Study of the *endo*- and *exo*-Isomers of 5-Acylbicyclo[2.2.1]hept-2-enes and their Ethynylated Products

[a]V. SUTORIS, [b]J. HRIVŇÁK, and [a]A. RICHTEROVÁ

[a]*Department of Organic Chemistry, Faculty of Natural Sciences, Komenský University, Bratislava 1*

[b]*Institute of Chemistry, Komenský University, Bratislava 1*

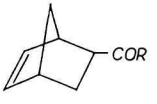
Received May 4, 1970

Accepted for publication January 3, 1971

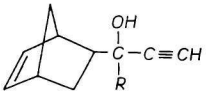
We have synthesized 5-acylbicyclo[2.2.1]hept-2-enes by diene addition and ethynylated with lithium aluminium acetylide. We have studied the ratio of *endo*- and *exo*-isomers in dependence on their preparation temperature and polarity of solvents as well as the kinetics of isomerization and the equilibrium of the *endo*- and *exo*-isomer mixture. We have calculated the rate constant of isomerization when sodium ethoxide was used as catalyst.

We synthesized ethynyl alcohols [1] by ethynylation of *exo*-cyclic ketones (adducts of 1,3-diene series with methyl vinyl ketones) and bicyclodicarboxyimides with lithium aluminium acetylide. After investigation of the herbicidic activity of the prepared ethynyl alcohols, it was evident that 3-hydroxy-3-methyl-3-bicyclo[2.2.1]hept-5′-en-3′-ylpropine showed almost the same activity as the standard substance 2,4-D.

In this work, we synthesized further 5-acylbicyclo[2.2.1]hept-2-enes (structure *I*) and on their ethynylation we obtained products of the structure *II*.



I



II

R = CH_2Cl (*a*); CH_2Br (*b*); CH_2CH_3 (*c*); $(CH_2)_2CH_3$ (*d*); $CH(CH_3)_2$ (*e*); $(CH_2)_3CH_3$ (*f*); $CH_2CH(CH_3)_2$ (*g*).

We studied the ratio of some *endo*- and *exo*-isomers in dependence on their preparation temperature and polarity of solvents by gas chromatography as well as their isomerization. These compounds will be tested whether they have any herbicidic activity.

Experimental

Characterization of all compounds synthesized is in Table 1. Gas chromatography was performed on a Perkin—Elmer Model F 11 apparatus with flame ionization detector.

Table I

Characterization of the prepared compounds

No.	Compound	Formula	*M*	Calculated/found		Yields	B.p.
				% C	% H	[%]	[°C/Torr]
*Ia**	5-chloroacetylbicyclo[2.2.1]hept-2-ene	$C_9H_{11}ClO$	170.6	83.21 83.09	6.47 6.50	62.9	111—114/15
*Ib***	5-bromoacetylbicyclo[2.2.1]hept-2-ene	$C_9H_{11}BrO$	215.1	50.27 50.32	5.15 5.22	53.8	108—113/15
Ic	5-propionylbicyclo[2.2.1]hept-2-ene	$C_{10}H_{14}O$	150.2	80.06 80.11	9.40 9.29	72.0	86— 89/14
Id	5-butyrylbicyclo[2.2.1]hept-2-ene	$C_{11}H_{16}O$	164.2	80.55 80.45	9.83 9.76	73.9	90— 95/12
Ie	5-isobutyrylbicyclo[2.2.1]hept-2-ene	$C_{11}H_{16}O$	164.2	80.55 80.61	9.83 9.71	58.4	88— 92/14
If	5-valerylbicyclo[2.2.1]hept-2-ene	$C_{12}H_{18}O$	178.2	80.96 81.04	10.19 10.15	68.9	101—103/13
Ig	5-isovalerylbicyclo[2.2.1]hept-2-ene	$C_{12}H_{18}O$	178.2	80.96 80.86	10.19 10.07	73.3	103—106/14
IIc	3-(bicyclo[2.2.1]hept-5-en-2-yl)-1-pentyn-3-ol	$C_{12}H_{16}O$	176.3	81.75 81.64	9.14 9.20	55.7	98—102/13
IId	3-(bicyclo[2.2.1]hept-5-en-2-yl)-1-hexyn-3-ol	$C_{13}H_{18}O$	190.2	81.99 81.80	9.53 9.60	66.6	110—113/12
IIe	4-methyl-3-(bicyclo[2.2.1]hept-5-en-2-yl)-1--pentyn-3-ol	$C_{13}H_{18}O$	190.2	81.99 81.84	9.53 9.36	49.1	105—108/11
IIf	3-(bicyclo[2.2.1]hept-5-en-2-yl)-1-heptyn-3-ol	$C_{14}H_{20}O$	204.2	82.41 82.00	9.88 9.77	55.5	117—119/ 9
IIg	5-methyl-3-(bicyclo[2.2.1]hept-5-en-2-yl)-1--hexyn-3-ol	$C_{14}H_{20}O$	204.2	82.41 82.08	9.88 9.76	49.5	112—115/ 9

* *Ia* % Cl calculated/found: 20.77 20,54

** *Ib* % Br calculated/found: 37.18 37,06

The injection space was adjusted according to [2]. Nitrogen was used as a carrier ga The chromatographic column (2 m × 2 mm) was filled with Chromosorb W (0.20—0.25 mm coated with 7% (w/w) of poly(ethylene glycol) succinate.

5-Propionylbicyclo[2.2.1]hept-2-ene

To the mixture of potassium acetate (4.9 g, 0.5 mole) and octyl alcohol (23 ml), β-chlor ethyl ethyl ketone (6.1 g, 0.5 mole) and cyclopentadiene (4.95 g, 0.75 mole) were adde at constant temperature. The reaction mixture was then allowed to react 1 hour und stirring. The addition was accomplished at temperatures 0, 20, 40, 60, 80, 100, 12 140, 160, and 180°C.

5-Halogenacetylbicyclo[2.2.1]hept-2-enes

To halogenmethyl vinyl ketone (0.16 mole), cyclopentadiene (11.0 g, 0.16 mol was added dropwise under cooling and the reaction mixture was allowed to stand a room temperature overnight. On vacuum distillation, 17.0 g of 5-chloroacetylbicycl [2.2.1]hept-2-ene (*Ia*) and 11.7 g of 5-bromoacetylbicyclo[2.2.1]hept-2-ene (*Ib*) wer obtained.

5-Acylbicyclo[2.2.1]hept-2-enes

To the mixture of diethylaniline (92 g, 0.6 mole) and dicyclopentadiene (32 g), β-di chloroethyl alkyl ketone (0.4 mole) mixed with cyclopentadiene (10 g; totally 0.63 mol was added within 15 minutes at 160°C. The reaction mixture was then heated 15 m nutes at 170°C and after cooling extracted with ether. The obtained extract was washe with hydrochloric acid and subsequently with sodium hydrogen carbonate and the dried with sodium sulfate. After the evaporation of solvent, vacuum distillation gav 5-propionyl- (*Ic*, 43.0 g), 5-butyryl- (*Id*, 48.5 g), 5-isobutyryl- (*Ie*, 38.3 g), 5-valery (*If*, 49.2 g), and 5-isovalerylbicyclo[2.2.1]hept-2-ene (*Ig*, 52.3 g).

3-(Bicyclo[2.2.1]hept-5-en-2-yl)-1-alkyn-3-ol

Into the mixture of tetrahydrofuran (150 ml) and lithium aluminium acetylide (3.8 0.01 mole), acetylene was introduced through a flask submerged in a freezing mixtur a bubbler with concentrated sulfuric acid and another with a solid potassium hydroxid When the reaction was complete (no more evolution of hydrogen), 5-acylbicyclo[2.2.1 hept-2-ene (0.2 mole) was added dropwise under stirring. The reaction mixture wa then stirred for 2 hours at 40—50°C and refluxed 1 1/2 hours. Tetrahydrofuran wa removed by distillation and the residue was poured onto ice with 10 g of ammoniu chloride. The organic components were extracted with ether and dried with sodiu sulfate. Vacuum distillation gave 3-(bicyclo[2.2.1]hept-5-en-2-yl) derivative of 1-pentyn -3-ol (*IIc*, 19.5 g), 1-hexyn-3-ol (*IId*, 25.3 g), 4-methyl-1-heptyn-3-ol (*IIe*, 18.6 g 1-heptyn-3-ol (*IIf*, 22.6 g), and 5-methyl-1-hexyn-3-ol (*IIg*, 20.2 g), respectively.

Results and Discussion

The dependence of the ratio of *endo*- and *exo*-isomers of 5-propionylbicyclo[2.2.1]hept -2-ene (*Ic*) on their preparation temperature is in Fig. 1. In spite of the communication [3 that only one stereoisomer (*endo* configuration) is formed on diene synthesis at low temp

Table 2

The effect of solvent on the ratio of *endo*- and *exo*-isomers

Solvent	The ratio of *endo*- and *exo*-isomers of compound		
	Ic	*Ie*	*Id*
n-heptane	4.7	3.0	4.0
carbon tetrachloride	—	5.0	3.8
tetrahydrofuran	6.0	6.2	3.9
dioxan	5.9	5.9	4.6
formamide	9.0	7.8	5.9

ratures, it is evident from Fig. 1 that the ratio of *endo*- and *exo*-isomers at 0°C is still 14.1. From the slope of the curve it is possible to presume the isomerization of the already formed *endo*-isomer to *exo*-isomer at high temperatures (above 100°C).

Ratios of *endo*- and *exo*-isomers of compounds *Ic*, *Id*, and *Ie* prepared in different solvents at 40°C are presented in Table 2. It is obvious that with the increasing polarity of solvents relatively larger amount of *endo*-isomer was formed. The longer the chain of alkylbicyclo[2.2.1]hept-2-enes the smaller is the amount of *endo*-isomer formed. It can be explained by decreased polarity of the medium.

Dinwiddie et al. [4] accomplished the isomerization of 5-acetylbicyclo[2.2.1]hept-2-ene with sodium methoxide in absolute methanol. We used sodium ethoxide as catalyst (the same amount for the used sample in twentyfold excess of ethanol under reflux) for the study of isomerization of the compound *Ic*. In the original sample the ratio of *endo*- and *exo*-isomers was 1.32. The equilibrium was achieved in 30 minutes and then the ratio was 0.81.

To follow the kinetics of isomerization of the compound *Ic*, we took that sample which contained 91.6% of *endo*-isomer. The dependence of $\log a/(a - x)$ on time is in Fig. 2. The reaction rate constant of the first order calculated from the graphical dependence was 4.37×10^{-2} min^{-1}.

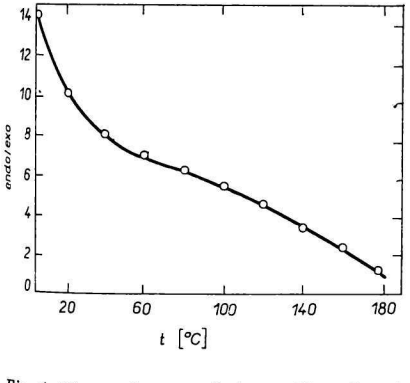


Fig. 1. Dependence of the ratio of *endo*- and *exo*-isomers of 5-propionylbicyclo-[2.2.1]hept-2-ene on the preparation temperature.

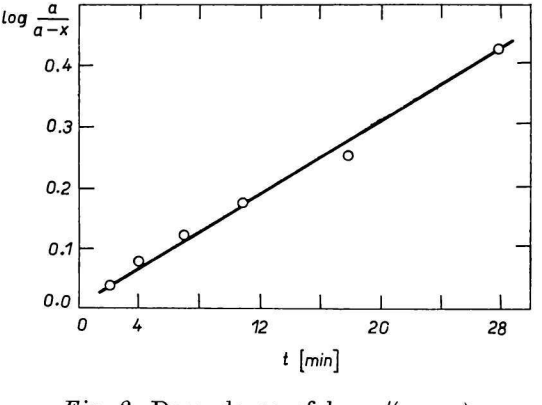


Fig. 2. Dependence of $\log a/(a - x)$ on time for 5-propionylbicyclo[2.2.1]hept-2-ene.

For dehydrohalogenation at diene synthesis of 3-chloroethyl-*tert*-butyl ketone a cyclopentadiene we used potassium acetate as base. The ratio of *endo*- and *exo*-isome in the diene adduct was 6.78. The yield, however, was very low (10%); therefore w could not accomplish the ethynylation.

When preparing the alkyl vinyl ketones, we found that the most suitable way w that from β-halogenethyl ketones, syntheses of which were accomplished by acylati of ethene with chlorides of fatty acids using anhydrous aluminium chloride as catal [6—9]. At acylation we used chloroform as solvent [6, 10—12] because in other solve or without them [13, 14], lower yields were obtained [15]. From alkyl vinyl keto we have isolated chloromethyl vinyl ketone and bromomethyl vinyl ketone only.

We used *N*,*N*-diethylaniline for dehydrohalogenation in all cases. As chlorometh and bromomethyl-β-chloroethyl ketones were easily dehydrohalogenated we allow to proceed the reaction for 12 hours at room temperature without stirring. In oth cases of dehydrohalogenation of β-chloroethyl alkyl ketones, the reaction mixture ha to be warmed up to 180°C and the reaction proceeded very vigorously. We have accompl shed the diene synthesis directly *via* corresponding alkyl vinyl ketones (which are ver unstable) and cyclopentadiene only in the case of chloromethyl vinyl ketone and brom methyl vinyl ketone. In other cases we added the solution of β-chloroethyl alkyl keto in cyclopentadiene dropwise to the warmed up mixture (170—180°C) of *N*,*N*-diethylanili and dicyclopentadiene.

Mahen [16] reported the evolution of chloroethane on dehydrohalogenation wit *N*,*N*-diethylaniline and thereupon the possibility of addition of *N*-ethylaniline to th double bond of the unsaturated ketone. In informative experiments, we did not fin nitrogen-containing substances by qualitative analysis. Therefore we preferred *N*,*N* -diethylaniline rather than potassium acetate in which case β-acetoxy ethyl keton could be formed by addition of the formed acetic acid to the α,β-unsaturated keton

On ethynylation of 5-acylbicyclo[2.2.1]hept-2-enes we found chromatographicall more compounds which could be different isomers regarding the stereo positions of alky and hydroxyl groups, respectively, in relation to the *endo*-methylene bridge.

References

1. Sutoris V., Furdík M., *Chem. Zvesti* ***21***, 329 (1967).
2. Hrivňák J., *Chem. Zvesti* ***19***, 942 (1965).
3. Furdík M., Sutoris V., *Chem. Zvesti* ***14***, 564 (1960).
4. Dinwiddie J. G., McManus S. P., *J. Org. Chem.* ***30***, 766 (1965).
5. Colonge J., *Bull. Soc. Chim. Fr.* ***3***, 2116 (1936).
6. Christ R. E., Fuson C., *J. Amer. Chem. Soc.* ***59***, 893 (1937).
7. Kondakov I. L., *J. Prakt. Chem.* ***48***, 647 (1893).
8. Blane G., *Bull. Soc. Chim. Fr.* ***19***, 699 (1898).
9. Kenner J., Statham F., *Ber.* ***69***, 16 (1936).
10. *German Patent* 625 758; *Chem. Abstr.* ***30***, 5591 (1936).
11. Darzens G., *C. R. Acad. Sci.* (Paris) ***150***, 707 (1910).
12. Taub W., Szmuszkovicz J., *J. Amer. Chem. Soc.* ***74***, 2117 (1952).
13. *Brit. Patent* 459 537; *Chem. Abstr.* ***31***, 3948 (1937).
14. *US Patent* 1 737 203; *Chem. Abstr.* ***24***, 626 (1930).
15. Norris J. F., Couch H. B., *J. Amer. Chem. Soc.* ***42***, 2329 (1920).
16. Mahen E. M., *J. Amer. Chem. Soc.* ***70***. 2971 (1948).

Translated by A. Kardošová