ACRYLOYLOXY AND METHACRYLOYLOXY DERIVATIVES OF PHENYLACETIC ACID AND THEIR POLYMERS

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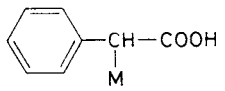
2-Methacryloyloxy-2-phenylacetic acid (*I*), 2-acryloyloxy-2-phenylacetic acid (*II*), 4-methacryloyloxyphenylacetic acid (*III*), and 4-acryloyloxyphenylacetic acid (*IV*), ethyl 4-methacryloyloxyphenylacetate (*V*) and ethyl 4-acryloyloxyphenylacetate (*VI*) were prepared. The new monomers were characterized by their melting points, IR, ^{1}H, and ^{13}C NMR spectra; their polymerization was also examined.

Earlier, we prepared high molecular mass analogs of 2-acetyloxybenzoic acid and 3-chloro-4-benzyloxyphenylacetic acid, and tested their pharmacological activity by treating an induced inflammation of a rat's limb[1,2]. Subsequently, six polymerizable analogs of phenylacetic acid *I* – *VI* with the antimicrobial and antimycotic effect[3] were prepared. We characterized these monomers and prepared their polymers. The latter will be used to study their pharmacological activity, especially their antimicrobial and antimycotic effect.

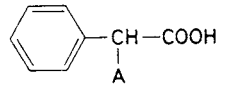
With the exception of acid *IV* which is ochre in colour, all monomers prepared in this study are colourless crystalline compounds. While the differences between the melting points of methacrylate and acrylate derivatives of acids from *I* to *IV* (Table I) reach almost 30°C, the difference between the melting points of esters *V* and *VI* is small. All monomers can be dissolved in alcohols, acetone, chlorinated aliphatic and aromatic hydrocarbons, diethyl ether, and 1,4-dioxane and do not dissolve in aliphatic hydrocarbons and water. Along with elemental composition (Table I), their assumed structure is confirmed also by the IR, ^{1}H NMR (Table II), and ^{13}C NMR spectra.

Table III summarizes data on the solution polymerization of monomers *I*, *II*, *III*, and *V* with 2,2′-azobis(isobutyronitrile) as initiator (In). The specific volume contraction, ΔV_{sp}, was calculated as the ratio of the final volume contraction and the mass of the isolated polymer. Using the value thus obtained, the recorded time dependences of contraction were recalculated to the conversion–time dependences which remained linear up to a 15% conversion. The polymerization rates were cal-

culated in mol dm^{-3} s^{-1} from the slopes at the beginning of these dependences. The data show, that the determined values of the rate of polymerization, R_p, and of the specific volume contraction of *II* in acetone and chloroform are very close, though in the chloroform solution the precipitation of the polymer of *II* occurred. Although the conditions of polymerization of all monomers were not the same, it is obvious that the ratio of R_p of monomers *I* and *II* to R_p of *III* and *V* increased more than merely the square root of the ratio of 2,2-azobis(isobutyronitrile) concentrations used.



I



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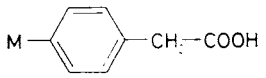

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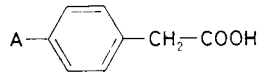

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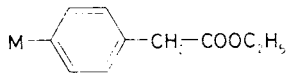

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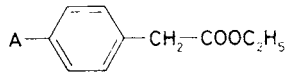
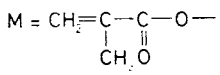
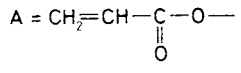


VI





Polymers of acids *I* to *IV* dissolve in acetone, alcohols, tetrahydrofuran, and in a mixture of diethyl ether with ethanol, but cannot be dissolved in aliphatic, aromatic or chlorinated hydrocarbons. The polymers of acids also dissolve in aqueous solutions of inorganic and organic bases, *e.g.* ammonia, alkali hydroxides and carbonates, pyridine, alkylamines or ethanol amines, from which they may be precipitated by acidifying with a mineral acid. Polymers of esters *V* and *VI* prepared in acetone are soluble in aromatic and chlorinated aliphatic solvents and insoluble in alcohols and aliphatic hydrocarbons.

Polymers of *IV* and *V* prepared in bulk were colourless, brittle, and crosslinked. Bulk polymer of *II* was light-brown, that of *VI* was colourless. Both polymers of *II* and *VI* were rubberlike and they only swelled in chloroform, tetrahydrofuran, and dimethylformamide.

TABLE I

Characteristics of acryloyloxy- and methacryloyloxyphenylacetic acids and their ethyl esters

Compound	Formula (rel. mol. mass)	M.p. °C	Found/calculated		Yield %
			% C	% H	
I	$C_{12}H_{12}O_4$ (220·22)	91–93	65·27 65·44	5·50 5·49	55·4
II	$C_{11}H_{10}O_4$ (206·19)	64–65	63·75 64·07	4·81 4·89	54·0
III	$C_{12}H_{12}O_4$	119–121	65·24 65·44	5·57 5·49	83·0
IV	$C_{11}H_{10}O_4$	79–80	63·85 64·07	4·99 4·89	82·2
V	$C_{14}H_{16}O_4$ (248·27)	35–36	67·43 67·72	6·61 6·49	79·8
VI	$C_{13}H_{14}O_4$ (234·24)	31–32	66·52 66·65	6·14 6·02	81·2

TABLE II

^{1}H NMR chemical shifts of monomers *I* to *VI* (in ppm with respect to the internal standard HMDS; relative intensities are given in brackets; s — singlet, t — triplet, q — quartet, m — multiplet)

Monomer	CH_3—	—CH_2—	—CH—	=CH_2 —CH=CH_2	CH aromatic	COOH
I	1·95(3) s	—	5·99(1) s	5·61(1) m 6·22(1) m	7·40(5) m	10·75(1) s
II	—	—	5·99(1) s	5·80–6·60(3) m	7·35(5) m	—
III	2·01(3) s	3·56(2) s	—	5·68(1) m 6·27(1) m	7·13(4) q	10·70(1) s
IV	—	3·57(2) s	—	5·90–6·60(3) m	7·13(4) q	10·10(1) s
V	1·18(3) t 1·98(3) s	3·55(2) s 4·11(2) q	—	5·65(1) m 6·27(1) m	7·13(4) q	—
VI	1·20(3) t	3·53(2) s 4·07(2) q	—	5·90–6·60(3) m	7·13(4) q	—

The intensive absorption bands in the IR spectra of acid *I* at 950 and 1 050 cm^{-1}, and of acid *II* at 980 and 1 040 cm^{-1} have virtually disappeared in the IR spectra of polymers of *I* and *II*. It is probable, therefore, that they belong to out-of-plane deformational vibrations of the C—H bonds of vinyl groups in *I* and *II*. The absorption bands in the range 1 400–1 410 cm^{-1} are more intensive in the spectra of monomeric acrylates *II*, *IV*, *VI* than in those of methacrylates *I*, *III*, *V* and of polymers of *II*. It is quite likely that the rise in the absorption of the acrylates is related to the planar deformational vibration of the =C—H bond in *II*, *IV*, *VI*. An intensive peak in the range 1 500–1 515 cm^{-1}, which appears in the spectra of both monomers and polymers, is probably due to the valence vibration of the aromatic C=C bonds[4]. Bands near 1 635 cm^{-1} are present in the spectra of all monomers, but not polymers. They may be attributed to the valence vibration of aliphatic C=C bonds. In the spectra of acids *III*, *IV* in the range 1 700–1 730 cm^{-1} two intensive peaks appear, which clearly belong to different carbonyl groups of the carboxylic group and of the acryloyloxy or methacryloyloxy groups. In the spectra of acids *I*, *II* and of ethyl esters *V*, *VI* the bands of both carbonyl groups overlap. The absorption bands of ethyl esters *V*, *VI* in the range 2 900–3 000 cm^{-1} may be assigned to the valence vibration of the C—H bonds of saturated carbon atoms. The broad absorption about 3 000 cm^{-1} in the spectra of monomer and polymer acids is probably due to the —COOH groups.

Chemical shifts of the ^1H NMR spectra of compounds from *I* to *VI* are given in Table II along with the relative line intensities and the type of splitting due to the spin–spin interaction between the adjacent ^1H nuclei. All these data are in agreement with the assumed structure of compounds from *I* to *VI*.

The structure of *I* and *II* was also checked by means of the ^{13}C NMR spectra.

TABLE III

Solution polymerization at 50°C: M monomer, In initiator, R_p polymerization rate, ΔV_{sp} specific volume contraction, $[\eta]$ limiting viscosity number of polymer

M	Solvent	[M]	[In]	$R_p \cdot 10^5$	ΔV_{sp}	$[\eta]$
		mol dm^3		mol dm^{-3} s^{-1}	cm^3 g^{-1}	
I	acetone	0·6	0·02	1·7	0·121	26
II	acetone	1·0	0·02	4·1	0·142	–
II	chloroform[a]	1·0	0·02	3·0	0·140	66
III	acetone	0·8	0·01	0·4	0·143	20
V	acetone	0·8	0·01	0·9	0·165	32

[a] Heterogeneous course of polymerization.

In the ^{13}C NMR spectra of *I* the following chemical shifts were identified (ppm): 16·18 (CH_3—), 72·28 (—CH—), 125·57 (CH_2=), 125·25, 126·90, 127·47 (CH aromatic), 131·34, 133·29 (=C—), and 164·59, 172·71 (CO). In the ^{13}C NMR spectra of *II* the following chemical shifts of lines (ppm) were detected: 72·07 (—CH—), 125·69 (=CH—), 125·30, 126·90, 127·47 (CH aromatic), 130·64 (=CH_2), 131·29 (=C—), and 163·45, 171·67 (CO). This assignment of lines in the ^{13}C NMR spectra was checked by means of ^{13}C NMR spectra with an unperturbed interaction between the ^{13}C and ^{1}H nuclei.

EXPERIMENTAL

Methods

Purity of the starting liquids was checked by means of a gas chromatograph CHROM 5 (Laboratorni přístroje, Prague, Czechoslovakia). The melting points were determined with a Mikroheiztisch Boëtius (F. Künstner, Dresden, G.D.R.). The ^{1}H NMR spectra of 10% solutions of monomers and polymers in C^2HCl_3 were recorded with a PS-100 JEOL spectrometer at 100 MHz, the FT ^{13}C NMR spectra were measured with an XL-200 Varian spectrometer at 50 MHz (acquisition time 1·60, pulse repetition time 5·60, 500 scans). The measurements were performed at room temperature using HMDS as the internal standard. The IR spectra of the monomers and polymers were recorded with a Perkin–Elmer 577 spectrometer using the KBr technique. The limiting viscosity numbers, $[\eta]$, of the polymers were obtained from measurements in tetrahydrofuran solutions with an Ubbelohde viscometer at 20°C.

Starting Compounds

2-Hydroxy-2-phenylacetic acid was prepared from monotopic dichloroacetophenone[5]; m.p. 118–119°C (benzene). 4-Hydroxyphenylacetic acid was prepared from 4-aminophenylacetic acid[6]; m.p. 149–150°C (water). Ethyl 4-hydroxyphenylacetate was prepared by acid esterification of 4-hydroxyphenylacetic acid[7]; b.p. 148–150°C/20 Pa; n_D^{20} 1·5222. Acryloyl chloride, b.p. 77–78°C, and methacryloyl chloride, b.p. 96–97°C (Fluka, A.G., Buchs, Switzerland) were redistilled at normal pressure in nitrogen and stabilized with copper(I) chloride. Methyl methacrylate was shaken with a 10% NaOH solution, washed with water, dried with calcium hydride and redistilled on a Vigreux column in nitrogen; the main fraction was 42°C/10 kPa. Styrene was purified by the same procedure; the main fraction 36°C/1·6 kPa. 2,2'-Azo-bis(isobutyronitrile) was recrystallized from ethanol, m.p. 105°C. Benzoyl peroxide was analyzed iodometrically (99·2%). The other liquids used were distilled prior to use. They were chromatographically pure.

Preparation of Monomers *I* to *VI* and their Polymerization

2-Methacryloyloxy-2-phenylacetic (I) *and 2-acryloyloxy-2-phenylacetic* (II) *acids*[8]: To a solution of 7·6 g (50 mmol) of 2-hydroxy-2-phenylacetic acid, 5 mg of hydroquinone and 5·75 g of methacryloyl chloride (55 mmol) in 25 cm^3 of 1,4-dioxan cooled with ice-cold water a solution of 5·6 g (55 mmol) of triethyl amine in 15 cm^3 of dioxan was added with stirring within 20 min. After that, the mixture was stirred at room temperature for one hour, then at 50°C for 15 min, and eventually it was poured into 250 cm^3 of water. The solution in water was extracted five times with 10 cm^3 of benzene. The joined extracts in benzene were gradually extracted with 15 cm^3 of 10% hydrochloric acid and twice with 15 cm^3 of water. After that, they were separated, dried

with anhydrous sodium sulfate, and solvents were removed from them by distillation at reduced pressure. The residue was dissolved in 50 cm^3 of benzene, and the solution was extracted with an aqueous solution of 8·4 g $NaHCO_3$ (100 mmol) in 100 cm^3 of water. After bubbling with nitrogen for 10 min, the alkaline aqueous solution was acidified with a solution of 10 cm^3 of conc. hydrochloric acid in 25 cm^3 of water. The oily acid *I* that separated from solution crystallized by the following day; 6·1 g (27·7 mmol), m.p. 84—89°C. Crystals dried in an evacuated desiccator over a mixture of solid NaOH and anhydrous $CaCl_2$ were reprecipitated twice from benzene solution with a fivefold volume of hexane (Table I). Acid *II* was prepared from 50 mmol of 2-hydroxy-2-phenylacetic acid and acryloyl chloride by a similar procedure. Yield 27 mmol (Table I).

4-*Methacryloyloxyphenylacetic* (III) *and* 4-*acryloyloxyphenylacetic* (IV) *acids*[9]: To a solution of 1 g (6·57 mmol) of 4-hydroxyphenylacetic acid and a crystal of hydroquinone in 7% aqueous solution of 0·54 g (13·5 mmol) NaOH cooled to −10°C, 0·77 cm^3 (7·9 mmol) of methacryloyl chloride was added, and the mixture was vigorously shaken. After 3 min the methacryloyl chloride phase disappeared, and the reaction mixture was clear. After further 5 min it became turbid and frothy. It was diluted with a solution of 0·34 g of sodium bicarbonate in 12 cm^3 of water and shaken for another 10 min. After that, the mixture was filtered and the filtrate was acidified with a solution of 1·2 g of conc. hydrochloric acid (12 mmol HCl) in 3 cm^3 of water. The white precipitate of acid *III* was removed by filtration, washed twice with 3 cm^3 of water and dried in the air; 1·2 g (5·45 mmol). The crystals were reprecipitated twice with water from methanol solution (Table I). Acid *IV* was prepared from 6·57 mmol of 4-hydroxyphenylacetic acid, and acryloyl chloride by employing a similar procedure; yield 1·11 g (5·4 mmol).

Ethyl 4-*methacryloyloxyphenylacetate* (V) *and ethyl* 4-*acryloyloxyphenylacetate* (VI): To a solution of 9 g (50 mmol) of ethyl 4-hydroxyphenylacetate and 5·6 g (60 mmol) of triethylamine in 20 cm^3 of dry tetrahydrofuran (THF) cooled with ice-cold water, a solution of 10·45 g (100 mmol) of methacryloyl chloride in 15 cm^3 THF was added dropwise with stirring, and the mixture was stirred at room temperature for 2 h. The precipitated triethylamine hydrochloride was filtered off, and the solvent was removed from the filtrate in the vacuum of the water pump by distillation. The distillation residue was diluted with 20 cm^3 of ether, the ether solution was shaken twice with water and three times with a 0·6M-$NaHCO_3$ solution, separated and dried with anhydrous sodium sulfate. Ether was then removed by distillation, the yellow oily residue was diluted with 15 cm^3 of methanol, and the methanolic solution was poured into 50 cm^3 of distilled water. Ester *V* recrystallized from solution in the refrigerator; 0·9 g (39·9 mmol). The crystals were reprecipitated twice from the methanolic solution with water (Table I). Ester *VI* was prepared similarly from 50 mmol of ethyl 4-hydroxyphenyl acetate and acryloyl chloride; yield 9·5 g (40·6 mmol).

Polymerization[10,11]: The solution polymerization of *I*, *II*, *III*, and *V* took place at 50°C in dilatometers c. 8 cm^3 in an acetone solution with 2,2′-azobis(isobutyronitrile) as initiator; *II* was polymerized under the same conditions in a chloroform solution. The polymers of acids *I*, *II*, and *III* were precipitated from the mixture with benzene, the polymer of ester *V* was precipitated with methanol. The polymers were precipitated from acetone by using the same precipitants and dried to constant mass in an evacuated desiccator.

Monomers *II*, *IV*, *V*, and *VI* were polymerized in bulk in glass ampoules with dibenzoyl peroxide (1% with respect to monomer) as initiator. The ampoule with *II* and *IV* was heated to 80°C for 24 h, the ampoules containing *V* and *VI* were heated to 50°C for 48 h.

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