8-ACYL-7-PHENYLBICYCLO[2.2.2]-2,6-DIONES BY REARRANGEMENT OF 3-ACYLOXY-5-(2-PHENYLETHENYL)-2-CYCLOHEXEN-1-ONES. ^{1}H AND ^{13}C NMR SPECTRAL EVIDENCE OF THEIR STRUCTURE

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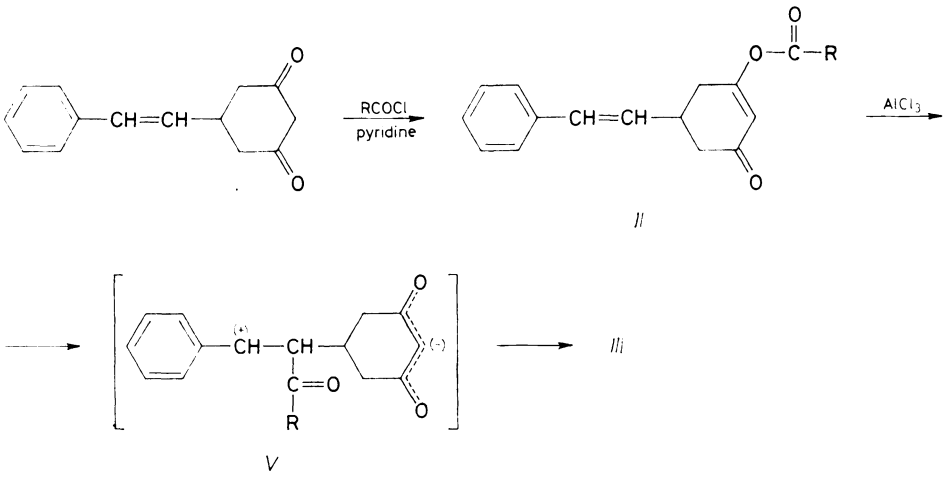
3-Acyloxy-5-(2-phenylethenenyl)-2-cyclohexen-1-ones *II* were prepared by O-acylation of 5-(2--phenylethenenyl)-1,3-cycloxanedione (*I*). Treatment of *II* with $AlCl_3$ resulted in rearrangement of the acyl group to the double bond of the phenylethenyl grouping followed by cyclization to 8-acyl-7-phenylbicyclo[2.2.2]octane-2,6-diones *III*. Their structure was evidenced by analysis of the ^{1}H and ^{13}C NMR spectral data.

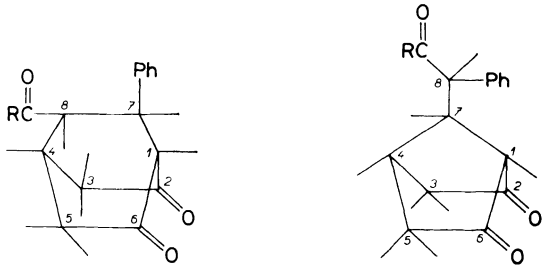
1,3-Dicarbonyl compounds can be acylated in position 2 either by a direct C-acylation or via O-acylation followed by rearrangement of the intermediate enol ester. The C-acylation products are obtainable from 1,3-diketones by a base-catalyzed reaction with acyl anhydrides at elevated temperatures[1,2], or by acylation with ketene[3]. Acylation of 1,3-hexanedione with acid chlorides in pyridine, or with acetic anhydride under catalysis with an acid takes exclusively place at oxygen[2,4,5]. Rearrangement of O-acyl derivatives to C-acyl ones can occur on treatment with Lewis acids[6], but also with imidazole or pyridine derivatives[7]. The latter procedure seems to be more economic[8] with derivatives of 1,3-cyclohexanedione provided acyl halides were used. We selected this method also for preparation of 2-acyl-5--(2-phenylethenyl)-1,3-cyclohexanedione. The O-acylation with acyl halides in chloroform in the presence of pyridine proceeded in high yields (85–92%) furnishing 3-acyloxy-5-(2-phenylethenyl)-2-cyclohexan-1-ones *II*; these compounds were rearranged with aluminium chloride in chloroform or 1,2-dichloroethane. The ^{1}H and ^{13}C NMR spectral data of the rearrangement products showed that the acyl group migrated to one of the carbon atoms of the phenylvinyl double bond and not to position 2 of the 1,3-cyclohexanedione system. Analysis of NMR spectra of the rearrangement products indicated that one product contains four sp^3 hybridized CH groups, and consequently, a possible involvement of cyclization under formation of bicyclic derivatives *III* or *IV*. An acceptable route leading to compounds *III* is illustrated in Scheme 1. Should compound *IV* be formed, the cyclization had to take place at the carbon atom adjacent to phenyl.



In formulae *II* - *V*: *a*, R = CH_3 *b*, R = C_2H_5 *c*, R = C_6H_5

SCHEME 1

Due mainly to the absence of a neutral correlation element of spectrum signals in the plain ^{13}C NMR spectra, the product could not unequivocally be identified. On the other hand, the ^1H–^1H spin–spin interaction in the ^1H NMR spectra enables us to correlate multiplets of protons localized from each other by few bands only and thus identify the skeleton of the molecule. Of most practical sense are interactions through two and three bonds (geminal and vicinal interactions) and the long-range ones of type W, ref.[9]. The greatest difference between the two structures suggested for the product was associated with the arrangement of bonds between C-1, C-8, C-7 and C-4; linear chain in *III* or branched one in *IV*. The 2D H and



H-COSY spectra[10,11] showed correlation peaks proving unambiguously the structure *III* (Fig. 1). Taking the signal of H-1 as reference one can simply identify signals

TABLE I

^{1}H NMR coupling constant values (Hz) for compound *IIIa*

Atom	J(A, B)[a]						
	H-8	H-7	H-5e	H-5a	H-4	H-3e	H-3a
H-1	1·8	—	—	—	—	—	—
H-3a	—	1·5	—	—	2·8	19·5	—
H-3e	—	—	3·1	—	2·9	—	
H-4	—	1	3·2	2·3	—		
H-5a	—	—	19·3	—			
H-5e	—	—	—				
H-7	7·7						

[a] The coupling constant values were obtained from standard ^{1}H NMR spectra, the FID was multiplied by a suitable weight function prior to FT in order to enhance the spectra resolution; digitalization of the spectra was 0·1 Hz per point, the accuracy of values presented is ±0·2 Hz.

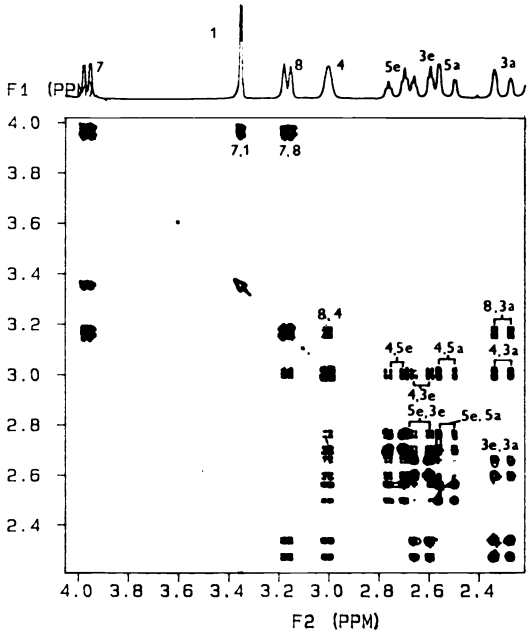


FIG. 1

The H–H DQ COSY spectrum of derivative *IIIa*

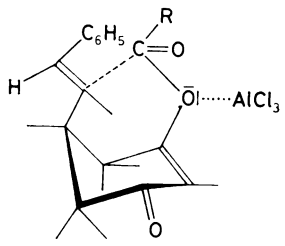
of H-7 and H-4. Protons H-7 and H-8 revealed two vicinal interactions, i.e. they have to be embodied in structure *III*, the skeleton of which is quite rigid. The RCO and phenyl groups affect the symmetry of six-membered rings C-1 – C-6, this being observed in the NMR spectra as a non-equivalence of positions 3 and 5 and also as a non-equivalence of carbonyls at C-2 and C-6.

The rigid structures have a well defined geometric arrangement of bonds, what makes it possible to ascribe all proton resonances. The crucial point for signal assignments was the identification of H-3a (a-pseudoaxial) according to its long-range interaction with H-7 of type W. The H-3 proton was in a strong geminal interaction with the H-3e (e-pseudoequatorial), which is in interaction with H-5e through a W-shaped bond system. The latter is in a strong geminal interaction with H-5a thus the identification of the whole proton system being solved. Proton H-4, revealing the most complicated multiplet, is in interaction with five protons H-3a, H-3e, H-5a, H-5e, and H-7. The coupling constant values for derivative R = $COCH_3$ are listed in Table I; those for the other two derivatives are equal within the measurement error and therefore, they were omitted. The ^1H and ^{13}C NMR chemical shift data are listed in Table II. The resonances of protonated carbons were identified by means of the H and C-COSY experiments[12]. Carbonyls were discerned by the selective transmission of coherence from H-3a and H-5a protons.

The presented spectral data do not allow to decide on the mutual orientation of H-7 and H-8. The coupling constant $J(7, 8) = 7{\cdot}7$ Hz holds for both dihedral angles 0° and 120° considering scattering of values for similar vicinal interactions. Therefore, the conformation of substituents at C-7 and C-8 was assigned from data for ^3J (H-7, C-2) and ^3J(H-7, C-6). Should H-7 be in a *trans* ($\varphi = 120°$) position to H-8, the bonds between H-7 and C-6 have to be in plane and therefore, it holds ^3J(H-7, C-6) > ^3J(H-7, C-2). On the other hand, bonds between H-7 and C-2 are in plane and consequently, ^3J(H-7, C-6) < ^3J(H-7, C-2). Values obtained from the selective INEPT 2D-J experiment[13] are: ^3J(H-7, C-2) = 5·1 Hz, ^3J(H-7, C-6) = 9·2 Hz. Substituents RCO and phenyl are, therefore, in a *trans* arrangement ($\varphi = 120°$) and as a result, the conformation of the whole molecule was unequivocally solved.

Rearrangement of *II* into *III* proceeds probably via the intermediate *V*, which has to be in an interaction with $AlCl_3$ present in the medium. The intermediate *V* does not undergo stabilization as is the case for a Fries rearrangement, i.e. by the loss of a proton from carbon to which an acyl was attached and by bonding the freed proton to oxygen from which acyl group had been detached; instead a bond was formed between the electrophilic and nucleophilic moieties of *V* to afford a bicyclo-[2.2.2]octane system. The finding that also a deacylated product *I* (25 – 30%) was obtained might indicate an intermolecular rearrangement of the acyl group to the ethenyl carbon under formation of *V*. Inspection of Dreiding models of *IIa* – *IIc* showed that the carbonyl carbon of the acyl group can enter into interaction with π-electrons of the ethenyl grouping prior to the cleavage of the oxygen–carbon bond

(structure *VI*), i.e. the intermediate *V* can be produced by an intramolecular rearrangement. Migration of acyl groups from oxygen to carbon of the phenylethenyl grouping could be explained by a lower electron density at the carbon atom in position 2 than at that of the phenylethenyl grouping due to interaction of compounds *IIa*–*IIc* with $AlCl_3$ through oxygen both of the acyl and carbonyl groups.



VI

TABLE II

^1H and ^{13}C NMR chemical shift values δ (ppm) for derivatives *IIIa*–*IIIc*

Position	*IIIa*		*IIIb*		*IIIc*	
	^1H	^{13}C	^1H	^{13}C	^1H	^{13}C
1	3·35	70·52	3·33	70·38	3·54	69·93
2	—	13·54	—	203·54	—	203·36
3a	2·31	38·57	2·30	2·26	2·26	38·19
3e	2·62		2·65		2·70	
4	3·01	30·43	2·96	30·52	2·91	32·00
5a	2·54	44·82	2·52	44·69	2·54	44·78
5e	2·73		2·72		2·87	
6	—	204·28	—	204·24	—	204·54
7	3·17	55·66	3·19	55·46	4·00	51·75
8	3·97	40·82	3·98	40·88	4·33	40·46
COR	—	206·59	—	209·49	—	198·49
Ph-1	—	140·37	—	140·22	—	140·22
Ph-2,6	7·06	127·15	7·06	126·90	7·1–8·2[b]	126·90
Ph-3,5	7·2–7·3[a]	129·19	7·2–7·3[a]	128·95	7·1–8·2[b]	128·95
Ph-4	7·2–7·3[a]	127·65	7·2–7·3[a]	127·41	7·1–8·2[b]	127·39
(R)CH_3	2·2	29·33	1·01	7·51	—	—
(R)CH_4	—	—	2·58[c]	35·21	—	—
			2·38[c]			

[a] Overlap of signals; [b] overlapped by COC_6H_5 proton signals; [c] AB multiplicity J (A, B) 17·9 Hz

Compounds *IIa*–*IIc* were synthesized from (*E*)-5-(2-phenylethenyl)-1,3-cyclohexanedione (*I*). The very *trans* arrangement of phenyl and 1,3-cyclohexanedion-5-yl groupings provides for compounds *II* a geometric system enabling an approach of the acyl carbonyl carbon to the ethenyl carbon. This geometry, as well as steric factors direct the stereospecific course of the rearrangement, in other words rearrangement afforded a single stereoisomer having the acyl and phenyl groups in a *trans* arrangement. It is worth noting that the rearrangement product to position 2 of the 1,3-cyclohexadienone system could not be traced even by a repeated chromatography; neither the presence of products stemming from an intermolecular interaction of electrophilic and nucleophilic centres of the intermediate *V* could be detected.

EXPERIMENTAL

The IR spectra of chloroform solutions were recorded with a Specord 75 IR (Zeiss, Jena) apparatus, the ^1H and ^{13}C NMR spectra of $CDCl_3$ solutions of compounds *IIa*–*IIc* were taken

TABLE III

Yields, analytical and spectral data of compounds *IIa*–*IIc* and *IIIa*–*IIIc*

Compound	M.p., °C Yield, %	Formula M.w.	Calculated/Found		IR spectrum, cm^{-1}	
			% C	% H	ν(C=O)	ν(C=C)
IIa	48–51[a] 89	$C_{16}H_{16}O_3$ 256·2	75·06 74·90	6·25 6·21	1 660 1 758	1 615
IIb	48–52[b] 92	$C_{17}H_{18}O_3$ 270·2	75·56 75·71	6·48 6·81	1 766 1 756	1 610
IIc	[c] 87	$C_{41}H_{18}O_3$ 318·3	79·23 78·94	5·65 5·91	1 650 1 730	1 610
IIIa	143–146 40	$C_{16}H_{16}O_3$ 256·2	75·06 74·83	6·25 6·31	1 748 1 738 1 726	
IIIb	105–108 45	$C_{17}H_{18}O_3$ 270·2	75·56 75·35	6·48 6·90	1 748 1 738 1 726	
IIIc	117–121 38	$C_{41}H_{18}O_3$ 318·3	79·23 78·81	5·65 6·10	1 746 1 720 1 705	

[a] After two weeks of standing in refrigerator, n_D = 1·5768; [b] ditto, n_D = 1·5700; [c] oil, n_D = = 1·6089.

with a Varian UXR-300 instrument operating at 300 and 75 MHz, respectively, and those of compounds *I* and *II* with a TESLA BS 487 spectrometer operating at 100 MHz, tetramethylsilane being the internal reference for all substances.

The starting (*E*)-5-(2-phenylethenyl)-1,3-cyclohexanedione (*I*) synthesized according to ref.[14] was prior to reaction recrystallized from acetonitrile; m.p. 182–183°C (ref.[14] does not report any m.p.).

3-Acyloxy-5-(2-phenylethenyl)-2-cyclohexan-1-ones (*IIa–IIc*)

Pyridine (1·74 g, 22 mmol) was added to a stirred solution of the diketone *I* (4·28, 20 mmol) in chloroform or 1,2-dichloroethane (100 ml) and then acyl chloride (22 mmol) was introduced within 20 min at 25°C. The mixture, after being stirred for additional 2 h at room temperature, was poured into 20% hydrochloric acid (30 ml), cooled to 0°C, the organic layer was separated, washed successively with water (30 ml), saturated aqueous sodium hydrocarbonate and water to neutral reaction and dried with $MgSO_4$. Products *IIa–IIc* obtained by removing the solvent are oily substances suitable for further use. The product for analysis was purified by column chromatography on silica gel with chloroform–hexane (20 : 1). Yields, IR spectra and analytical data are listed in Table III.

IIa. ^{1}H NMR spectrum: 2·20 s, 3 H (CH_3), 2·35–2·70 m, 4 H (CH_2); 2·80–3·30 m, 1 H (CH); 5·95–6·60 m, 3 H (CH=); 7·10–4·40 m, 5 H (C_6H_5).

IIb. ^{1}H NMR spectrum: 1·19 t, 3 H (CH_3, J = 7); 2·30–2·70 m, 5 H (C_6H_5).

IIc. ^{1}H NMR spectrum: 2·35–2·75 m, 4 H (CH_2); 2·85–3·30 m, 1 H (CH); 6·00–6·35 m, 3 H (CH=); 7·10–8·10 m, 10 H (C_6H_5).

8-Acyl-7-phenylbicyclo[2.2.2]octane-2,6-diones *IIIa–IIIc*

Aluminium chloride (3·41 g, 25·6 mmol) dissolved in a minimal amount of 1,2-dichloroethane was poured into stirred 1,2-dichloroethane (50 ml) cooled to −10°C. At this temperature acyl derivative *II* (12·8 mmol) was added to this solution (derivative *IIc* at 25°C) and stirring was continued for 2 h. The pasty interphase removed with the aqueous layer was extracted with 1,2-dichloroethane (3 × 15 ml) and added to the organic layer which was washed with water to a neutral reaction and dried with $MgSO_4$. The solvent was removed and the residue was purified by column chromatography on silica gel with chloroform–hexane (20 : 1) as eluent. The first fractions yielded compound *III*, the pasty product dissolved in acetone was chromatographed on silica gel, ethanol–chloroform being the eluent. The last fraction crystallizing from ethanol or acetonitrile afforded the diketone *I*. Yields, IR and analytical data of compounds *IIIa–IIIc* are presented in Table III, the ^{1}H and ^{13}C NMR spectral data in Table II.

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