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The Isomerization of Some *cis*-Cinnamic Esters under the Influence of Iodine Atoms[*]

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The *cis–trans* isomerization of a number of *cis*-cinnamic esters under the influence of thermally generated iodine atoms was studied at 100° and 120°C, using carbon tetrachloride as the solvent. Most of the esters could be made by direct esterification of pure *cis*-cinnamic acid; the *t*-butyl ester was obtained as a mixture of *cis*- and *trans*-cinnamate by UV irradiation of the *trans* ester. Isomerization rates were measured by following the increase in the extinction at 272 mμ. The methyl, ethyl, *n*-propyl, isopropyl, and cyclopentyl ester reacted 2 to 2 1/2 times more readily than *cis*-cinnamic acid; the *t*-butyl ester was more than three times as reactive as the free acid.

These results are interpreted in terms of a rapidly reversible addition of atomic iodine at the β carbon atom, followed by a rotation about the C_α—C_β bond through opposition of the phenyl group and the iodine atom. Rate differences are believed to be mainly due to differences in the release of strain upon formation of the primary adduct-radical.

INTRODUCTION

Cis–trans isomerization of unsaturated compounds in the absence of light may be effected in various ways. Two main categories may be distinguished. The first group proceeds through rotation about the central carbon–carbon bond, which has been "opened up" by the intermediate addition of a catalytic fragment. Uncatalyzed *cis–trans* isomerization, which generally involves much higher activation enthalpies, may proceed through a triplet state (*1*).

Noyes, Dickinson, and Schomaker (*2*) investigated the iodine-atom–catalyzed isomerization of *cis*-1,2-diiodoethene, using radioactive iodine; they found that iodine exchange is much faster than *cis–trans* isomerization, indicating that the primary step is rapidly reversible and that rotation about the C—C bond occurs relatively slowly (Fig. 1).

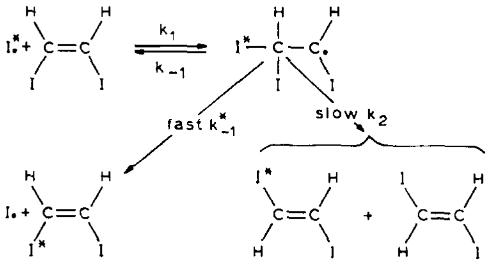

FIG. 1. Isomerization of *cis*-1,2-diiodoethene under the influence of radioactive iodine.

Dickinson and Lotzkar (*3*) studied the isomerization of *cis*-cinnamic acid in benzene solution under the influence of iodine atoms, generated both thermally and photochemically. Rates were followed by determining *cis*- and *trans*-cinnamic acid from the conductivities of the reaction products in water. The reactions were found to be first order with respect to *cis*-cinnamic acid and half-order relative to the iodine concentration. From their results they concluded that the isomerization under the influence of atomic iodine involved an Arrhenius activation energy of about 5 kcal.

We have investigated the *cis–trans* isomerization of a series of *cis*-cinnamic esters under the influence of iodine atoms in carbon tetrachloride solution in sealed ampoules at 100° and 120°C. Following Dickinson and Lotzkar we have assumed that the reactions

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[*] Cf. E. A. R. Visscher, Thesis, Leiden, June, 1963.

are first order with respect to ester and half order with respect to iodine concentration. As a consequence of nonplanarity of the conjugated system in the *cis* compounds, the equilibrium is far towards the *trans* side for the methyl cinnamates (*4*)†; *trans* → *cis* conversion was therefore neglected. Rates of isomerization were followed spectroscopically, taking advantage of the increasing extinction at 272 mμ accompanying the *cis–trans* conversion.

The pure methyl, ethyl, *n*-propyl, isopropyl, and cyclopentyl ester could be prepared through acid-catalyzed esterification of pure *cis*-cinnamic acid under mild conditions. The latter acid was synthesized starting from phenylpropiolic acid, the methyl ester of which was selectively hydrogenated by using a Lindlar-type catalyst; pure methyl *cis*-cinnamate was then hydrolyzed to yield *cis*-cinnamic acid. The *t*-butyl ester was obtained in the form of a 50/50 *cis–trans* mixture, prepared by UV irradiation of *trans*-*t*-butyl cinnamate.

In a series of exploratory experiments it was established that no *cis–trans* isomerization occurred under the influence of the stable diphenyl-picrylhydrazyl radical (10^{-2} *M* in pure methyl *cis*-cinnamate at 60°C) or of cyanoisopropyl radicals generated by thermal decomposition of azoisobutyronitrile at 80°C.

METHODS

Starting Materials

Methyl ester of phenylpropiolic acid. Pure phenylpropiolic acid (100 g) (*5*) (m.p. 137°C; halogen-free) was dissolved in 200 ml of methanol and refluxed in the presence of 10 ml of concentrated sulfuric acid for 10 hr. The mixture was diluted with an excess of water and extracted with benzene. The benzene layer was repeatedly extracted with an aqueous solution of sodium bicarbonate; it was then dried over anhydrous magnesium sulfate and fractionated. The ester boiled at 120°C at 0.01 mm Hg; m.p. 26°C [lit. 25–26°C (*6*)]. Yield about 100 g (nearly 95% of the theoretical). Gas-liquid chromatography analysis showed this product to be homogeneous.

Methyl ester of *cis*-cinnamic acid. Lindlar catalyst (20 g) (*7*) was shaken in a hydrogenation apparatus with 100 ml of purified petroleum ether (b.p. 60–80°C) until no further hydrogen consumption occurred. Then 25 ml of methylphenyl propiolate was added. Hydrogen was absorbed at a rate of about 1 liter/10 min. The process was continued until the theoretical amount of hydrogen had been absorbed. The catalyst was then filtered off and extracted with 50 ml of pure petroleum ether. Fractional distillation yielded the reduction product at 125–130°C at 0.01 mm Hg. It was then several times recrystallized from petroleum ether at −70°C. In this way a product was obtained which melted at −2°C; gas-liquid chromatography indicated this material to be quite pure.

***Cis*-cinnamic acid.** Methyl *cis*-cinnamate (25 g) was dissolved in aqueous ethanol containing 2 moles of sodium hydroxide per mole of the ester. The mixture was stirred at room temperature for 1 hr and then acidified by addition of 20% sulfuric acid with rapid stirring. The solution was seeded with a few crystals of pure *cis*-cinnamic acid. The free acid thus liberated was collected by filtration and melted at 68°C [lit. m.p. 68°C (*8*)].

Ethyl, *n*-propyl, isopropyl, and cyclopentyl *cis*-cinnamate. Pure *cis*-cinnamic acid (25 g) was dissolved in a 20-fold excess of the corresponding alcohol, 1 ml of concentrated sulfuric acid was added, and the mixture was refluxed for 10 hr. The esters obtained had boiling points between 120° and 150°C at 0.01 mm Hg. The yields were generally better than 75% of the theoretical. None of these compounds could be brought to crystallization. Gas-liquid chromatography indicated that each product consisted of a single compound, impurities occurring to an extent of less than 5%. All chromatograms were made at 184°C using asphalt bitumen as the stationary phase; hydrogen was used as the carrier gas. Elementary compositions and other properties of the products are given in Table 1.

***Cis*- and *trans*-*t*-butyl cinnamates.** *trans*-*t*-Butyl cinnamate (5 g) (9) was dissolved in

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† Williams (*4*) found a difference of 4 kcal in the heats of hydrogenation of these two isomers.

TABLE 1

ANALYTICAL DATA FOR THE COMPOUNDS Ph—CH=CH—COOR

R[a]	Elemental analysis (%)			n^{25}	d_4^{25}	MR_D (Lorenz-Lorentz)	Log Σ mol	
	Calc.	Found					*cis*	*trans*[b]
H	—	—		—	—	—	4.025	4.245
CH_3	C 74.04	C 74.1	74.2	1.5542	1.0776_5	48.22	3.969	4.268
	H 6.17	H 6.4	6.3					
C_2H_5	C 75.00	C 74.4	74.5	1.5422	1.0431	53.15	4.046	4.286
	H 6.81	H 6.8	6.9					
n-C_3H_7	C 75.78	C 75.6	75.7	1.5334	1.0189	57.84	4.031	4.279
	H 7.36	H 7.5	7.5					
i-C_3H_7	C 75.78	C 76.1	75.9	1.5290	1.0127	57.79	3.977	4.192
	H 7.36	H 7.6	7.4					
Cyclopentyl	C 77.77	C 77.6	77.7	1.5512	1.0653_5	64.76	4.040	4.292
	H 7.47	H 7.7	7.6					
t-C_4H_9	—	—		—	—	—	3.988	4.290

[a] The methyl, ethyl, and *n*-propyl ester have been mentioned in literature but were not adequately characterized (*11*). The fairly constant increments in the molar refractions suggest that our samples had a high degree of purity.

[b] Derived from the extinctions at the end of the reactions.

2 liters of ether and irradiated by means of 2 Biosol lamps (Philips) (250 watt) for 9 hr, using the apparatus described by Havinga and Bots (*10*). The filters employed were a nickel sulfate/cobalt sulfate solution of 1 cm thickness (transmission in the 2200–3500 Å region of 90%) and a cupric sulfate solution of 0.5 cm thickness (transmission less than 20% at 2800 Å). The cupric sulfate solution contained 16.2 g $CuSO_4 \cdot 5H_2O$ per liter of water; the other filter contained 220 g $NiSO_4 \cdot 7H_2O$ and 20 of $CoSO_4 \cdot 7H_2O$ per 100 g of water. The photoisomerization was followed by withdrawing samples by means of a syringe and determining the extinction at 272 mμ. The irradiation was terminated after no further decrease in the extinction was observed; this appeared to be the case after a decrease in extinction of about 30%. Gas chromatographic analysis as well as nuclear magnetic resonance indicated that about 50% of the *cis*-ester was formed. The coupling constants agreed with the values reported by Pople (*12*), viz., *J cis* = 13 *Hz*, *J trans* = 16.5 *Hz*.

Kinetic Methods

Two sets of standard solutions were made, viz. 1/5 and 1/50 *M* in pure carbon tetrachloride. One milliliter samples of these solutions were pipetted into a blackened 3 ml ampoule. One milliliter of a 1/50 *M* solution of pure iodine in carbon tetrachloride was added. The ampoules were sealed and then heated in a thermostated oil bath at 100°C or 120°C. Check experiments indicated that no reaction occurred other than during the heating process.

The contents of the ampoules were rinsed into blackened volumetric flasks of 50 ml contents by means of carbon tetrachloride. One milliliter of these diluted solutions was again diluted to 50 ml; optical densities of the final solutions were then determined at 272 mμ in quartz cuvettes (10 mm width), using a Cary-14 recording spectrophotometer. For each complete run 10–12 ampoules were used at different reaction times. From determinations of extinction coefficients of series of standard solutions it followed that Lambert-Beer's law applied. Rate constants were determined from the extinctions measured with the aid of the following equation (*13*):

$$\log (V_\infty - V_t) = \log (V_\infty - V_0) - kt \log \mathrm{e}$$

in which V_0, V_t, and V_∞ are the measured extinctions at times 0, t, and ∞. Straight lines were obtained when plotting $\log (V_\infty - V_t)$ against time. The slopes of these plots yield values for k^{10} log e. Values for V_0 were obtained from the extinction at zero time; the value of V_0 for the *t*-butyl ester was derived from the extinctions of the *trans* ester and that of the starting material in combination with the data on the material as obtained by irradiation (cf. p. 422). The iodine concentration used was so low that the extinction of the iodine at 272 mμ could be practically neglected in determining the extinctions.

RESULTS AND DISCUSSION

Rate Constants

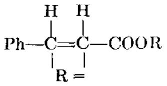
Four sets of kinetic runs were made, at 100° and 120°C and with initial concentrations of *cis* ester (C_0) of 0.01 and 0.1 *M*; the iodine concentration amounted to 0.01 *M* in all runs.

In each run, plots of log C_0/C_t versus time led to straight lines, which supports our assumption as regards the reactions being first order with respect to *cis* ester. Pseudo-first-order rate constants were computed from these plots in the usual fashion, using the method of least squares. They are presented in Table 2.

Attention is called to the fact that rate constants derived from the runs at the lower initial ester concentration were generally somewhat higher than those found at 0.1 *M*; this applies particularly to the runs with the ethyl and isopropyl esters. Duplicate runs with these esters led to the same result. In view of this uncertainty, the significance of our rate constants should be regarded as hardly more than semiquantitative; the same would apply to the Arrhenius activation energies. Probably, our findings can be best expressed by stating that the methyl, ethyl, propyl, isopropyl, and cyclopentyl esters are about 2–2.5 times more reactive than the free acid and that the *t*-butyl ester is slightly more reactive than the other esters. The Arrhenius activation energies are about 26 ± 4 kcal; the high value computed for the *t*-butyl ester (30.5 kcal) should be regarded as doubtful.

A possible explanation for the discrepancy between the runs at 0.1 and 0.01 *M* might consist in complex formation between I_2 and ester, which should lower the concentration of free iodine, particularly in the runs at high ester concentrations. No attempts were made to test this hypothesis, e.g. by varying the iodine concentration. Dickinson and Lotzkar (*3*) also reported lower rates for the runs at high concentrations.

TABLE 2
RATES OF ISOMERIZATION OF *cis*-CINNAMATES UNDER THE INFLUENCE OF THERMALLY GENERATED IODINE ATOMS

 $\mathrm{Ph{-}C(H){=}C(H){-}COOR}$, R =	Rate constants[a] (hr^{-1})				Relative rates[b]		Arrhenius activation energy[c] (kcal)
	100°C		120°C		100°C	120°C	
H	0.019_5	0.022	0.091	0.091	1	1	22 ± 1
CH_3	0.036	0.039	0.17	0.17	$1.9 \pm 0.0_5$	1.9	22 ± 1
C_2H_5	0.030	0.042	0.21	0.26	1.8 ± 0.3	2.6 ± 0.3	28 ± 5
	0.030	0.043					
n-C_3H_7	0.032	0.035	0.22	0.24	1.6 ± 0.1	2.5 ± 0.1	28 ± 3
i-C_3H_7	0.038	0.054	0.24	0.19	2.3 ± 0.3	2.4 ± 0.2	23 ± 5
	0.042	0.054					
Cyclopentyl	0.034	0.041	0.21	0.22	1.8 ± 0.1	$2.4 \pm 0.0_5$	26 ± 1
t-C_4H_9		0.062	0.43	0.57	3.0	5.5 ± 0.9	30.5 ± 2

[a] Pseudo-first-order rate constants from the linear plot of ln (C_0/C_t) versus time. Initial concentrations of esters (C_0) 0.1 *M* first (column) and 0.01 *M* (second column); iodine concentrations 0.01 *M* in carbon tetrachloride.

[b] Rates relative to those for the free acid (R=H), using the mean value from rate constants found at the two concentrations; limits apply to deviations from the averaged values.

[c] From the averaged rate constants by means of the Arrhenius equation; limits are relating to the deviations between the rate constants at the two concentrations.

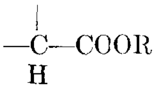
Assuming—with Dickinson and Lotzkar (*3*)—that the temperature coefficient for the iodine concentration equals one-half the dissociation energy of the iodine molecule (38/2 = 19 kcal), this leaves for the Arrhenius activation energy of the iodine-atom–catalyzed *cis–trans* isomerization of our esters a value of $26 \pm 4 - 19 = 7 \pm 4$ kcal. Assuming that the rates are obeying the expression: rate = k_b (*cis* ester) $\times (I_2)^{1/2}$ the "true" over-all rate constants can be computed by dividing the pseudo-first-order constants by the square root of the iodine concentration $[(0.01)^{1/2} = 0.1]$. For *cis*-cinnamic acid, this leads to the rate constants 0.20_5 at 100°C and 0.91 at 120°C, expressed as $\text{moles}^{-1/2} \times \text{liters}^{-1/2} \times \text{hr}^{-1}$. Dickinson and Lotzkar found 0.15 at 99.4°C and 1.01 at 122.5°C for the reaction in benzene; the Arrhenius activation energy reported by Dickinson and Lotzkar amounted to 24 kcal as compared with our value of 22.

Mechanisms

The above trends observed in the structural effects on rates of *cis–trans* isomerization, homogeneously catalyzed by iodine atoms, are at first sight perhaps somewhat surprising. Thus, rate differences are relatively small whereas the *t*-butyl ester is the *most* reactive of the series. The latter result should not have been anticipated if the approach of the catalytic iodine atom to the double bond were to be rate determining. Thus, according to the Newman Rule of Six (*14*), the approach of the catalytic species should be subject to increasing steric shielding as the number of atoms in the 6-position with respect to the carbon atom attacked increases. Moreover, one should expect a steep decrease in reactivity somewhere in the series propyl, isopropyl, *t*-butyl, just as is found in the acid-catalyzed esterification of fatty acids. Whereas, in these reactions, the effect may be enhanced as a result of hindrance to solvation of the intermediate (i.e., the protonated acid molecule), one should still expect some indication for shielding in our catalytic process if the primary interaction were rate-determining.

It seems plausible, therefore, to interpret the present results in terms of a rapidly reversible addition of an iodine atom, followed by a relatively slow rotation about the C_α—C_β bond of the radical formed. Such an interpretation is analogous to that proposed by Noyes and his co-workers (*1*) for the reaction between radioactive iodine and *cis*-1,2-diiodoethene (cf. Fig. 1).

It will be assumed that iodine atom addition occurs at the end of the "styrene-type" double bond because of the greater stability of a benzyl radical as compared to a



$$-\overset{|}{\underset{H}{C}}-COOR$$

radical (*15*). Bond strength data (*16*) then suggest that the primary step is only weakly exothermic. Thus, the C—I bond strength in isopropyl iodide amounts to 42 kcal, which is about equivalent to the loss of a double bond (41 kcal). The resonance energy of the benzyl-type radical formed (20 kcal?) will not be much greater than the coupling energy due to mesomeric interaction between a phenyl group, the double bond, and the ester group, which is lost in the process; this may be estimated to be 10–15 kcal. On these grounds, the addition of an iodine atom is probably less than 10 kcal exothermic, e.g. of the order of 5 kcal. The energy diagram of the various processes involved may be therefore about as shown in Fig. 2. This diagram illustrates our above semiquantitative assumptions as well as a few others to be discussed further on.

According to this scheme rates may be expressed as

$$(k_1/k_{-1}) \times k_2 \times (I\,\cdot)(cis\ \text{ester})$$

in which k_1 and k_{-1} apply to the reversible addition of $I\cdot$ to *cis* ester and k_2 to the rotation step. Rotation about the central carbon–carbon bond in the adduct radical might occur either through opposition of a phenyl group and an iodine atom or through opposition of phenyl and ester grouping. However, because of the greater steric requirements of an ester group as compared to the iodine atom the former process would seem to be the more plausible (cf. Fig. 3). Thus, the free energy difference between cyclohexanes containing an axial and an equatorial COOR

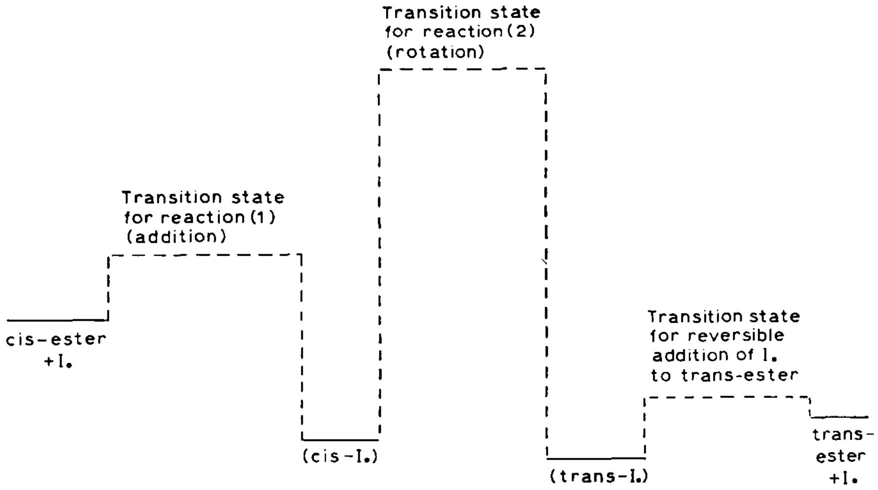


FIG. 2. Energy diagram for *cis–trans* isomerization through reversible addition (1) followed by rotation (2).

group is about 1.1 kcal. For axial and equatorial iodine the difference amounts to 0.4 kcal (*17*).

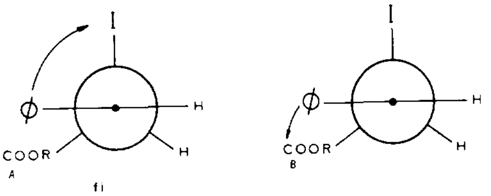


FIG. 3. (a) Rotation about central C—C bond in *cis*–I· through opposition of phenyl group and I atom. (b) Rotation about central C—C bond in *cis*–I· through opposition of phenyl group and COOR group.

From this point of view, differences in rates of isomerization should be mainly due to differences in the equilibrium constant k_1/k_{-1} rather than to differences in k_2, the second step being more or less *independent of the nature of R* (cf. Fig. 3); the barrier height for this rotation step should be of the order of 10 kcal.

Shielding effects on step (1) should then be completely compensated by similar effects on step (−1); since both addition and its reversal are going through the same transition state the equilibrium position remains unaffected by strain in the transition state. It seems plausible, however, to assume that *cis* isomers will be more highly strained as the size of R increases. Formation of the *cis*-I radical involves a lengthening of the C_α—C_β bond, and, accordingly, an appreciable release of strain in the radical with respect to the ester (cf. Figs. 3 and 4). *This release of strain will therefore probably favor the equilibrium position derived from the more highly strained esters.* These assumptions have already been incorporated in Fig. 2 since the levels of *cis*-I · and *trans*-I · are drawn fairly close together (little strain in both the adduct radicals) and since the heat effect in the addition of I · to *cis* ester is greater than for the addition to the *trans* ester.

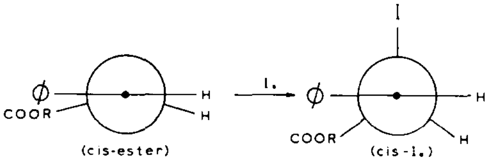


FIG. 4. Illustrating relief of strain in the addition of I· to *cis* ester.

The assumption that rotation about the central C—C bond proceeds according to path shown in Fig. 3a rather than by the path in Fig. 3b may at least partly explain why neither the diphenyl picrylhydrazyl radical—used in a very high concentration as compared with that of the iodine atoms—nor the cyanoisopropyl radicals are effective as a catalytic species. If an adduct with such a very bulky fragment were formed, rotation should have to take place through opposition of phenyl and COOR, which involves more strain than opposition of phenyl and I ·; it also seems possible, however, that a covalent adduct cannot be formed anyway, because of the extreme weakness of the new bond. According to the above scheme the most effective catalytic species should be small in size and form a weak—but not too weak—bond with the ester.

In any case, the failure of the above stable and bulky radicals to effect isomerization indicates that the mere presence of a paramagnetic species is an insufficient requirement for isomerization.

Admittedly, the present results do not provide a clue as to whether a *classical covalent intermediate* (*cis*-I ·) is actually formed. The available data suggest, however, that the present isomerizations will proceed through a species permitting rotation about the central carbon–carbon bond, which is "opened up" by the iodine atom in a reversible process. Formation of a covalent intermediate would then seem to be the most simple assumption, a possible alternative being, for example, an ion pair ($cis^{+}I^{-}$).

Since the Arrhenius parameters computed from our rate data are of insufficient accuracy, no conclusions can be drawn as regards the effects of "strain" on activation enthalpies or entropies.

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