The Mechanism of Decarboxylation of α-*p*-Nitrophenyl-*trans*-cinnamic Acids

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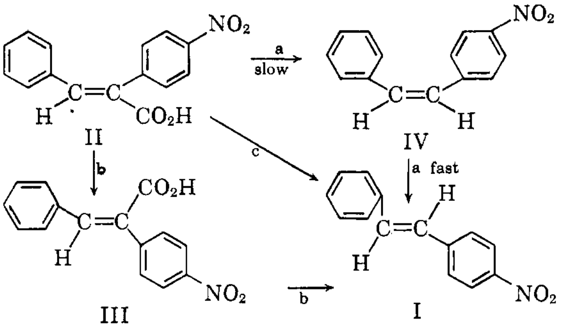
The piperidine-catalyzed condensation of *p*-nitrophenylacetic acid with aromatic aldehydes to give *trans-p*-nitrostilbenes has been shown to proceed through formation of α-*p*-nitrophenyl-*trans*-cinnamic acids. These intermediates undergo decarboxylation with concurrent rearrangement in a one-step process to afford exclusively *trans-p*-nitrostilbenes.

A direct synthetic approach to variously substituted *trans-p*-nitrostilbenes is the piperidine-catalyzed condensation of *p*-nitrophenylacetic acid with aromatic aldehydes. This procedure, originally developed by Pfeiffer and Sergiewskaja[2] for the synthesis of *p*-nitrostilbene (I) has been extended to the synthesis of a number of disubstituted stilbenes.[3] The similarity between this and the amine-catalyzed Perkin condensation[4] of phenylacetic acids and aromatic aldehydes suggested that α-*p*-nitrophenyl-*cis*- and *trans*-cinnamic acids might be intermediates which, on decarboxylation, afford the corresponding stilbene. However, such intermediates have not been reported. In the Perkin condensation, the major product is normally the α-phenyl-*trans*-cinnamic acid[4] which, if it underwent decarboxylation without rearrangement, would have given the corresponding *cis*-stilbene. On the contrary, the only product reported has been the *trans*-stilbene; one unsuccessful attempt to isolate a *cis*-stilbene has been reported.[5]

We, therefore, attempted to establish whether α-phenylcinnamic acids might be intermediates in the reaction and, if so, what course was taken in the decarboxylation process.

In addition to *trans-p*-nitrostilbene (I), we found that the piperidine-catalyzed condensation of *p*-nitrophenylacetic acid with benzaldehyde yielded small quantities of α-*p*-nitrophenyl-*trans*-cinnamic acid (II) and α-*p*-nitrophenyl-*cis*-cinnamic acid (III). The *cis* acid was the major component of the acidic fraction. No *cis-p*-nitrostilbene (IV) could be detected in the neutral fraction. Similarly, condensations of *p*-nitrophenylacetic acid with anisaldehyde and *p*-nitrobenzaldehyde afforded only the corresponding *trans*-stilbenes in the neutral fraction, in addition to mixtures of α-phenyl-*cis*- and *trans*-cinnamic acids.

In the formation of *trans-p*-nitrostilbene (I), the reaction path must involve transformation of II (phenyl groups *cis*) to I. One can envision three possible pathways for this process: (a) decarboxylation to IV followed by rapid isomerization to I; (b) isomerization of II to III followed by decarboxylation to I; or (c) direct decarboxylation of II accompanied by rearrangement to I. These possibilities are outlined.



When II was heated under reflux with piperidine for 1 hr., there was obtained I, unchanged II, and a small amount of III. When the reaction time was decreased to fifteen minutes, only I and unchanged II were found in the reaction mixture. When III was heated under reflux in piperidine for 15 min., no I was formed, but III did yield some I when the reaction time was increased to sixteen hours. These observations indicate that the *cis* acid (III) is not an intermediate in the transformation so that path b must be eliminated. The *cis–trans* ratios of the acids isolated in the three condensations with *p*-nitrophenylacetic acid are considerably higher than the ratios obtained in the amine-catalysed Perkin condensation.[4e] Thus, the *cis* acids which neither isomerize nor decarboxylate are accumulated in the product mixture.

cis-4-Nitrostilbene (IV) does not isomerize in refluxing piperidine, but, in piperidine–acetic acid (4:1), IV is isomerized to the extent of 24% in fifteen minutes. This rate, however, is not sufficiently large to account for failure to detect any *cis-p*-nitrostilbene in the product mixture.

Thus, the only logical path is the direct decarboxylation of II to I. Consideration of the geometry of α-phenyl-*trans*-cinnamic acids[4a] and the probable mechanism of decarboxylation suggests that this should be a highly favorable path. Zimmerman has shown[4a] and we have confirmed[4e] that, in α-phenyl-*trans*-cinnamic acid, the α-phenyl group must be perpendicular to the plane of the cinnamic acid system.

Decarboxylation of the *trans* acid (II) to the *trans*-stilbene (I) should follow the path shown, starting presumably from the carboxylate ion (IIa). The only function of the piperidine in the decarboxylation is formation of this anion. (See p. 2183.)

If the carbanion (Va) resulting from loss of carbon dioxide is stabilized by participation of the allenic system (Vb), the nitrophenyl group would be perpendicular to the plane of the other phenyl ring. Furthermore, the two central ethylenic carbons and the 1 and 4 carbons of the nitro-substituted benzene ring should

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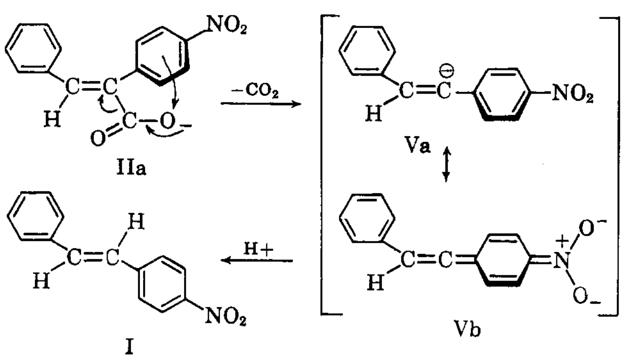
(1) To whom inquiries should be directed.

(2) (a) P. Pfeiffer and S. Sergiewskaja, *Ber.*, **44**, 1109 (1911); (b) J. T. Hewitt, W. L. Lewcock, and F. G. Pope, *J. Chem. Soc.*, **101**, 606 (1912).

(3) (a) H. Kaufmann, *Ber.*, **54**, 801 (1921); (b) N. Cullinane, *J. Chem. Soc.*, 2060 (1923); (c) H. Harrison and H. Wood, *ibid.*, 580 (1926).

(4) (a) H. E. Zimmerman and L. Ahramjian, *J. Am. Chem. Soc.*, **81**, 2086 (1959); (b) L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., D.C. Heath and Co., Boston, Mass., p. 182; (c) R. E. Buckles, M. P. Bellis, and W. D. Coder, Jr., *J. Am. Chem. Soc.*, **73**, 4972 (1951); (d) J. R. Johnson, "Organic Reactions," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942; (e) R. Ketcham and D. Jambotkar, *J. Org. Chem.*, **28**, 1034 (1963).

(5) P. Ruggli and F. Long, *Helv. Chim. Acta*, **21**, 38 (1938).



lie in a straight line.[6] Thus in the decarboxylation step the carboxylate ion (IIa) loses carbon dioxide to give the carbanion (Va ↔ Vb), during which process the α-phenyl group has only to move about 60° (arrows) in the direction from which the carbon dioxide was expelled. No twisting is necessary. This intermediate then accepts a proton to give the more stable *trans* isomer (I).[7] The geometry of the *cis* acid (III), having nearly co-planar phenyl groups, is not so similar to that of the intermediate carbanion.

The significance of stabilization of the carbanion by the nitro group is emphasized by the fact that the isomeric acid, α-phenyl-*trans*-*p*-nitrocinnamic acid, does not undergo decarboxylation when heated under reflux in piperidine for sixteen hours. The piperidine-catalyzed condensation of phenylacetic acid with anisaldehyde yields a mixture of α-phenyl-*cis*- and *trans*-*p*-methoxy-cinnamic acids rather than any decarboxylation product.

It is interesting to note that the copper chromite-catalyzed decarboxylations of II[8] and of α-phenyl-*trans*-cinnamic acid[9] in the presence of quinoline at about 220° afford the *cis* isomers as the major products. This indicates a fundamental difference in the heterogenously catalyzed decarboxylation. Perhaps the reaction involves free radical intermediates, but, if this is so, it is necessary to explain the need for the quinoline. Taylor and Crawford[9] have indicated that it stabilizes *cis*-stilbene under the conditions of the reaction. It has been shown[10] that benzoic acid is decarboxylated at about 250° on a similar catalyst in the absence of a base. It is probable that the acid is absorbed on the catalyst surface and is held in its original geometry during decarboxylation so that isomerization is prevented. However, the presence of copper chromite in the piperidine-catalyzed decarboxylation does not cause any change in the course of the reaction; that is, only I is obtained.

Experimental[11]

Condensation of *p*-Nitrophenylacetic Acid with Benzaldehyde.—Nine grams (0.05 mole) of *p*-nitrophenylacetic acid, 5.6 g. (0.055 mole) of benzaldehyde, and 2.5 ml. of piperidine were heated under reflux for 45 min. The reaction mixture was taken up in chloroform and washed free of piperidine with 5% hydrochloric acid. The acidic components were extracted with 5% sodium hydroxide. The alkaline extract was acidified with acetic acid to a pH of 4.5; yield, 1.16 g. (7.2%) of α-*p*-nitrophenyl-*trans*-cinnamic acid; m.p. 214–219° (lit.[12] m.p. 219–221°). Acidification of filtrate with concentrated hydrochloric acid gave 1.54 g. (11.5%) of the *cis* isomer, m.p. 143–145° (lit.[12] m.p. 149–151°). Concentration of the chloroform extract gave 7.2 g. (54%) of *trans*-*p*-nitrostilbene, m.p. 150–153° (lit.[2] m.p. 155°). The infrared spectrum of this crude product gave no evidence of any *cis* isomer.

Condensation of *p*-Nitrophenylacetic Acid and Anisaldehyde.—A suspension of 18.1 g. (0.1 mole) of *p*-nitrophenylacetic acid and 15.0 g. (0.11 mole) of anisaldehyde and 5 ml. piperidine was heated under reflux for 45 min. The reaction mixture was dissolved in 200 ml. of methylene chloride and extracted with 0.1 *N* sodium hydroxide. Evaporation of methylene chloride left 12.5 g. (49%) of residue, m.p. 132–133° (lit.[13] m.p. 132–134°). An infrared spectrum of this residue showed it to be composed entirely of *trans*-*p*-nitro-*p*′-methoxystilbene. The alkaline extract on acidification with concentrated hydrochloric acid yielded 2.0 g. (9%) of a mixture of α-*p*-nitrophenyl-*trans*- and *cis*-*p*-methoxycinnamic acids.[4c,e] The ultraviolet spectrum of this mixture showed it to be 53% *trans* and 47% *cis*.

Condensation of *p*-Nitrophenylacetic Acid with *p*-Nitrobenzaldehyde.—To a solution of 18.1 g. (0.1 mole) of *p*-nitrophenylacetic acid and 16.6 g. (0.11 mole) of *p*-nitrobenzaldehyde at 100° was added 5 ml. of piperidine, whereupon the reaction proceeded spontaneously to give a thick solid mass. The reaction mixture was dissolved in 1000 ml. of methylene chloride. After extracting the acidic material with 0.1 *N* sodium hydroxide and evaporation of methylene chloride, there was obtained 15.2 g. (56%) of residue m.p. 283–285° (lit.[14] m.p. 286°). Infrared analysis on this residue showed it to consist entirely of *trans*-*p*-*p*′-dinitrostilbene. The alkaline extract on acidification gave 3.1 g. (10%) of a mixture of α-*p*-nitrophenyl-*cis*- and *trans*-*p*-nitrocinnamic acids.[4c,e] The ultraviolet spectrum of this mixture showed it to be 37% *cis* and 63% *trans*.

Piperidine-Catalyzed Decarboxylation of α-*p*-Nitrophenyl-*trans*-cinnamic Acid (II).—A 3-g. (0.011 mole) sample of α-*p*-nitrophenyl-*trans*-cinnamic acid[4e] was heated under reflux in 7 ml. of piperidine for 1 hr. The reaction mixture, when worked up as described earlier, afforded 0.38 g. (13%) of α-*p*-nitrophenyl-*trans*-cinnamic acid, m.p. 209–210°; 0.05 g. (1.7%) of α-*p*-nitrophenyl-*cis*-cinnamic acid, m.p. 145–148°; and 2.0 g. (80%) of *trans*-*p*-nitrostilbene, m.p. 149–150°. The infrared spectrum of the crude stilbene showed no evidence for the presence of the *cis* isomer. Essentially the same results were observed when cuprous chromite was added to the reaction mixture.

When the reaction time was decreased to 15 min. (by which time the reaction mixture had become homogeneous), there was recovered 2.0 g. of unchanged acid and 0.60 g. of *trans*-*p*-nitrostilbene. None of the isomeric acid or the *cis*-stilbene were obtained.

Piperidine-Catalyzed Decarboxylation of α-*p*-Nitrophenyl-*cis*-cinnamic Acid (III).—When 3 g. of α-*p*-nitrophenyl-*cis*-cinnamic acid[4e] was heated under reflux in 7 ml. of piperidine for 15 min., there was isolated 2.9 g. (97%) of the unchanged starting material. None of the isomeric acid or the stilbene was obtained. When the reaction time was extended to 16 hr., there was isolated 1.20 g. of unchanged starting material, 100 mg. of *trans*-*p*-nitrostilbene, and a trace of α-*p*-nitrophenyl-*trans*-cinnamic acid.

Stability of *cis*-*p*-Nitrostilbene (IV) under Decarboxylation Conditions.—When an authentic sample[8] of *cis*-*p*-nitrostilbene was heated under reflux in piperidine–acetic acid 4:1 for 15 min., 24% (ultraviolet spectrum) of the product was found to be *cis*-*p*-nitrostilbene

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[6] *Cf.* D. Y. Curtin and J. W. Crump, *J. Am. Chem. Soc.*, **80**, 1922 (1958), who suggest a similar intermediate for the interconversion of the organolithium salts of *cis*- and *trans*-stilbene.

[7] The referees made the valuable observation that, if the allenic carbanion is protonated directly, it should afford *cis*-stilbene resulting from attack on the least hindered side [H. E. Zimmerman, *J. Org. Chem.*, **20**, 549 (1955)]. The suggestion that the carboxylate ion loses carbon dioxide to give the *cis* carbanion (i) and that this is converted to the thermodynamically more stable *trans* carbanion (ii) *via* (Va ↔ Vb) appears to be in conflict with some of the facts. It does not adequately account for the need of the nitro group. This, and the failure of the *cis* acid (phenyl groups *trans*) to decarboxylate are both best accounted for by the primary intermediacy of the allenic carbanion in which the nitro group is in direct conjugation with the developing negative charge and the phenyl groups are perpendicular to each other. We propose that the allenic carbanion (Va ↔ Vb) is formed first and that it rearranges to ii before being protonated to give I. Experiments designed to learn more about this intermediate carbanion are in progress.

[8] R. Stroemer and H. Oehlert, *Ber.*, **55**, 1239 (1922).

[9] T. W. J. Taylor and E. J. Crawford, *J. Chem. Soc.*, **1934**, 1130.

[10] C. R. Kinney and D. P. Langois, *J. Am. Chem. Soc.*, **53**, 2189 (1931).

[11] Melting points are uncorrected. Analyses are by the microchemical laboratory, Department of Chemistry, University of California, Berkeley, Calif.

[12] T. R. Lewis, M. G. Pratt, E. D. Homiller, B. F. Tullar, and S. Archer, *J. Am. Chem. Soc.*, **71**, 3749 (1949).

[13] M. Calvin and H. Alter, *J. Chem. Phys.*, **19**, 765 (1951).

[14] P. Pfeifer and B. Eistert, *J. prakt. Chem.*, (2) **124**, 168 (1930).

Attempted Piperidine-Catalyzed Decarboxylations of α-Phenyl-*cis*- and *trans*-*p*-nitrocinnamic Acids.—After heating 3 g. of either acid[4e,15] with 7 ml. of piperidine for 1 hr. under reflux, no stilbene was found in the neutral fraction.

Ultraviolet and Infrared Spectra.—Ultraviolet spectra were recorded on a Carey Model 11 spectrophotometer and infrared spectra on a Beckman IR5 spectrophotometer.

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(15) M. Bakunin, *Gazz. chim. ital.*, **25**, 137 (1895).

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Synthesis of 1,1-Dimethyl-*trans*-decalin-10-carboxylic Acid[1a,b]

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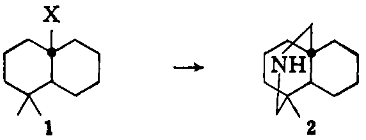
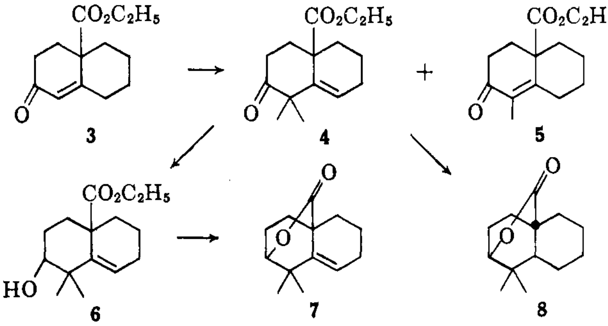
A convenient six-step stereoselective synthesis of 1,1-dimethyl-*trans*-decalin-10-carboxylic acid (**15**) from 6-carbethoxy-2,2-dimethylcyclohexanone (**9**) is described. This proceeds in 30% yield by condensation of the β-keto ester **9** with methyl vinyl ketone, catalytic reduction of the resulting 10-carbethoxy-1,1-dimethyl-Δ^8-7-octalone (**11**), conversion of the saturated keto ester **13** into its thioketal, desulfurization, and cleavage of the resulting saturated ester **14** with lithium iodide. Attempts to prepare the acid **15** from 10-carbethoxy-1,1-dimethyl-Δ^8-2-octalone (**4**) also are discussed.

In connection with an investigation of the structural selectivity of a variety of photochemical reactions which might afford derivatives of the tricyclic amine **2**,[2] we required a series of 1,1-dimethyl-*trans*-decalin derivatives (**1**) containing angular substituents (X) capable of undergoing suitable photolysis. It appeared that most of these would be readily accessible from 1,1-dimethyl-*trans*-decalin-10-carboxylic acid (**15**),[3] and thus a convenient synthesis of the latter was developed. This synthesis and several interesting observations on unsuccessful approaches to the problem are described in the present paper.



The 1,1-Dimethyl-Δ^8-2-octalone Approach.—The most direct route to the acid **15** initially appeared to involve dimethylation of 10-carbethoxy-$\Delta^{1,9}$-2-octalone (**3**), followed by a suitable reductive sequence to remove the ketone and olefin from the product. Accordingly, the carbethoxyoctalone **3**[4] was treated with potassium *t*-butoxide and excess methyl iodide,[5] producing a major product readily recognized as the desired 10-carbethoxy-1,1-dimethyl-Δ^8-2-octalone (**4**) by its lack of ultraviolet absorption in the 240-mμ region, its infrared absorption at 5.85 μ (ester and nonconjugated ketone), and its n.m.r. spectrum, which had a singlet at 8.82 τ (two quaternary C-methyl groups), a triplet at 4.27 τ (one vinyl proton), and the quartet (5.93 τ) and triplet (8.78 τ) from the ethoxyl group.[6] Unfortunately, however, none of the subsequent sequences which we examined for removal of nuclear functionality from the dimethyl enone **4** led efficiently to the desired acid **15**. Although unsuccessful for their intended synthetic purpose, certain of these results were not without interest, however, for they appear to be strikingly illustrative of the influence which the *gem*-dimethyl group can have on the behavior of the decalin system.



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(1) (a) Abstracted in part from the Ph.D. dissertation of A. S. Levinson, Indiana University, 1963; (b) preliminary communication, W. L. Meyer and A. S. Levinson, *Proc. Chem. Soc.*, 15 (1963); (c) Communication no. 1140.

(2) W. L. Meyer and A. S. Levinson, *J. Org. Chem.*, in press.

(3) For the sake of clarity all *gem*-dimethyldecalins herein discussed are named with the methylated position as C-1. The configurational notations α and β are used in the steroid sense, *i.e.*, a β substituent is *cis* to the angular group. Although only one enantiomer is depicted in each of the structural formulas and the prefix *dl* is omitted, all compounds discussed are racemic.

(4) E. C. DuFeu, F. J. McQuillin, and R. Robinson, *J. Chem. Soc.*, 53 (1937); A. S. Hussey, H. P. Liao, and R. H. Baker, *J. Am. Chem. Soc.*, **75**, 4727 (1953); A. S. Dreiding and A. J. Tomasewski, *ibid.*, **77**, 411 (1955); M. Idelson, Ph.D. thesis, Brooklyn Polytechnic Institute, 1955; M. Idelson and E. I. Becker, *J. Am. Chem. Soc.*, **80**, 908 (1958).

(5) R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelly, *J. Chem. Soc.*, 1131 (1953).

(6) The dimethyl enone **4** was accompanied by 10–15% of 10-carbethoxy-1-methyl-$\Delta^{1,9}$-2-octalone (**5**) [F. J. McQuillin and R. Robinson, *ibid.*, 586 (1941)], the product of monomethylation. Retreatment of this mixture of ketones with potassium *t*-butoxide and methyl iodide under the conditions of its formation resulted in no increase in the ratio of di- (**4**) to monomethylation product **5**, clearly demonstrating that the dimethyl enone **4** is produced without intermediacy of the conjugated monomethyl enone **5**, and providing insight into the sequence of steps involved in such methylations. The initial product of methylation of the enolate of **3** is, of course, the unconjugated 1-methyl-Δ^8-2-ketone i, and it seems clear that this must be the intermediate from which the monomethyl enolate ii is formed. Enolate ii then undergoes the second methylation and, to a lesser extent, competitive protonation to produce the monomethyl ketone **5**. Proton abstraction from C-8 of the latter (to re-form the enolate ii) is apparently quite slow under these conditions. See H. J. Ringold and S. K. Malhotra, *J. Am. Chem. Soc.*, **84**, 3402 (1962), for other recent evidence supporting such a sequence in related dimethylations.