mine gave pure L-isoglutamine and L-glutamine, respectively. It may therefore be concluded that the isolation of a mixture of glutamine and isoglutamine from either ester after treatment with alkali is due to the intermediate formation of carbobenzoxy-α-aminoglutarimide.

The esters were dissolved in one equivalent of aqueous sodium hydroxide, stored at room temperature for 2 hours, neutralized with 1 *N* hydrochloric acid, and hydrogenated at room temperature with palladium black. The chromatographic analysis was carried out on Whatman No. 1 paper, using the solvent systems *n*-butyl alcohol, acetic acid, water (4:1:5) and phenol saturated with water.

The R_f values for the components of the hydrolyzed and hydrogenated preparations corresponded with those found for pure L-glutamine and L-isoglutamine. Evidence for the formation of traces of L-glutamic acid was also obtained. The R_f values found at 25° for L-glutamic acid, L-glutamine and L-isoglutamine are 0.25, 0.15 and 0.25 in the *n*-butyl alcohol system and 0.25, 0.6 and 0.6, respectively, in the phenol system.

GENEVA, NEW YORK

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

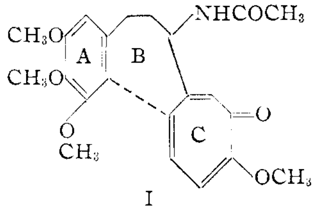
Synthetic Studies on the Colchicine Problem. The Preparation and Properties of Some Styryltropolones[1]

BY D. S. TARBELL, RICHARD F. SMITH AND V. BOEKELHEIDE

RECEIVED DECEMBER 21, 1953

The condensation of benzaldehyde, and of its 2-nitro, 2-acetamino and 3,4,5-trimethoxy derivatives, with α-carboxy-β-carboxymethyltropolone in the presence of acetic anhydride and triethylamine proceeds with the liberation of carbon dioxide. The products are the corresponding α-carboxy-β-styryltropolones, usually mixed with the O-acetyl derivatives. These compounds have been separated and characterized. The *o*-nitrostyryltropolone has been reduced by hydrazine–Raney nickel to the amino compound, which on diazotization and treatment with copper powder fails to cyclize. It is found from infrared and cyclization studies that, contrary to the usual results, the Perkin–Oglialoro reaction between the benzaldehydes studied and α-carboxy-β-carboxymethyltropolone yields only the *trans* isomers.

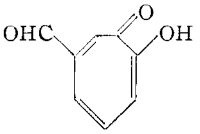
Most of the approaches to the synthesis of colchicine (I) which have been described so far[2] have projected the formation of rings A and B, followed by the elaboration of the tropolone ring C either by cyclization, or by introduction of the necessary oxygen functions and unsaturation into a relatively saturated seven-membered ring C.



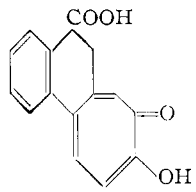
I

It occurred to us that a promising alternative scheme would be the formation of a compound containing an aromatic ring (A) connected to a tropolone ring (C) by a three-carbon chain, with an amino group in the one ring or the other, so situated that the bond between rings A and C (indicated with a dotted line in structure I) could be established by application of the Pschorr reaction. The present paper describes some model experiments designed to test the feasibility of this synthetic scheme.

Thus, β-formyltropolone[3] (II) might be condensed with oxindole, and the resulting product treated by the Windaus modification[4] of the Pschorr

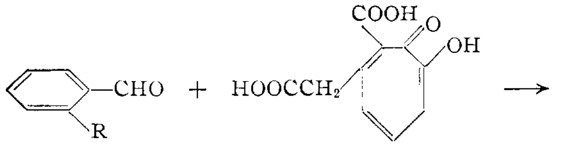


II

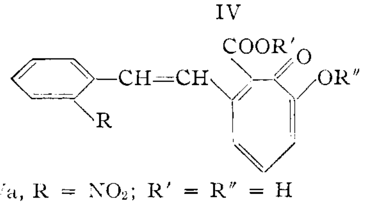


III

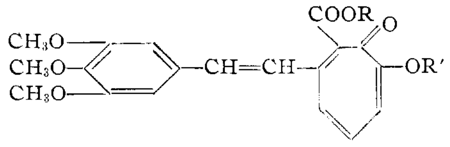
cyclization to form the tricyclic tropolone III. However, the much greater accessibility of α-carboxy-β-carboxymethyltropolone[3] (IV) suggested the investigation of the condensation of aromatic aldehydes with the active methylene group of IV.



IV



Va, R = NO_2; R′ = R″ = H
Vb, R = NO_2; R′ = H, R″ = $COCH_3$
Vc, R = NO_2; R′ = R″ = CH_3
Vd, R = NH_2; R′ = R″ = H
Ve, R = $NHCOCH_3$; R′ = R″ = H
Vf, R = R′ = R″ = H
Vg, R = R′ = H; R″ = $COCH_3$



VIa, R = R′ = H
VIb, R = H; R′ = $COCH_3$
VIc, R = R′ = CH_3

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[1] This research was aided by a grant from the National Cancer Institute of the National Institutes of Health, Public Health Service.

[2] For example: H. Rapoport and J. E. Campion, THIS JOURNAL, **73**, 2239 (1951); C. D. Gutsche and K. L. Seligman, *ibid.*, **75**, 2579 (1953); P. D. Gardner and W. J. Horton, *ibid.*, **75**, 4976 (1953); A. G. Anderson, Jr., and H. F. Greef, *ibid.*, **74**, 5203 (1952); E. Ott and D. S. Tarbell, *ibid.*, **74**, 6266 (1952); G. A. Page and D. S. Tarbell, *ibid.*, **75**, 2053 (1953); A. Eschenmoser and H. H. Rennhard, *Helv Chim. Acta*, **36**, 290 (1953); V. Boekelheide and F. C. Pennington, THIS JOURNAL, **74**, 1558 (1952).

[3] R. D. Haworth and J. D. Hobson, *J. Chem. Soc.*, 561 (1951).

[4] A. Windaus and W. Eickel, *Ber.*, **57**, 1871 (1924); A. Windaus H. Jensen and A. Schramme, *ibid.*, **57**, 1875 (1924).

It was found that aromatic aldehydes—benzaldehyde, *o*-nitrobenzaldehyde, *o*-acetaminobenzaldehyde, 3,4,5-trimethoxybenzaldehyde—condensed readily with IV in the presence of acetic anhydride and triethylamine[5] to eliminate carbon dioxide with formation of compounds of type V. With all of the aromatic aldehydes except *o*-acetaminobenzaldehyde, the condensation under these conditions led to two products: the derivatives with the free hydroxyl group in the tropolone ring (Va, Ve, Vf, VIa) and the compounds in which the hydroxyl group had been acetylated (Vb, Vg, VIb). These were separated by crystallization, characterized, and the relationship between each pair was established by hydrolysis and, in some cases, by reacetylation.

During the course of our work, Nozoe and his collaborators[6-8] reported on experiments directed along lines very similar to our own. Our results will be reported in detail only as they extend or supplement the published results.[6,8]

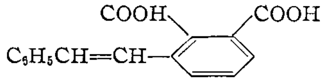
We studied the series from *o*-nitrobenzaldehyde in most detail because of its significance for the projected synthetic method. The condensation, carried out at room temperature, gave 44% of the tropolone Va, and 24% of the corresponding acetate Vb, which were separated by crystallization from alcohol. The tropolone Va was characterized by analysis and titration as a dibasic acid, with pK_a values of 4.1 and 8.8; it showed absorption in the hydroxyl region in the infrared and also showed a band at 970 cm.$^{-1}$. The acetate showed no absorption in the hydroxyl region, showed very weak absorption at 970 cm.$^{-1}$ and titrated as a monobasic acid; acidic hydrolysis of Vb gave the hydroxy compound Va.

Reduction experiments on Va with ferrous hydroxide, ammonium sulfide, sodium hydrosulfite or hydrogen and platinum in dioxane were unpromising; however, treatment with hydrazine and Raney nickel in aqueous alcohol[9] gave a very high melting insoluble compound, probably a polymeric amide, which, when boiled with dilute hydrochloric acid, yielded the hydrochloride of the expected amino acid Vd. Addition of water to an alcoholic solution of the hydrochloride liberated the free amino acid Vd.

The structure of the amino acid Vd was checked by the condensation of *o*-acetaminobenzaldehyde[10] with α-carboxy-β-carboxymethyltropolone (IV) to yield the *o*-acetamino compound Ve; hydrolysis of this with hydrochloric acid yielded Vd.

The free amino acid Vd was diazotized very slowly by the usual procedure; the hydrochloride, however, in ethanol saturated with dry hydrogen chloride was readily diazotized by isoamyl nitrite. The diazotized solution gave red precipitate with alkaline β-naphthol, but application of modified Pschorr procedures (addition of copper powder to the diazonium solution under acetone)[11] yielded only tars and small amounts of undiazotized amine.

The reason for the failure of the Pschorr cyclization soon became apparent; all of the styryltropolones, V and VI, have the *trans* configuration of the aromatic ring and the tropolone ring around the central double bond. This assignment is based on our observation of the infrared spectra of V and VI, all of which show a band at about 970 cm.$^{-1}$, which is characteristic of the *trans* R—CH=CHR′ system.[12] Furthermore, Nozoe[7] synthesized VII, the product derived from Vf by aromatization of the tropolone ring, by a method which would be expected to yield the *trans* isomer.[13] This synthesis also proved the position of the carboxyl group in Vf; confirmatory evidence for this in the other compounds in the series is given by the infrared spectra, as discussed below.



VII

The formation of *trans* compounds in the condensation of IV and the benzaldehydes is unexpected because the analogous reactions between phenylacetic acids and benzaldehyde usually lead exclusively or predominantly to *cis*-α-arylcinnamic acids (*cis* with respect to the two aryl groups).[14,15] Furthermore, the condensation of *o*-nitrobenzaldehyde with homophthalic acid, which is analogous to IV in structure, leads, without decarboxylation, to the *cis* (aryl to aryl) product.[16] The behavior of IV, in yielding *trans* products, may be caused by the greater steric requirement of the carboxytropolone ring, compared to the phenyl group in the other examples; the double bond is introduced more readily with the tropolone ring as far from the phenyl ring as possible.

The condensation of IV with 3,4,5-trimethoxybenzaldehyde yielded the expected product VIa and its acetate VIb; the product had the *trans* configuration, from the infrared spectra, and attempts to cyclize the acid VIa by acylation of the trimethoxyphenyl ring by the carboxyl group were unsuccessful, in agreement with the assigned configuration.

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(5) These conditions for the Perkin-Oglialoro condensation are recommended by P. Kalnin, *Helv. Chim. Acta*, **11**, 982 (1928), and M. Bakunin and D. Peccerillo, *Gazz. chim. ital.*, **65**, 1145 (1935); *cf.* J. R. Johnson, in "Organic Reactions" (edited by Roger Adams), Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 210 ff.

(6) T. Nozoe, Y. Kitahara, K. Doi and M. Endo, *Proc. Japan Acad.*, **28**, 32 (1952).

(7) T. Nozoe, Y. Kitahara, K. Doi and S. Masamune, *ibid.*, **28**, 291 (1952).

(8) T. Nozoe, Y. Kitahara and S. Masamune, *ibid.*, **29**, 17 (1953).

(9) D. Balcom and A. Furst, THIS JOURNAL, **75**, 4334 (1953).

(10) L. I. Smith and J. W. Opie, *Org. Syntheses*, **28**, 11 (1948); P. Cohn and L. Springer, *Monatsh.*, **24**, 96 (1903).

(11) D. H. Hey and J. M. Osbond, *J. Chem. Soc.*, 3168 (1949).

(12) For a summary of examples, see K. Mislow, THIS JOURNAL, **74**, 5156 (1952).

(13) H. Meerwein, E. Buchner and K. van Emster, *J. prakt. Chem.*, **152**, 237 (1939).

(14) M. Bakunin and D. Peccerillo, ref. 5; R. Pschorr, *Ber.*, **29**, 497 (1896); P. Pfeiffer, *Ann.*, **465**, 29 (1928). D. H. Hey and J. M. Osbond, *J. Chem. Soc.*, 3172 (1949), report that over 120 Pschorr cyclizations have been carried out with derivatives of *o*-amino-α-phenylcinnamic acids, which means that all these compounds, usually prepared by Perkin reactions, had the *cis* (aryl to aryl) configuration. The steric requirement of the *cis* configuration for the Pschorr cyclization, which is obvious, has been demonstrated experimentally by P. Ruggli and A. Straub, *Helv. Chim. Acta*, **19**, 1288 (1936); **20**, 37 (1937).

(15) E. D. Amstutz and E. R. Spitzmiller, THIS JOURNAL, **65**, 367 (1943), and H. Richtzenhain and B. Alfredson, *Acta Chem. Scand.*, **7**, 1173 (1953).

(16) R. Pschorr, *Ber.*, **39**, 3115 (1906). The mechanism of the condensation between benzaldehyde and phenylacetic acid is discussed by R. E. Buckles and K. G. Bremer, THIS JOURNAL, **75**, 1487 (1953).

The acid VIa was converted in low yield by diazomethane to the methyl ester VIc and, because of their relationship to colchicine, these three compounds have been submitted to the Sloan–Kettering Institute for screening for tumor-inhibiting properties.

Tropolones show a strong band near 1620 cm.$^{-1}$ in the infrared[17] which is believed to be the carbonyl stretching frequency, lowered below its normal value by conjugation and hydrogen bonding. The styryltropolones prepared in the present work all showed a shift of this band to 1570–1580 cm.$^{-1}$; this is probably due to increased hydrogen bonding of the tropolone carbonyl group by the *o*-carboxyl group, which is additional evidence for assigning the carboxyl group in V and VI to the tropolone ring.[18] In α-carboxy-β-carboxymethyltropolone itself (IV), the carbonyl absorption is shifted to 1587 cm.$^{-1}$.

Experiments on the reduction or isomerization of the double bond in the styryltropolones were unpromising, and it appears that other methods of synthesis will be required to prepare suitable intermediates for the Pschorr cyclization.

Experimental[19]

α-Carboxy-β-carboxymethyltropolone was prepared from purpurogallin by essentially Haworth's method[3] in 34–39% yield.

α-Carboxy-β-(*o*-nitrostyryl)-tropolone (Va) and the Acetate Vb.—The acid IV (7.0 g., 0.031 mole) was suspended in 40 cc. of reagent acetic anhydride, containing 4.3 cc. (0.031 mole) of triethylamine; addition of 4.75 g. (0.031 mole) of *o*-nitrobenzaldehyde resulted in vigorous bubbling with the formation of a deep red homogeneous solution. After standing 1 hr. at room temperature, the reaction mixture was poured into 100 cc. of 10% hydrochloric acid containing crushed ice. The mixture was stirred, and the addition of an equal volume of water precipitated a brown taffy-like mass. This was separated, and extracted with 400 cc. of boiling ethanol. This treatment left 1.6 g. of an almost white solid undissolved, which was the crude acetate Vb, m.p. 173–178° dec.; an additional 750 mg. of this compound (making the total yield 24%) was obtained by diluting the aqueous solution with a large volume of water. The acetate gave a deep green ferric chloride test, and formed an orange salt with sodium carbonate.

In other runs, the acetate was separated from the free tropolone by dissolving the crude product in methanol and seeding with the pure acetate. The ratio of acetate to free tropolone varied considerably in different runs. The analytical sample of the acetate was prepared by several recrystallizations from methanol, as pale greenish-yellow prisms, m.p. 185–186° dec. (cor.). The reported[6] m.p. is 196° dec.

Anal. Calcd. for $C_{18}H_{13}NO_7$: C, 60.85; H, 3.69; N, 3.94; neut. equiv., 355. Found: C, 60.92; H, 3.55; N, 4.25; neut. equiv., 340.

The ethanolic solution described above was concentrated to a small volume and decolorized with charcoal; cooling yielded 3.7 g. (44%) of the free tropolone Va, m.p. 188–192° dec. This compound gave a green ferric chloride test, and an orange insoluble salt with sodium carbonate; the analytical sample, after several crystallizations from aqueous ethanol, was obtained as greenish-yellow glistening plates, m.p. 198–199° dec. (cor.). The reported m.p. is 206° dec. The two breaks in the titration curve correspond to pK_a of 4.1 and 8.8.

Anal. Calcd. for $C_{16}H_{11}NO_6$: C, 61.34; H, 3.54; N, 4.47; neut. equiv., 157. Found: C, 61.59; H, 3.79; N, 4.46; neut. equiv., 155.

Because of the similarity in percentage composition of the tropolone Va and its acetate Vb, it was at first thought that they were *cis–trans* isomers. This was disproved by the absence of hydroxyl absorption in the infrared spectrum of the acetate, and by the hydrolysis of the acetate, by *refluxing* in equal volumes of acetic and 6 *N* hydrochloric acids, to the free tropolone Va. Identity of the sample of Va prepared by hydrolysis with the sample obtained from the condensation reaction was established by m.p. and by the fact that the two had identical infrared spectra.

α-Carbomethoxy-β-(*o*-nitrostyryl)-tropolone Methyl Ether (Vc).—Ethereal diazomethane prepared from 10 g. of nitrosomethylurea was added to a solution of the styryltropolone Va (2.0 g.) in 100 cc. of pure acetone. A vigorous evolution of gas was observed and the reaction was allowed to proceed at room temperature for 2 hr. (negative ferric chloride test). The solvents were evaporated, and the brown oil partially crystallized after a day; the crude dimethyl compound after several crystallizations from alcohol, formed yellow needles, m.p. 179–180° dec. (cor.).

Anal. Calcd. for $C_{18}H_{15}NO_6$: C, 63.34; H, 4.43. Found: C, 63.41; H, 4.56.

The reported[6] m.p. for this compound is 187–188°, but calculated and found analytical values reported[6] are in error. The yield of the dimethyl compound was only 40%, but no other isomeric compound could be isolated from the oily residue by crystallization or chromatography on Florisil.

α-Carboxy-β-(*o*-aminostyryl)-tropolone (Vd).—To 1 g. of the nitrostyryltropolone Va in 44 cc. of hot absolute ethanol was added 1.0 cc. of hydrazine hydrate (67%). Water was added to dissolve the orange hydrazine salt which precipitated at first. A small amount of Raney nickel[9] was added, and after an additional 1.0 cc. of hydrazine hydrate had been put in, a vigorous bubbling ensued. The reaction mixture was heated on the steam-bath for 1.5 hr., the catalyst was removed by filtration, and the resulting clear orange solution was acidified with acetic acid to yield 810 mg. of a bright orange powder. This material, presumably a polyamide, was insoluble in all common organic solvents, and did not melt but began to char and shrink above 200°. The compound turned brown on prolonged exposure to the air, and a satisfactory analysis could not be obtained.

The polyamide (50 mg.) was boiled for a few minutes with 20% hydrochloric acid, and the clear solution, on cooling in ice, deposited the hydrochloride of the amino acid (48 mg.) as reddish-brown rods, m.p. 183–185° dec. Dilution of an ethanolic solution of the hydrochloride with water liberated the amino acid quantitatively as a brown powder, m.p. 194–195° dec. The amino acid was insoluble in common organic solvents; both it and the hydrochloride gave a deep green ferric chloride test, the amino acid being tested in a methanol suspension.

The hydrochloride was recrystallized for analysis several times from water containing a few drops of hydrochloric acid, and was obtained as yellow needles, m.p. 184–185° dec. The analytical sample was dried *in vacuo* over phosphorus pentoxide; drying at higher temperatures and air exposure caused much darkening.

Anal. Calcd. for $C_{16}H_{14}ClNO_4$: C, 60.10; H, 4.41; N, 4.38. Found: C, 59.89; H, 4.59; N, 4.10.

The pure amino acid was obtained by adding water to a solution of the analytically pure hydrochloride in ethanol; it formed a brown powder, m.p. 194–195° dec.

Anal. Calcd. for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63. Found: C, 67.94; H, 4.88.

The reduction of α-carboxy-β-(*o*-nitrostyryl)-tropolone acetate (Vb) was carried out in a similar fashion, but methanol was used as a solvent to keep the hydrazine salt in solution. After filtration of the catalyst, evaporation of the methanol and treatment of the residue with boiling 20% hydrochloric acid, the monohydrated amino acid hydrochloride was obtained in 60% yield as red crystals, m.p. 175–178°. The analytical sample of this compound was

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[17] G. P. Scott and D. S. Tarbell, This Journal, **72**, 240 (1950); H. P. Koch, *J. Chem. Soc.*, 512 (1951).

[18] It is well known (*e.g.*, I. M. Hunsberger, This Journal, **72**, 5632 (1950)) that hydrogen bonding markedly decreases the carbonyl stretching frequency.

[19] Melting points are uncorrected unless otherwise stated; microanalyses are by Micro-Tech Laboratories, Miss Viola Williams and Miss Annette Smith. We are indebted to Mr. Carl Whiteman for the infrared spectra, which were determined in Nujol mulls with a Perkin–Elmer spectrometer, Model 12-A. Mrs. Cecile Friedman Rosenthal gave valuable assistance with the preparation of α-carboxy-β-carboxymethyltropolone.

also prepared by recrystallization from dilute hydrochloric acid; red crystals, m.p. 179–180° dec.

Anal. Calcd. for $C_{16}H_{14}NO_4Cl \cdot H_2O$: C, 56.89; H, 4.78; N, 4.15. Found: C, 56.85; H, 4.81; N, 3.85.

The infrared spectra of the monohydrated amino acid hydrochloride and the anhydrous salt obtained by the reduction of the free tropolone were identical. The amino acid obtained by treating an ethanolic solution of the hydrated salt with water melted at 190–191° dec. and the infrared spectrum of this compound was also identical with that of the amino acid liberated from the anhydrous salt.

α-Carboxy-β-(*o*-acetylaminostyryl)-tropolone (Ve).—This compound was obtained in 31% yield by condensation of IV and *o*-acetylaminobenzaldehyde[10] by essentially the same procedure described above for the nitro compound; none of the acetylated tropolone could be isolated. The product melted at 208–209° dec. in agreement with Nozoe's report.[7,20]

Hydrolysis of α-carboxy-β-(*o*-acetylaminostyryl)-tropolone (Ve) by refluxing with 20% hydrochloric acid yielded the hydrochloride of α-carboxy-β-(*o*-aminostyryl)-tropolone, which showed the same properties and gave no depression on mixed m.p. with the compound prepared by the reduction of the nitro compound above. The free amino acids from the two sources also showed identical properties.

Typical Attempted Pschorr Reaction.—α-Carboxy-β-(*o*-aminostyryl)-tropolone hydrochloride (817 mg.) was dissolved in 40 cc. of absolute ethanol and was saturated with anhydrous hydrogen chloride. The red solution was cooled to 0° and 1.2 cc. of isoamyl nitrite was added slowly from a pipet with stirring. The reaction was allowed to proceed at 0° for 15 min. and some precipitation of the diazonium salt was observed. The diazotized solution gave an immediate deep red precipitate with alkaline β-naphthol solution. The reaction mixture was then poured into 500 cc. of absolute ether to precipitate completely the diazonium salt. The salt was filtered (always wet), and washed with dry acetone, transferred with acetone into a beaker and covered with 100 cc. of dry acetone. Copper powder (1.0 g. freshly precipitated from copper sulfate with zinc dust) was added and a vigorous bubbling ensued. The reaction proceeded at room temperature for one hour and the solution turned black. The copper was filtered and the acetone evaporated to yield a black tar. On trituration with hexane, 110 mg. of undiazotized amino acid hydrochloride was obtained. The remainder of the material was intractable brittle tar. The amino acid was diazotized very slowly with nitrous acid in dilute hydrochloric acid and Pschorr reactions were similarly unsuccessful.

α-Carboxy-β-styryltropolone Vf and its Acetate Vg.—These compounds were obtained in 43% and 13% yield, respectively, from IV and benzaldehyde by essentially the procedure described above for the nitro compound. The acetate melted at 102–104° dec. (cor.) and had the proper carbon–hydrogen analysis; the reported[6] m.p. is 106° dec. Hydrolysis of the acetate in acetic acid–hydrochloric acid gave the free tropolone, as shown by identity of mixed m.p. and of infrared spectra.

The styryltropolone Vf was obtained after several recrystallizations from dilute acetic acid, as yellow needles, m.p. 170–172° dec. (cor.). Extensive purification did not raise the m.p., which is reported[6] as 182° dec. The compound was recovered unchanged after attempted cyclization with polyphosphoric acid and with anhydrous hydrogen fluoride.

Anal. Calcd. for $C_{16}H_{12}O_4$: C, 71.63; H, 4.51; neut. equiv., 134. Found: C, 71.68; H, 4.72; neut. equiv., 135.

Attempted Isomerization of Vf.—A solution of 500 mg. of the tropolone in 40 cc. of absolute ethanol was placed in a quartz flask and irradiated with a mercury arc lamp in the dark for 4 days. The solution was reduced to a small volume and water added to precipitate 450 mg. of the pure starting material. The melting point and the infrared spectrum of the irradiated material were identical with those of the tropolone obtained from the starting material.

α-Carboxy-β-(3,4,5-trimethoxystyryl)-tropolone (VIa) and the Corresponding Acetate VIb.—A mixture of 5.0 g. (0.022 mole) of the acid IV, 3.1 cc. (0.022 mole) of triethylamine and 4.4 g. (0.022 mole) of 3,4,5-trimethoxybenzaldehyde[21] was allowed to stand at room temperature for 2 hr.; the mixture was poured into 200 cc. of 10% hydrochloric acid containing crushed ice, and a dark green solid precipitated. This was recrystallized from methanol (with charcoal treatment) to yield 4.10 g. (46%) of the acetylated compound VIb, as orange needles, m.p. 170–171° dec. The product gave a green ferric chloride test, which developed slowly, and the analytical sample, prepared by three crystallizations from methanol, formed orange cotton-like needles, m.p. 175–176° dec. (cor.).

Anal. Calcd. for $C_{21}H_{20}O_8$: C, 62.99; H, 5.04; neut. equiv., 400. Found: C, 62.95; H, 5.28; neut. equiv., 396.

The methanolic filtrate from the isolation of the acetyl compound was concentrated to a very small volume and cooled in ice to precipitate 1.90 g. (24%) of the styryltropolone VIa as yellow crystals, m.p. 190–192° dec. The compound gave an immediate green ferric chloride test; the analytical sample, obtained as yellow plates by crystallization from a small volume of methanol, had m.p. 199–201° dec. (cor.).

Anal. Calcd. for $C_{19}H_{18}O_7$: C, 63.68; H, 5.06; neut. equiv., 179. Found: C, 63.61; H, 5.26; neut. equiv., 187.

The ratio of acetylated to non-acetylated material varied considerably in different runs. The relationship of the acetylated and non-acetylated products VIb and VIa was established by alkaline hydrolysis of the acetate to yield the unacetylated product, and acetylation of the latter with acetic anhydride–pyridine to yield the former. Identity of the samples obtained was shown in each case by mixed m.p. and identity of the infrared spectra.

Attempts to cyclize VIa with anhydrous hydrogen fluoride or polyphosphoric acid were unsuccessful.

α-Carbomethoxy-β-(3,4,5-trimethoxystyryl)-tropolone Methyl Ether (VIc).—Treatment of 2.0 g. of the styryltropolone VIa overnight with diazomethane in acetone gave a brown oil, which was chromatographed on Florisil and eluted with chloroform–ether (2:1) followed by chloroform. The residue from the chloroform–ether after removal of the solvent did not crystallize, and was taken up in benzene; this was seeded with some pure product which was obtained in a previous run in very poor yield by fractional crystallization of the crude product. Refrigeration of the benzene solution yielded 320 mg. of crude product, m.p. 88–95°. The benzene filtrate was combined with the residues of chloroform eluate from the column, and yielded, after seeding and cooling, an additional 120 mg. of crude product. An analytical sample prepared by crystallization from benzene gave high values for carbon and hydrogen, but a sample of m.p. 119–120° (cor.) obtained as yellow crystals from ethyl acetate–pentane, gave the following analysis.

Anal. Calcd. for $C_{21}H_{22}O_7$: C, 65.27; H, 5.74. Found: C, 65.00; H, 5.50.

ROCHESTER, N. Y.

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(20) Our sample gave the proper analysis for carbon, hydrogen and nitrogen.

(21) Prepared by Dr. Leo Zeftel (Ph.D. Thesis, University of Rochester, 1951) by the Rosenmund reduction of 3,4,5-trimethoxybenzoyl chloride (D. S. Tarbell, H. T. Huang and H. R. V. Arnstein, THIS JOURNAL, **70**, 4181 (1948)).