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The Preparation of Geometrical Isomers of β-Nitrostyrene and Their Addition Reactions with Ethanol

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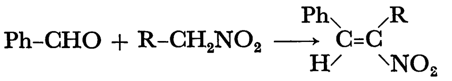
The preparation of the geometrical isomers of ethyl α-nitrocinnamate and α-nitrochalcone is described. Ethyl (*E*)-α-nitrocinnamate and (*Z*)-α-nitrochalcone were obtained by the thermal- or photoisomerization of the corresponding geometrical isomers, which were themselves produced predominantly through the Knoevenagel reaction. The facile addition of ethanol to the double bonds of β,β-dinitrostyrene, ethyl α-nitrocinnamates, and α-nitrochalcones without any catalyst at room temperature is also described.

The Knoevenagel condensation of benzaldehyde with primary nitroalkanes leads to the preferential formation of *trans*-β-nitrostyrenes, in which the nitro group and the phenyl group are on opposite sides of the carbon-carbon double bond.[1]



$$\text{Ph-CHO} + \text{R-CH}_2\text{NO}_2 \longrightarrow \begin{matrix} \text{Ph} & & \text{R} \\ & \text{C=C} & \\ \text{H} & & \text{NO}_2 \end{matrix}$$

$R = \text{-H}, \text{-CH}_3, \text{-C}_6\text{H}_5$

On the other hand, it is known that the base-catalyzed condensation reactions of benzaldehyde with ethyl phenylacetate and with desoxybenzoin afford predominantly ethyl (*E*)-α-phenylcinnamate with a *trans*-cinnamic ester moiety and (*E*)-α-phenylchalcone with a *trans*-chalcone moiety respectively.[2,3] Therefore, it seems to be worthwhile to examine the configurations of ethyl α-nitrocinnamate (β-carbethoxy-β-nitrostyrene) (I) and α-nitrochalcone (β-benzoyl-β-nitrostyrene) (II), obtained by the condensation of

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[1] a) E. A. Braude, E. R. H. Jones, and G. G. Rose, *J. Chem. Soc.*, **1947**, 1104; b) J. P. Freeman and T. E. Stevens, *J. Org. Chem.*, **23**, 136 (1958); c) G. Drefahl and G. Heublein, *Chem. Ber.*, **93**, 497 (1960).

[2] I. Shahak, *J. Chem. Soc.*, **1961**, 3160.

[3] A. Dornow and F. Boberg, *Ann.*, **578**, 101 (1952).

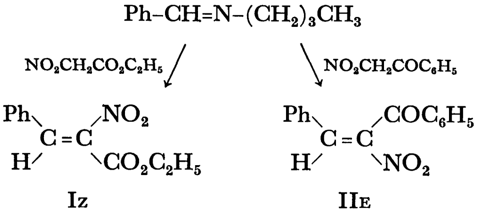
benzaldehyde with ethyl α-nitroacetate or ω-nitroacetophenone, since I and II can be regarded as β-nitrostyrene derivatives as well as α-nitrocinnamate and α-nitrochalcone respectively. The formation of a single geometrical isomer of I or II has been reported with no configurational assignment.[4]

The present paper will deal with the preparation of *cis*- and *trans*-isomers of I and II, and with the isomerization reaction of these compounds. The nucleophilic addition of ethanol to the carbon-carbon double bonds of these compounds under very mild conditions is also described.

The nitro valence vibrations and the ultraviolet spectra of these β-nitrostyrenes in correlation with their stereochemical configurations have been reported in a previous paper.[5]

Results and Discussion

Preparation. The condensations of *N*-benzal-*n*-butylamine with ethyl α-nitroacetate and with ω-nitroacetophenone according to the method reported by Dornow *et al.*[4] afforded ethyl α-nitrocinnamate (I) and α-nitrochalcone (II) in 88 and 82% yields respectively. The stereochemical configurations of the compounds were identified as ethyl (*Z*)-α-nitrocinnamate (Iz) with a *cis*-β-nitrostyrene moiety and (*E*)-α-nitrochalcone (IIE) with a *trans*-β-nitrostyrene moiety respectively, on the basis of their IR and UV spectroscopic behavior.[5] The formation of Iz is noteworthy, because the formation of the *cis*-β-nitrostyrene derivative as a main product of the condensation of benzaldehyde with an aliphatic nitro compounds has never been reported in the literature. The only compounds having a well-established *cis*-β-nitrostyrene configuration are α-nitrostilbene[6] and its derivatives.[7]



The geometrical isomers of Iz and IIE were obtained by the thermal isomerization and/or by the photoisomerization of each compound. Ethyl (*Z*)-α-nitrocinnamate (Iz), on heating at 175°C for 8 hr, gave a mixture from which an oily yellow material has been isolated. The structure of the oily material was identified as ethyl (*E*)-α-nitrocinnamate (IE). Both isomers, IE and Iz, gave the same equilibrium mixture when treated for 8 hr at this temperature, and the ratio of IE/Iz was found to be *ca.* 1:1. This ratio seemed inconsistent with the finding that IE was not formed in the Knoevenagel reaction. Since, however, the gradual conversion of IE into Iz was observed at room temperature in the dark, Iz appears to be thermodynamically the more stable isomer.

(*E*)-α-Nitrochalcone (IIE) was recovered unchanged when subjected to the same thermal treatment, while under much more drastic conditions it gave tarry substances, along with a trace of benzoic acid. On the other hand, the (*Z*)-α-nitrochalcone (IIz) obtained by the photoisomerization of IIE could isomerize very readily to give IIE in a 90% yield when treated for 3 hr at 170°C, thus indicating the greater stability of IIe.

All the geometrical isomers of I and II easily isomerized to their counterparts when the benzene solution was irradiated with a high-pressure mercury lamp. Starting from both isomers of I, photoequilibrium was established for 8 hr, the ratio IE/Iz was found to be *ca.* 1:1. In the case of II, photoequilibrium was established more rapidly under the same conditions, and the ratio IIe/IIz at equilibrium was found to be 2:3 (as is shown in Fig. 1).

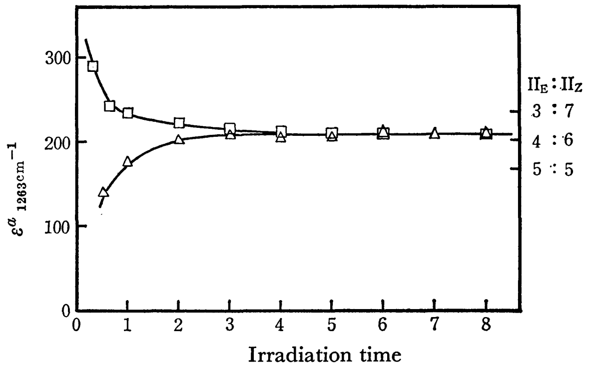


Fig. 1. Plots of the apparent molar absorbance of characteristic band of IIz(1263 cm^{-1}) *vs.* irradiation time in the photoisomerization of IIE and IIz.

-□—□- IIz → IIE

-△—△- IIE → IIz

The Addition of Ethanol. It was observed that the intensity at the absorption maxima in the region of $\pi \rightarrow \pi^*$ of ethyl α-nitrocinnamates, IE and Iz, and α-nitrochalcones, IIE and IIz, decreased considerably

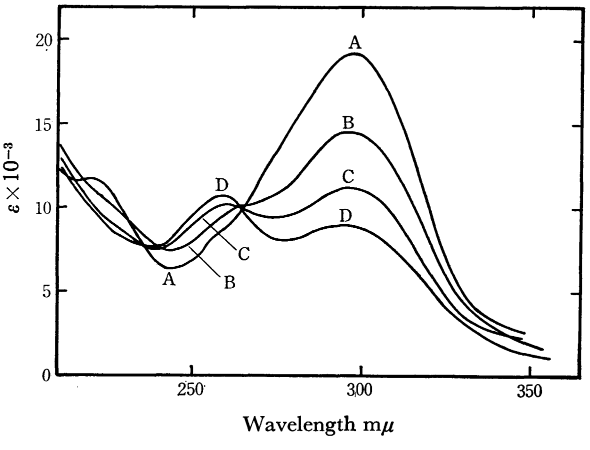


Fig. 2. Variations of UV spectra of (*Z*)-α-nitrochalcone (IIz) in ethanol at 20°C.

A: 0 hr, B: 1 hr, C: 2 hr, D: 3 hr

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[4] a) A. Dornow and H. Menzel, *Ann.*, **588**, 40 (1954); b) A. Dornow, A. Müller, and S. Lupfer, *ibid.*, **594**, 191 (1955).

[5] S. Watarai, K. Yamamura, and T. Kinugasa, This Bulletin, **40**, 1448 (1967).

[6] a) F. Heim, *Ber.*, **44**, 2013 (1911); b) B. Flurscheim and E. L. Holmes, *J. Chem. Soc.*, **1932**, 1463.

[7] a) R. Reichert and W. Kuhn, *Ber.*, **74B**, 328 (1941); b) T. E. Stevens and W. D. Emmons, *J. Amer. Chem. Soc.*, **80**, 338 (1958).

with the time when the ethanolic solutions were left standing at room temperature, even in the dark (Fig. 2). Also, β-bromo-β-nitrostyrene (III) showed a slight but evident decrease in the intensity at the absorption maximum under the present conditions. These results can be explained by assuming the addition of ethanol to the carbon-carbon double bonds of these compounds.

Actually, colorless needles were isolated from the ethanolic solutions of each geometrical isomer of II after keeping the solutions in the dark at room temperature for 24 hr, they were found to be identical with authentic 1-ethoxy-1-phenyl-2-nitro-2-benzoylethane (IV).[8] When the ethanolic solution of IIE or IIz was refluxed, ω-nitroacetophenone was produced together with IV. It might be thought that ω-nitroacetophenone was formed *via* IV, because ω-nitroacetophenone was also obtained by refluxing the ethanolic solution of IV. Similarly, 1-ethoxy-1-phenyl-2-nitro-2-carbethoxyethane (V), an ethanol adduct of I, was obtained from either of the geometrical isomers. β-Bromo-β-nitrostyrene (III) was less reactive toward ethanol than was either I or II, and its ethanol adduct, 1-ethoxy-1-phenyl-2-nitro-2-bromoethane (VI), could be obtained by refluxing the ethanolic solution of III for 120 hr or by treating III with equimolar sodium ethoxide in THF. Upon the treatment of VI with sodium ethoxide, ω-nitroacetophenone was formed. Recently, Hata *et al.* reported that ω-nitroacetophenone and its diethyl acetal were obtained from III upon treatment with excess sodium ethoxide.[9]

On the other hand, in the cases of (*E*)- and (*Z*)-α-nitrostilbenes (VIIE and VIIz), β-methyl-β-nitrostyrene and β-nitrostyrene, the addition of ethanol did not occure when their ethanolic solutions were allowed to reflux for an extended period. Additionally, α-benzoylchalcone, ethyl α-benzoylcinnamate, and diethyl benzalmalonate were recovered unchanged from their ethanolic solutions.

Although the reaction of nucleophilic reagents at the carbon-carbon double bond conjugated with the electron-withdrawing groups is well known,[10] it is noteworthy that the β-nitrostyrenes, which hold the nitro group and other strong electron-withdrawing groups at the same carbon atom, readily undergo the addition of ethanol without any catalyst at room temperature. In particular, β,β-dinitrostyrene (VIII) is very reactive to ethanol. The addition of ethanol seemed to come to completion instantaneously when VIII was dissolved in ethanol, since the solution had no maximum in the π→π* region, but showed a lower intensity absorption near 370 *m*μ. Its UV spectrum was identical with that of 1-ethoxy-1-phenyl-2,2-dinitroethane (IX), which was otherwise obtained from the ethanolic solution of VIII after it had stood at room temperature. The UV spectrum of VIII in *n*-hexane did not vary even when the mixture stood for a long time, but in the *n*-hexane-ethanol mixture (97: 3) the absorption intensity at the maximum in the π→π* region decreased very rapidly, as was expected (Fig. 3).

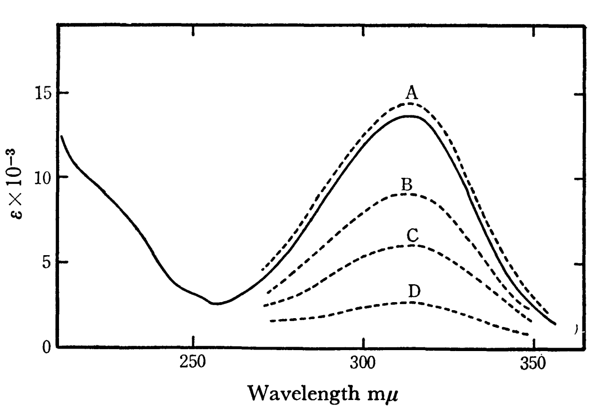
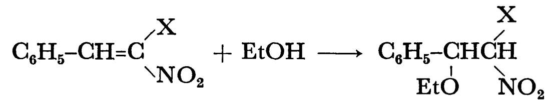


Fig. 3. UV spectra of β,β-dinitrostyrene (VIII).
—— in *n*-hexane
------ variations of UV spectra in ethanol-*n*-hexane (3:97) at 20°C; A: 0 hr, B: 0.5 hr, C: 1 hr, D: 2 hr

Thus, very significant differences in reactivities toward nucleophilic reagents, such as alcohol, were observed among various β-nitrostyrene derivatives, some rate coefficients (*k*), summarized in Table 1, for these ethanol-addition reactions were also measured.

TABLE 1. FIRST-ORDER RATE COEFFICIENTS AND ETHANOL ADDUCTS



$$C_6H_5\text{–}CH{=}C(X)(NO_2) + EtOH \longrightarrow C_6H_5\text{–}CH(OEt)CH(X)(NO_2)$$

Substituent X	β-Nitro-styrenes	*k* *k*×10/hr (at 25°C)	Ethanol adducts Compds. No.	Mp (bp)°C
$CO\cdot OC_2H_5$	IE	1.05	V	39 — 40
	Iz	0.587		
$CO\cdot C_6H_5$	IIE	0.965	IV	118 —121
	IIz	3.41		
Br	III	0.07[a)]	VI	(143/9 mmHg)
NO_2	VIII	very fast	IX	29 — 30
C_6H_5	VIIE & VIIz	—	b)	93.5— 94.0

a) Value at 30°C.
b) This compound was obtained by treating VIIE or VIIz with sodium ethoxide in the ethanolic solution.

Of the three pairs of *cis-trans* isomers of β-nitrostyrenes investigated, I, II, and VII, (*Z*)-α-nitrochalcone (IIz) gave the largest *k* value, six times the value of ethyl (*Z*)-α-nitrocinnamate (Iz). On the other hand, IIE, with a *cis*-chalcone moiety, showed almost the same degree of value as IE, with a *cis*-cinnamic ester moiety. These data indicate that the *trans*-chalcone conjugation, which is sterically little affected in IIz, contributes effectively to this addition reaction, although the extent of its contribution is far less than that of the *trans*-β-nitrostyrene conjugation in the case of VIII.

The *k* values of Iz and IIE, which were the major products of the Knoevenagel reaction, were evidently smaller than those of their counterparts, IE and IIz respectively.

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[8] H. Wieland, *Liebig's Ann. Chem.*, **328**, 154 (1903).

[9] M. Shiga, M. Tsunashima, H. Kono, I. Motoyama, and K. Hata, This Bulletin, **43**, 841 (1970).

[10] For a review, see S. Patai and Z. Rappoport, in S. Patai, "The Chemistry of Alkenes," Interscience Publishers, Inc., New York, N. Y. (1964), p. 469.

Further studies of the difference in the *cis*- and *trans*-compounds of this series are in progress.

Experimental

All the melting points and boiling points are uncorrected. The UV spectra were obtained with a Hitachi model EPS-3 spectrophotometer; the data of some β-nitrostyrenes in *n*-hexane are presented in Table 2. The measurements of the IR spectra were made in chloroform on a Nihon-Bunko model DS-402G grating infrared spectrophotometer.

TEBLE 2. UV SPECTRA OF *cis*- AND *trans*-β-NITROSTYRENES IN *n*-HEXANE[a)] (C_6H_5–CH=C(X)–NO_2)

Substituent	Compds. No.	λ_{max}	
		mμ	ε
$CO\cdot OC_2H_5$	IE	285	14200
	Iz	282	17200
$CO\cdot C_6H_5$	IIE	301	16300
	IIz	298	17100
C_6H_5	VIIE	307	13300
	VIIz	282	21500
NO_2	VIII	313	13500

a) Data in the ethanolic solutions were presented in the previous paper.[5)]

Materials. β-Nitrostyrene,[11)] β-methyl-β-nitrostyrene,[12)] β-bromo-β-nitrostyrene (III),[13)] (*E*)- and (*Z*)-α-nitrostilbenes (VIIE and VIIz),[6a)] β,β-dinitrostyrene (VIII),[14)] α-benzoylchalcone,[15)] ethyl α-benzoylcinnamate,[16)] and diethyl benzalmalonate[17)] were prepared as has been described in the literature. Ethyl (*Z*)-α-nitrocinnamate (Iz, mp 72.5—73.5°C, yield 88%) and (*E*)-α-nitrochalcone (IIE, 91.5—92.5°C, yield 82%) were prepared essentialy according to the procedures reported by Dornow *et al.*,[4)] but each compound was obtained in a far better yield than that described in the literature (lit,[4)] yield: Iz, 45%; IIE, 48%).

Thermal Isomerizations of IE and Iz. Iz (30 g) was heated at 175°C for 8 hr under reduced pressure (3 mmHg). Cooling for 24 hr below −10°C, followed by filtration, gave the recovery of Iz (15 g). The filtrate was chromatographed over Wako-gel Q-22 using a mixture of benzene-petroleum ether(1:2.5) as an eluent. The first fraction contained Iz, while the subsequent fractions gave a yellow oil, which, when purified by chromatography until the refractive index indicated a constant value, gave 15.0 g of ethyl (*E*)-α-nitrocinnamate (IE); n_D^{20} 1.5780; yield 50%.

Found: C, 59.88; H, 5.28; N, 6.24%. Calcd for $C_{11}H_{11}$-O_4N: C, 59.72; H, 5.01; N, 6.33%.

Starting from IE, Iz was obtained in about a 50% yield under similar conditions.

Thermal Isomerization of IIz. IIz, obtained by the photoisomerization of IIE, was isomerized in a manner similar to that described above to give (*E*)-α-nitrochalcone (IIE) in a 90% yield.

Photoisomerizations of α-Nitrochalcones (IIE and IIz). A solution of IIE (20 g) in 1650 m*l* of benzene was irradiated for 3 hr, and then the solvent was evaporated *in vacuo*. Fractional crystallization from benzene-petroleum ether gave colorless flakes of IIz; mp 103—104°C.

Found: C, 71.04; H, 4.77; N, 5.35%. Calcd for $C_{15}H_{11}$-O_3N: C, 70.88; H, 4.79; N, 5.68%.

In a similar manner, IIE was obtained from IIz.

Photoisomerization of IE and Iz. Under conditions similar to those described above, *cis*- and *trans*-isomers of ethyl α-nitrocinnamate isomerized each other without any difficulty.

Preparation of IV. IIE (1 g) was dissolved in 60 m*l* of ethanol, and this solution was kept in the dark for 24 hr. The solvent was then evaporated *in vacuo*. Fractional crystallization from benzene gave 0.3 g of an ethanol adduct, IV, as colorless needles; mp 118—121°C.

Found: C, 68.16; H, 5.97; N, 4.72%. Calcd for $C_{17}H_{17}$-O_4N: C, 68.21; H, 5.73; N, 4.68%.

Preparation of V. In a manner similar to that described above, Iz gave the ethanol adduct (V) as colorless plates; mp 39—40°C.

Found: C, 58.20; H, 6.48; N, 5.23%. Calcd for $C_{13}H_{17}$-O_5N: C, 58.42; H, 6.41; N, 5.24%.

Preparation of VI. III (1 g) was dissolved in 80 m*l* of ethanol and was heated under reflux for 72 hr, and then the solvent was evaporated *in vacuo*. The ethanol adduct, VI, was thus obtained almost quantitatively. Yellow oil; bp 143°C/9 mmHg.

Found: C, 43.75; H, 4.64; N, 5.07%. Calcd for $C_{10}H_{12}$-NO_3Br: C, 43.78; H, 4.36; N, 5.11%.

This compound was also prepared as follows. To a solution of III (2.3 g, 0.01 mol) in THF (60 m*l*), sodium ethoxide (0.7 g, 0.01 mol) was added at room temperature. The mixture was stirred for 1 hr and then poured into 200 m*l* of ice water. Then, CO_2 gas was bubbled through the mixture for 1 hr. The aqueous mixture was extracted with three 300 m*l*-portions of benzene. After the removal of the benzene, the ethanol adduct, VI, was obtained by distillation under reduced pressure.

Preparation of IX. VIII (1 g) was dissolved in 50 m*l* of ethanol, and the mixture was kept at 30°C for 24 hr. After the ethanol had then been evaporated *in vacuo*, the residual pale yellow liquid was chromatographed on Wako-gel Q-22, using *n*-hexane as the eluent. The first fraction gave 0.9 g of pale yellow crystals of IX; mp 29—30°C; yield, 72.8% (lit,[14)] 29—31°C).

Equilibrium Ratios in the Isomerizations. The equilibrium ratios in the thermal- and photoisomerizations were determined by comparison with the known ratio of isomers and the characteristic absorption bands of the isomerization mixtures, at appropriate time intervals, as is shown in Fig. 1.

Kinetic Measurements. The ethanolic solutions of the β-nitrostyrenes (about 10^{-5}M concentrations) were thermostated, and the UV spectra, at appropriate time intervals, were measured. The logarithm of molar absorbance at the wavelength in the $\pi\rightarrow\pi^*$ region against the time was linear. The first-order rate coefficients (k) were calculated by the usual method.

The authors are indebted to Miss Masuko Nishinaka for her IR measurements and elemental analyses.

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