DIENOIC ACIDS, SYNTHESIS AND ¹³C NMR SPECTRAL ANALYSIS

Nelson FRIGHETTO, Carmen L.P. SILVEIRA, Francisco de A.M. REIS, Eva G. MAGALHÃES and Edmundo A. RÚVEDA

Instituto de Química, Universidade Estadual de Campinas, C.P. 1170, 13100 Campinas, São Paulo, Brasil

Received October 26th, 1977 accepted January 9th, 1978

A preparation of E,E-2,4-dienoic acids, together with the assignments of their ¹³C NMR signals and the shifts observed after transformation into their sodium salts, is described. The stereochemistry of the double bonds of 3,5-dienoic esters, obtained from 2,4-dienoic acids, on the basis of ¹³C NMR data, is also presented.

I. Introduction

Recently, effort has been devoted to the synthesis of E,E-2,4-dienoic acids [1]. In this connection, and as part of a project on the synthesis of unsaturated carboxylic acids, we wish to report a simple preparation of 2,4-dienoic acids, their ¹³C NMR analysis and their transformation into 3,5-dienoic acid derivatives.

II. Methods

The synthetic procedure is illustrated with the preparation of methyl E,E-2,4nonadienoate^{*}. By treatment of methyl E-2-nonenoate (1) – readily prepared from



heptanal and malonic acid in pyridine [2], followed by esterification – with N-bromosuccinimide in carbon tetrachloride, the corresponding bromo ester (2) was obtained in 71% yield**. The dehydrohalogenation reaction of (2) proved to be more difficult than expected, even if very effective amines such as 1.5-diazabicyclo-(4.3.0)-nonene-5

^{*} For another procedure for preparation of (3), see R.A. Gato, M.Sc. Dissertation, Universidade de Sao Paulo, 1976.

^{**} All compounds have been fully characterized (IR, ¹H NMR, mass spectra).

(DBN) and 1,5-diazabicyclo-(5.4.0)-undecene-5 (DBU) were used under a variety of reaction conditions. It was found, however, that the reaction could be successfully carried out (85% yield) by using lithium carbonate-lithium chloride in dimethyl-formamide*, a well-known method for dehydrobromination of bromoketones. The stereochemistry of (3) was assigned on the basis of the ¹H NMR spectrum and by using lanthanide shift reagents [3].

III. Results and Discussion

The availability of fatty acids with relatively short carbon chains, with one and two conjugated double bonds, and the considerable interest focused on the ¹³C NMR spectral analysis of this type of compound [4,5], prompted us to undertake an analysis of these substances.

The ¹³C NMR chemical shifts of several unsaturated fatty acids, presented in Table 1, were assigned on the basis of previous results [6] and on parameters proposed by Bus et al. [7]. Although we were dealing with carboxylic acids, instead of methyl esters, a good correlation was obtained between experimental and calculated values. The interesting result that emerges from this analysis is the assignment of the 27.5 and 27.8 ppm signals to the homoallylic carbons of E-2-octenoic and E-2-nonenoic acids. Since these values are within the normal range for an allylic carbon shift of a Z-disubstituted double bond, care should be taken with a double configuration assignment in unsaturated carboxylic acids on the basis of ¹³C NMR data alone.

In order to extend the study of the effect of ionization on chemical shifts of unsaturated carboxylic acids [8], the ¹³C NMR spectra of the corresponding sodium salts were also analyzed. As expected, C-2 and C-3 are deshielded and shielded respectively, while the remaining carbons are deshielded in all salts, in comparison with similar sites of the corresponding acids, as shown in table 1. Part of these effects, however, could be attributed to the change of solvent (CDCl₃ \rightarrow D₂O) used for recording the spectra of both series of compounds [8,9].

Table 2 shows the shifts of four E,E-2,4-dienoic acids and the effect observed on the sp^2 carbons by ionization. The changes are similar to the previously reported ones [8].

As part of the work on dienoic acids and in connection with another project, esterification reactions with sterically hindered alcohols were also studied. We have found that, by reaction of sorboyl chloride with 1-ethynylcyclopentanol in triethyl-

^{*} A magnetically stirred mixture of 2 (11.28 g), lithium carbonate (4.48 g) and lithium chloride (3.16 g) in dry dimethylformamide (50 ml) was heated in an oil bath at $125-130^{\circ}$ C for 1.5 hr. The reaction mixture was then poured into water and thoroughly extracted with ether. The combined ether extracts were washed twice with 10% aqueous hydrochloric acid, with water, dried (Na₂SO₄) and evaporated. The residue gave (3) (6.47 g) after distillation, b.p. 75-78°C/0.5 torr. Compound (3) has approximately 90% purity on GLC, carbowax 20 M at 200°C; the remaining 10% is probably a stereoisomer since by catalytic hydrogenation only methyl nonanoate was detected on GLC.

	Ŀ	C-2	C-3	5 7	C-5	C-6	C-7	C-8	6-9
E-2-Hexenoic acid*	171.9	120.7	151.9	34.3	21.1	13.6			
				34,30	21.15	13,55**			
Sodium salt ***	176.5	128.4	146.4	35.1	22.8	14.9			
E-2-Heptenoic acid*	172.1	120.7	152.1	32.0	30.0	22.2	13.7		
				31.90	30.30	22.20	13,70**		
Sodium salt ***	175.9	128.5	145.4	32.6	31.7	23.4	15.0		
E-2-Octenoic acid*	172.2	120.5	152.2	32.2	27.5	31.3	22.4	14.0	
				32.20	27,80	31,35	22.20	13.95**	
Sodium salt ***	176.0	128.6	145.0	33.1	29.4	32.7	23.0	14.9	
E-2-Nonenoic acid*	172.0	120.6	1519	32.2	27.8	28.8	31.5	22.5	13.8
				32.20	28.05	28.85	31.50	22.60	14.05**
Sodium salt ***	175.8	128.7	144.8	33.1	29.7	30.1	32.8	23.8	15.0
* The spectra were re values are in ppm d	corded on a V ownfield from	arian XL-100 TMS.	-15 spectron	neter at 25.2	MHz in the]	Fourier transfo	rm mode and ir	n CDCl ₃ solutio	ns. The δ

Table 1

** Calculated values according to ref. 17.
*** In D₂O solutions having 0.1% of DMSO as internal reference, 6(TMS) = 6(DMSO) + 40.5 ppm.

	C-I	C-2	C-3	0 4	C-5	C-6	C-7	6 8 C	6-)
E,E-2,4-Hexadienoic acid***	169.9	118.3	145.8	129.8	139.4	18.0			
Sodium salt**	176.0	127.3	142.1	131.4	138.0	19.6			
E,E-2,4-Hepadienoic acid*	172.6	118.3	147.3	127.2	147.2	26.0	12.7		
Sodium salt **	176.6	127.3	142.6	129.1	144.9	27.0	14.2		
E,E-2,4-Octadienoic acid*	172.5	118.3	147.1	128.2	145.5	35.0	21.8	13.5	
Sodium salt**	175.6	128.0	141.7	130.4	141.5	35.9	23.1	14.7	
E,E-2,4-Nonadienoic acid*	172.8	118.2	147.3	128.0	145.9	32.7	30.7	22.2	13.8
Sodium salt*	175.4	128.2	141.6	130.3	141.3	33.4	32.0	23.2	14.9
* The spectra were recorded c	on a Varian X	L-100-15 spe	ctrometer at	t 25.2 MHz ii	1 the Fourier	transform n	ode and in C	DCI, solutior	ıs. The δ
values are in ppm downfield	d from TMS.							,	
** In D O solutions having 0 1			(L) 3		2 27 - 20				

Table 2

** In D₂O solutions having 0.1% of DMSO as internal reference; 6(TMS) = 6(DMSO) + 40.5 ppm.
*** In CDCl₃ solution containing some methanol.

amine at room temperature, the corresponding 3,5-hexadienoic ester was obtained as sole reaction product in 72% yield. By using cyclopentanol and isopropanol the respective unconjugated esters were also obtained, although in lower yield (46%). With methanol, however, a 1 : 1 mixture of conjugated and unconjugated methyl esters was shown to be the product in 54% yield (GLC and ¹H NMR).

In order to study this reaction*, which can be explained by an addition of the alcohol to an intermediate unsaturated ketene, from the point of view of the stereochemistry of the isomerized double bonds, a careful analysis of the methylene region of the ¹³C NMR spectrum of the ester obtained from E,E-2,4-octadienoic acid and cyclopentanol was carried out.

By reaction of E,E-2,4-octadienoyl chloride with cyclopentanol in triethylamine an approximately 1 : 1 mixture of stereoisomeric Δ 3,5-esters (GLC and ¹H NMR) was obtained in 85% yield. The ¹³C NMR spectrum of this mixture showed methylene signals at 20.9, 25.4, 38.2 and 38.4 ppm. The signals at 38.4 and 38.2 ppm, which were assigned to C-2 and the ones at 20.9 and 25.4 ppm assigned to C-7, show that it was a mixture of E,Z-3,5- and E,E-3,5- octadienoic esters, respectively, on the basis of the known shielding effect of an allylic carbon of a Z-disubstituted double bond. This was further confirmed since isomerization with iodine [10] gave a product where mainly the signals corresponding to the E,E-isomer were observed**.

Acknowledgements

We thank the World Health Organization and FINEP, Financiadora de Estudos e Projetos, for financial support and Professor E. Wenkert for helpful suggestions and encouragement. N.F. thanks CAPES for a fellowship, and C.L.P.S. thanks U.F.F. for a leave of absence and CAPES for a fellowship.

References

- [1] J. Tsuji, H. Nagashima, T. Takahasi and K. Masaoka, Tetrahedron Lett. (1977) 1917
- [2] M. Jacobson, I. Keiser, D.L. Chambers, D.H. Miyashita and C. Harding, J. Med. Chem. 14 (1971) 236
- [3] J.H. MacMillan and S.S. Washburne, Org. Magn. Resonance 6 (1974) 250

^{*} For other procedures of deconjugation of methyl sorbate see K. Torssell, Tetrahedron Lett. (1974) 623, and for deconjugation of unsaturated acids P.E. Pfeffer and L.S. Gilbert, J. Org. Chem. 36 (1971) 3290.

^{**}The ¹³C NMR spectrum of the stereoisomeric mixture of cyclopentyl-3,5-octadienoates in CDCl₃ solution showed the following signals: 13.4, 14.1, 20.9, 23.6, 25.4, 32.5, 38.2, 38.4, 77.0, 122.5, 124.7, 127.1, 128,5, 133.1, 133.5, 135.5, 170.9 and 171.0 ppm. After isomerization, and recording the spectrum also in CDCl₃ solution, the following signals were observed: 13.4, 23.6, 25.4, 32.5, 38.2, 77.0, 122.5, 128.5, 133.6, 135.6 and 171.0 ppm downfield from TMS.

- [4] F.D. Gunstone, M.R. Pollard, C.M. Scrimgeour and H.S. Vedanayagam, Chem. Phys. Lipids 18 (1977) 115, and references cited herein
- [5] J. Bus, I. Sies and M.S.F. Lie Ken Jie, Chem. Phys. Lipids 18 (1977) 130, and references cited therein
- [6] E. Lippmaa, T. Pehk, K. Anderson and C. Happe, Org. Mag. Resonance 2 (1970) 109
- [7] J. Bus, I. Sies and M.S.F. Lie Ken Jie, Chem. Phys. Lipids 17 (1976) 501
- [8] E. Wenkert, B.L. Buckwalter, I.R. Burfitt, M.J. Gasic, H.E. Gottlieb, E.W. Hagaman, F.M. Schell and P.M. Wovkulich, Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Naturally Occurring Substances, in: Topics in Carbon-13 NMR Spectroscopy, Vol. 2 (G.C. Levy, ed.) Wiley-Intersciences, New York, 1976
- [9] J.G. Batchelor, J.H. Prestegard, R.J. Cushley and S.R. Lipsky, J. Am. Chem. Soc. 95 (1973) 6358
- [10] W.D. Ceimer and I.A. Solomons, J. Am. Chem. Soc. 75 (1973) 3430.