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Note

Mechanistic studies on the formation
of phenylpropionic acid from *trans*-
cinnamic acid

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Mechanistic studies on the formation of phenylpropionic acid from *trans*-cinnamic acid by bromination and step-wise dehydrobromination are reported.

Phenylpropionic acid is prepared¹ by the bromination of ethyl *trans*-cinnamate yielding ethyl dibromocinnamate which on treatment with alc. KOH undergoes dehydrobromination and hydrolysis to give the expected product. In an alternate synthesis², phenylpropionic acid is prepared by the bromination of *trans*-cinnamic acid to give (±)-dibromocinnamic acid, followed by treatment with alc. KOH. In this communication we report the isolation of intermediates and the mechanism involved in the formation of phenylpropionic acid from *trans*-cinnamic acid by the latter process.

Commercial cinnamic acid **1** is a *trans* compound as observed from its ¹H NMR spectrum in CDCl₃/TMS solution which shows peaks at δ 6.47 (1H, d, ³J_{H-H}=18 Hz), 7.3-7.6 (5H, complex, m, phenyl protons), 7.8 (1H, d, ³J_{H-H}=18 Hz), 12.4 (1H, broad s, -COOH). It was brominated with liquid bromine in refluxing CCl₄ to obtain (±)-dibromocinnamic acid **2** in good yield. The IR spectrum of **2** in KBr showed peaks at ~3000 (m, vb, bonded OH and -CH-), 1715 (unsplit doublet, vs, -CO-), 1460 (m), 1433 (m), 1323 (w), 1300 (m), 1284 cm⁻¹ (s), etc. Its ¹H NMR spectrum in CDCl₃/TMS showed signals at δ 5.29 [1H, d, J=12 Hz, Ph-CH(Br)-], 5.525 [1H, d, J=12 Hz, -

CH(Br)-CO-], 7.25-7.62 (5H, complex m, phenyl protons), 14.0 (1H, broad s, -COOH). Its ¹³C NMR spectrum showed signals at δ 47.37 [Ph-CH(Br)-], 51.99 [-CH(Br)-CO-], 128.41, 128.69, 129.07 (five phenyl carbons carrying hydrogens), 138.25 (quaternary phenyl carbon), 169.11 (-CO-). Its electron impact mass spectrum recorded at 70 eV showed peaks at m/z 310 (2.34%, M+4), 308 (7.08%, M+2), 306 (3%, M⁺), 229 (26.5%), 227 (27.6%), 184 (28.9%), 182 (31.4%), 148 (31.8%), 147 (49.7%), 131 (13.2%), 107 (20.6%), 104 (24.7%), 103 (100%), 102 (25.4%), 91 (10.5%), 82 (15.9%), etc.

The (±)-dibromocinnamic acid (**2**) on treatment with two equivalents of alc. KOH followed by simple processing gave a compound with m.p. 98-100° (yield 56%, based on monodehydrobromination). Its IR spectrum in KBr showed peaks at ~2900 (m, vb, bonded -OH and -CH-), 1680 (vs, unsplit doublet, -CO-), 1600 (m), 1573 (w), 1511 (vw), 1425 cm⁻¹ (s), etc. Its ¹H NMR spectrum showed signals at δ 7.2-7.45 (5H, complex m, phenyl protons), 7.55 (1H, s, Ph-CH=), 11.8 (1H, broad s, -COOH). Its ¹³C NMR spectrum showed signals at δ 110.6 [=C(Br)-COOH], 128.49, 128.51, 128.57, 129.37, 129.40, 134.44 (six phenyl carbons), 143.73 [Ph-C(H)=], 169.37 (-CO-). Its electron impact mass spectrum recorded at 70 eV showed peaks at m/z 227 and 229 (4.24 and 1.92%, M+1 ion peaks corresponding to ⁷⁹Br and ⁸¹Br, respectively), 226 and 228 (twin peaks, 18.6 and 20.12%, M⁺), 147 (100%), 129 (17.38%), 103 (9.31%), 102 (20.6%), 77 (13.5%), 50 (13.8%), 49 (10.5%), etc. Based on these data, the compound was formulated as bromocinnamic acid.

In the dehydrobromination of **2** to bromocinnamic acid, four stereoisomers are possible. Appropriate chemical shift values for these stereoisomers were calculated³ as shown in Tables I and II.

By comparing the calculated ¹³C chemical shift values of the isomeric bromocinnamic acids (Table I) with the actual values of the bromocinnamic acid obtained in our work, it may be concluded that the compound obtained in the present study is α-bromocinnamic acid. Furthermore, by compar-

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Table I—Calculation of ^{13}C NMR chemical shift values for vinylic carbons of isomeric bromocinnamic acids

Sl.No.	Name of isomer	Structure of the isomer	α -Carbon	Chemical shift value β -Carbon
1.	α -Bromocinnamic acid	$\text{Ph} \begin{array}{c} \diagup \text{COOH} \\ \diagdown \text{H} \end{array} \text{Br}$ (or) $\text{H} \begin{array}{c} \diagup \text{COOH} \\ \diagdown \text{Ph} \end{array} \text{Br}$	Base value=123.3 One pair of <i>cis</i> -substituent=−1.1 One pair of <i>geminal</i> substituent on C_1 =−4.89 Br on C_1 =−7.9 −COOH on C_1 =+6.3 Ph on C_2 =−11.0	Base value=123.3 One pair of <i>cis</i> -substituent=−1.1 One pair of <i>geminal</i> substituent on C_2 =+2.5 Ph on C_1 =+12.5 Br on C_2 =−1.4 −COOH on C_2 =+7.0 $\delta=104.8$
2.	β -Bromocinnamic acid	$\text{Br} \begin{array}{c} \diagup \text{COOH} \\ \diagdown \text{Ph} \end{array} \text{H}$ (or) $\text{Ph} \begin{array}{c} \diagup \text{COOH} \\ \diagdown \text{Br} \end{array} \text{H}$	Base value=123.3 One pair of <i>cis</i> -substituent=−1.1 One pair of <i>geminal</i> -substituent on C_2 =+2.5 −COOH on C_1 =+6.3 Br on C_2 =−1.4 Ph on C_2 =−11.0	Base value=123.3 One pair of <i>cis</i> -substituent=−1.1 One pair of <i>geminal</i> -substituent on C_1 =4.8 Br on C_1 =−7.9 Ph on C_1 =+12.5 −COOH on C_2 =+7.0 $\delta=142.8$
			$\delta=118.6$	$\delta=129.0$

Table II—Calculation of ^1H NMR chemical shift values for vinylic proton of isomeric bromocinnamic acids

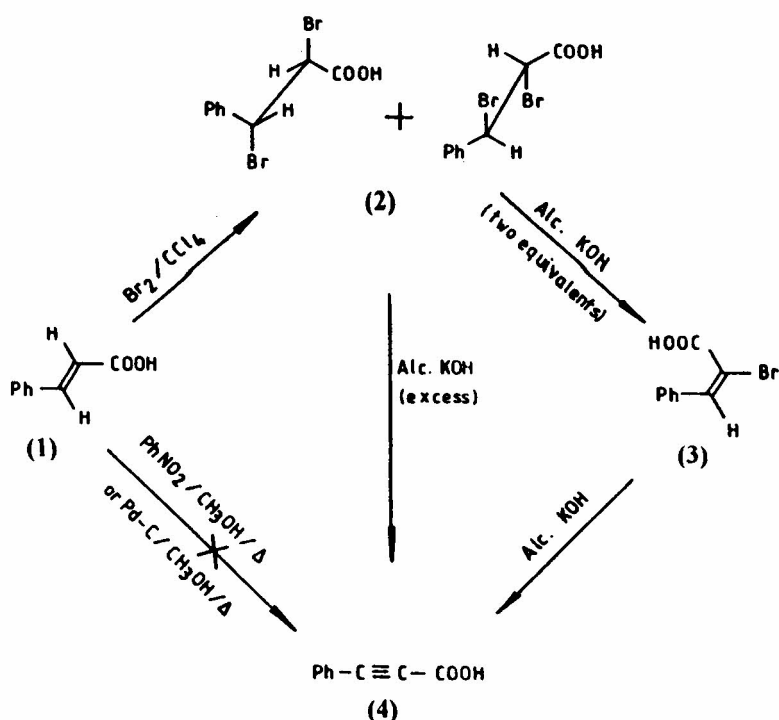
Sl. No.	Name of the isomer	Structure of the isomer	Chemical shift value (ppm units)
1.	(<i>E</i>)- α -Bromocinnamic acid	$\text{Ph} \begin{array}{c} \diagup \text{COOH} \\ \diagdown \text{H} \end{array} \text{Br}$	Base value <i>geminal</i> 'Ph' <i>cis</i> 'Br' <i>trans</i> -conjugated −COOH $\delta=7.40$
2.	(<i>Z</i>)- α -Bromocinnamic acid	$\text{Ph} \begin{array}{c} \diagup \text{Br} \\ \diagdown \text{H} \end{array} \text{COOH}$	Base value <i>geminal</i> 'Ph' <i>trans</i> 'Br' <i>cis</i> -conjugated −COOH $\delta=8.16$
3.	(<i>E</i>)- β -Bromocinnamic acid	$\text{Ph} \begin{array}{c} \diagup \text{COOH} \\ \diagdown \text{Br} \end{array} \text{H}$	Base value <i>trans</i> 'Ph' <i>cis</i> 'Br' <i>geminal</i> -conjugated −COOH $\delta=6.43$
4.	(<i>Z</i>)- β -Bromocinnamic acid	$\text{Ph} \begin{array}{c} \diagup \text{H} \\ \diagdown \text{Br} \end{array} \text{COOH}$	Base value <i>cis</i> 'Ph' <i>trans</i> 'Br' <i>geminal</i> -conjugated −COOH $\delta=6.96$

ing the calculated ^1H chemical shift values of the isomeric (*E*)- α - and (*Z*)- α -bromocinnamic acids (Table II) with the actual values of the bromocinnamic acid obtained in our work, it may be concluded that the compound in question is decisively (*E*)- α -bromocinnamic acid 3.

It may be mentioned here that Dalcanale *et al.*⁴ reported the preparation of the so called (*E*)- α -bromocinnamic acid (m.p. 129–30°) by the $\text{NaClO}_2\text{-H}_2\text{O}_2$ oxidation of α -bromocinnamaldehyde. These authors assumed the configuration of α -

bromocinnamaldehyde to be (*E*)- and assigned the configuration (*E*)- α to the bromocinnamic acid obtained from its oxidation. Moreover, the chemical shift value for the vinyl proton of the bromocinnamic acid was reported to appear at δ 8.1. It is obvious from Table II that the configuration assigned by Dalcanale *et al.*⁴ to the bromocinnamic acid they obtained (m.p. 129–30°) is erroneous and that it actually has (*Z*)- α -configuration.

The (*E*)- α -bromocinnamic acid 3 obtained in our work, m.p. 98–100°, on treatment with alc.



Scheme I

KOH gave phenylpropionic acid 4 which was also obtained by treating 2 with excess of alc. KOH for a prolonged period. Attempted preparation of 4 directly from *trans*-cinnamic acid 1 by dehydrogenation over Pd-C or over nitrobenzene in refluxing methanol led to the recovery of the starting material. All these reactions are briefly summarised in Scheme I.

The structure of 4 was supported by its m.p., TLC and spectral data. Its IR spectrum in KBr showed peaks ~ 2900 (m, vb, bonded $-\text{OH}$ and $-\text{CH}-$), 2236 and 2203 (unequal, sharp, strong doublet, $-\text{C}\equiv\text{C}-$), 1680 (vs, $-\text{CO}-$), 1495 (w), 1417 (s), 1307 (s), 1208 cm^{-1} (s), etc. Its ^1H NMR spectrum in CDCl_3/TMS showed resonances at δ 7.25-7.63 (5H, complex m, phenyl protons), 11.76 (1H, sharp s, $-\text{COOH}$). Its ^{13}C NMR spectrum showed peaks at δ 80.10 (acetylenic carbon α to $-\text{COOH}$), 89.26 (acetylenic carbon β to $-\text{COOH}$), 119.04 (quaternary carbon of phenyl group), 128.68, 131.22, 133.32 (two *ortho*, two *meta* and one *para* carbons of phenyl ring), 159.1 ($-\text{CO}-$). Its electron impact mass spectrum at 70 eV showed peaks at m/z 147 (9.33%, $M+1$), 146 (97.4%, M^+), 130 (9.9%), 129 (100%), 118 (56.2%), 102 (74.3%), 101 (11.2%), 98 (6.7%), 89 (18.9%), 77

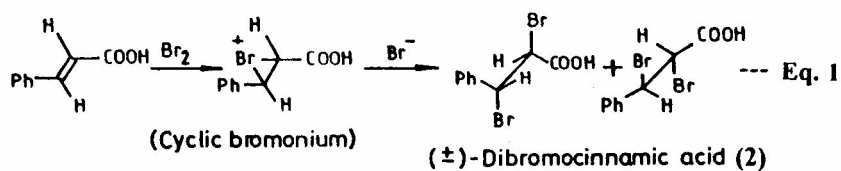
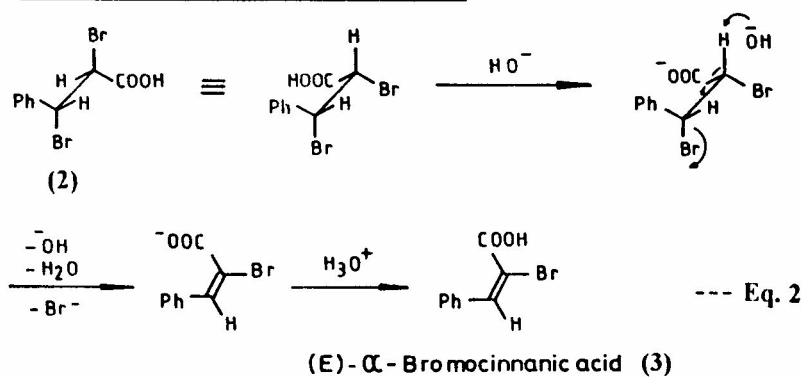
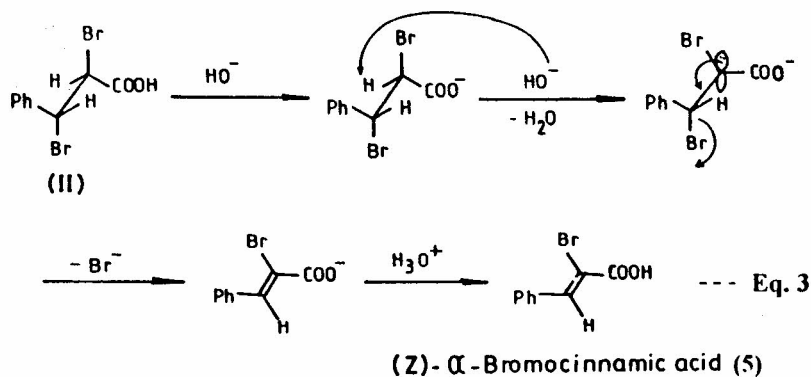
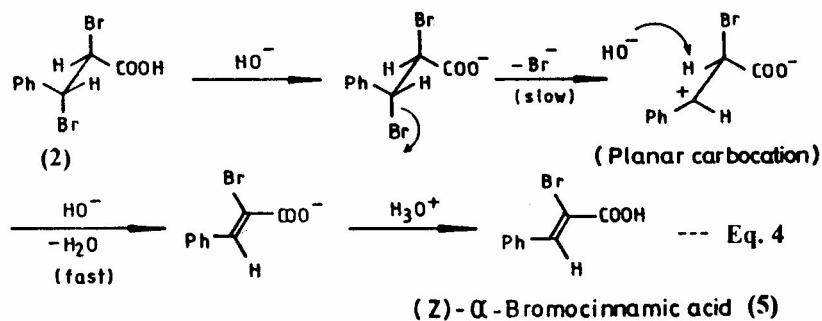
(5.4%), 76 (28.6%), 75 (79.6%), 74 (41.1%), 73 (9.3%), 62 (20.5%), 51 (14.9%), 50 (30.4%), etc.

Based on these results, the formation of phenylpropionic acid 4 from *trans*-cinnamic acid can be shown to take place mechanistically⁵ in three steps as given below:

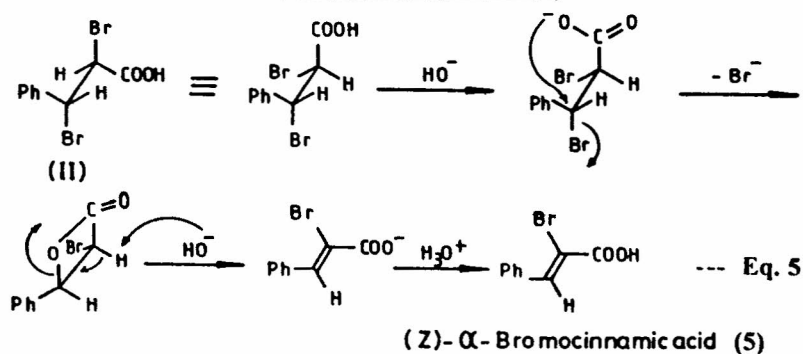
(i) *trans*-Cinnamic acid 1 undergoes *trans* bromination to yield ($\pm$)-dibromocinnamic acid 2 via a cyclic bromonium ion intermediate (Eq. 1 of Scheme II).

(ii) ($\pm$)-Dibromocinnamic acid 2 undergoes selective monodehydrobromination when treated carefully with two equivalents of alc. KOH to yield (*E*)- α -bromocinnamic acid 3. This is a regio-specific process in which the proton α to $-\text{COOH}$ group is preferentially abstracted by HO^- because of its more acidic nature compared with β -proton (see the ^1H NMR of 2 given above). The abstraction of α proton by HO^- is followed by simultaneous loss of bromine as Br^- similar to an E_2 -elimination process and proceeds through a transition state in which the proton α to $-\text{COOH}$ and Br atom β to $-\text{COOH}$ group are anti to each other (Eq. 2 of Scheme II).

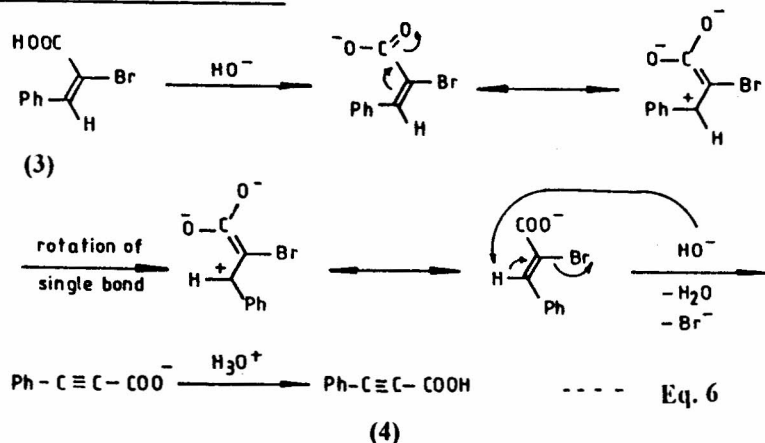
If the monodehydrobromination of 2 to give (*E*)- α -bromocinnamic acid 3 was not an E_2 -elimination. assuming it to be E_1CB , E_1 or anchi-

Addition of Bromine to cinnamic acid:Elimination of HBr (E₂-mechanism)Elimination of HBr (E₁CB mechanism)Elimination of HBr (E₁ mechanism)

Elimination of HBr (Anchimeric assistance)



Conversion of 3 to 4



Scheme II

merically assisted mechanism, a different isomer of (*E*)- α -bromocinnamic acid would have been formed in which the phenyl and $-\text{COOH}$ groups are present on the opposite sides of the double bond (*Z*- α -bromocinnamic acid 5) thus decreasing the steric crowding in the product (see Eqns 3, 4 and 5 respectively of Scheme II).

(iii) (*E*)- α -Bromocinnamic acid 3 thus formed has hydrogen and bromo groups in *cis*-orientation to each other. Further loss of HBr from such a molecule would normally be very difficult since *cis*-eliminations do not occur easily. Nevertheless, the fact is that 3 undergoes facile dehydrobromination on treatment with alc. KOH under relatively mild conditions to yield phenylpropionic acid 4. This is probably due to rotation across the double bond, on heating in alc. KOH, of (*E*)- α -bromocinnamic acid 3, facilitated by the carbonyl moiety of carboxyl group resulting in an intermediate with H and Br groups *trans* oriented to each other followed by loss of HBr similar to an E_2 -elimination. This is shown in equation 6 of Scheme

II. Thus, what appears apparently as a *cis*-elimination is in reality a *trans*-elimination process.

Experimental Section

Melting points are uncorrected and have been recorded in open capillary tubes in sulphuric acid-bath. TLC examination was done on small glass plates using silica gel G as adsorbant and UV lamp for visualisation purposes. IR spectra were recorded on a Perkin-Elmer 2000 FT-IR Spectrometer. NMR spectra were recorded on a Bruker instrument at 250 MHz for proton probe and at 62.9 MHz for carbon probe. Mass spectra were recorded on a CEC 21-110 Mass spectrometer at 70 eV.

Preparation of ($\pm$)-dibromocinnamic acid 2 from *trans*-cinnamic acid 1. To a refluxing solution of *trans*-cinnamic acid (7.4 g, 50 mmoles) in CCl_4 (200 mL) was added slowly, dropwise, a solution of bromine (3 mL, 55 mmoles) in CCl_4 (10

mL) during 30 min. After the addition was over, the reaction mixture was cooled to room temperature. The solid that separated was filtered, washed with CCl_4 and dried, yield 14.8 (96.7%). A sample of this material was recrystallised from boiling benzene to obtain pure **2**, m.p. 200-201° (lit.², m.p. 203-4°).

Preparation of (*E*)- α -bromocinnamic acid **3 from ($\pm$)-dibromocinnamic acid **2**.** A solution of KOH (1.684 g, 30 mmoles) in methanol (25 mL) was added at room temperature to solid **2** (4.62 g, 15 mmoles) in a china dish. The contents were heated on water-bath till all the methanol was evaporated. The residue was dissolved in water and pH of the solution was adjusted to 3-4 with conc. HCl. The mixture was cooled and the separated solid filtered, washed with cold water (2×20 mL) and dried, yield 1.906 g (56%, based on monodehydrobromination). A portion of this product was recrystallised from hot benzene. It was found to be homogeneous on TLC and melted at 98-99°.

Preparation of phenylpropionic acid **4 from (*E*)- α -bromocinnamic acid **3**.** A solution of KOH (1.0 g, 18 mmoles) in methanol (15 mL) was added at room temperature to solid **3** (1.13 g, 5 mmoles) in a china dish. The contents were heated on water-bath till all the methanol was evaporated. The residue was dissolved in water (20 mL) and pH was adjusted to 3-4 with conc. HCl. The solid, which separated after cooling, was filtered, washed with cold water (2×5 mL) and dried, yield 0.42 g (57.5%). A sample of this material was recrystallised from hot CCl_4 to obtain TLC-pure **4**, m.p. 132-34° (lit.^{1,2}, m.p. 134-35°).

Preparation of phenylpropionic acid **4 from ($\pm$)-dibromocinnamic acid **2**.** A solution of KOH (5 g, 0.09 mole) in methanol (20 mL) was added at room temperature to solid **2** (5 g, 0.0163 mmole) in a china dish. The contents were heated on water-bath till all the methanol was evaporated. Once again, methanol (20 mL) was added and the china dish heated on water-bath until all the methanol

evaporated. The residue was then dissolved in water and pH of the solution adjusted to 3-4 with conc. HCl. The mixture was cooled, and the separated solid filtered, washed with water (2×5 mL) and dried, yield 1.4 (58.7%). A sample of this product was recrystallised from hot CCl_4 to obtain pure **4**, m.p. 133-34° (lit.^{1,2}, m.p. 134-35°).

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