

SODIUM SALT, SULFONATES AND CARBOXYLATES OF (*E*)- AND (*Z*)-3-(HYDROXYMETHYLENE)-5-METHYLDIHYDRO- -2(3*H*)-FURANONE

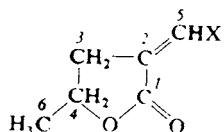
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In the solid state, sodium salt of 3-(hydroxymethylene)-5-methyldihydro-2(3*H*)-furanone can be prepared in the form of the (*Z*)-isomer, (*E*)-isomer or as a mixture of both isomers; in solutions the salt exists exclusively as the (*E*)-isomer. Reaction of the corresponding isomers of this sodium salt with sulfonyl or acyl chlorides afforded sulfonates or carboxylates derived from (*E*)- or (*Z*)-3-(hydroxymethylene)-5-methyldihydro-2(3*H*)-furanone. Configurations of the obtained isomeric sulfonates and carboxylates were confirmed by their ^1H and ^{13}C NMR spectra. Dihedral angles, calculated from the observed coupling constants, were used in the discussion of preferred conformation of the prepared compounds.

Recently, it has been found that, in the solid state, sodium salt of 3-(hydroxymethylene)dihydro-2(3*H*)-furanone (*I*) can be prepared both as the (*Z*)- and (*E*)-isomer and this fact has been utilized for preparation of isomeric (*E*)- and (*Z*)-3-(hydroxymethylene)dihydro-2(3*H*)-furanone sulfonates and carboxylates¹⁻⁴. We have now investigated to what extent these findings may be applied to the behaviour of sodium salt of 3-(hydroxymethylene)-5-methyldihydro-2(3*H*)-furanone (*II*). The sodium salt *II* was for the first time prepared by Korte and coworkers⁵ and used without isolation for further reaction. Vaidya and collaborators⁶ assigned (*Z*)-configuration to the sodium salt *II*, as well as to 3-(4-toluenesulfonyloxymethylene)-5-methyldihydro-2(3*H*)-furanone (*III*), prepared from it in aqueous acetone. The sodium salt *II* was used as nucleophile also in the preparation of synthetic analogues of strigol⁷.



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| <i>II</i> , X = ONa | <i>V</i> , X = C ₆ H ₅ CO ₂ |
| <i>III</i> , X = 4-CH ₃ C ₆ H ₄ SO ₃ | <i>VI</i> , X = CH ₃ SO ₃ |
| <i>IV</i> , X = C ₆ H ₅ SO ₃ | <i>VII</i> , X = CH ₃ CO ₂ |

We have found that, like the sodium salt *I*, the sodium salt *II* is polymorphous in the solid state, its polymorphism being due to configurational change at the C=C double bond. We proved three crystalline modifications of the sodium salt *II*: (Z), (E) and (E + Z). The (Z)-modification is obtained when the salt *II* is prepared according to ref.⁵ but at temperatures -20°C to -30°C . It is unstable and at room temperature it turns into the stable modification (E) (half-time in hours). The modification (E + Z), containing a variable admixture of modification (E), is formed in diethyl ether or toluene at room temperature or in boiling toluene and is very slowly converted into the modification (E) (half-time in months). These phase transitions can be considerably accelerated by heating to 110°C or suspending in a polar solvent such as acetone. Dissolution of any of the crystalline modifications of *II* e.g. in water, dimethyl sulfoxide or dimethylformamide leads immediately to the formation of the (E)-isomer. The structure of all modifications was proved by Debye-Scherrer diagrams (Table I); the population of the (E)- and (Z)-isomers was determined by IR spectra in nujol or dimethylformamide, where the (E)-(Z)-isomer mixture is characterized by strong absorption bands at 727, 770, 777 and 790 cm^{-1} and the (E)-isomer by a narrow doublet at 770 and 727 cm^{-1} . Both the configurational homogeneity and the (Z)-configuration of the salt prepared at -20°C to -30°C were confirmed by preparative results at -75°C ; its rapid isomerisation to the (E)-modification was shown, besides the powder diagrams, also by the fact that the salt, isolated at room temperature, reacted with 4-toluenesulfonyl chloride at -75°C to give a 9 : 1 mixture of (E)-*III* and (Z)-*III*. Configurational homogeneity of *II* in solutions was proved by the IR, ^1H and ^{13}C NMR spectra (Tables II and III), its (E)-configuration being identified by the preparative results. The presence of both configurations in the crystalline modification (E + Z) was confirmed by the IR spectra in nujol and by the preparative results: the isolated sodium salt *II*, prepared in boiling toluene, reacted with 4-toluenesulfonyl chloride at -75°C to afford a 2 : 3 mixture of (E)-*III* and (Z)-*III*.

We made use of these results for the preparation of pure sulfonates and carboxylates of (E)- and (Z)-3-(hydroxymethylene)-5-methyldihydro-2(3H)-furanone. A suspension of the sodium salt *II*, prepared at -20°C to -30°C essentially according to ref.⁵, reacted with 4-toluenesulfonyl, benzenesulfonyl and benzoyl chloride in acetone at -75°C to give pure (Z)-*III*, (Z)-3-(benzenesulfonyloxymethylene)-5-methyldihydro-2(3H)-furanone ((Z)-*IV*) and (Z)-3-(benzoyloxymethylene)-5-methyldihydro-2(3H)-furanone ((Z)-*V*), respectively. The salt *II* is a weaker nucleophile than the salt *I* and the isomer (Z)-*II* reacts with the mentioned sulfonyl chlorides and benzoyl chloride about five times more slowly than the salt (Z)-*I*. The reaction of the sodium salt (Z)-*II* with methanesulfonyl chloride in diethyl ether-acetone proceeds practically only above -50°C , however, its isomerization is faster and a mixture (6 : 1) of (E)-3-(methanesulfonyloxymethylene)-5-methyldihydro-2(3H)-furanone ((E)-*VI*) and (Z)-3-(methanesulfonyloxymethylene)-5-methyldihydro-2(3H)-furanone ((Z)-*VI*) is ob-

tained. Under the same conditions, the reaction with acetyl chloride gives pure (*E*)-3-(acetoxymethylene)-5-methyldihydro-2(3*H*)-furanone ((*E*)-*VII*). When treated for 30 minutes with the corresponding sulfonyl chlorides and acyl chlorides in aqueous acetone in the presence of triethylamine at room temperature, the salt *II* gives the pure sulfonates (*E*)-*III*, (*E*)-*IV*, (*E*)-*VI* and the carboxylates (*E*)-*V* and (*E*)-*VII*.

Configuration of the prepared sulfonates and carboxylates was again determined using chemical shifts of the vinyl protons and their coupling constants in the ^1H NMR spectra^{1,8} (Table II). In the spectra of (*E*)-isomers the vinyl proton signals are shifted

TABLE I

Diffraction angles (θ , deg), interplane distances (d , Å) and intensities (I) derived from powder diagrams of sodium salt of 3-(hydroxymethylene)-5-methyldihydro-2(3*H*)-furanone (*II*)

Mixture of (<i>E</i>) and (<i>Z</i>) ^a			(<i>E</i>) ^b			(<i>E</i> + <i>Z</i>) ^c		
2θ	d	I	2θ	d	I	2θ	d	I
—	—	—	13.8	6.41	8	—	—	—
—	—	—	—	—	—	18.5	4.79	12
19.0	4.67	16	—	—	—	—	—	—
—	—	—	22.0	4.04	4	22.0	4.04	8
—	—	—	24.0	3.70	4	—	—	—
—	—	—	—	—	—	24.5	3.63	20
25.0	3.56	20	—	—	—	—	—	—
—	—	—	26.0	3.43	4	—	—	—
—	—	—	—	—	—	27.3	3.26	8
—	—	—	28.0	3.18	4	—	—	—
—	—	—	—	—	—	29.5	3.03	8
31.0	2.88	20	31.0	2.88	20	31.0	2.88	12
—	—	—	32.5	2.75	8	—	—	—
35.2	2.55	12	—	—	—	—	—	—
—	—	—	35.5	2.53	12	35.5	2.53	8
—	—	—	37.8	2.38	8	—	—	—
—	—	—	—	—	—	38.7	2.33	4
42.3	2.13	12	—	—	—	42.4	2.13	8
—	—	—	46.3	1.96	8	—	—	—
—	—	—	49.8	1.83	8	—	—	—
53.8	1.70	16	53.8	1.70	16	53.8	1.70	12
—	—	—	59.0	1.57	4	—	—	—
—	—	—	67.3	1.39	4	—	—	—

^a Prepared according to ref.⁵ at -25°C and isolated at room temperature; ^b isolated from aqueous solution by azeotropic distillation with benzene; ^c prepared at room temperature according to ref.⁵ or in boiling toluene.

0.65–0.75 ppm downfield, their coupling constants being in the range 2.8–3.0 Hz (as compared with 2.2–2.3 Hz for the (Z)-isomers). In the ^{13}C NMR spectra of the prepared compounds (Table III) the chemical shifts of the C(1) and C(5) carbon signals are important: for the (E)-isomers they are shifted 3–4 ppm downfield. Our spectral and preparative results show that 3-(4-toluenesulfonyloxymethylene)-5-methyldihydro-2(3H)-furanone, described in ref.⁶, has the (E)-configuration.

The observed anisochronism of the diastereotopic hydrogen atoms H(3) and H(3') enabled us to study the conformation of the lactone ring in the synthesized compounds. The fact that the coupling constants $^4J_{\text{H}(5),\text{H}(3)}$ and $^4J_{\text{H}(5),\text{H}(3')}$ differ very little (mostly only within the limits of the digital resolution used) can be interpreted (as shown by data of Barfield and collaborators⁹) by practically identical dihedral angles C(5)—C(2)—C(3)—H(3) and C(5)—C(2)—C(3)—H(3'), as measured from the C(5)—C(6)—C(3) plane. The same may be concluded from the identical values of $^3J_{\text{C}(5),\text{H}(3)}$ and $^3J_{\text{C}(5),\text{H}(3')}$ in the ^{13}C NMR spectra. This, together with the calculated dihedral angles ϕ_1 (H(4)—C(4)—C(3)—H(3)) and ϕ_2 (H(4)—C(4)—C(3)—H(3')) (Table IV) agrees best with the preferred chair conformation (A) of the exomethylene lactone ring with isoclinal atoms H(3) and H(3'), an axial H(4) atom and an equatorial methyl group C(6)H(6)₃. A more detailed analysis of the fine ($^1J_{\text{C}(6),\text{H}(6)}$ coupling) and superfine (coupling across more than one bond) structure

TABLE II

^1H NMR Spectral data for compounds II–VII (in deuteriochloroform, chemical shifts δ , ppm^a, and coupling constants J , Hz^b)

Compound	δ_5	δ_4	δ_3	$\delta_{3'}$	δ_6	$^3J_{4,6}$	$^2J_{3,3'}$	$^4J_{5,3}$	$^4J_{5,3'}$	$^3J_{3,4}$	$^3J_{3,4'}$
(E)-II ^c	8.48	4.47	2.89	2.30	1.26	6.3	14.1	1.6	1.6	8.7	6.3
(E)-II ^d	8.43	^e	2.93	2.37	1.35	6.3	14.2	1.6	1.7	8.6	5.9
(E)-III	7.57	4.65	3.01	2.41	1.35	6.1	17.4	2.8	3.1	7.8	5.8
(Z)-III	6.92	4.58	2.99	2.47	1.34	6.3	16.0	2.0	2.5	7.4	6.5
(E)-IV	7.59	4.64	3.01	2.41	1.35	6.3	17.4	2.8	3.1	7.8	5.8
(Z)-IV	6.94	4.58	3.00	2.47	1.35	6.1	16.0	2.1	2.5	7.3	6.4
(E)-V	8.46	4.76	3.27	2.67	1.46	6.1	17.0	2.8	3.0	7.9	5.7
(Z)-V	7.81	4.69	3.12	2.60	1.44	6.3	15.8	2.1	2.4	7.4	6.4
(E)-VI	7.69	4.73	3.13	2.54	1.44	6.3	17.4	2.8	3.1	7.8	5.8
(Z)-VI ^f	6.94	—	—	—	—	—	—	2.2	2.2	—	—
(E)-VII	8.20	4.72	3.12	2.53	1.42	6.1	17.2	2.8	3.0	7.8	5.6

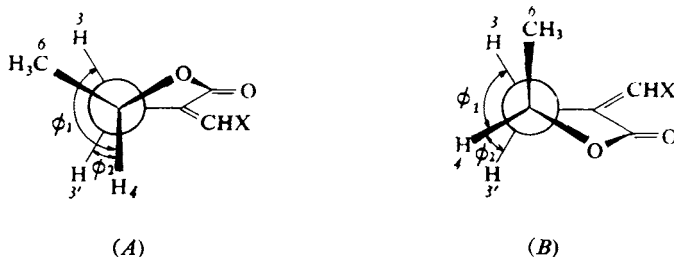
^a Experimental error ± 0.0025 ppm; ^b digital resolution 0.24 Hz; ^c in $^2\text{H}_2\text{O}$ -hexadeuterioacetone (1:2); ^d $^2\text{H}_2\text{O}$; ^e not measurable because of solvent signal; ^f measured as a 6:1 mixture of (E)-VI and (Z)-VI.

TABLE III
 ^{13}C NMR Spectral data for II—VII (in 0.75 mol l^{-1} solutions in deuteriochloroform, chemical shifts δ , ppm,^a coupling constants J , Hz^b)

Compound	δ_1	δ_2	δ_3	δ_4	δ_5	δ_6	$^1J_{\text{C}(4),\text{H}(4)}$	$^1J_{\text{C}(3),\text{H}(3)}$	$^3J_{\text{C}(5),\text{H}(3),\text{H}(3')}$
(E)-II ^c	178.7	93.1	32.6	74.5	172.9	22.6	153.1	133.3	1.0
(E)-II ^d	181.7	96.5	33.9	77.9	174.6	24.0	—	—	—
(E)-III	169.6	114.8	31.6	74.8	142.8	21.9	154.0	135.7	4.7
(Z)-III	165.7	114.0	32.8	74.2	139.0	21.5	153.1	136.2	4.7
(E)-IV	160.5	115.1	31.6	74.8	142.6	21.9	153.1	135.7	4.7
(Z)-IV	165.7	114.2	32.8	74.3	138.9	21.5	153.1	132.8	4.7
(E)-V	170.7	112.1	31.9	74.7	142.3	22.2	152.1	135.2	4.2
(Z)-V	167.1	110.5	32.9	74.2	139.2	21.7	154.0	134.8	4.3
(E)-VI	169.6	114.7	31.7	75.0	142.4	22.0	154.0	136.2	4.7
(E)-VII	170.7	111.4	31.8	74.6	142.0	22.1	153.1	135.7	4.7

^a Experimental error ± 0.04 ppm; ^b digital resolution 0.94 Hz; ^c in $^2\text{H}_2\text{O}$ -hexadeuterioacetone (1 : 2); ^d in $^2\text{H}_2\text{O}$.

of the ^{13}C NMR spectra shows that for all the prepared sulfonates and carboxylates the superfine structure signals due to the C(6) atom have character of doublet of doublets with coupling constants of about 3 and 6 Hz. According to a selective decoupling of the H(4) signal, carried out for (Z)-V, the larger coupling constant is due to the $^2J_{\text{C}(6),\text{H}(4)}$ coupling which means that the C(6) atom interacts with only one of the H(3) and H(3') atoms. Selective decoupling of the H(3) and H(3') signals revealed that the interacting atom is the H(3) proton, defined in A. As follows from the dependence of vicinal coupling constants $^3J_{\text{C,H}}$ on the dihedral angle¹⁰, such situation may exist only in the mentioned conformation (A) in which the dihedral angle



C(6)—C(4)—C(3)—H(3) is about 35° (large $^3J_{\text{C,H}}$ value) whereas the dihedral angle C(6)—C(4)—C(3)—H(3') is about 80° (minimum value of $^3J_{\text{C,H}}$). In the inverted conformation (B) with an axial methyl group C(6)H(6)₃, the C(6)—C(4)—C(3)—H(3) angle is about 30° and the C(6)—C(4)—C(3)—H(3') angle about 145° and thus both the coupling constants $^3J_{\text{C}(6),\text{H}(3)}$ and $^3J_{\text{C}(6),\text{H}(3')}$ should be of measurable magnitude.

On the basis of this consideration we assume that the suggested form (A) may be regarded as the sole conformation.

TABLE IV

Calculated dihedral angles ϕ_1 (H(4)—C(4)—C(3)—H(3)) and ϕ_2 (H(4)—C(4)—C(3)—H(3')) (deg)

Compound	ϕ_1	ϕ_2	Compound	ϕ_1	ϕ_2
(E)-II	158.0	40.0	(E)-V	151.2	44.0
(E)-III	150.4	43.4	(Z)-V	147.4	39.4
(Z)-III	147.4	38.8	(E)-VI	150.4	43.4
(E)-IV	150.4	43.4	(E)-VII	150.4	44.7
(Z)-IV	146.8	39.3			

EXPERIMENTAL

The temperature data are uncorrected. The ^1H and ^{13}C NMR spectra were measured on a Tesla BS 567 instrument at 100.034 MHz and 25.156 MHz respectively, using hexamethyldisiloxane or sodium 4,4-dimethyl-4-silapentanesulfonate as internal standard. The chemical shifts are related to tetramethylsilane as the internal standard. All the coupling constants $J_{\text{H,H}}$ except $J_{\text{H(4),H(6)}}$ were evaluated by simulation of AB spectrum of hydrogen atoms H(3) and H(3') using the LAOCN program. In all cases the differences between the experimental and simulated chemical shifts were smaller than the digital resolution. The IR spectra were measured on a Zeiss UR 20 spectrometer in nujol mull or dimethylformamide solution. Debye-Scherrer diagrams were obtained using a chamber of 57.3 mm diameter, Cu α K radiation, 40 kV, 30 mA, exposition 16 h. The diagrams were measured with a comparator, the low accuracy (0.1 mm) being due to diffuse diffraction lines. The dihedral angles Φ_1 and Φ_2 were calculated according to Janowski¹¹ using the relationships (1) and (2).

$$^3J_{\text{H(4),H(3)}} = 8.79 \cos^2 \Phi_1 + C \quad (1)$$

TABLE V

Sulfonates and carboxylates of (*E*)- and (*Z*)-3-(hydroxymethylene)-5-methyldihydro-2(3*H*)-furanone

Compound (yield, %)	M.p., °C (solvent)	Formula (mol.wt.)	Calculated/Found	
			% C	% H
(<i>E</i>)-III (45)	61—62 (CCl ₄) ^a	C ₁₃ H ₁₄ O ₅ S (282.3)	55.31 55.13	5.00 4.79
(<i>Z</i>)-III (60)	125—127 (C ₂ H ₅ OH—H ₂ O (4 : 1)) ^a	C ₁₃ H ₁₄ O ₅ S (282.3)	55.31 55.27	5.00 4.87
(<i>E</i>)-IV (60)	oil —	C ₁₂ H ₁₂ O ₅ S (208.3)	53.72 53.79	4.51 4.48
(<i>Z</i>)-IV (50)	70—72 (C ₂ H ₅ OH)	C ₁₂ H ₁₂ O ₅ S (268.3)	53.72 53.46	4.51 4.36
(<i>E</i>)-V (50)	113.5—114 (C ₆ H ₆)	C ₁₃ H ₁₂ O ₄ (232.2)	72.45 72.11	5.21 5.04
(<i>Z</i>)-V (65)	128—129 (C ₆ H ₆)	C ₁₃ H ₁₂ O ₄ (232.2)	72.45 72.39	5.21 5.07
(<i>E</i>)-VI (60)	81—82 (CH ₃ OH)	C ₇ H ₁₀ O ₅ S (206.2)	40.77 40.58	4.89 4.81
(<i>E</i>)-VII (45)	^b	C ₈ H ₁₀ O ₄ (170.2)	56.46 56.30	5.92 5.85

^a Cf. ref.⁶; ^b b.p. 114°C/660 Pa, n_D^{20} 1.4838.

$$^3J_{H(4),H(3')} = 8.79 \cos^2 \Phi_2 + C, \quad (2)$$

where $C = 0.004(^1J_{C(3),H(3)} + ^1J_{C(4),H(4)})$.

The starting 5-methyldihydro-2(3H)-furanone was prepared by reduction of sodium levulinate with sodium borohydride followed by cyclization¹².

(E + Z)-Modification of Sodium Salt II

A suspension, prepared according to ref.⁵ or in boiling toluene, was filtered and the solid was dried under diminished pressure; yield 75–85% of the sodium salt II. IR Spectrum (nujol): 727, 770, 777 and 790 cm^{-1} . Reaction with 4-toluenesulfonyl chloride at -75°C in diethyl ether–acetone mixture (1 : 1) afforded a 2 : 3 mixture of (E)-III and (Z)-III.

(E)-Modification of Sodium Salt II

The title compound was prepared by heating the (E + Z)-modification of sodium salt II to 110°C for 42 h or by azeotropic dehydration with benzene of an aqueous solution of II. IR Spectrum (nujol): 770, 777 cm^{-1} ; (dimethylformamide): 770, 777 cm^{-1} .

Sulfonates and Carboxylates of (Z)-3-(Hydroxymethylene)-5-methyldihydro-2(3H)-furanone (Z)-III, (Z)-IV and (Z)-V

A solution of 5-methyldihydro-2(3H)-furanone (4.3 g; 0.043 mol) and ethyl formate (3.7 g; 0.050 mol) in diethyl ether (20 ml), pre-cooled to -25°C , was added in one portion to a suspension of sodium (1.0 g; 0.043 mol) in diethyl ether (100 ml) cooled to -25°C . The mixture which gradually deposited a yellowish precipitate of the sodium salt of II was stirred at -20°C to -30°C for 60 h, cooled to -75°C and mixed with a cold (-75°C) solution of the corresponding sulfonyl or acyl chloride (0.043 mol) in acetone (100 ml). After stirring and cooling for 10 h, the mixture was left to attain room temperature, taken down under diminished pressure and shaken with water (100 ml). Solid products were filtered, washed with water, dried under diminished pressure and crystallized, liquid products were extracted with chloroform, the extract was dried over sodium sulfate, filtered, taken down under diminished pressure and the residue was crystallized or distilled *in vacuo*. Thus, methanesulfonyl chloride afforded a 6 : 1 mixture of the corresponding sulfonates (E)-VI and (Z)-VI which was not further separated, acetyl chloride gave pure (E)-VII. For physico-chemical characteristics of the prepared sulfonates and carboxylates see Table V.

Sulfonates and Carboxylates of (E)-3-(Hydroxymethylene)-5-methyldihydro-2(3H)-furanone (E)-III, (E)-V, (E)-VI and (E)-VII

The sodium salt II (1.5 g; 0.01 mol) was dissolved in water (10 ml) with triethylamine (1 g; 0.01 mol) and the solution was diluted with acetone (20 ml). The corresponding sulfonyl or acyl chloride (0.01 mol) was added in one portion either neat (if liquid) or as a solution in a mixture of acetone (15 ml) and water (7.5 ml) (if solid). After stirring for 30 min, the mixture was concentrated under diminished pressure and the residue was mixed with water (50 ml).

Solid products were filtered, washed with water, dried *in vacuo* and crystallized, liquid products were taken up in chloroform, the extracts were dried over sodium sulfate, filtered, concentrated under diminished pressure and the residue was crystallized or distilled *in vacuo*. Properties of the prepared sulfonates and carboxylates are given in Table V.

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