yielded 3-isobutyl-6-*sec*-butyl-2-hydroxypyrazine (0.2 g) as colorless needles, mp 99–100°, whose structure was confirmed by comparison (mixture melting point determination and identity of infrared spectra) with an authentic sample.[14]

1-Chloro-4-methyl-2-oximinopentane (3e). A. From 4-Methyl-2-nitro-1-pentene.—The reduction with stannous chloride and hydrogen chloride was performed in the manner reported previously,[15] bp 84–87° (7.5 mm).

B. From 1-Chloro-4-methyl-2-pentanone.—An aqueous solution of hydroxylamine from the hydrochloride (8.0 g, 175 mmoles) in water (10 ml) and sodium carbonate decahydrate (16 g, 56 mmoles) in water (10 ml) was added dropwise, with stirring, to 1-chloro-4-methyl-2-pentanone (8.0 g, 59 mmoles) at 0°. After the addition was complete, stirring was continued for 4 hr. The mixture was extracted with ether and the extract was washed with water and dried over anhydrous sodium sulfate. The ether was evaporated and the residue was distilled to give a colorless oil (3.9 g, yield 45%), bp 80–84° (2.5 mm).

Both oximes obtained by A and B methods gave an identical product (**6e**) in the following reactions.

N-[4-Methyl-2-(4-methyl-2-oxopentylamino)valeryl]-O-benzylhydroxylamine (6e) Hydrochloride.—To a solution of **4** (15 g, 63 mmoles) in methanol (170 ml) was added 1-chloro-4-methyl-2-oximinopentane (**3e**, 4.5 g, 30 mmoles). After 6 days the solution was concentrated under reduced pressure and the residue was treated with ether (150 ml). After removal of the insoluble, crystalline product, the ethereal solution was washed twice with water and dried over anhydrous sodium sulfate. The ether was evaporated and the residue was dissolved in a mixture of methanol (65 ml), 3 *N* hydrochloric acid (40 ml), and benzaldehyde (5 g, 47 mmoles). The resultant solution was left to stand at room temperature for 90 hr. The solution was concentrated under reduced pressure to 20–30 ml, to which ether (100 ml) and water (10 ml) were added, whereupon colorless crystals separated gradually. The mixture was kept in a refrigerator overnight, and then the crystals (3.3 g) were collected and washed with ether and ethyl acetate. Recrystallization from 30% aqueous methanol gave two products. As the first crop, a small quantity of colorless needles was obtained, mp 147–147.5°. The product was confirmed to be 3,6-diisobutyl-2-hydroxypyrazine by comparison (mixture melting point determination and identity of infrared spectra) with an authentic sample.[16]

After removal of the first crop, the filtrate was left to stand overnight to separate clusters of colorless small needles as the main product, mp 134–135° dec. The infrared spectrum (KBr) had a complex series of absorptions between 2800 and 2300 cm^{-1} and sharp bands at 3220, 2950, 1690, 750, and 700 cm^{-1}.

Anal. Calcd for $C_{19}H_{30}N_2O_3 \cdot HCl$: C, 61.46; H, 8.36; N, 7.55. Found: C, 61.47; H, 8.51; N, 7.82.

4-Methyl-2-(4-methyl-2-oxopentylamino)valerohydroxamic Acid (7e).—The hydrochloride of **6e** (2.5 g) was dissolved in 1 *N* aqueous sodium hydroxide (30 ml) and treated with activated charcoal. The clear solution was saturated with carbon dioxide to give an oil, which was extracted with ether and dried over anhydrous sodium sulfate. Evaporation of the ether gave the oily free base (1.5 g), which was reduced under the same conditions as in **7a**. After removal of the catalyst, the methanol was evaporated and the residual crystals were washed with ether, yield 0.5 g, 45%. An analytical sample was obtained by recrystallizing twice from 80% aqueous methanol as clusters of colorless needles, mp 141–142° dec. The infrared spectrum (KBr) had a broad band at 2700–2200 and sharp bands at 3160, 2950, 1725, and 1610 cm^{-1}.

Anal. Calcd for $C_{12}H_{24}N_2O_3$: C, 58.99; H, 9.90; N, 11.47. Found: C, 58.72; H, 9.87; N, 11.64.

3,6-Diisobutyl-2-hydroxypyrazine 1-Oxide (Neoaspergillic Acid, 1e).—A suspension of **7e** (1.1 g, 4.5 mmoles) in methanol (30 ml) was saturated with gaseous ammonia. After 3 days the resultant solution was concentrated under reduced pressure and the residue was dissolved in a mixture of methanol (20 ml) and 1 *N* aqueous sodium hydroxide (10 ml). The solution was treated with activated charcoal and then again concentrated under reduced pressure. A solution of the residue in water (20 ml) was saturated with carbon doxide. After removal of an oily material (all attempts to crystallize it were unsuccessful), the solution was acidified to pH 1.5 with 3 *N* hydrochloric acid, whereupon crystals separated gradually. The mixture was left to stand in a refrigerator for 3 hr and the crystals were collected. Recrystallization from 80% aqueous methanol yielded neoaspergillic acid (0.1 g, yield 9.9%) as yellow needles, mp 127.5–128.5°.

Anal. Calcd for $C_{12}H_{20}N_2O_2$: C, 64.25; H, 8.99; N, 12.49. Found: C, 64.31; H, 9.08; N, 12.67.

3-Isobutyl-6-phenyl-2-hydroxypyrazine (2g).—A solution of **4** (2.4 g, 10 mmoles) in methanol (30 ml) was saturated with gaseous ammonia, and phenacyl bromide (1.9 g, 9.5 mmoles) was added to the solution, which was then left to stand in a refrigerator for 4 days. The crystalline solid (0.6 g) was removed by filtration. [Recrystallization from methanol gave 3,6-diphenylpyrazine, mp 196° (lit. mp 196°,[17a] 195–196°[17b]).] The filtrate was concentrated under reduced pressure and the residue was extracted with 1 *N* aqueous sodium hydroxide. After treatment with activated charcoal, the extract was saturated with carbon dioxide to separate hydroxypyrazine **2g** (0.6 g, 2.6 mmoles). Recrystallization from ethyl acetate gave yellow, long needles, mp 167°.

Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.06; N, 15.27. Found: C, 73.42; H, 7.63; N, 15.21.

(15) M. Masaki and M. Ohta, *Bull. Chem. Soc. Japan*, **36**, 922 (1963).
(16) M. Masaki and M. Ohta, *ibid.*, **36**, 1177 (1963).
(17) (a) L. Wolff, *Ber.*, **20**, 432 (1887); (b) E. Braun and V. Meyer, *ibid.*, **21**, 1278 (1888).

The Decarboxylation of α-Nitrophenylcinnamic Acids

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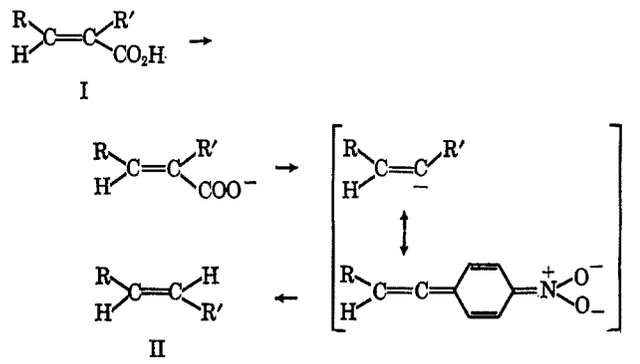
The decarboxylation of α-nitrophenylcinnamic acids in the presence of piperidine was found to proceed *via* the Michael addition of the piperidine to the double bond of the cinnamic acid derivative and the loss of carbon dioxide from the Michael adduct, with and without the regeneration of piperidine, to afford *trans*-4-nitrostilbenes and tertiary amines, respectively.

The decarboxylation of α-4-nitrophenyl-*trans*-cinnamic acid in the presence of piperidine at 150–160° was first reported in 1911.[1] Earlier studies had shown that decarboxylation did not occur in the absence of piperidine, decomposition of the cinnamic acid derivative taking place at 260°.[2] In view of these results Pfeiffer and Sergiewskaja attempted the condensation of benzaldehyde with 4-nitrophenylacetic acid in the presence of piperidine at 150–160° and found *trans*-4-nitrostilbene to be afforded in good yield.[1] Although this decarboxylation procedure has been successfully used in the synthesis of substituted stilbenes,[3] no mechanistic studies were reported until 1963.

(1) P. Pfeiffer and S. Sergiewskaja, *Ber.*, **44**, 1107 (1911).
(2) R. Walther and A. Wetzlich, *J. Prakt. Chem.*, [2] **61**, 181 (1900).
(3) (a) H. Kaufmann, *Ber.*, **54**, 795 (1921); (b) N. Cullinane, *J. Chem. Soc.*, 2060 (1923); (c) H. Harrison and H. Wood, *ibid.*, 580 (1926); (d) R. Ketcham and D. Jambotkar, *J. Org. Chem.*, **28**, 1034 (1963).

Jambotkar and Ketcham have proposed a direct decarboxylation path for the formation of *trans*-4-nitrostilbene (II) from α-4-nitrophenyl-*trans*-cinnamic acid (I) in which the role of the piperidine lies in the generation of the carboxylate ion of I which in turn loses carbon dioxide to afford a resonance-stabilized carbanion.[4]



I

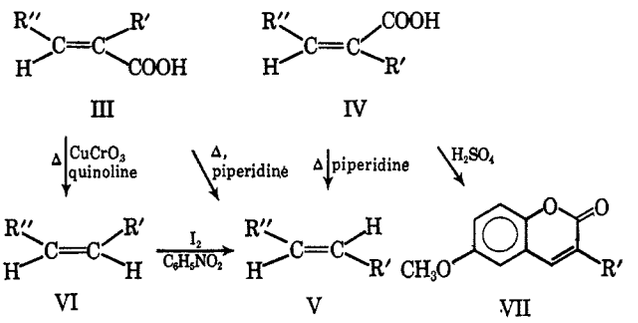
II

R = phenyl
R′ = *p*-nitrophenyl

Evidence for this one-step decarboxylation mechanism included the exclusive formation of the *trans*-stilbene II from I, the failure of I to form its *cis* isomer under the reaction conditions, and the failure of both α-phenyl-*trans*-4-nitrocinnamic acid and its *cis* isomer to decarboxylate in the presence of piperidine.[4]

We have found the reaction of 2,5-dimethoxybenzaldehyde with 4-nitrophenylacetic acid in the presence of piperidine to afford both α-4-nitrophenyl-*trans*-2,5-dimethoxycinnamic acid (III) and α-4-nitrophenyl-*cis*-2,5-dimethoxycinnamic acid (IV). Trace amounts of *trans*-2,5-dimethoxy-4′-nitrostilbene (V) and 4-nitrotoluene[5] were also formed.

The assignment of structures to III and IV was made primarily from the three following experimental results. (a) The copper chromite catalyzed decarboxylation of α-4-nitrophenyl-*trans*-cinnamic acid (I) is known to afford the *cis*-4-nitrostilbene as the major product.[7] The isomer which we assigned as α-4-nitrophenyl-*trans*-2,5-dimethoxycinnamic acid (III), on treatment with copper chromite in quinoline, afforded the *cis*-stilbene VI. Compound VI was isomerized in refluxing nitrobenzene in the presence of iodine to the *trans*-stilbene V. (b) The *trans*-stilbene V and the *cis* acid IV exhibited a characteristic absorption in the ultraviolet at 380 mμ (ε 20,000) and 375 mμ (ε 14,000), respectively, while both the *cis*-stilbene VI and the *trans* acid III were nearly transparent in this region.[8] (c) The *cis* acid IV, on solution in concentrated sulfuric acid and hydrolysis, afforded 3-(4′-nitrophenyl)-6-methoxycoumarin (VII). Under the same reaction conditions the *trans* acid III was recovered unchanged. This reaction is similar to one in which coumarin is afforded in 79% yield from the treatment of methyl *cis*-2-methoxycinnamate with polyphosphoric acid at 30°.[9] With the *trans* ester, 95% of the starting material was recovered.[9]

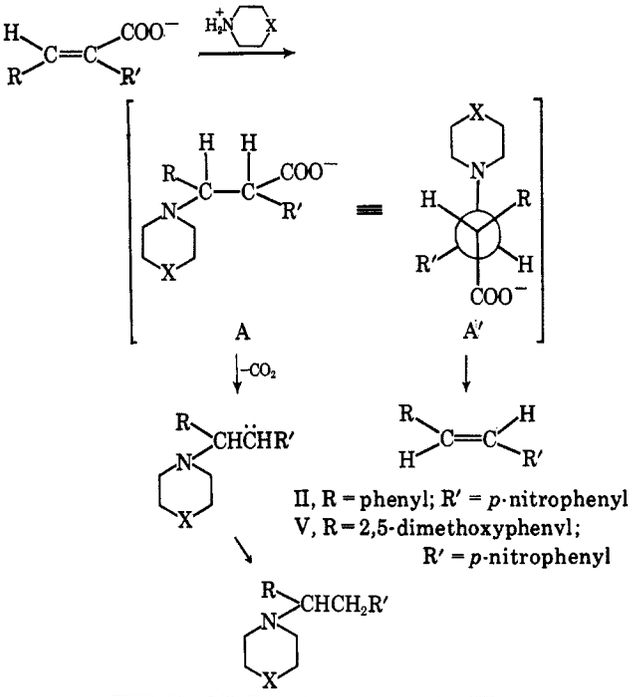


III IV VI V VII

R′ = *p*-nitrophenyl
R″ = 2,5-dimethoxyphenyl

The cinnamic acids III and IV form stable piperidine salts (mp 174–175° and 155–156°, respectively) which melt with decarboxylation. In solution, however, these salts undergo an intramolecular Michael addition at a much lower temperature. For example, heating of III in refluxing piperidine (106°) for 6 hr results in complete decarboxylation, with formation of 59% of V and 38.8% of VIII. However, refluxing of III in chlorobenzene (130°), in the presence of a catalytic amount of piperidine for 24 hr results in almost complete recovery of the cinnamic acid. The participation of piperidine as a reactant, rather than a catalyst, is thus demonstrated.

Although the intermediate A could not be isolated, its *threo* configuration A′ can clearly undergo a *trans* elimination to afford the observed *trans*-stilbene V. The free rotation around the carbon–carbon bond in



A A′

II, R = phenyl; R′ = *p*-nitrophenyl
V, R = 2,5-dimethoxyphenyl; R′ = *p*-nitrophenyl

VIII, R = 2,5-dimethoxyphenyl; X = CH_2; R′ = *p*-nitrophenyl
IX, R = 2,5-dimethoxyphenyl; X = O; R′ = *p*-nitrophenyl
X, R = phenyl; X = CH_2 R′ = *p*-nitrophenyl

(4) D. Jambotkar and R. Ketcham, *J. Org. Chem.*, **28**, 2182 (1963).

(5) The 4-nitrotoluene arises from the decarboxylation of 4-nitrophenylacetic acid. The decarboxylation of 2-nitrophenylacetic acid at temperatures above 90° has been observed.[6]

(6) P. Ruggli and O. Schmid, *Helv. Chim. Acta*, **18**, 1229 (1935).

(7) R. Stroemer and H. Oehlert, *Ber.*, **55**, 1239 (1922).

(8) The interaction of the *cis*-phenyl groups in III and VI gives rise to skewed or nonplanar configurations. Thus, the absorption resulting from the resonance in IV and V is prevented in III and VI.

(9) N. Narayana, J. F. Dash, and P. D. Gardner, *J. Org. Chem.*, **27**, 4704 (1962).

the intermediate A can account for the inversion of configuration.

Morpholine was similarly allowed to react with III to yield a mixture of V and 1-(2,5-dimethoxyphenyl)-1-morpholino-(1)-2-(4-nitrophenyl)ethane (IX), but secondary amines such as dimethylamine, N-methylaniline, and 2-methylpiperidine were found to be ineffective. The failure of these amines well demonstrates the rigid, steric requirement for the reaction.[10]

Likewise, α-4-nitrophenyl-*cis*-2,5-dimethoxycinnamic acid (IV) decarboxylates in the presence of piperidine to afford the *trans*-stilbene V and 1-(2,5-dimethoxyphenyl)-1-piperidino(1)-2-(4-nitrophenyl)ethane (VIII).

The decarboxylation of α-4-nitro- and α-2-nitrophenylcinnamic acids is also made explicable by this mechanism, once the intermediate A is rightfully recognized as a nitrophenylacetic acid derivative, compounds known to decarboxylate readily. We have also isolated the hydrochloride of 1-phenyl-1-piperidino-(1)-2-(4-nitrophenyl)ethane (X) in the decarboxylation of α-4-nitrophenyl-*trans*-cinnamic acid (I),[1,4] which lends support to our proposed mechanism. The structures of the amines VIII, IX, and X were established by elementary analysis and by infrared spectrography.

Experimental Section[11]

Condensation of 4-Nitrophenylacetic Acid with 2,5-Dimethoxybenzaldehyde.—To a solution of 83 g (0.5 mole) of 2,5-dimethoxybenzaldehyde and 90.5 g (0.5 mole) of 4-nitrophenylacetic acid in 500 ml of benzene was added 8.3 g (0.1 mole) of piperidine and the mixture was refluxed for 6 hr during which time 8.5 ml of water was azeotropically distilled. Cooling of the reaction mixture gave 115.8 g (70%) of α-4-nitrophenyl-*trans*-2,5-dimethoxycinnamic acid (III): mp 224–225°; λ_{max}^{KBr} 3.45, 5.95, 6.2, 6.25, 6.55, 6.7, 6.79, 7.05, 7.4, 7.95, 8.15, 8.6, 9.02, 9.6, 11.6, 12.2, and 14.0 μ.

Anal. Calcd for $C_{17}H_{15}NO_6$: N, 4.25. Found N, 4.30.

The benzene was evaporated from the mother liquor and the residue was then stirred with 150 ml of 5% NaOH to give 9.8 g (6.9%) of *trans*-2,5-dimethoxy-4′-nitrostilbene (V), mp 115° (lit.[3a] mp 118°). Acidification of this basic mother liquor afforded 33.8 g (20.5%) of a mixture of III and α-4-nitrophenyl-*cis*-2,5-dimethoxycinnamic acid (IV), mp 150–190°. Upon fractional crystallization of the mixture from ethanol 6.1 g (3.7%) of pure IV was obtained: mp 174–175°; λ_{max}^{KBr} 3.45. 5.95, 6.25, 6.68, 7.0, 7.43, 7.7, 7.9, 8.15, 8.45, 8.98, 9.6, 10.0, 11.73. 12.4, 13.26, 13.75, 14.1, 14.25, and 14.48 μ.

Anal. Calcd for $C_{17}H_{15}NO_6$: C, 62.00; H, 4.59; N, 4.25. Found: C, 61.87, H, 4.67, N, 4.45.

Piperidine (0.85 g, 0.01 mole) was added to 3.29 g (0.01 mole) of α-4-nitrophenyl-*trans*-2,5-dimethoxycinnamic acid (III) suspended in 50 ml of benzene and after several minutes there was separated 3.85 g (93%) of the piperidine salt, mp 174–175° dec.

The heating of 17.6 g (0.043 moles) of the piperidine salt of III at 172–181° (12 mm) for 6 hr followed by treatment with aqueous base afforded 5.9 g (39%) of the *trans*-stilbene (V), mp 116–117°. Upon acidification of the aqueous mother liquor 3.2 g (21.5%) of a mixture of the cinnamic acids III and IV, mp 180–190°, was obtained.

Piperidine (0.85 g, 0.01 mole) was added to 3.29 g (0.01 mole) of α-4-nitrophenyl-*cis*-2,5-dimethoxycinnamic acid (IV) suspended in 50 ml of benzene and the mixture was stirred for 1 hr to yield 2.5 g (67.5%) of the salt, mp 155–156° dec. Evaporation of the mother liquor gave an additional 1.0 g, mp 154–155° dec, a total yield of 3.5 g (94.5%) of the piperidine salt of IV being obtained.

Decarboxylation of α-4-Nitrophenyl-*trans*-2,5-dimethoxycinnamic Acid (III). Method A. Copper Chromite in Quinoline.—Copper chromite (1.5 g) was added to 60 ml of quinoline, followed by the addition of III (15 g, 0.045 mole) at 205–255° over 10 min. Gas evolution occurred immediately and continued for 5 min after the addition of III had been completed. The mixture was then cooled to 8° and 300 ml of 10% HCl was added. A dark tar separated and was extracted with diethyl ether, the evaporation of the ether extract giving 10.5 g (79%) of *cis*-2,5-dimethoxy-4′-nitrostilbene (VI): mp 60–61° (from ethanol); λ_{max}^{KBr} 3.43–3.55, 6.12, 6.27, 6.65, 6.78 7.02 7.45 7.77 8.20 8.5, 8.68, 9.05, 9.78, 11.35, 11.65, 12.15, 12.30, 12.88, 13.32, 13.92, 14.12, and 14.38 μ.

Method B. Catalytic Amount of Piperidine in Chlorobenzene.—Piperidine (47.5 mg, 0.005 mole) was added to 6.6 g (0.02 mole) of III in 50 ml of chlorobenzene and the mixture was refluxed for 24 hr. On cooling there was obtained 5 g (75.7%) of III, mp 225–226°. The evaporation of solvent from the mother liquor followed by trituration with 5% aqueous sodium hydroxide afforded minute quantities of alkali-insoluble materials which were removed by filtration. Acidification of the filtrate gave 1.1 g (16.7%) of a mixture of the cinnamic acids III and IV, mp 165–175°.

Method C. Excess Piperidine.—To 300 ml of piperidine was added 100 g (0.304 mole) of III and the mixture was refluxed for 6 hr after which time none of the starting acid could be detected (by infrared). The piperidine was removed by evaporation *in vacuo* and the residue was extracted with three 500-ml portions of hot ligroine to yield 50.9 g (59%) of pure *trans*-2,5-dimethoxy-4′-nitrostilbene (V): mp 117–118°; λ_{max}^{KBr} 3.45–3.55, 6.12, 6.27, 6.68, 7.0, 7.49, 7.77, 8.03, 8.23, 8.4–8.5, 8.9, 8.99, 9.53, 9.78, 10.28, 10.45, 11.43, 11.59, 12.33, 13.25, 13.92, and 14.53 μ. Evaporation of the mother liquor gave 43.7 g (38.8%) of 1-(2,5-dimethoxyphenyl)-1-piperidino-(1)-2-(4-nitrophenyl)-ethane (VIII): mp 78–81°; λ_{max}^{KBr} 3.43–3.6, 6.24, 6.65, 6.78, 7.48, 7.80, 8.20, 9.13, 9.54, 10.00, 10.22, 11.2, 11.6, 12.25, 13.32, 14.22, and 14.38 μ. The further purification of VIII by dissolution in 50% aqueous HCl, precipitation by base, and crystallization from ethanol afforded pale yellow crystals, mp 85–86°.

Anal. Calcd for $C_{21}H_{26}N_2O_4$: N, 7.56. Found N, 7.72.

Method D. Excess Morpholine.—To 132 ml of morpholine was added 13.2 g (0.04 mole) of III and the mixture was refluxed for 3 hr. The morpholine was evaporated from the reaction mixture and ethanol was added to cause precipitation of 12.8 g of a crude mixture, mp 104–110°. After stirring the mixture in 50% aqueous HCl there was afforded 35% of V, mp 115–116°. Neutralization of the aqueous mother liquor caused precipitation of 5.6 g (43.8%) of 1-(2,5-dimethoxyphenyl)-1-morpholino-(1)-2-(4-nitrophenyl)ethane (IX), mp 123–124°.

Anal. Calcd for $C_{20}H_{24}N_2O_5$: C, 64.50; H, 6.50; N, 7.52. Found: C, 64.36; H, 6.46; N, 7.33.

Decarboxylation of α-4-Nitrophenyl-*cis*-2,5-dimethoxycinnamic Acid (IV) in Piperidine.—To 13.2 g of piperidine was added 3.29 g (0.01 mole) of IV and the mixture was refluxed for 4 hr. The piperidine was evaporated from the reaction mixture and 91% isopropyl alcohol was added to cause precipitation of 2 g of a mixture of the *trans*-stilbene V and the Michael adduct VIII, mp 105–110°, as evidenced by infrared spectroscopy.

3-(4′-Nitrophenyl)-6-methoxycoumarin (VII).—To 10 ml of concentrated H_2SO_4 was added 2.5 g (0.0076 mole) of α-4-nitrophenyl-*cis*-2,5-dimethoxycinnamic acid (IV) and the mixture was stirred for 5 min and then poured into 125 ml of water to give 2.1 g (93%) of 3-(4′-nitrophenyl)-6-methoxycoumarin (VII), mp 270–271°. Recrystallization of VII from dioxane afforded yellow crystals: mp 278°; λ_{max}^{KBr} 5.85, 6.35, 6.65, 7.43, 7.79, 8.02, 8.9, 9.62, 10.38, 11.75, 12.15, 12.8, and 14.8 μ.

Anal. Calcd for $C_{16}H_{11}NO_5$: C, 64.64; H, 3.73; N, 4.71; MeO, 10.44. Found: C, 64.97; H, 3.75; N, 4.98; MeO, 10.92.

Isomerization of *cis*-2,5-Dimethoxy-4′-nitrostilbene (VI) to the *trans* Isomer (V).—To 50 ml of nitrobenzene was added 2.5 g (0.009 mole) of VI and one crystal of iodine. The mixture was refluxed for 10 min and cooled. Removal of the nitrobenzene by evaporation *in vacuo* yielded 2.2 g (88%) of *trans*-2,5-dimethoxy-4′-nitrostilbene (V), mp 115–116°.

Stability of *cis*- and *trans*-2,5-Dimethoxy-4′-nitrostilbene under

(10) One of the referees has suggested that the fact that sterically hindered amines, such as dimethylamine and 2-methylpiperidine, are ineffective, lends additional support to the postulation that addition of the base occurs prior to decarboxylation. Hindered amines add across carbon double bonds less readily, but the ionization of carboxylic acids depends upon the basicity of the amine. If ionization of the acid were the important feature in the decarboxylation, as in Jambotkar and Ketcham's mechanism, then hindered amines ought to be effective as well as unhindered amines in promoting this reaction.

(11) Melting points are uncorrected. Analyses are by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Decarboxylation Conditions.—To 12 g of piperidine was added 2.85 g (0.01 mole) of V and the mixture was refluxed for 6 hr. Evaporation of the piperidine afforded 2.85 g of the starting material V.

Under similar conditions compound VI was also found to be unchanged.

Decarboxylation of α-4-Nitrophenyl-*trans*-cinnamic Acid (I) in Piperidine.—To 50 ml of piperidine was added 5.4 g (0.02 mole) of α-4-nitrophenyl-*trans*-cinnamic acid (I), mp 224–225° (lit.[12] mp 224.5°), and the mixture was refluxed for 5 hr. Evaporation of the piperidine followed by the addition of ethanol to the semi-solid residue caused precipitation of 1.5 g (33.5%) of *trans*-4-nitrostilbene (II), mp 150–152° (lit.[4] mp 150–153°). Work-up of the mother liquor by evaporation of the ethanol, addition of 50% aqueous HCl, stirring for 1 hr at room temperature, extraction with chloroform, and evaporation of the chloroform gave a residue which was recrystallized from ethyl acetate to afford 2.1 g (30.4%) of the hydrochloride of 1-phenyl-1-piperidino-(1)-2-(4-nitrophenyl)ethane (X): mp 230–232°; λ_{max}^{KBr} 2.95, 3.43, 3.83, 4.1, 6.2, 6.55, 6.85, 7.4, 9.0, 11.6, 11.75, 12.1, 13.15, 13.4, 14.18, and 14.35 μ.

Anal. Calcd for $C_{19}H_{23}ClN_2O_2$: C, 65.79; H, 6.65; N, 8.07. Found: C, 65.84; H, 6.87, N, 7.84.

(12) F. K. Beilstein, "Handbuch der Organischen Chemie," Vol 9, 4th ed, 1919, p 693.

Acknowledgment.—We are indebted to Benjamin Tucker and Martha Reiter for their assistance in the experimental aspects of this work.

Studies on Cyclic Polyols. VI. Synthesis of Anhydrocyclopentanetetrols and Aminocyclopentanetriols[1]

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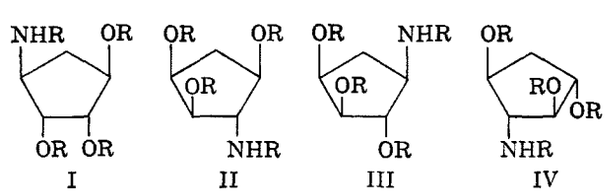
The isomeric cyclopentenediols and their diacetates are converted to the corresponding epoxides (anhydrotetrols) by treatment with *m*-chloroperoxybenzoic acid. The epoxidation obeys Henbest's rule that an allylic OH is *cis* directing in the epoxidation reaction. By nucleophilic opening with NaN_3 the epoxide group is converted to a *trans*-azido alcohol. After acetylation the azido compounds are reduced with Pd–C catalyst to aminotriol derivatives. The position of nucleophilic attack by Br^- and OH^- was previously shown to be governed by steric hindrance and electrostatic factors. In the present study one case was found in which N_3^- attacked the epoxide at the electrostatically less favorable position. A *trans*-OAc group adjacent to one end of the oxirane ring is a powerful directing influence for hydrolytic epoxide opening, and when both ends of the oxirane ring have adjacent *trans*-OAc groups the nucleophilic attack does not take place; hydrolysis of the epoxide occurs instead. Four acetamidocyclopentanetriol triacetates, DL-(1,4/2,3)-1-acetamido-2,3,4-tri-O-acetylcyclopentanetriol (Id), DL-(1,2,4/3)-3-acetamido-1,2,4-tri-O-acetylcyclopentanetriol (IId), DL-(1,2,4/3)-4-acetamido-1,2,3-tri-O-acetylcyclopentanetriol (IIId), and DL-(1,3/2,4)-2-acetamido-1,3,4-tri-O-acetylcyclopentanetriol (IVd), and the corresponding acetamido-tri-O-benzoylcyclopentanetriols (If–IVf) are described. An improved method for preparing DL-*trans*-3,4-di-O-acetylcyclopentenediol (XIIIb) has been developed.

Although aminocyclitols derived from cyclohexane are known as components of many carbohydrate antibiotics,[3,4] such as streptomycins, kanamycins, and neomycins, and the synthesis of cyclohexane aminocyclitols has been studied in several laboratories,[3,5–7] the analogous cyclopentane derivatives have been unknown. As part of our systematic study of cyclopentane cyclitols we have now synthesized several aminocyclopentanetriols which are described in the present communication (see Chart I). Some aminocyclopentanediols, aminocyclopentanetetrols, and diaminocyclopentanediols are described elsewhere.[8a]

In earlier studies the configurational uncertainties were resolved,[9,10] and some anhydrotetrols were described.[11] Epoxidation of the cyclopentenediols with

CHART I

AMINOCYCLOPENTANETRIOLS



R = H or Ac

m-chloroperoxybenzoic acid, which proceeded according to Henbest's rule,[12] produced[11] anhydrotetrols Va–VIIa, whereas VIIIa was prepared[11b,13] from the known[9a] epoxybromohydrin VIIIc by reactions of known stereospecificity. The anhydrotetrols have served as starting materials for the synthesis of many of the aminocyclitols to be reported, and the preparation of some new isomers and derivatives of anhydrotetrols (V–XI) is described below (see also Chart II).

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