PREPARATION AND SPECTRAL PROPERTIES OF IMIDAZO- AND TRIAZOLOQUINOLINES WITH ANGULAR RING FUSION

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Received July 22nd, 1987

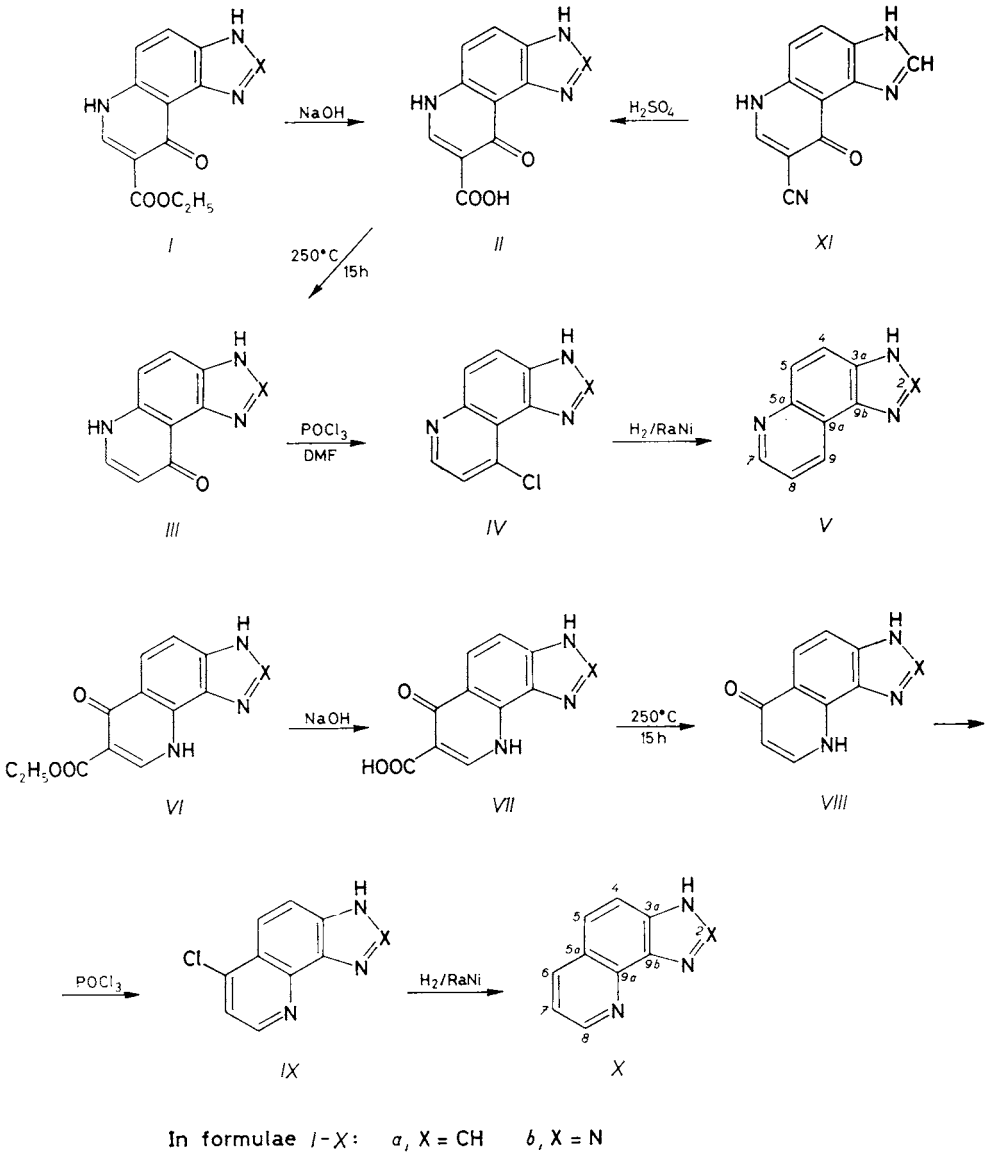
The imidazo- and triazolo[4,5-*f*]quinolines (*Va*, *Vb*) and imidazo- and triazolo[4,5-*h*]quinolines (*Xa*, *Xb*) have been synthetized by the Gould–Jacobs reaction starting from the quinolinecarboxylic acids *II* and *VII* prepared by base-catalyzed hydrolysis of the esters *I* and *VI*, resp. The decarboxylation of the acids *II* and *VII* gives the quinolones *III* and *VIII*, resp., which are aromatized to the corresponding chloroquinolines *IV* and *IX*. The latter compounds give the azoloquinolines *V* and *X* on catalytic reduction. The structure of the condensed heterocyclic compounds with angular ring fusion has been proved by ^{1}H and ^{13}C NMR, IR, UV, and mass spectra.

Imidazo[4,5-*f*]quinoline *Va* and triazolo[4,5-*f*]quinoline *Vb* were synthetized by the Skraup reaction from 5-aminobenzimidazole[1] and 5-aminobenzotriazole[2], by the reaction of 5,6-diaminoquinoline with formic acid[3,4], and by basic hydrolysis of the 2-trifluoromethyl derivative[5]. The analogous synthesis from the starting 7,8-diaminoquinoline via 2-trifluoromethyl derivative gave imidazo[4,5-*h*]quinoline[5] *Xa*. Triazolo[4,5-*h*]quinoline *Xb* was isolated from mother liquors after diazotization of 8-tosylamino-5,7-diaminoquinoline in the presence of cupric sulphate and trisodium arsenite[6].

The reaction of 5-aminobenzimidazole with diethyl 2-ethoxymethylenpropanedioate and subsequent cyclization of the product under the conditions of the Gould–Jacobs reaction (boiling at 250°C in the inert medium of Dowtherm) gave angular anelated 8-ethoxycarbonyl-9-oxo-6,9-dihydroimidazo[4,5-*f*]quinoline[7,8] *Ia*. The preparation of analogous triazolo[4,5-*f*]quinoline from 5-aminobenzotriazole is described in a patent[9].

In the present work we have examined the possibility of synthesis of non-substituted angular-ring-fused skeletons of the azoloquinolines *V* and *X* (Scheme 1) by application of the Gould–Jacobs reaction and subsequent removal of the functional groups from ethyl esters *I* and *VI* (ref.[11]). The base-catalyzed hydrolysis of *I* and *VI* gave the corresponding acids *II* and *VII* in high yields. The acid *IIa* was also prepared by acid-catalyzed hydrolysis of the nitrile *XI*, but the yield was lower and the reaction needed a longer time.

The decarboxylation of acids *II* and *VII* (15 h heating at 250°C in quinaldine under argon) gave the azoloquinolones *III* and *VIII*, resp. Their chlorination with phosphoryl trichloride in dimethylformamide gave the chloroazoloquinolines *IV* and *IX*, resp., which were submitted to hydrogenation on the Raney nickel catalysts to give the non-substituted skeletons of the azoloquinolines *V* and *X*, resp.



In formulae *I*–*X*: *a*, X = CH *b*, X = N

SCHEME 1

TABLE I

The azoloquinolines *II*—*V*, *VII*—*X*

Compound	Formula mol. mass	M.p., °C (yield, %)	Calculated/found			
			% C	% H	% N	% Cl
IIa	$C_{11}H_7N_3O_3$	312—314[a]	57·65	3·08	18·33	—
	229·2	(99)	57·69	3·02	18·29	
IIb	$C_{10}H_6N_4O_3$	>400	52·18	2·63	24·34	—
	230·2	(85)	52·16	2·53	24·22	
VIIa	$C_{11}H_7N_3O_3$	296—303	57·65	3·08	18·33	—
	229·2	(86)	57·68	2·92	18·02	
VIIb	$C_{10}H_6N_4O_3$	>400	52·18	2·63	24·34	—
	230·2	(93)	52·06	2·56	24·51	
IIIa	$C_{10}H_7N_3O$	375—379[a]	64·86	3·81	22·69	—
	185·2	(92)	64·93	3·60	22·31	
IIIb	$C_9H_6N_4O$	>400	58·06	3·25	30·09	—
	186·2	(93)	57·83	3·09	30·22	
VIIIa	$C_{10}H_7N_3O$	353—357	64·86	3·81	22·69	—
	185·2	(96)	64·68	3·68	22·58	
VIIIb	$C_9H_6N_4O$	>400	58·06	3·25	30·09	—
	186·2	(84)	57·93	3·19	30·01	
IVa	$C_{10}H_6N_3Cl$	>400[a]	58·98	2·97	20·64	17·41
	203·6	(46)	59·12	3·06	20·47	17·21
IVb	$C_9H_5N_4Cl$	>400	52·83	2·46	27·38	17·33
	204·6	(95)	53·02	2·38	27·23	17·31
IXa	$C_{10}H_6N_3Cl$	>400	58·98	2·97	20·64	17·41
	203·6	(48)	59·12	2·97	20·55	17·28
IXb	$C_9H_5N_4Cl$	>400	52·83	2·46	27·38	17·33
	204·6	(39)	52·80	2·42	27·40	17·20
Va	$C_{10}H_7N_3$	212—214	70·99	4·17	24·84	—
	169·2	(56)	71·16	4·13	24·66	
Vb	$C_9H_6N_4$	242—244	63·52	3·55	32·92	—
	170·2	(52)	63·54	3·50	32·90	
Xa	$C_{10}H_7N_3$	209—212	70·99	4·17	24·84	—
	169·2	(49)	71·09	4·06	24·69	
Xb	$C_9H_6N_4$	240—244	63·52	3·55	32·92	—
	170·2	(38)	63·64	3·44	32·89	

[a] Ref.[7]: *IIa* m.p. 310°C, *IIIa* m.p. 368°C, *IVa* m.p. below 400°C.

TABLE II

The IR and UV spectra of compounds *II*—*V*, *VII*—*X*

Compound	$\tilde{\nu}$, cm^{-1}			λ_{max}, nm ($\log \varepsilon_{max}$, $m^2\ mol^{-1}$)[a]				
	ν(C=O)	γ(C—H)	ν(CH, NH)					
IIa[b]	1 630 1 700	800	2 840—3 415	—	255	—	317	330
IIb	1 635 1 720	810	3 000—3 500	—	260	—	329	342
VIIa	1 630 1 710	810	2 850—3 415	—	247	—	327	337
VIIb	1 635 1 720	830	3 050—3 350	—	246	—	322	336
IIIa[b]	1 640	800	3 055, 3 390	237 (3·42)	250 (3·42)	261 (3·14)	313 (3·03)	326 (3·03)
IIIb	1 645	830	2 840, 3 375	243 (3·30)	249 (3·30)	266 (3·00)	328 (2·95)	341 (3·00)
VIIIa	1 645	800	2 920, 3 400	234 (3·19)	259 (3·37)	267 (3·32)	314 (2·95)	328 (2·92)
VIIIb	1 640	815	2 740, 3 245	246 (3·32)	253 (3·34)	269 (3·14)	317 (3·10)	332 (3·10)
IVa	—	810	3 090, 3 440	217 (2·92)	255 (3·39)	—	—	—
IVb	—	845	2 750, 3 400	219 (3·34)	254 (3·76)	—	—	—
IXa	—	810	3 015, 3 410	222 (3·30)	253 (3·50)	—	—	—
IXb	—	850	3 060, 3 425	223 (3·17)	252 (3·37)	—	—	—
Va	—	805	2 780, 3 455	—	253 (3·47)	—	315 (2·60)	—
Vb	—	800	2 920, 3 440	—	251 (3·55)	—	288 (2·85)	—
Xa	—	830	3 080, 3 440	—	252 (3·47)	—	315 (2·52)	—
Xb	—	815	2 810, 3 440	—	252 (3·51)	—	288 (2·64)	—

[a] The saturated solutions were measured in the cases where no $\log \varepsilon$ values are given; [b] ref.[8]: *IIa* 1 730, 1 700, 3 000, and 3 500; *IIIa* 1 610, 2 900, and 3 400.

The azoloquinolines were prepared in an overall yield of 15–20% by a sequence of seven reactions starting from 4-and 5-nitrobenztriazole or benzimidazole[11] and involving the Gould–Jacobs reaction, the lowest yields being just those of the last two reaction steps. By the Skraup reaction we only obtained *Va* in a yield of 15% (ref.[1] gives 47%), by the cyclization of 1,2-diaminoquinolines we obtained, in a high yield, only *Va* from 5,6-diaminoquinoline, whereas the respective triazole derivative *Vb* could be obtained from 5,6-diaminoquinoline in a very low yield only, and the Skraup reaction starting from 5-aminobenzimidazole gave no *Vb* at all. The preparation of *Xa* and *Xb* involves the difficult synthesis of the starting 7,8-diaminoquinoline. From the facts given it follows that the synthesis of the non-substituted skeletons with application of the Gould–Jacobs reaction represents a suitable synthetic pathway to angular-ring-fused azoloquinolines (Table I).

TABLE III

The ^{1}H NMR spectra of compounds *II*–*V* and *VII*–*X*

Compound	Solvent[a]	H-2	H-4	H-5	H-7	H-8	H-6(9)	^3J(7, 8)
IIa	A	9·09 s	7·99 d	8·39 d	9·13 s	—	—	—
IIb	A	—	7·91 d	8·33 d	9·21 s	—	—	—
IIa	B	7·95 s	7·35 d	7·95 d	8·51 s	—	—	—
IIb	B	—	7·43 d	7·96 d	8·51 s	—	—	—
IIa	C	9·66 s	8·01 d	8·29 d	8·79 s	—	—	—
IIIa	B	8·06 s	7·46 d	7·77 d	8·15 d	6·38 d	—	6
IIIb	B	—	7·17 d	7·64 d	7·88 d	6·32 d	—	6
IIIa	C	7·95 s	7·33 d	7·70 d	7·94 d	6·14 d	—	6
IVa	C	8·43 s	7·71 d	7·85 d	8·74 d	7·71 d	—	5
IVb	C	—	7·94 d	8·23 d	8·85 d	7·86 d	—	5
Va	C	8·36 s	7·96 d	7·77 d	8·81 dd	7·55 dd	8·77 dd	4·5
Vb	C	—	8·01 d	7·54 d	8·72 dd	7·49 dd	8·83 dd	4·5
VIIa	A	9·19 s	8·00 d	8·48 d	—	9·24 s	—	—
VIIb	A	—	7·89 d	8·33 d	—	9·20 s	—	—
VIIa	B	8·23 s	7·82 d	8·13 d	—	8·80 s	—	—
VIIb	B	—	7·63 d	8·04 d	—	8·81 s	—	—
VIIIa	B	8·24 s	7·88 d	8·09 d	6·70 d	8·48 d	—	5·5
VIIIb	B	—	7·73 d	7·99 d	6·43 d	8·32 d	—	5·75
IXa	C	8·29 s	7·89 d	8·02 d	7·70 d	8·81 d	—	5
IXb	C	—	7·98 d	8·16 d	7·83 d	8·89 d	—	5
Xa	C	8·36 s	7·81 d	7·66 d	7·48 dd	8·89 dd	8·42 dd	4·5
Xb	C	—	8·03 d	7·81 d	7·65 dd	8·97 dd	8·50 dd	4·5

[a] A — CF_3COO^2H; B — $NaO^2H/^2H_2O$; C — hexadeuteriodimethyl sulphoxide.

The imidazo[4,5-*f*]quinoline *Va* was prepared independently by the modified Gould–Jacobs reaction and found identical with the products of the Skraup reaction[1] and with those of the cyclization of 5,6-diaminoquinoline with formic acid[3].

Compounds *V* and *X* exhibit the most intensive band at 253 nm, which represents a typical $\pi \rightarrow \pi^*$ transition of an aromatic system[10]. The imidazoloquinolines *Va* and *Xa* have their longest-wavelength band (of very low intensity) at 315 nm, whereas the isoelectronic triazoloquinolines *Vb* and *Xb* have their longest-wavelength band (appearing as an inflection) at 285–290 nm. A change of ring fusion has no distinct effect on the shape or position of the absorption curve. The λ_{max} values and the respective absorption coefficients are listed in Table II.

TABLE IV
The ^{13}C NMR spectra of compounds *V* and *X*[a]

Atom	*Va*	*Vb*	*Xa*	*Xb*
C-2	141·12	—	141·18	—
	142·0		142·0	
C-3a	135·10	137·14	138·49	138·02
	136·6	137·6	139·5	140·5
C-4	116·51	118·72	119·12	116·73
	116·9	116·4	114·0	113·5
C-5	123·75	126·61	119·94	125·79
	123·6	127·9	121·6	125·9
C-5a	145·39	146·80	124·62	126·61
	142·4	146·7	122·0	126·3
C-6(9)	129·42	130·42	136·56	136·91
	136·1	136·1	136·1	136·1
C-7	147·97	149·08	121·82	122·34
	150·9	150·9	121·7	121·7
C-8	121·06	121·87	148·96	150·02
	121·7	121·7	150·9	150·9
C-9a	112·50	120·99	130·59	134·16
	115·9	115·4	136·3	135·8
C-9b	136·46	138·02	140·77	142·00
	138·1	139·1	140·1	141·1

[a] The data given in the lower lines are the calculated values (see the text); the other data were measured in hexadeuteriodimethyl sulphoxide.

In all the IR spectra of compounds *II*–*V* and *VII*–*X* (Table II) there are deformation out-of-plane vibrations in the region of 800–850 cm^{-1} which are typical of 1,2,3,4-tetrasubstituted benzene derivatives. The vibrations of carboxylic carbonyl groups of compounds *II* and *VII* are seen in the region of 1 700–1 720 cm^{-1}, whereas the more conjugated carbonyl of the pyridone nucleus absorbs in the region of 1 630–1 645 cm^{-1}. The presence of this vibration and of the absorption bands in the long-wavelenghth region of compounds *II* and *VII*, *III* and *VIII* confirm their existence in the oxo and not hydroxy form[11].

The ^{1}H NMR spectra of *II*–*V* and *VII*–*X* (Table III) exhibit signals of protons of a benzene nucleus with the coupling constant $^3J(4, 5) = 9$ Hz, which supports the angular ring fusion in these compounds. The proton signals of pyridine nucleus in compounds *II*–*IV* and *VII*–*IX* exhibit the coupling constants of 5–6 Hz, those of the azoloquinolines *V* and *X* are about 8, 4·5, and 1·8 Hz. These values of coupling constants are comparable with those of the pyridine nucleus in quinoline[12]. The signals of the protons at C-8 and C-7 in compounds *V* and *X*, resp., are split by the interaction of 8 and 4·5 Hz, resp., with the adjacent protons. The coupling constants $^4J(7, 9)$ of *V* and $^4J(6, 8)$ of *X* are 1·8 Hz (ref.[12]). The application of trifluoroacetic acid as the solvent for compounds *II* and *VII* causes downfield shifts of the imidazole and pyridine proton signals, resp., due to protonation[8].

From the ^{13}C NMR spectra of benzimidazole[13], benzotriazole[14], and quinoline[15] we calculated the shifts of carbon atoms of the benzene ring in azoloquinolines *V* and *X* and compared them with the measured ones: the calculated and measured values agreed well. It can be stated that the azole nucleus has no great influence on the shifts of carbon atoms of pyridine ring in azoloquinolines *V* and *X*. Table IV

TABLE V

The relative intensities (in %) of the most important ions in the mass spectra of compounds *Va*–*Vd*

m/z	*Va*	*Vb*	*Xa*	*Xb*
170 ($M^{\cdot+}$)	—	70	—	56
85 (M^{2+})	—	4	—	5
169 (M^{+})	100	—	100	—
84·5 (M^{2+})	8	—	3·8	—
142	18	100	24	100
115	14	57	13	70
114	14	26	12	33
88	7	24	7	22

lists the measured and calculated shift values for carbon atoms in compounds *V* and *X*.

The mass spectra of compounds *V* and *X* (Table V) always exhibit the respective molecular ion and the most important ions with *m/z* 142, 115, 114, and 88. The basic peaks in the mass spectra of imidazole derivatives *Va* and *Xa* belong to their molecular ions, whereas in the case of triazoles *Vb* and *Xb* the basic peak has *m/z* 142. The presence of the ion 142 in the mass spectra of all the azoloquinolines *V* and *X*, and the absence of the ion with *m/z* 143 indicate that the splitting of these azoloquinolines starts, at the azole ring, by splitting off of a nitrogen molecule (*Vb*, *Xb*) or a hydrogen cyanide molecule (*Va*, *Xa*), which is proved by the presence of the metastable ions with *m/z* 119·61 and 118·61. The fragmentation continues by splitting off of two hydrogen cyanide molecules to give the ion with *m/z* 88, which is also confirmed by the presence of the metastable ions with *m/z* 93·13 and 67·33. The mass spectra of compounds *V* and *X* exhibit the less intensive $(M-1)^+$ ions formed by splitting off of the proton from the azole ring and ions with two charges. Also observed was the fragmentation $(M-1)^+ \rightarrow 141 \rightarrow 114$, proved by the presence of the metastable ions with *m/z* 118·34, 117·64, and 92·17.

EXPERIMENTAL

The melting temperatures were determined on a Kofler apparatus and their values were not corrected. The IR spectra were measured with a Specord IR 75 spectrometer (Zeiss, Jena) in KBr disc. The UV spectra were measured with a Specord UV VIS (Zeiss, Jena) in ethanolic solutions of (1 to 5) . 10^{-5} mol l^{-1} concentration. The ^{1}H NMR spectra were measured with a Tesla BS 497 C apparatus at the operation frequence of 80 MHz. The ^{13}C NMR spectra were measured with a JEOL FX-100 and FX-60 apparatus at the operation frequences of 25·047 and 15·036 MHz, resp. Hexamethyldisiloxane was used as the internal standard for ^{1}H NMR, whereas for the ^{13}C NMR we used — as an indirect internal standard — the central signal of hexadeuteriodimethyl sulphoxide (39·5 ppm) or the carbonyl group signal of trifluoroacetic acid (164·2 ppm). The mass spectra were measured with an MS 902S spectrometer using the direct inlet system and 70 eV energy of the ionizing electrons, the ionizing current of 100 μA, and the temperature of ion source 100—130°C. Table I lists the reaction yields and the melting temperatures of products.

Preparation of Azoloquinolonecarboxylic Acids *II* and *VII*

A mixture of 10 mmol ester *I* or *VI* and 20 ml 10% sodium hydroxide solution was refluxed 4 h, boiled with charcoal, filtered, and the filtrate was neutralized with hydrochloric acid. The solid precipitated on cooling was collected by suction, washed with water, and dried under reduced pressure at 80°C. For analyses the samples were purified by reprecipitation of the solutions in 20% sodium hydroxide with hydrochloric acid, washing with water, and drying under reduced pressure at 80°C for 6 h.

Decarboxylation of Acids *II* and *VII*

A mixture of 2 g acid *II* or *VII* and 20 ml quinaldine was refluxed under argon 15 h. The product

was collected by suction, washed with 50 ml diethyl ether, dried, and purified by dissolution in 20% sodium hydroxide, boiling with charcoal, filtration, and neutralization of the filtrate with hydrochloric acid. The precipitate was collected by suction and dried under reduced pressure at 80°C 6 h.

Preparation of Chloroazolo[4,5-*f*]- and [4,5-*h*]quinolines *IV* and *IX*

A mixture of 0·74 g quinolone *III* or *VIII* and 5 ml phosphorus trichloride was stirred and treated with 5 ml dimethylformamide added drop by drop. The reaction mixture was cooled and stirred overnight. Then the viscous liquid was poured onto 300 ml water, boiled with charcoal, and filtered. After cooling the solution was neutralized with 20% sodium hydroxide solution. The precipitated solid was collected by suction, washed with water, and dried under reduced pressure at 60°C 4 h. The products were recrystallized from ethanol (*IVb* and *IXb*) or dimethylformamide (*IVa* and *IXa*).

Preparation of Azoloquinolines *V* and *X*

A mixture of 0·51 g *IV* or *IX*, 0·15 g sodium hydroxide, 30 ml absolute ethanol and the Raney nickel catalyst prepared from 2 g Raney alloy was hydrogenated with continuous stirring (120 kPa hydrogen pressure) until the consumption of hydrogen ceased (the consumption: observed 60 ml, theoretical 56 ml H_2). The catalyst was removed by filtration, the filtrate was neutralized with hydrochloric acid and evaporated under reduced pressure until dry. The residue was extracted with 3 × 30 ml boiling benzene. The combined extracts were discoloured with charcoal, filtered, and evaporated under reduced pressure until dry or submitted to column chromatography (silica gel, chloroform–methanol 10 : 1).

Hydrolysis of Nitrile of 9-Oxo-6,9-dihydroimidazo[4,5-*f*]quinoline-8-carboxylic Acid *XI*

A mixture of 0·42 g *XI* and 4 ml 50% sulphuric acid was refluxed 15 h. Then it was poured onto 50 ml water and neutralized with 20% aqueous sodium hydroxide. After cooling, the precipitate was collected by suction, washed with water, and dried under reduced pressure at 80°C 6 h. Yield 0·2 g (44%) acid *IIa*, m.p. 313°C.

The technical assistance of the following co-workers is acknowledged: J. Kovárová (mass spectra), S. Markusová (IR spectra), K. Kováčová (UV spectra), L. Livařová (^{1}H NMR spectra), and M. Ondrejkovičová (elemental analyses).

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Translated by J. Panchartek.