

THE FORMATION OF *cis*- AND *trans*-ISOMERS DURING PROTOTROPIC ISOMERIZATION

V.SVÁTA and M.PROCHÁZKA

Department of Organic Chemistry,
Charles University, 128 40 Prague 2

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During prototropic isomerization of 4-penten-2-one catalysed with triethylamine at 35°C *cis*-3-penten-2-one (II) and *trans*-3-penten-2-one (III) are formed at the beginning of the reaction in a 1:24:1 ratio. At equilibrium the ratio of II/III was $0.7 \cdot 10^{-2}$, i.e. the *cis*-isomer is not an intermediary stage in this reaction. The results were compared with the isomerization of ethyl 4-butenic acid and explained by the equilibrium of isomeric carbanions. Relative stabilization energies of the double bond system $\text{>C}=\overset{\text{I}}{\text{C}}-\text{C}=\text{O}$ (R; OR) were also measured.

We studied the problem of the ratio of *cis-trans* isomers during base catalysed prototropic isomerization at thermodynamical equilibrium and kinetically controlled reaction. Up till today a series of examples is known in which in the kinetically controlled process (*cis/trans*) $t \rightarrow 0$ (time t at the beginning of the reaction) a *cis*-propenyl derivative is formed from the allylic compound independently of the fact of whether it is thermodynamically more stable¹; for example in the base catalysed isomerization of $\text{CH}_2=\text{CH}-\text{CH}_2-\text{X}$ it has been found [X ; (*cis/trans*) $t \rightarrow 0$; (*cis/trans*) $t \rightarrow \infty$] CH_3 47.4; 0.25 (ref.^{2,3}); C_2H_5 10.8; 0.23 (ref.²); $\text{CH}(\text{CH}_3)_2$ 3.2; 0.23 (ref.²); $\text{C}(\text{CH}_3)_3$ 0.25; 0.001 (ref.²); C_6H_5 $7.55 \cdot 10^{-2}$; $2.25 \cdot 10^{-2}$ (ref.⁴); $\text{O}-\text{C}_2\text{H}_5$ 50; 1.38 (ref.⁵⁻⁷); $\text{N}(\text{CH}_3)_2$ ≈ 8.5 ; $1 \cdot 10^{-2}$ (ref.^{8,9}); CN 3.1 or 1.85; 1.2 (ref.^{10,11}); NO_2 0.78; $2.5 \cdot 10^{-2}$ (ref.^{12,13}). The formation of the *cis*-isomer may be correlated with the geometrical stability of the allylic anion, because an analysis of the NMR spectrum of butenyl lithium demonstrated *cis*- and *trans*-isomeric carbanions¹⁴, and, similarly, for anions formed from 4-phenyl-2-butenes¹⁵ it was shown that they attain equilibrium at 0°C, at which the *cis*-isomer predominates. The anion formed from *trans*-2-pentanal¹⁵ exists exclusively in the form in which the $-\text{CH}_3$ group is in the *cis* position and the hydrogen atom on carbon atom two (Formula A). These results exclude both a conformational control of the reaction by the ground state of the reaction product, and the theory based on the sterical inhibition of the solvation of the transition state¹. On the basis of the study of carbanion structure^{16,17} it seems probable that the nature of the products in kinetically controlled isomerization may be correlated directly with the thermodynamical

stability of possible carbanions or similar reaction intermediates (it is known that a proton transfer usually takes place by an intramolecular mechanism)¹.

In this paper we investigated the isomerization of 4-penten-2-one ($X = -\text{COCH}_3$) from the point of view of the formation of *cis*-*trans* isomers of 3-pentenone, equilibrium of all isomers, and we compared them with the results obtained with analogous esters ($X = -\text{COOC}_2\text{H}_5$). The isomerization of unsaturated ketones has been studied by a series of authors, but without differentiating *cis* and *trans* isomers; for example, during the isomerization of 4-penten-2-one the authors mentioned 75% of conjugated isomer¹⁸ at equilibrium, in the case of 5-methyl-4-hepten-3-one¹⁹ 57–67% of conjugated isomer were found at equilibrium, in the case of 6-methyl-5-nonen-4-one the percentage was 73%, and great attention was also paid to cyclic ketones^{20,21}; Mialhe and Vessière¹⁰ state that during the isomerization of 5-hexen-3-one 100% of *trans* isomer is formed under the effect of a secondary amine and in the case of ethyl 3-butenate 80–85% of *trans* isomer; the type of base and solvent had little effect on the ratio of isomers. In this case isomerization can take place both by addition and elimination.

During the isomerization of 4-penten-2-one (Table I, Fig. 1, 2) it was found that the *cis* isomer is formed simultaneously with the *trans* isomer (*III*); the ratio of *cis* *II*/*trans* *III*, $t \rightarrow 0$ (at the reaction beginning) was 0.84 at 20°C, at 35°C it was 1.24, at 50°C 1.86, in consequence of temperature dependence of reaction rates. From the

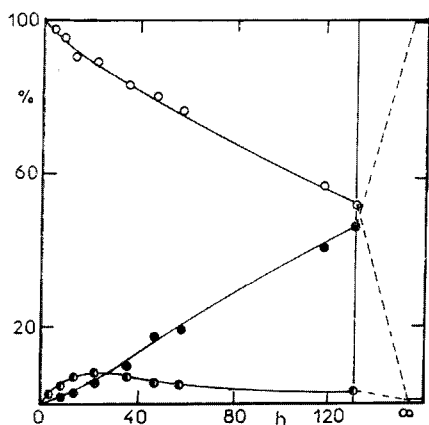


FIG. 1
Isomerization of 1M Solution of *cis*-3-Penten-2-one at 50°C in Tetrahydrofuran in the Presence of 0.1M Triethylamine

○ *cis*-3-Penten-2-one, ● *trans*-3-penten-2-one, ● 4-penten-2-one.

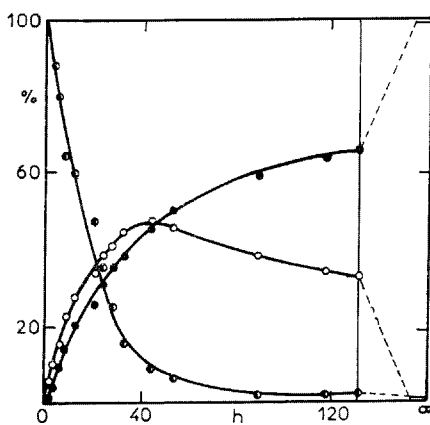
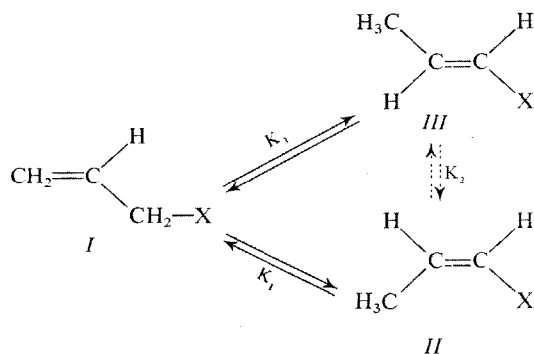


FIG. 2
Isomerization of 1M Solution of 4-Penten-2-one at 50°C in Tetrahydrofuran in the Presence of 0.1M Triethylamine

○ *cis*-3-Penten-2-one, ● *trans*-3-penten-2-one, ● 4-penten-2-one.

course of the reaction it may be judged that both isomers are converted into each other by rotation of the bonds in the carbanion and that the *cis* isomer is not an intermediate in *trans* isomer formation. At equilibrium the conjugated isomer distinctly prevails. These results may be compared with those from a paper²² where the isomerization of ethyl 3-butenolate has been studied under catalysis with potassium tert-butoxide in tert-butyl alcohol. In this case too it could be inferred from the reaction rates that the *cis* isomer *II* is not an intermediate in the formation of the *trans* isomer *III* of ethyl 2-butenolate. The ratio of the formation of *cis-trans* isomers of ethyl 2-butenolate was determined only approximately for the reaction rate and the competing Michael addition of 3-butenic acid ester to the *trans* isomer of ethyl 2-butenolate²³.



I 4-penten-2-one (or ethyl 3-butenolate)
II *cis*-3-penten-2-one (or ethyl 2-butenolate)
III *trans*-3-penten-2-one (or ethyl 2-butenolate)

SCHEME 1

TABLE I
 Equilibria of *cis*- and *trans*-Isomeric Ketones and Esters

—X	<i>T</i> , °C	(<i>cis/trans</i>) <i>t</i> → 0	(<i>cis/trans</i>) <i>t</i> → ∞	(<i>cis/trans</i>) <i>t</i> → 0 ^a (<i>cis/trans</i>) <i>t</i> → ∞
—COCH ₃	35	1.24	0.97 · 10 ⁻²	128
—COC ₂ H ₅	45	0.13	4.14 · 10 ⁻²	3.2

^a (*cis/trans*) *t* → 0 ratio concentrations of *II* and *III* at the beginning of the reaction, (*cis/trans*) . *t* → ∞ ratio of concentrations of *II* and *III* at equilibrium.

If comparing ketones and esters, then the equilibrium of the *cis-trans* isomerism is shifted to the *trans* isomer *III*, probably due to larger steric requirements of the $-\text{CH}_3$ group in comparison with the $-\text{O}-\text{C}_2\text{H}_5$ group, which can be derived from *A*-values²⁴, steric constants of substituents E_s (ref.²⁵) and conformational energy $-\Delta G_x^0$ (ref.²⁶). Similarly the deduction can be made from the equilibrium ratio of the conjugated and unconjugated isomer, that the resulting stabilization by the $-\text{COCH}_3$ group is approximately 1.8 kcal/mol higher (for $-\text{COCH}_3$, $\Delta G(\alpha\beta \Delta/\beta\gamma \Delta) = 4.3$ kcal/mol; for $-\text{COOC}_2\text{H}_5$ 2.5 kcal/mol).

In both carbonyl compounds the formation of an enol form by protonation of the carbanion on oxygen atom also should be considered. The enol could not be proved. It is formed probably in concentrations common in other saturated ketones ($K_r = 10^{-20}$). It is known that the anions derived from α,β -unsaturated ketones are converted to β,γ -unsaturated ketones²⁷ on careful acidification, and it may be supposed that the enol, if formed, possesses the structure with conjugated double bonds²⁸. In the case of pentenones we found during the isomerization a small amount of β,γ -unsaturated ketone only, and therefore it may be supposed that the proton transfer takes place predominantly on the carbon atom and that the dienol is not an intermediate in the reaction (Figs 1 and 2).

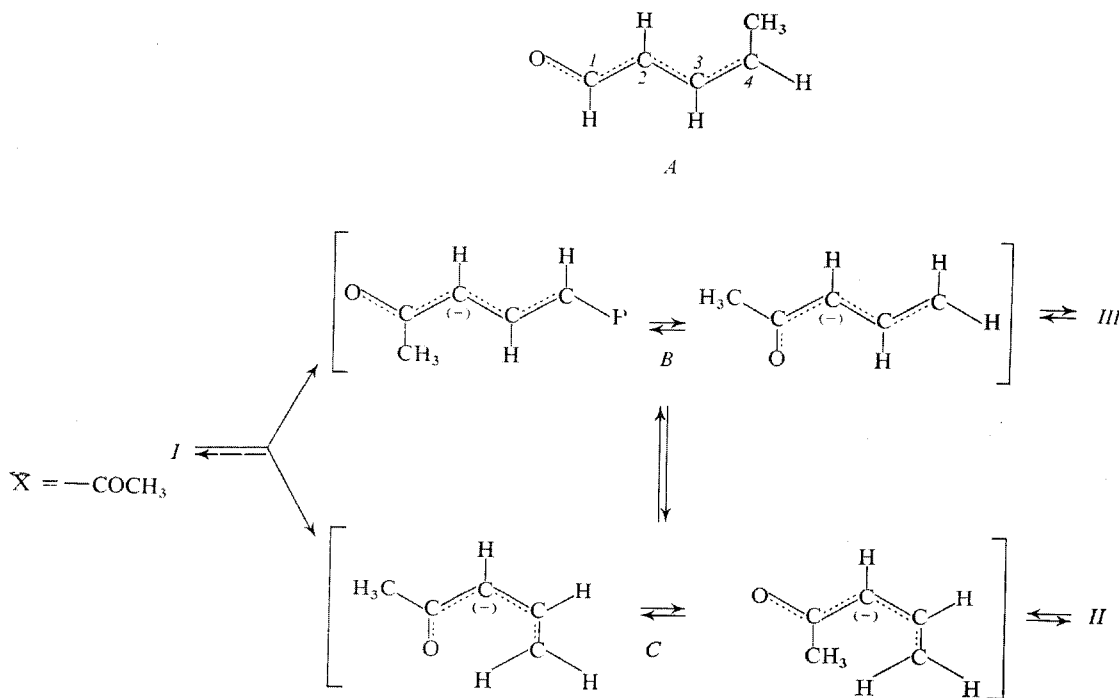
As both isomers play an important role at the beginning of the isomerization we can suppose that also in the equilibrium of carbanions, which shows a considerable temperature dependence, *cis* and *trans* isomeric carbanions (*B*, *G*) or analogous intermediates are also present (Scheme 2).

In ketones and esters substantially more *cis* isomers are formed at the reaction beginning than would correspond to equilibrium and this reaction can be utilized for their preparation (Table II).

TABLE II
Isomerization of Unsaturated Ketones and Esters

-X	T, °C	Equilibrium concentration of isomers, %								
		<i>I</i>	<i>II</i>	<i>III</i>	K_1^a	ΔG_1^b	K_2^a	ΔG_2^b	K_3^a	ΔG_2^b
-COCH ₃	20	0.01 ± 0.02	0.66 ± 0.1	99.4 ± 0.1	66	2.44	150	2.91	9.940	5.36
	35	0.05 ± 0.02	0.70 ± 0.1	99.3 ± 0.1	14	1.61	142	3.03	1.980	4.65
	50	0.1 ± 0.02	0.95 ± 0.1	98.9 ± 0.1	9.5	1.45	104	2.98	989	4.33
-COC ₂ H ₅ ^c	45	1.4 ± 0.7	3.9 ± 0.4	94.7 ± 0.7	2.75	0.63	24.3	2.0	67.8	2.65
	60	1.4 ± 0.4	2.7 ± 0.3	96.3 ± 0.3	1.92	0.43	35.6	2.35	69	2.78

^a Equilibrium constants of the reactions according to Scheme 1; ^b kcal/mol; ^c ref.²².



SCHEME 2

EXPERIMENTAL

4-Pentan-2-one was prepared according to literature²⁹ in 43% yield. From 100 g of 4-hydroxypentan-2-one³⁰ a mixture (70 g) of isomeric unsaturated ketones was formed on boiling with 2 g of oxalic acid, b.p. 117.5–121°C/750 Torr, of the composition 6% 4-penten-2-one, 8% *cis*-3-penten-2-one and 86% of *trans*-3-penten-2-one. *cis*-3-Penten-2-one³¹ was obtained by distillation of 50 g of the *trans* isomer with 1 g of hydroquinone and 0.5 g of *p*-toluenesulfonic acid on a 40 TP column filled with etched glass rings. A mixture (10 g) was obtained containing 90% *cis*- and 8% *trans*-3-penten-2-one and 2% 4-penten-2-one. The separation and the purification of the isomers of penten-2-one was carried out by preparative gas chromatography on a 3–6 m column containing 10% GE XE-60 on 0.20–0.25 mm Chromaton N-AW-DMCS. Single ketones were obtained in the following purities: *cis*-3-penten-2-one 99.5% and 0.5% of *trans*-isomer, *trans*-3-penten-2-one 99.9%, 4-penten-2-one 95.5% and 4.5% of *cis*-isomer. IR Spectra: 4-penten-2-one $\delta(\text{CH})$ 938, 995 cm^{-1} , $\nu(\text{C}=\text{C})$ 1642 cm^{-1} , $\nu(\text{C}=\text{O})$ 1725 cm^{-1} ; *cis*-3-penten-2-one $\delta(\text{CH})$ 740 cm^{-1} , $\nu(\text{C}=\text{C})$ 1625 cm^{-1} , $\nu(\text{C}=\text{O})$ 1700 cm^{-1} , 1648 cm^{-1} ; *trans*-3-penten-2-one $\delta(\text{CH})$ 952, 978 cm^{-1} , $\nu(\text{C}=\text{C})$ 1640 cm^{-1} , $\nu(\text{C}=\text{O})$ 1680 cm^{-1} .

Isomerization

Ampoules of 0.3 ml volume were filled with 50 μl of a 1M solution of corresponding ketone and 10 mol% of triethylamine in tetrahydrofuran and sealed. Isomerization was slowed down at the

required interval by cooling to -60°C . The analysis of the samples was carried out by gas chromatography, using a calibration straight line. For chromatography a 2 m column was used, packed with 10% of GE XE-60 on Chromaton N-AW-DMCS 0.20–0.25 mm, 6 mm diameter, at 37°C and nitrogen flow 1.5 ml/s, and the following retention times were observed: isomer *I* 5.8 min, *II* 4.6, *III* 10.5 min. Triethylamine, which was present in the sample, did not cause changes in the equilibrium mixture of ketones during gas chromatography. This was checked by samples which had been prepared immediately before the analysis.

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