Study of the Radical Mechanism of Iodine-Catalyzed Isomerization of Conjugated Diene Systems

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The iodine-catalyzed *Z/E*-isomerization of internal conjugated dienes in the dark, to form a thermodynamic equilibrium mixture, was found to be a radical process with an activation energy of 12.4±1.2 kcal/mol. The effects of antioxidants on the reaction, both in the dark and in sunlight, were studied. In both processes the radical isomerization was slowed down, probably through radical scavenging.

In the light iodine serves as a catalyst in *Z/E*- isomerization of double bonds (1). In conjugated diene systems this process is very effective in obtaining the (*E,E*)-isomer as the predominant one in the thermodynamic equilibrium (1,2). The light facilitates the reaction, and two mechanisms have been suggested, depending on the wavelength of the applied light (3):

UV region, shorter wavelength:

$$\text{(Z)-olefin} + I_2 \rightleftharpoons [(Z)I_2] \overset{hv}{\rightleftharpoons} [(Z)I_2]^*$$

$$(Z)\text{-olefin} + [(Z)I_2]^* \rightleftharpoons 2\cdot(Z)I$$

$$\cdot(Z) \rightleftharpoons \cdot(E)I \rightarrow (E)\text{-olefin} + I\cdot$$

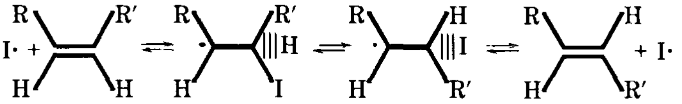
Visible region, longer wavelength:

$$I_2 \overset{hv}{\rightleftharpoons} 2I\cdot$$

$$(Z)\text{-olefin} + I\cdot \rightleftharpoons \cdot(Z)I$$

$$\cdot(Z)I \rightleftharpoons \cdot(E)I \longrightarrow (E)\text{-olefin} + I\cdot$$

It has been suggested that the isomerization process itself involves rotation around the σ-bond, after reaction of I· with the π-bond (4):



According to this mechanism the rate-determining step is either the formation of the carbon radical or the rotation around the σ-carbon-carbon bond. It has been shown (4) that in the gas phase the addition reaction of I atoms is rate controlling.

Our studies with I_2 as a catalyst in the *Z/E*-isomerization of conjugated diene systems showed that the process also takes place in the dark, albeit much slower than in the light (Table 1), thus hinting at a thermal radical mechanism for the reaction. In this paper we describe our studies on the mechanism and the estimation of the activation energy of the I_2-catalyzed *Z/E*-isomerization in dark. The reaction was studied on three conjugated diene systems which appear, among many others, in long chain compounds, such as sex pheromones of moths: (*Z,E*)-9,11-tetradecadien-1-yl acetate [(*Z,E*)-9,11-$C_{14}OAc$)] (TDDA) (I), the main component of the sex pheromone of the female Egyptian cotton leafworm (*Spodoptera littoralis*) (5,6); (*E,Z*)-7,9- dodecadien-1-yl acetate [(*E,Z*)-7,9- $C_{12}OAc$)] (DDA) (II), the sex pheromone of the female grapevine moth (*Lobesia botrana*) (7,8); and (*E,E*)-10,12-hexadecadien-1-yl acetate [(*E,E*)-10,12-$C_{16}OAc$)] (HDDA) (III), which is the analog of (*E,E*)-10,12-hexadecadienal (IV), the sex pheromone of the female spiny bollworm (*Earias insulana*) (9).

(*Z,E*)- $CH_3CH_2CH{=}CHCH{=}CH\,(CH_2)_8OAc$
I
(*E,Z*)- $CH_3CH_2CH{=}CHCH{=}CH\,(CH_2)_6OAc$
II
(*E,E*)-$CH_3(CH_2)_2\,CH{=}CHCH{=}CH\,(CH_2)_9OAc$
III
(*E,E*)-$CH_3(CH_2)_2\,CH{=}CHCH{=}CH\,(CH_2)_8CHO$
IV

EXPERIMENTAL PROCEDURES

The three pheromones I, II and IV and the analog III were synthesized and found to be ≥98% pure (10,11).

TABLE 1

Iodine-Catalyzed Isomerization of Conjugated Dienes in the Sunlight and in the Dark

			% Composition				
Diene[a]	Conditions	Exposure time (hr)	*Z,E*-	*E,Z*-	*Z,Z*-	*E,E*-	Ref.
TDDA	Sunlight	3	12	14	2	72	This work
	Dark	24	14	15	1	70	12
DDA	Sunlight	4	11	12	2	75	12
	Dark	26	11	12	2	75	12
HDDA	Dark	6	13	14	1	72	13

[a] Each sample contained 50 or 100 mg of diene and 5 mg of I_2 in 5 ml cyclohexane at room temperature in dark or in sunlight.
TDDA, (*Z,E*)-9,11-$C_{14}OAc$; DDA, (*E,Z*)-7,9-$C_{12}OAc$, and HDDA, (*E,E*)-10,12-$C_{16}OAc$.

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TABLE 2

Isomerization of (*Z,E*)-9,11-C_{14}OAc in the Presemce of Iodine in the Dark

I_2in TDDA			Time	% Composition				Time	% Composition			
mg	mmol	%	(min)	*Z,E*-	*E,Z*-	*Z,Z*-	*E,E*-	(min)	*Z,E*-	*E,Z*-	*Z,Z*-	*E,E*-
2.5	0.01	5	60	70	7	-	23	120	45	11	-	44
5.1	0.02	10	40	60	12	-	28	120	45	13	-	42
15.2	0.06	30	60	67	12	-	21	120	52	15	-	33
25.4	0.1	50	60	60	15	-	25	120	45	19	-	36
50.8	0.2	100	60	39	15	-	46	120	17	15	<1	68
76.2	0.3	150	60	36	15	-	49	120	19	15	<1	66
101.6	0.4	200	60	23	18	-	59	120	16	15	<1	69

[a] Each sample contained 50.4 mg of TDDA (0.2 mmol) in 5 ml t-BuOH at room temperature with different amounts of I_2. Percentage of I_2 was relative to 50.4 mg of TDDA.

A.R. grade solvents were used without further purification. Antioxidants were purchased from Aldrich and used as such. UV spectra were determined on a Bausch and Lomb Spectronic 2000 spectrophotometer in spectroscopic grade cyclohexane or t-butanol. Depending on the pheromone studied, GLC analyses were performed on a Packard-417 instrument with FID, using a 30-m × 0.25-mm fused silica capillary column coated with SP 2340, and with a flow rate (He) of 0.4 ml/min at 130-160°C, or on a WCOT silar 9 25-m x 0.5-mm column with a flow rate (He) of 2.7 ml/min at 130-160° C. In all reactions fixed amounts of diene were dissolved in the appropriate solvent (details are given in all tables), and other components were added to the solution. Samples were withdrawn at intervals, washed with $NaHSO_3$ solution, dried over Na_2SO_4 and injected into GLC as such or diluted as needed. Aliquots (1-2μl) were injected twice (± 1%) from each sample. Dark reactions were conducted in aluminum foil-wrapped flasks in a closed cabinet. Reactions in sunlight were usually run on the roof of the building in diffused light except for the experiment shown in Table 4, in which the flasks were held in direct sunlight at noon (in the summer).

UV spectra of antioxidants in cyclohexane: BHT (V): $\lambda_{\max}^{C_6H_{12}}$ 229nm (ϵ=5130), 280 (3100); BHA(VI): $\lambda_{\max}^{C_6H_{12}}$ 228 (3980), 290 (2190); TBHQ (VII): $\lambda_{\max}^{C_6H_{12}}$ 229 (4870), 275(4010). Iodine: $\lambda_{\max}^{t\text{-BuoH}}$ 525(300); $\lambda_{\max}$ 438(765). UV spectra of mixtures of antioxidants or pheromones and I_2 were obtained in solutions with the same ratio of components as mentioned in Tables 1 and 3.

RESULTS AND DISCUSSION

The dark isomerization of the diene system catalyzed by iodine can be explained by the above-mentioned radical mechanism. Thermal dissociation of the iodine molecule into two iodine radicals takes place because the I-I bond energy is relatively low, 37 kcal/mol (14). Still another mechanism can be proposed in which a π-complex is formed between I_2 and the π-bond of the olefin, as occurs with an aromatic system (15), and as proposed for the short wavelength isomerization in light (*vide supra*). The π-complex may activate the π-system as the starting point for the isomerization. However, we do not consider this π-complex route to be the main path, as no change was observed in the UV spectrum of the mixture of each of the diene systems (I-III) with I_2 as compared with the spectra of the individual pure components. If a π-complex were formed, then we might expect either a shift in the absorption bands or the appearance of new ones, as found with aromatic systems such as benzene, toluene and others (15).

We thus decided to study the postulated radical mechanism. The first step was to clarify the catalytic behavior of iodine. We measured the isomerization rate with increasing quantities of iodine, relative to the diene system. The measurements were conducted in t-BuOH solution, because we have found that cyclohexane dissolves

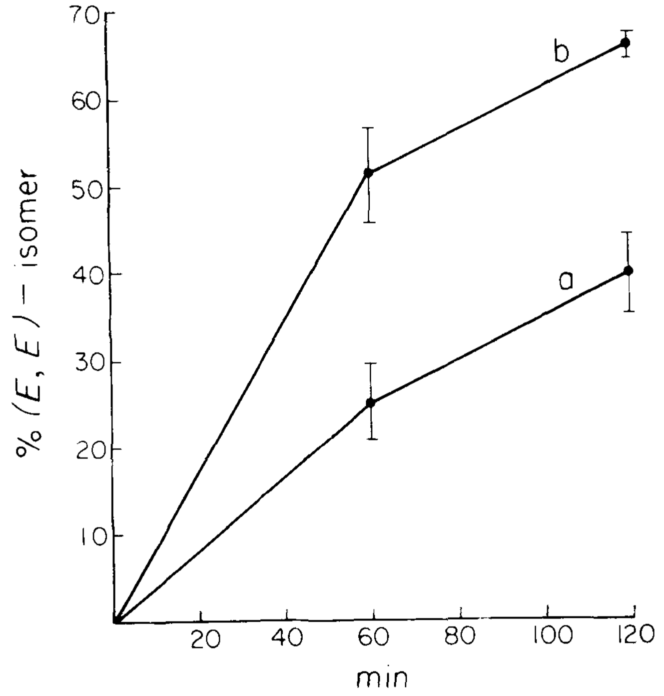


FIG. 1. Average rate of isomerization (±s.d.) of (*Z,E*)-9,11-C_{14}OAc at low (5-50%) (a) and high (100-200%) (b) concentration of I_2 in the reaction, for 60- and 120-min reaction period (based on data presented in Table 2).

TABLE 3

Isomerization of TDDA, DDA and HDDA with I_2 in the Presence of Antioxidant in the Dark[a]

Entry	Diene[b]	Antioxidant[c]	Time (hr)	% Composition *Z,E*-	*E,Z*-	*Z,Z*-	*E,E*-	Ratio of *E,E*- formed or reacted
1	TDDA	-	25	14	12	2	72	1
2		BHT	26	53	12	<1	35	0.49
3		BHA	24	34	15	<1	50	0.69
4		TBHQ	24	28	14	2	56	0.78
5		DBHA	23	33	19	1	47	0.65
6	DDA	-	26	11	12	2	75	1
7		BHT	23	5	72	-	23	0.31
8		BHA	23	13	18	1	68	0.91
9		TBHQ	23	13	19	1	67	0.89
10	HDDA	-	2	10	10	-	80	1
11		BHT	2	4	4	-	92	0.4
12		BHA	2	7	7	-	86	0.7
13		TBHQ	2	7	7	-	86	0.7

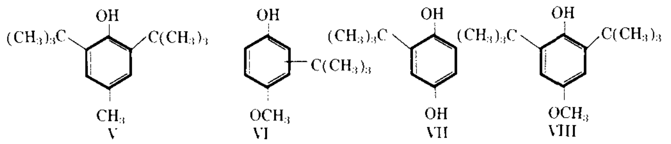
[a] Each sample contained 50 mg of diene, 50 mg of antioxidant and 2.5 mg of I_2 in 5 ml cyclohexane, at room temperature.
[b] For abbreviations see Table 1.
[c] BHT, (butylated hydroxy toluene) or 2,6-di-t-butyl-4-methylphenol (V); BHA, (butylated hydroxy anisole) or 2(3)-t-butyl-4-methoxyphenol (VI); TBHQ, (butylated hydrouinone), or 2-t-butylhydroquinone (VII); DBHA, 3,5-di-t-butyl-4-hydroxyanisole (VIII).

only small amounts of iodine (up to 10-15 mg in 5 ml), and the results of isomerization were not consistent using larger amounts of iodine. We found that for up to 50% by weight of iodine in the diene solution (25 mg of I_2 and 50 mg of TDDA, which is 1:2 in molar ratio), there is no increase in the isomerization rate, as shown in Table 2 and Figure 1. Therefore, we may conclude that at low concentrations of I_2 (5-10%, 2.5-5.1 mg of I_2 and 50 mg of TDDA) the reaction is a catalytic process, first order only in the conjugated diene system. This suggests that the amountof iodine radicals is large enough to induce the catalytic isomerization at 5% I_2, and thus no increase in the rate process is observed when larger quantities (up to 50%) of I_2 are used. Therefore, together with the low activation energy (*vide infra*) of the isomerization, only a low concentration of iodine radicals is needed for the catalytic process. Any further reduction of iodine concentration (1-2% would be 0.5-1 mg) could lead to erroneous results.

It is interesting to note that with much larger quantities of I_2 (100-200%), the amount of isomerization is again constant but is about double that of the smaller quantities (5-50%), which is clear from Figure 1. This may indicate a different mechanism and kinetics of isomerization.

Assuming that iodine reacts through a radical, the effect of radical scavengers ought to slow the isomerization. Phenolic antioxidants react with ground state triplet oxygen ($^3O_2$) as radical scavengers, thus protecting sensitive molecules from radical oxidation. Three such antioxidants [BHT (V), BHA (VI) and TBHQ (VII)] (for abbreviations see Table 3) markedly inhibited the I_2-catalyzed isomerization of the three studied dienes (Table 3).

The results clearly show the effect of all three antioxidants on the isomerization. BHT is the most effective (entries no. 2,7,11), and BHA and TBHQ show similarly inhibitory activity but are less efficient than BHT.



V VI VII VIII

It could be argued that the effect of the phenolic antioxidants is not only radical scavengers, but also through deactivation of the iodine by formation of a π-complex (15), i.e., "binding" the I_2 molecules to the aromatic systems to yield fewer I· radicals. Measurement of the UV spectra of the mixtures of the antioxidants and I_2 in the same ratio as that used in the experiments summarized in Table 3 does not show any change as compared with the spectra of individual components. Thus, we may assume that the dark isomerization probably proceeds through a thermal-radical mechanism.

TABLE 4

Isomerization of (*Z,E*)-9-11-C_{14}OAc with I_2 in the Presence of Antioxidants in the Sunlight[a]

Entry	Antioxidant[b]	Time (min)	% Composition *Z,E*-	*E,Z*-	*Z,Z*-	*E,E*-
1	-	40	16	14	3	67
2	BHT	45	34	16	3	47
3	BHA	40	49	11	2	38
4	TBHQ	45	24	17	3	56
5	DBHA	30	41	13	1	45

[a] Each sample contained 50 mg of TDDA, 50 mg of antioxidant (for abbreviations see Table 3) and 2.5 mg of I_2 in 5 ml of cyclohexane.
[b] For abbreviations see Table 3.

TABLE 5

Iodine Catalyzed Isomerization of (*Z,E*)-9,11-C_{14}OAc at Different Temperatures in the Dark[a]

Solvent[a]											
t-BuOH[b]						Cyclohexane[c]					
Temp (°C)	Time (min)	Composition *Z,E*-	*E,Z*-	*Z,Z*-	*E,E*-	Temp (°C)	Time (min)	% Composition *Z,E*-	*E,Z*-	*Z,Z*-	*E,E*-
90	20	22	14	<1	64	90	15	24	15	-	61
64	20	63	10	-	27	70	15	40	17	-	43
64	60	16	15	1	68	70	50	27	13	-	60
25	30	65	9	-	26	58	120	45	8	-	47
25	120	45	11	-	44	23	120	50	12	-	38
2[b]	60	90	4	-	6						
2[b]	240	83	5	-	12						

[a] Each sample contained 50 mg of TDDA and 2.5 mg I_2 in 5 ml of solvent.

[b] Because of freezing of t-BuOH, ethanol was used as a solvent.

[c] Erratic results were obtained because of low solubility of I_2 in cyclohexane at 2°C.

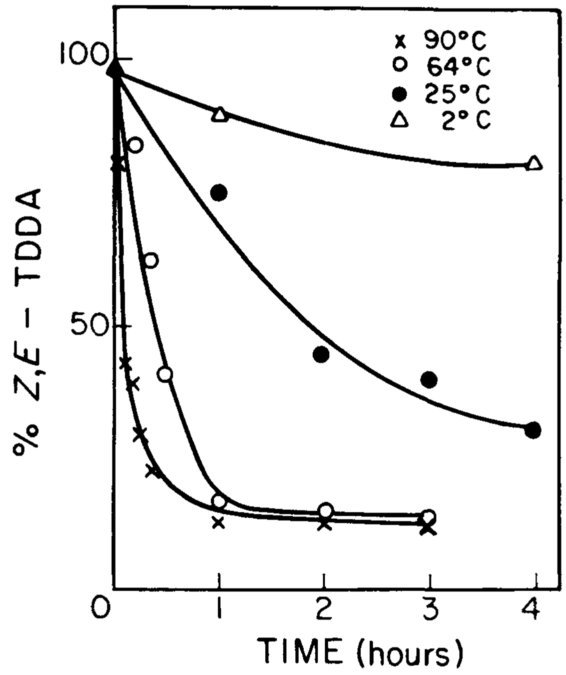


FIG. 2. Decrease in (*Z,E*)-9,11-C_{14}OAc (TDDA) concentration in t-BuOH solution at different temperatures with I_2 in the dark (based on Table 5).

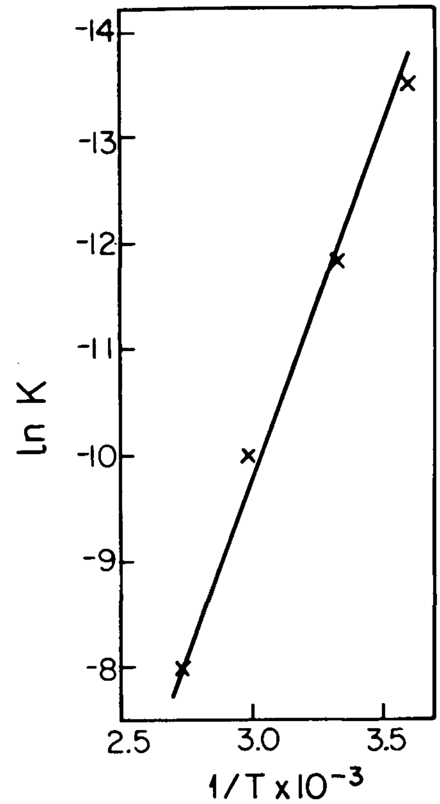
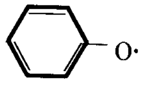


FIG. 3. Relationship between ln k and 1/T for the dark isomerization of (*Z,E*)-9,11-C_{14}OAc (TDDA) by I_2 in t-BuOH at different temperatures.

There are two differences in the structure of BHT as compared with BHA and TBHQ: BHT has two t-butyl groups and BHA and TBHQ have a second phenolic (ether) oxygen. Entry 5 in Table 3 clearly shows that the second t-butyl group in the anisole ring (3,5-di-t-butyl-4-hydroxyanisole, DBHA, VIII) does not have any effect on the isomerization. Thus, the difference in the radical scavenging behavior apparently stems from the second OH (OR) group (Entries 3,4,8,9,12 and 13 in Table 3). A substituent



(i)

TABLE 6

Isomerization of TDDA, DDA and HDDA Induced by Thiophenol in Toluene at 100°C[a]

Diene[b]	Time (min)	% Composition *Z,E-*	*E,Z-*	*Z,Z-*	*E,E-*
TDDA	20	22	13	<1	65
DDA	20	13	18	3	66
HDDA	5	14	16	3	67

[a]Each sample contained 50 mg of diene and one drop of thiophenol in 5 ml toluene at 100°C.
[b]For abbreviations see Table 1.

such as RÖ- on the ring can donate its unshared n-electrons on the oxygen to the π-system of the benzene ring, thus destabilizing the phenoxy radical (i) and rendering it less effective as an iodine radical scavenger.

As described earlier, the iodine-catalyzed photochemical isomerization with longer wavelength light starts with the formation of $I\cdot$. We found that the antioxidants used by us can also slow down the iodine-catalyzed isomerization of the conjugated diene system in sunlight, as summarized in Table 4.

In sunlight the reaction is fast, and even diffused light in the laboratory is sufficient for the iodine-catalyzed isomerization to proceed.

The above described findings support the assumption of the radical characteristic of the isomerization. If the key step in the reaction is cleavage of the I-I bond (37 kcal/mol) by thermal energy, then the temperature effect should be important. We thus measured the rate of isomerization as a function of the temperature (Table 5 and Fig. 2).

The reaction was conducted in two solvents, t-BuOH and cyclohexane, which differ both in polarity and protic ability. The rates and compositions are similar, thus hinting at the nonionic character of the reaction. As expected, at the higher temperature (90°C) the isomerization was much faster than at room temperature, and it proceeded very slowly at the low temperature (2°C). The dependence of the isomerization rate on temperature is illustrated in Figure 3, from which the activation energy of the iodine-catalyzed isomerization of (*Z,E*)-TDDA, an internal conjugated diene system, in the dark is calculated to be 12.4 ± 1.2 kcal/mol. The processes leading to the isomerization which require energy are the breaking of the π bond [(64 kcal/mol (14)], the loss of resonance energy of the conjugated diene system [(5-7 kcal/mol (14)], and rotation around the C-C bond [at least 4-5 kcal/mol, as the rotation barrier in butane is 3.8 kcal/mol (16)], giving a total of 73-75 kcal. The processes in which energy is evolved or saved are formation of the C-I bond [52 kcal/mol (14)] and the stabilization of the allylic radical formed [12 kcal/mol (4)], giving a total 64 kcal. The difference of 9-11 kcal/mol is in good agreement with our experimental result of the relatively low activation energy of ca. 12 kcal/mol.

It is interesting to note that the rate of radical isomerization of the conjugated diene system by thiophenol in toluene at 100°C (Table 6) is about the same as that of iodine isomerization at 90°C (Table 5) in the light (Table 4), both processes bringing the mixture close to the thermodynamic equilibrium.

We have previously shown that light and photosensitizer promote singlet oxygen reaction with an (*E,E*)-conjugated diene system (17,18) to form a cyclic peroxide, which later collapses to a furan derivative. We have obtained large-scale isomerization (hundreds of grams) of conjugated diene systems with I_2 in sunlight and found that a significant portion of the material is lost during the process. It could be that this loss occurs through the oxidation process. It seems, therefore, that fast thermal iodine-catalyzed isomerization might be a better approach when the (*E,E*)-isomer is required. An inert atmosphere in the flask is also desirable (2).

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