between the π orbitals of the quinolinone ring and the styrene double bond (torsion angle, C(11a)–C(6a)–C(7)–C(8), 40°). Even the benzene ring is incompletely conjugated with the double bond (torsion angle, C(6P)–(C(1P)–(C(7)–C(8), 38°).

Catalytic hydrogenation (Pt–HCl) of melochinone provided two compounds whose structures may be rationalized from II. An octahydro derivative, mp 274°, showed a molecular ion at m/e 339 and lost the elements of cyclohexyl (benzylic cleavage) to produce the most intense ion in the spectrum at m/e 256 (m* 194.0). The uv spectrum (qualitative) was very similar to II (max 248 nm) but lacked the shoulder at 270 nm assigned to the styryl system; accord-
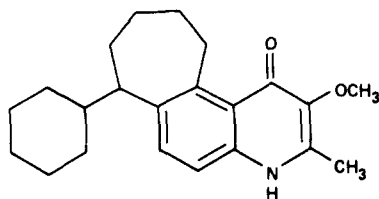
**III**

ingly it is formulated as III. A dodecahydro derivative (mp 174°) was also isolated by chromatography on silicic acid. The molecular ion at m/e 343.2496 (C$_{22}$H$_{33}$NO$_2$, 343.2511) again lost the cyclohexyl ring to give the most in-

tense ion in the spectrum at m/e 260.1662 (C$_{16}$H$_{22}$NO$_2$, 260.1650, m* 197.5). The uv (qualitative) showed maxima at 220 and 270 nm in methanol shifting to 247 and 265 nm in dilute acid where it absorbed with a lower intensity. 2-Methyl-3-methoxy-4-(1H)-pyridinone absorbs at 266 nm (ϵ 13370) shifting in acid to 241 nm (ϵ 5580) and 259 (5329),[26] and therefore the dodecahydro derivative is assigned structure IV of undetermined stereochemistry.
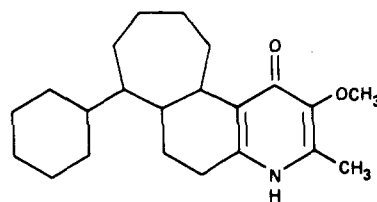
IV

While 2- and 4-quinolinones are common enough among, for example, the *Rutaceae* and *Angostura* alkaloids, we were able to find only one other example of a 3-methoxyquinolinone, japonine (V) from *Orixa japonica*.[27] This seems surprising from the apparently obvious biosynthesis
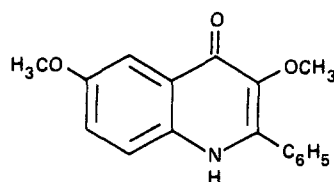
V

of this system from anthranilate and phenylpyruvate or, in the case of melochinone, pyruvate itself.

The origin of the seven-membered ring in melochinone is considerably more of a problem, biosynthetically. An arene oxide intermediate similar to that proposed by Luckner[28] in the formation of the 7,8-dialkoxyquinolinones from kynurenic acid is attractive. One might imagine it to condense with

Table II. Crystal and Refinement Data for Melochinone

Molecular formula:	C$_{22}$H$_{21}$NO$_2$
Asymm. unit weight:	331.4 Daltons
Habit:	Monoclinic prismatic
Crystal size:	Irregular fragment 0.13 × 0.43 × 0.55 mm
Radiation:	Cu Kα (graphite monochromatic λ 1.5418 A)
Space group:	$P2_1/a$ (No. 14)
Cell dimensions:	From LS refinement of $\pm\theta$ data
a:	13.086 (1) Å
b:	10.160 (1) Å
c:	14.682 (1) Å
β:	112.65 (1) deg
V:	1801.5 Å^3
Z:	4
d_m:	1.214 g/cm^3
d_x:	1.221 g/cm^3
μ:	6.25 cm^{-1}
Reflections:	3590 (652 unobserved, 3σ)
Maximum sin θ/λ:	0.62 A^{-1}
Diffractometer:	Nonius CAD-4
Computer programs:	XRAY72, general[30]
	Silverton, direct methods[8]
Scattering factors:	C,N,O, International Tables[31]
	H, Stewart, Davidson, and Simpson[32]
Refinement:	Full matrix least-squares
	(Partitioned because of molecular size)
Function minimized:	$\Sigma w\Delta^2$, Peterson–Levy weights[33]
R:	0.046 (observed reflections only)[34]

**Table III.** Parameters of the Heavier Atoms ($\times 10^4$)[a]

Atom	x/a	y/b	z/c	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	2297 (1)	3120 (1)	6593 (1)	288 (5)	347 (6)	550 (7)	−12 (5)	208 (5)	16 (5)
C(2)	2475 (1)	1914 (1)	6174 (1)	305 (5)	337 (6)	495 (7)	−35 (5)	167 (5)	−2 (5)
C(3)	3481 (1)	1567 (1)	6162 (1)	344 (6)	357 (6)	495 (7)	26 (5)	180 (5)	2 (5)
N(4)	4351 (1)	2387 (1)	6563 (1)	267 (5)	400 (6)	568 (6)	38 (4)	187 (5)	−32 (5)
C(4A)	4276 (1)	3567 (1)	6987 (1)	271 (5)	363 (6)	438 (6)	21 (4)	143 (5)	15 (5)
C(5)	5229 (1)	4359 (1)	7368 (1)	243 (5)	462 (7)	525 (7)	1 (5)	137 (5)	13 (6)
C(6)	5168 (1)	5555 (1)	7759 (1)	306 (6)	433 (7)	472 (7)	−61 (5)	105 (5)	8 (6)
C(6A)	4174 (1)	6019 (1)	7809 (1)	374 (6)	377 (6)	423 (6)	−24 (5)	153 (5)	−6 (5)
C(7)	4115 (1)	7395 (1)	8138 (1)	465 (7)	403 (7)	498 (7)	−75 (6)	201 (6)	−78 (6)
C(8)	3224 (1)	8147 (1)	7658 (1)	527 (8)	367 (7)	696 (9)	−36 (6)	228 (7)	−89 (7)
C(9)	2251 (1)	7716 (2)	6763 (1)	460 (8)	453 (8)	734 (10)	32 (6)	137 (7)	−37 (7)
C(10)	1539 (1)	6649 (2)	6958 (1)	413 (7)	463 (8)	873 (11)	38 (6)	276 (8)	−149 (8)
C(11)	2249 (1)	5656 (2)	7708 (1)	453 (7)	457 (8)	707 (10)	−42 (6)	358 (7)	−123 (7)
C(11A)	3241 (1)	5204 (1)	7502 (1)	349 (6)	354 (6)	485 (7)	−4 (5)	207 (5)	0 (5)
C(11B)	3267 (1)	3977 (1)	7040 (1)	285 (5)	332 (6)	470 (7)	2 (4)	181 (5)	11 (5)
C(M2)	813 (2)	1470 (2)	4839 (1)	511 (9)	802 (13)	623 (10)	−204 (9)	68 (8)	−52 (9)
C(M3)	3682 (1)	307 (2)	5728 (1)	508 (8)	421 (8)	787 (11)	23 (6)	326 (8)	−126 (7)
C(1P)	80 (1)	7079 (2)	8987 (1)	521 (8)	565 (8)	476 (7)	91 (6)	207 (6)	133 (6)
C(2P)	422 (1)	5775 (2)	8987 (1)	605 (9)	638 (10)	649 (10)	192 (8)	294 (8)	207 (8)
C(3P)	6317 (2)	9724 (2)	9766 (1)	722 (12)	928 (15)	920 (14)	−340 (11)	353 (11)	−466 (12)
C(4P)	6889 (2)	8936 (3)	552 (1)	764 (14)	1350 (23)	781 (15)	−155 (14)	99 (12)	−487 (15)
C(5P)	6579 (2)	7656 (3)	570 (1)	1015 (18)	1291 (23)	554 (12)	80 (16)	11 (11)	−138 (13)
C(6P)	5676 (2)	7138 (2)	9790 (1)	854 (13)	838 (14)	536 (10)	−44 (11)	125 (9)	−44 (9)
O(1)	1348 (1)	3425 (1)	6547 (1)	296 (4)	461 (5)	1034 (8)	−57 (4)	362 (5)	−156 (5)
O(2)	1595 (1)	1053 (1)	5779 (1)	376 (5)	376 (5)	656 (6)	−93 (4)	201 (4)	−45 (4)

[a] Estimated standard deviations are given parenthetically and refer to the last one or two figures as appropriate. The temperature factor used had the form: $\exp[-2\Pi^2(\Sigma_i\Sigma_j U_{ij}a_i{}^*a_j{}^*h_ih_j)]$.

Table IV. Parameters of the Hydrogen Atoms ($\times 10^3$)[a]

Atom	x/a	y/b	z/c	U
4	1 (1)	282 (2)	651 (1)	63 (4)
5	590 (1)	403 (1)	729 (1)	58 (4)
8	320 (1)	902 (2)	789 (1)	60 (4)
6	83 (1)	886 (1)	799 (1)	52 (4)
9	178 (1)	850 (2)	641 (1)	72 (5)
9′	252 (1)	735 (2)	627 (1)	66 (5)
10	100 (1)	705 (2)	720 (1)	70 (5)
10′	108 (1)	616 (2)	631 (1)	63 (4)
11	253 (1)	610 (2)	834 (1)	56 (4)
11′	179 (1)	486 (1)	777 (1)	56 (4)
2P	505 (1)	980 (2)	843 (1)	57 (5)
3P	655 (1)	70 (2)	974 (1)	83 (6)
4P	260 (2)	567 (3)	113 (2)	126 (8)
5P	703 (2)	707 (3)	105 (2)	155 (11)
6P	539 (2)	620 (2)	977 (1)	105 (7)
M2	46 (2)	240 (3)	489 (2)	161 (11)
M2′	112 (2)	141 (3)	428 (2)	146 (10)
M2″	30 (2)	77 (2)	458 (2)	115 (8)
M3	414 (2)	41 (2)	541 (2)	113 (8)
M3′	301 (2)	986 (2)	533 (2)	130 (9)
M3″	394 (2)	960 (3)	624 (2)	170 (12)

[a] Numbering indicates attachments. Estimated standard deviations given parenthetically and referring to the last one or two figures.

Paracotoin
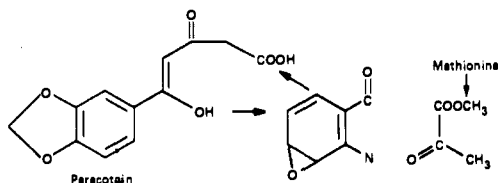
a C_6-C_3-C_2 unit of the type presumably responsible for the biosynthesis of paracotoin,[29] but the details of the condensation are not obvious from structure II.

Experimental Section

Isolation of Melochinone. Powdered root of *Melochia tomentosa* (800 g) was extracted for 24 hr in a continuous extractor with pe-

Table V. Torsion Angles (Degrees)

C(11B)	C(1)	C(2)	C(3)	1.3
O(1)	C(1)	C(2)	C(3)	−176.8
O(1)	C(1)	C(2)	O(2)	4.4
C(1)	C(2)	C(3)	N(4)	−0.2
O(2)	C(2)	C(3)	C(M3)	−1.0
C(1)	C(2)	O(2)	C(M2)	−76.0
C(3)	C(2)	O(2)	C(M2)	105.1
C(2)	C(3)	N(4)	C(4A)	0.0
C(3)	N(4)	C(4A)	C(11B)	1.1
C(5)	C(4A)	C(11B)	C(11A)	0.9
N(4)	C(4A)	C(11B)	C(1)	2.3
C(6)	C(5)	C(4A)	C(11B)	2.4
C(6A)	C(6)	C(5)	C(4A)	−1.0
C(11A)	C(6A)	C(6)	C(5)	−3.8
C(11A)	C(6A)	C(7)	C(8)	40.4
C(11)	C(6A)	C(11A)	C(6)	−171.0
C(7)	C(6A)	C(11A)	C(11B)	−169.7
C(1P)	C(7)	C(6A)	C(11A)	−141.6
C(1P)	C(7)	C(6A)	C(6)	41.7
C(6A)	C(7)	C(8)	C(9)	1.7
C(7)	C(8)	C(9)	C(10)	−69.0
C(8)	C(9)	C(10)	C(11)	38.1
C(9)	C(10)	C(11)	C(11A)	46.2
C(10)	C(11)	C(11A)	C(6A)	−81.1
C(11)	C(11A)	C(6A)	C(7)	12.2
C(11B)	C(11A)	C(6A)	C(6)	7.0
C(11)	C(11A)	C(11B)	C(4A)	172.3
C(6A)	C(11A)	C(11B)	C(1)	172.9
C(11A)	C(11B)	C(1)	O(1)	−2.8
C(4A)	C(11B)	C(1)	C(2)	−2.3
C(4A)	C(11B)	C(1)	O(1)	175.7
C(1)	C(11B)	C(4A)	C(5)	−177.7
C(11A)	C(11B)	C(4A)	N(4)	−179.1
C(4A)	C(11B)	C(11A)	C(6A)	−5.9
C(2P)	C(1P)	C(7)	C(6A)	−141.2
C(2P)	C(1P)	C(7)	C(8)	36.9
C(6P)	C(1P)	C(7)	C(6A)	37.8
C(6P)	C(1P)	C(7)	C(8)	−144.1
C(2P)	C(1P)	C(6P)	C(5P)	−0.6
C(3P)	C(2P)	C(1P)	C(6P)	0.7
C(4P)	C(3P)	C(2P)	C(1P)	−0.5
C(5P)	C(4P)	C(3P)	C(2P)	0.1
C(6P)	C(5P)	C(4P)	C(3P)	0.2
C(1P)	C(6P)	C(5P)	C(4P)	0.1

troleum ether (60–80°). The defatted plant material was then similarly extracted with benzene. The benzene extract was evaporated under vacuum to yield 2.8 g of residue. The residue was dissolved in chloroform (~10 ml) and the solution chromatographed on a silicic acid column (3.5 × 35 cm). The column was eluted first with 500 ml of petroleum ether, 500 ml each of petroleum ether–benzene 4:1, 3:1, 2:1, 1:1, 1:2, 1:3, 1:4, benzene, and benzene–chloroform 3:1, 2:1, 1:1, 1:2, 1:3. Although several of these fractions gave a positive Dragendorff's test for alkaloids, only the benzene–chloroform (3:1) and benzene–chloroform (2:1) eluates afforded crystalline products.

The residue from the benzene–chloroform (3:1) eluate yielded, on crystallization from aqueous methanol, a compound, mp 152–153° (44 mg). On silicic acid TLC, the material showed two spots which were not easily resolved. The less polar component appears to be an artifact arising during the chromatographic procedure and could not be obtained in a pure state. Further characterization of this product is in progress.

Concentration of the benzene–chloroform (2:1) fraction yielded crystalline melochinone, mp 312–316°, which on recrystallization from alcohol afforded 82 mg of product (mp 316–318° dec). Purity of the product was established by TLC on silicic acid plates using 10% methanol in chloroform. Anal. Calcd for $C_{22}H_{21}NO_2$: C, 79.78; H, 6.38; N, 4.23. Found: C. 79.13; H, 6.42; N, 4.12.

Hydrogenation of Melochinone. The compound (40 mg) was dissolved in 10 ml of ethanol, 3 N in hydrochloric acid, and hydrogenated for 2–5 days at 42 psi using 100 mg of Adam's catalyst. The reaction mixture was filtered and the filtrate evaporated to dryness. The residue was dissolved in 5 ml of chloroform containing 2% methanol and chromatographed on silicic acid (1.5 × 16 cm). The column was eluted with petroleum ether, benzene, chloroform, and chloroform containing 2% methanol and 5% methanol (50 ml each). The residue from the 2% methanol–chloroform eluate afforded colorless needles on crystallization from methanol, mp 274°, and showed a molecular ion at m/e 339 and a maximum in the uv at 248 nm (qualitative). The 5% methanol fraction produced colorless needles on evaporation and recrystallization from aqueous methanol, mp 174°. It showed a molecular ion at m/e 343 and gave one maximum in the uv at 270 nm (methanol) shifting to 266 nm with an additional maximum at 247 nm upon acidification.

Solution and Refinement of the Crystal Structure. X-Ray experimental results are given in Table II. The intensity data were corrected for Lorentz and polarization effects, but no corrections for absorption were made (azimuthal scans indicated very little intensity variation). While all the heavier atoms were not found in the E map, a combination of least-squares refinement and difference maps gave the rest of the structure including hydrogen atoms. Some hydrogen atoms, especially those attached to methyl carbon atoms, had high temperature factors, but they were visible as reasonably clear peaks in a difference map (all had peak intensities at least twice the noise level) and refined to satisfactory positions, and it seems unnecessary to suggest rotation or disorder.

Final atomic parameters for the heavier atoms are given in Table III and those for hydrogen atoms in Table IV. Estimated standard deviations of heavier atom bond lengths are all less than 0.003 Å except for those involving peripheral atoms of the highly vibrating phenyl ring [esd of the bond lengths C(3p)–C(4p) and C(6p)–C(5p) are slightly greater than 0.003 Å, and the bond C(4p)–C(5p) has an esd of 0.0046 Å]. Bond angles involving the heavier atoms all have esd of ca. 0.1° except for those at the five

outermost atoms of the phenyl ring where the corresponding value is ca. 0.2°. Relevant torsion angles are given in Table V.

References and Notes

(1) (a) Part III of the series on Potential Carcinogens. (b) Studies at Howard University were supported by contract No. N01 CP 33266 from the National Cancer Institute.
(2) (a) Howard University; (b) National Heart and Lung Institute.
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(4) *Melochia tomentosa* (Family *Sterculiaceae*) is a shrub 1.5 m high, abundant close to the coast in Curacao, and common at sea level and on the nearby mountains in Coro, Venezuela. The plant is also found in Florida, Texas, the Bahamas, throughout Mexico, and extending as far south as Brazil. Two species of *Melochia, M. corchorifolia* and *M. pyramidata* L., have been examined previously. In the former, the peptide alkaloids frangufoline, franganine, and adouetine, also found in *Rhamnus* species, were noted[5] and, in the latter, uncharacterized tertiary and quaternary bases were found.[6] One of these, designated melochin, has been implicated in a local cattle disease "derrengue".
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(34) See paragraph at end of paper regarding supplementary material.