isomerizes to azulene without any intervention of **2a**. These findings support our previous assumption[5,14] on the role of the pentafulvene moiety during the ring opening of azulvalene. The activation energy for **2a** is also small as compared with that of **2b** (36.7 kcal/mol).[5] The observed rate retardation by methoxy substitution in **2b** is mainly due to the increase in repulsive force with the progress of the disrotatory bond fission of **2b** with antiaromatic transition state.[15]

Under the strictly selected irradiations with monochromatic light,[16] **1a** isomerizes almost quantitatively throughout the overall reaction whereas **2a** isomerizes in ~60%, at least in the initial stage of the photolysis. It should be pointed out that the quantum yields for isomerizations of **1a** and **2a** in argon-purged cyclohexane with the irradiation in their first and second absorption bands are Φ_{S_1}(excited at 460 nm) = 5×10^{-4} and Φ_{S_2}(excited at 300 nm) = 0.35 for **1a**; Φ_{S_1}(excited at 400 nm) ~ 10^{-6} and Φ_{S_2}(excited at 280 nm) = 1.8×10^{-2} for **2a**.[16] Since addition of isoprene (E_T = 60.1 kcal/mol) or 1,3-cyclohexadiene (E_T = 52.4 kcal/mol) does not affect the above data, **1a** and **2a** presumably isomerize from their two distinct singlet excited states. The higher quantum yields in excitation of upper states of each compound should be ascribed to the longer lifetimes of these states as compared with those of S_1 states.[17]

This synthetic achievement permits access to a full understanding of the ground- and excited-state properties of these prototype molecules. We plan to examine such matters in due course.

Registry No. 1a, 92622-71-4; **2a**, 92622-72-5; **4**, 73566-86-6; **5**, 92622-73-6; **6**, 92622-74-7; **7**, 92622-75-8; azulene, 275-51-4; 9-chlorotetracyclo[5.3.0.0^{2,4}.0^{3,5}]dec-1(7)-en-6-one, 92622-76-9; tricyclo[5.3.0.0^{3,5}]deca-3,9-dien-6-one, 73566-88-8; 7-bromotricyclo[5.3.0.0^{2,5}]deca-3,9-dien-6-one, 92622-77-0.

(14) Dewar, M. J. S.; Kirschner, S. *J. Am. Chem. Soc.* **1975**, *97*, 2932. Turro, N. J.; Renner, C. A.; Katz, T. J.; Wiberg, K. B.; Connon, H. A. *Tetrahedron Lett.* **1976**, 4133.

(15) For the disrotatory ring opening of Dewar benzene with antiaromatic transition state, see: Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Verlag Chemie: Weinheim/Bergstr., Germany, 1970.

(16) For the photoisomerizations of **1a** in excitation at 460 nm and **2a** in excitation at 400 nm, Toshiba Y-43 (>430 nm) and UV-35 (>350 nm) were used, respectively, to shut off the leaking of shorter wavelength light.

(17) Kent, J. E.; Harman, P. J.; O'Dwyer, F. *J. Phys. Chem.* **1981**, *85*, 2726.

Temperature Dependence of Tautomeric Equilibria in the Solid State: The Case of Citrinin

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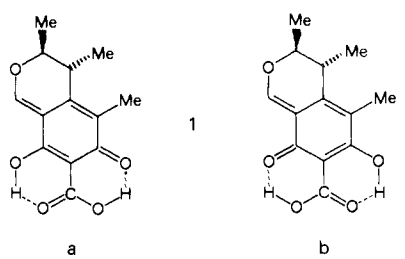
Citrinin (**1**) is an extensively studied[2] fungal metabolite, whose



a b

chemical structure was determined years ago by degradative, synthetic and spectroscopic techniques.[3-6] The absolute configurations of its asymmetric centers have also been established,[7,8] but no experimental evidence could be found to distinguish between the *p*-quinonemethide formulation **1a**, usually adopted as the true structure, and the *o*-quinone form **1b**. The results of an early investigation by single-crystal X-ray diffraction have been interpreted[9] in terms of structure **1a**, but anomalous values for some of the few published molecular dimensions seem rather in favor of either a resonance hybrid between the extreme structures **1a** and **1b**, as recently proposed,[10] or, more likely, a disordered structure corresponding to the superimposition of different amounts of **1a** and **1b**. Indeed, the position of the carboxylic group with respect to the hydroxyl and quinonoid oxygen atoms strongly suggests the occurrence of intramolecular proton exchange, reminiscent of the well-known case of naphthazarin,[11] and hence the existence of a tautomeric equilibrium between the para and the ortho isomers. If both forms are present in the crystal (i.e., the structure is disordered), two distinct positions for each proton involved in the intramolecular hydrogen bonds should be found, while the formulation of the structure as a resonance hybrid would require the detection of each hydrogen atom in a single position.

Table I. Crystal Data for Citrinin (**1**)[a]

	290 (2) K	147 (5) K
a, Å	13.441 (3)	13.358 (4)
b, Å	7.291 (2)	7.226 (5)
c, Å	12.241 (3)	12.170 (3)
V, Å^3	1199.6 (5)	1174.8 (9)
D_m, g cm^{-3}	1.385	
D_x, g cm^{-3}	1.386	1.415

[a] $C_{13}H_{14}O_5$, fw 250.25, Z = 4, orthorhombic, space group $P2_12_12_1$-(D_2^4), μ(Mo Kα) = 1.00 cm^{-1}.

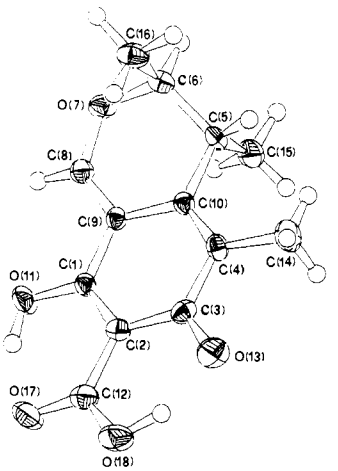


Figure 1. Perspective view of the molecule of citrinin at 147 K, with atomic numbering scheme. The thermal ellipsoids are drawn at a 50% probability level.

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(2) (a) Turner, A. B. *Prog. Chem. Org. Nat. Prod.* **1966**, *24*, 288–328. (b) Colombo, L.; Gennari, C.; Potenza, D.; Scolastico, C.; Aragozzini, F.; Merendi, C. *J. Chem. Soc. Perkin Trans. 1* **1981**, 2594–2597 and references therein.

(3) (a) Brown, J. P.; Robertson, A.; Whalley, W. B.; Cartwright, N. J. *J. Chem. Soc.* **1949**, 867–879. (b) Cartwright, N. J.; Robertson, A.; Whalley W. B. *J. Chem. Soc.* **1949** 1563–1567. (c) Johnson, D. H.; Robertson, A.; Whalley, W. B. *J. Chem. Soc.* **1950**, 2971–2975.

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(6) Mathieson, D. W.; Whalley, W. B. *J. Chem. Soc.* **1964**, 4640–4641.

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(8) Hill, R. K.; Gardella, L. A. *J. Org. Chem.* **1964**, *29*, 766–767.

(9) Rodig, O. R.; Shiro, M.; Fernando, Q. *J. Chem. Soc., Chem. Commun.* **1971**, 1553–1554.

(10) Sankawa, U.; Ebizuka, Y.; Noguchi, H.; Isikawa, Y.; Kitaghawa, S.; Tamamoto, Y.; Kobayashi, T.; Iitak, Y. *Tetrahedron* **1983**, *39*, 3583–3591.

(11) (a) Shiau, W. I.; Duesler, E. N.; Paul, I. C.; Curtin, D. Y.; Blann, W. G.; Fyfe, C. A. *J. Am. Chem. Soc.* **1980**, *102*, 4546–4548 and references cited therein. (b) de la Vega, J. R.; Busch, J. H.; Schauble, J. H.; Kunze, K. L.; Haggert, B. E. *J. Am. Chem. Soc.* **1982**, *104*, 3295–3299.

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To clarify the situation, an accurate single-crystal X-ray diffraction analysis of citrinin (**1**) has been performed, both at room temperature and at 147 ± 5 K.

Crystal data at the two temperatures are listed in Table I, while details of data collection and refinement are given in the supplementary material, Table II.[13] The atomic numbering scheme adopted for the analysis is shown in Figure 1. The solution of the structure by direct methods and its subsequent refinement by least-squares techniques were based on the room-temperature data set. Difference maps indicated the positions of all 14 hydrogen atoms, although some of them appeared as poorly resolved peaks. At convergence (max parameter shift $< 0.15\sigma$), the molecular model showed the following relevant features: (i) the lengths of the carboxylic C–O bonds, 1.239 (3) and 1.293 (3) Å, were indicative of partial disorder[14] for this group of atoms; (ii) concomitantly, neither of the C–O bonds of the quinonoid system could qualify as a double bond, their lengths being 1.279 (2) and 1.310 (2) Å; (iii) the values of the C–O–H angles, both 106 (1)°, were anomalously small and the O–H distances, 1.07 (3) and 1.15 (4) Å, unusually long; (iv) the temperature factors of the two protons participating in the intramolecular OH···O bonds and those of the hydrogen atoms of the methyl group C(14) were anomalously large.

A difference map was then calculated in the least-squares plane through the carboxyl group and the adjacent oxygen atoms, with the two hydrogen atoms excluded from the calculated structure factors. As seen in Figure 2a, this map clearly indicated that each of the two protons is distributed between two sites, unequally occupied. Similar difference maps, calculated in the planes of the methyl hydrogen atoms, indicated that the methyl group C(14) also has two different conformations, again with unequal occupancy.[15] At convergence of the least-squares refinement of this disordered model the *p*-quinone isomer appeared significantly favored, the site occupancy of the corresponding protons amounting to approximately 60%.[16] Selected molecular dimensions derived from the final coordinates are given in Figure 2a. As expected, bond distances and angles involving non-hydrogen atoms are virtually coincident with those from the nondisordered model, the differences rarely exceeding the corresponding esd's.[17]

Room-temperature positional parameters were used as the starting point for the refinement based on the 147 K data set; the thermal parameters were all halved, in view of the ratio between the two temperatures. After a few least-squares cycles it became evident that the disordered model was inconsistent with the low-temperature data, and the hydrogen atoms in the minor (40%) sites were removed. Rapid convergence was then obtained for a model where each hydrogen atom occupies a single site. As indicated by the difference map of Figure 2b, only the *p*-quinone isomer is present in the crystal at low temperature, at least within the limits of detection on the basis of the measured Bragg diffraction data.

Comparison of the geometries reported in Figure 2 shows that, on going from the disordered to the ordered structure, a substantial lenghthening [0.016 (2) Å] occurs for both the C(1)–O(11) and the C(12)–O(18) bonds, while of the three formally double bonds

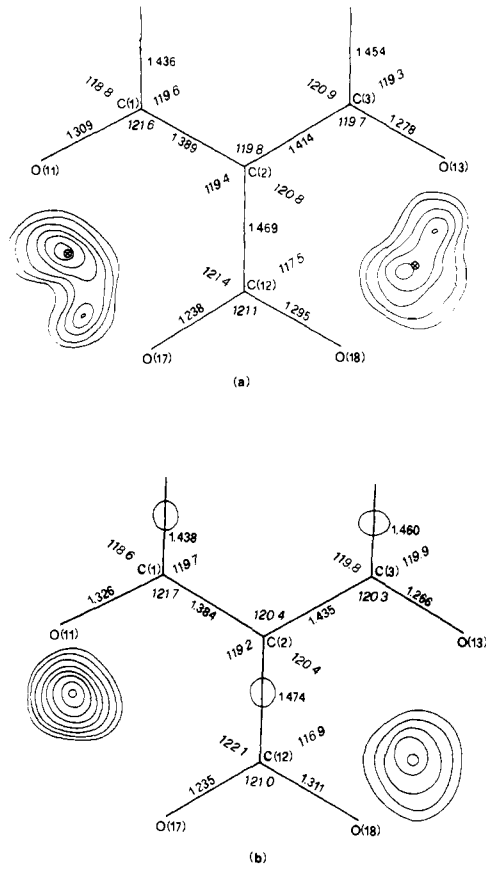

Figure 2. Different-density maps in the region of the intramolecular hydrogen bonds, without contribution of the two H atoms to the calculated structure factors. (a) 290 K; the contours start at 0.15 eÅ^{-3}, with increments of 0.03 e Å^{-3}. The symbol ⊗ denotes the positions of the H atoms in the nondisordered (single-hydrogen) refined model. Bond distances (esd's in the range 0.002–0.003 Å) and the angles (esd's 0.1–0.2°) are those of the final disordered model (see text). (b) 147 K; the contours start at 0.25 e Å^{-3}, with increments of 0.05 e Å^{-3}. Esd's are about 0.002 Å for bond lengths and 0.1° for bond angles.

C(1)–C(2), C(12)–O(17), and C(3)–O(13), apparently only the latter undergoes a significant shortenings, by 0.012 (2) Å. (If values corrected for thermal motion are used in the comparison, the shortening of these bonds amount to 0.010, 0.008, and 0.017 Å, respectively, whereas the lenghthening of the two C—O single bonds is reduced to 0.011 Å.) The quinonoid C=O bond is still much longer here than, for instance, in *p*-benzoquinone at 113 K,[19] 1.266 (2) vs. 1.222 (3) Å. On the other hand, single and double bonds in the latter compound have values of 1.473 (2) and 1.334 (3) Å, respectively, to be compared with 1.435 (2) Å for C(2)–C(3) and 1.384 (2) Å for C(1)–C(2) in **1a**. It may be concluded that extensive conjugation occurs between the double bonds in this region of the quinonoid system of citrinin.

At low temperature, the orientation of the methyl group C(14) corresponds to the favored (60%) conformer of the room-temperature structure. In this conformation (Figure 1), two hydrogen atoms of the methyl group are staggered with respect to O(13), as found, for instance, in 2,5-dimethyl-1,4-benzoquinone.[20] The minor conformation at room temperature involves a rotation of about 60° about the C(4)–C(14) bond and brings one hydrogen atom cis to the carbonyl, only 2.22 (6) Å from the oxygen atom O(13). On the basis of the parallel population factors of the five hydrogen atoms, it seems plausible to assign this second conformation to the ortho isomer, with the implication that the hydroxyl group prefers a neighboring methyl proton but the carbonyl group

(12) Cromer, D. T.; Waber, J. T. "International Tables for X-ray Crystallography"; Kynock Press: Birmingham, England, 1974; Vol. IV, Table 2.2B.

(13) See the paragraph at the end of paper regarding supplementary material.

(14) Leiserowitz, L. *Acta Crystallogr., Sec. B* **1976**, *B32*, 775–802.

(15) A well-ordered arrangement of atoms was detected for the other two methyl groups at C(15) and C(16).

(16) The population parameters for the disordered H atoms, as judged on the basis of the peak heights on the difference maps, had initial values of 0.55 and 0.45, both for the methyl group and the OH protons. These parameters were not included in the refinement, owing to the possible high correlation with positional and thermal parameters. Prior to the final least-squares cycles, however, they were changed to 0.60 and 0.40, respectively, to obtain an even distribution of values for the temperature factors of the pertinent H atoms.

(17) The geometry of our nondisordered model is also substantially similar to that obtained in the recent X-ray study reported in ref 10, although some bond lengths differ by as much as 0.01–0.02 Å.

(18) In the last least-squares cycle, no parameter shift exceeded 0.05σ.

(19) Bolhius, F. van; Kiers, C. Th. *Acta Crystallogr., Sec. B* **1978**, *B34*, 1015–1016.

(20) Hirshfeld, F. L.; Rabinovich, D. *Acta Crystallogr.* **1967**, *23*, 989–1000.

does not. However, since a cis arrangement has also been found in benzoquinone deviates, e.g., duroquinone,[21] this argument is to be taken with caution. In both isomers the carboxyl group adopts the somewhat unusual anti conformation which is stabilized by the intramolecular hydrogen bond.

While the room-temperature X-ray data are best explained by a disordered model, they provide no information as to whether the disorder is static or dynamic. However, taken in conjunction with the low-temperature results, they suggest that a proton-transfer process may take place in the solid state. As pointed out[11] in the similar case of naphthazarin, the problem of whether crystal sites are occupied exclusively by molecules with structures **1a** and **1b** is open to question, as is the mechanism of proton exchange. Further studies, especially by low-temperature solid-state NMR techniques, should provide answers to these problems.

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Registry No. 1a, 518-75-2; **1b**, 92720-00-8.

Supplementary Material Available: Table with details of data collection and refinement, final positional and thermal parameters at 290 and 147 K, and lists of observed and calculated structure factors at the two temperatures (22 pages). Ordering information is given on any current masthead page.

(21) Rabinovitch, D.; Schmidt, G. M. J.; Ubell, E. *J. Chem. Soc. B* **1967**, 131–139.

1,2-Migration of Hydrogen during the Biosynthesis of Tropic Acid from Phenylalanine

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(*S*)-Tropic acid (**4**) is the acid moiety of the ester alkaloids hyoscyamine (**1**) and scopolamine (**2**) which are found in *Datura* and related species of the Solanaceae. It is formed from phenylalanine (**3**) by an intramolecular 1,2-migration of the carboxyl group from C-2 to C-3.[2] No definitive work has appeared on the mechanism of this rearrangement.[3] This communication describes work on the fate of the hydrogens present at the C-3 position of phenylalanine.[4]

Since it was anticipated that the loss of hydrogen from the prochiral C-3 position of phenylalanine would be stereospecific, preliminary feedings (by the wick method) to *Datura innoxia* and *Datura stramonium* plants were carried out with a mixture of equal amounts of the four possible stereoisomers of [1-^{14}C,3-^{3}H]phenylalanine.[5] It was expected that the resultant alkaloids would retain 50% of the ^{3}H relative to ^{14}C. The results of the feeding to *D. innoxia* are recorded in Table I. The alkaloids were isolated and separated as previously described.[3,6] Both scopolamine (>95% optically pure) and hyoscyamine (58% optically pure)[7] retained significantly more than 50% of the ^{3}H. The tropic acid, mp 118 °C, obtained by hydrolysis of the scopolamine with barium hydroxide[8] had $[\alpha]^{25}_{D}$ −13.9° (ca. 18% optically pure).[9] The reduction in the ^{3}H/^{14}C ratio in this tropic acid corresponds to this degree of loss of tritium from the chiral center. The tropic acid was dehydrated to atropic acid (**6**), which was oxidized to afford formaldehyde (assayed as its dimedine derivative) and benzoylformic acid (assayed as its oxime) (**5**) as previously described.[8] Activities of these degradation products clearly indicate that tritium was located on the methylene group of the tropic acid. Similar results were obtained with the alkaloids isolated from *D. stramonium* plants, except that the degree of incorporation of radioactivity was somewhat lower.

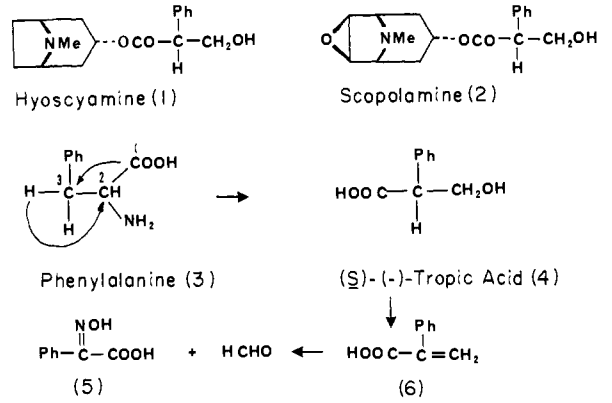
It is thus apparent that when the carboxyl group of phenylalanine migrates, there is also a migration of one of the hydrogens at C-3 to the carbon that ultimately becomes the hydroxymethyl group of tropic acid. In the scheme, this migration is represented as occurring with retention of configuration, and investigations with (3*S*)- and (3*R*)-[3-^{3}H]phenylalanine are in progress to settle this point. Although the formation of tropic acid from phenyl-

Table I. Activities of the Alkaloids, and Their Degradation Products, Derived from [1-^{14}C,3-^{3}H]Phenylalanine (0.5 mM) Fed to 3-Month Old *Datura innoxia* Plants for 10 Days

compound	activity,[a] dpm/mM ^{14}C	^{3}H	^{3}H/^{14}C
[1-^{14}C,3-^{3}H]phenylalanine	4.23×10^{7}	5.26×10^{8}	12.4
scopolamine HCl (^{14}C inc,[b] 0.18%)	7.6×10^{4}	9.0×10^{5}	11.8
tropic acid	7.1×10^{4}	5.2×10^{5}	7.3
oscine picrate[c]	$<0.1 \times 10^{4}$	$<0.1 \times 10^{4}$	
atropic acid (**6**)	7.0×10^{4}	4.3×10^{5}	6.1
formaldehyde-dimedone	$<0.1 \times 10^{4}$	4.2×10^{5}	
benzoylformic acid oxime (**5**)	6.8×10^{4}	$<0.1 \times 10^{5}$	
hyoscyamine HCl (^{14}C inc,[b] 0.20%)	8.4×10^{4}	7.9×10^{5}	9.4
tropic acid	8.3×10^{4}	5.1×10^{5}	6.2
tropine picrate[c]	$<0.1 \times 10^{4}$	$<0.1 \times 10^{4}$	

[a] Determined in duplicate with consistent results (within 5%). [b] inc = total radioactivity in the isolated alkaloid/total activity in the administered phenylalanine. [c] The tropane base isolated from the basic hydrolysis of the alkaloids.

Scheme I. Biosynthesis of Tropic Acid (Structures 3 and 4 are Fischer Projections



(1) Contribution 193 from this laboratory. Part 34 in the series "Chemistry of the Tropane Alkaloids". For Part 33, see: Leete, E. *J. Am. Chem. Soc.* **1983**, *105*, 6727.

(2) Leete, E.; Kowanko, N.; Newmark, R. A. *J. Am. Chem. Soc.* **1975**, *97*, 6826.

(3) Leete, E. *Phytochemistry* **1983**, *22*, 933 and references cited therein.

(4) Previous work related to this problem is ambiguous. When [1-^{14}C,2-^{3}H]phenylalanine was fed to a sterile culture of *Datura metel* roots the resultant tropic acid had lost 93% of the ^{3}H relative to ^{14}C: (a) Liebisch, H. W.; Bhavsar, G. C.; Schaller, H. J. *Biochem. Physiol. Alkaloide, Int. Symp., 4th, 1969* **1972**, 233. (b) Schutte, H. R.; Liebisch, H. W. *Z. Pflanzenphysiol.* **1967**, *57*, 440. (c) Liebisch, H. W. *Symp. Pap.—IUPAC Int. Symp. Chem. Nat. Prod., 7th* **1970**, 557. These authors also reported that tropic acid derived from [2-^{14}C,2,3-^{3}H$_3$]phenylalanine retained 39% of the ^{3}H relative to ^{14}C. However, the stereochemical location of ^{3}H at C-3 of the phenylalanine was not determined, and no comments were made on the loss of ^{3}H from the chiral center of tropic acid during basic hydrolysis of the labeled tropane alkaloids.

(5) The isomers 2*R*,3*R*, 2*R*,3*S*, 2*S*,3*R*, and 2*S*,3*S* were prepared from [1-^{14}C]glycine and [*formyl*-^{3}H]benzaldehyde as previously described: Wightman, R. H.; Staunton, J.; Battersby, A. R.; Hanson, K. R. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2355.

(6) Leete, E. *Phytochemistry* **1972**, *11*, 1713.

(7) Esters of tropic acid are readily racemized in basic solution (Frankland, P. F. *J. Chem. Soc., Trans.* **1913**, *103*, 713); however, scopolamine, for unknown reasons, is much less susceptible to racemization than hyoscyamine.

(8) Louden, M. L.; Leete, E. *J. Am. Chem. Soc.* **1962**, *84*, 4507.

(9) Watson and Youngson (Watson, M. B.; Youngson, M. B. *J. Chem. Soc., Perkin Trans 1*, **1972**, 1597) record $[\alpha]_D$ +74.4° for (*R*)-(+)-tropic acid, which has mp 129 °C.

0002-7863/84/1506-7271$01.50/0