

REACTION OF 4-SUBSTITUTED BENZALDEHYDES AND ACETOPHENONES WITH CHLOROACETONITRILE

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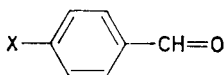
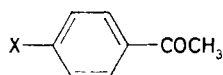
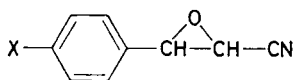
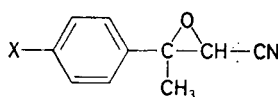
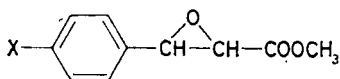
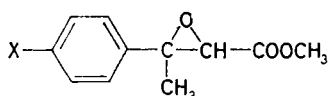
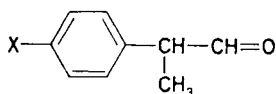
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Under conditions of phase-transfer catalysis or in homogeneous solution of potassium tert-butoxide the title compounds give stereoisomeric mixtures of substituted 2,3-epoxy nitriles *III* and *IV*. Alkaline hydrolysis of epoxy nitriles *IV* afforded the corresponding 2-arylpropanals in low yields. On treatment with methanol and potassium carbonate, epoxy nitriles *III* and *IV* were converted into epoxy esters in good yields.

The classical execution of Darzens glycidester synthesis¹ has found wide application in the preparation of substituted arylpropionic acids with analgetic and antiinflammatory activity^{2,3}. Replacement of α -halogeno alkanooates with α -halogeno nitriles made it possible to introduce the phase-transfer catalysis technique⁴ into the carbanion generation step. However, there was no systematic study of the effect of reaction conditions, of the substituent at the aromatic ring and of the oxo compound type. The aim of our work has been to investigate the effect of the substituent in 4-substituted benzaldehydes *I* and acetophenones *II* on the reaction course. The substituents bonded to the aromatic ring were chosen so as to achieve the widest possible range of the Hammett σ -constants. In all cases the required carbanion was generated from chloroacetonitrile at 5–10°C using two standard methods: either in a two-phase system (water–benzene or water–dichloromethane) by treatment with 50% sodium hydroxide in the presence of benzyltriethylammonium chloride as the phase-transfer catalyst (method *A*), or in a homogeneous medium using potassium tert-butoxide in tert-butyl alcohol (method *B*).

We have proven that in all cases the reaction affords the desired 2,3-epoxy-3-arylpropanenitriles *III* or 2,3-epoxy-3-arylbutanenitriles *IV*. The physico-chemical characteristics of the products *III* and *IV* are given in Tables I and II. As seen from Table I, the phase-transfer method affords the nitriles *III* in higher yields (74–84%). The relatively low yield of the nitro derivative *IIIk* (32%) may be due to an undesired reaction of the nitro group with concentrated sodium hydroxide, leading to unidentified polymers. An analogous behaviour of the nitro group was described already earlier^{5,6}. The nearly identical yields of the epoxy nitriles *III* indicate that the reaction is practically unaffected by electronic effects of the substituent in position 4 of the aromatic nucleus.

*Ia-Ic, If-Ih, Ik**IIa, IIc-IIg, IIi-IIk**IIIa-IIIc, IIIf-IIIh, IIIk**IVa, IVc-IVg, IVi-IVk**Va-Vc, Vf-Vh, Vk**VIc-VIg, VIi-VIk**VIIc, VIIf, VIIi*

In formulae I-VII: *a*, X = CH₃O *b*, X = (CH₃)₃C *c*, X = CH₃ *d*, X = CH₃CH₂CH₂
e, X = (CH₃)₂CHCH₂ *f*, X = H *g*, X = C₆H₅ *h*, X = Cl
i, X = Br *j*, X = CN *k*, X = NO₂

On the other hand, yields of the epoxy nitriles *IV* from the substituted acetophenones *II* vary considerably (35–85%; see Table II), particularly under conditions of the phase-transfer catalysis. We have found that, in addition to the desired epoxy nitrile *IV*, the crude product contains the starting ketone *II* and variable amounts of polymers. This finding, together with difficult isolation of the methoxy derivative *IVa* (which was not obtained in analytical purity), indicate low stability of the epoxy nitriles *IV*. An analogous observation was reported for epoxy esters⁷. We may thus assume that the yields of epoxy nitriles *IV* depend not only on the reactivity of the carbonyl compound but also on the stability of the product which is influenced by electronic effects of the substituent in position 4 of the aromatic nucleus.

The structure of the compounds has been confirmed by infrared and ¹H NMR spectra. As follows from the ¹H NMR spectra, the obtained epoxy nitriles *III* and *IV*

are approximately equimolecular mixtures of (*Z*)- and (*E*)-isomer (Tables I and II). The isomer ratio was determined from intensities of signals due to the oxirane protons. Spectra of (*Z*)-isomers of compounds *III* exhibit signals of H-2 and H-3 at 4.19–4.42 ppm and 3.72–3.93 ppm, respectively ($J = 4.0$ Hz) whereas the respective values for the (*E*)-isomers are 4.23–4.45 ppm and 3.35–3.52 ppm ($J = 2.0$ Hz) (Table III). For compounds *IV*, the H-2 and H-4 signals in the spectra of (*Z*)-isomers appear at 3.43–3.72 ppm and 1.66–1.86 ppm, respectively, and the corresponding resonances for the (*E*)-isomers are 3.20–3.42 ppm and 1.87–2.01 ppm, respectively. These chemical shifts agree with those given in the literature^{8,9} for similar epoxy nitriles. In order to check the accuracy of the *Z* : *E* ratios obtained from the ¹H NMR spectra, we separated the individual geometric isomers of compounds *IVb*, *IVc*, *IVg*, *IVi*, and *IVk* by column chromatography. The physico-chemical data of the separated isomers are given in Table II. The results of the two methods are practically identical within the experimental error.

TABLE I
Yields and physico-chemical characteristics of epoxy nitriles *III*

Compound	Yield, % (<i>Z/E</i>)		B.p., °C/kPa (m.p., °C)	Formula (mol. w.)	Calculated/found		
	method <i>A</i>	method <i>B</i>			% C	% H	% N
<i>IIIa</i>	77	43	105–114/0.04 ^a	C ₁₀ H ₉ NO ₂ (175.2)	68.54	5.18	8.00
	(47/53)	(49/51)			68.36	5.26	7.74
<i>IIIb</i>	80	46	120–126/0.2	C ₁₃ H ₁₅ NO (201.3)	77.58	7.51	6.96
	(48/52)	(44/56)			77.44	7.66	6.88
<i>IIIc</i>	74	45	140–145/2.27	C ₁₀ H ₉ NO (159.2)	75.45	5.70	8.80
	(45/55)	(44/56)			75.28	5.59	8.54
<i>IIIf</i>	77	58	132–134/2.40 ^b	C ₉ H ₇ NO (145.2)	74.47	4.86	9.65
	(46/54)	(50/50)			74.51	4.65	9.77
<i>IIIg</i>	76	54	<i>Z</i> : 105–107, <i>E</i> : 131–132)	C ₁₅ H ₁₁ NO (221.3)	81.43	5.01	6.33
	(46/54)	(50/50)			81.44	5.16	6.41
<i>IIIh</i>	77	61	<i>Z</i> : 79–81, <i>E</i> : 68–69 ^c	C ₉ H ₆ ClNO (179.6)	60.19	3.37	7.80
	(48/52)	(45/55)			60.01	3.46	7.48
<i>IIIk</i>	32	43	<i>Z</i> : 108–110, <i>E</i> : 104–107)	C ₉ H ₆ N ₂ O ₃ (190.2)	56.85	3.18	14.73
	(52/48)	(57/43)			56.49	3.43	14.55

^a Reported²³ b.p. 156–157°C/0.3 kPa; ^b reported²⁴ b.p. 86°C/0.7 kPa; ^c reported⁸ b.p. 110 to 115°C/0.6 kPa.

In accord with the literature¹⁰, the *Z* : *E* ratios show that, unlike the ester group, the nitrile group does not influence the stereoselectivity of the studied reaction.

We tried to convert the obtained epoxy nitriles *IV* into the corresponding aldehydes by the usual method¹, i.e. alkaline hydrolysis followed by acid-catalyzed decarboxylation. Compounds *IVc*, *IVf*, and *IVi* afforded the respective 2-arylpropanals *VIIIc*, *VIIIf*, and *VIII* in low yields (14–38%). We also isolated some starting ketones *II* and a great amount of polymeric material. We assume that in the basic medium the desired hydrolysis of epoxy nitriles *IV* is accompanied by partial decomposition to the starting carbonyl compound and polymers.

Epoxy nitriles can be converted into epoxy esters by treatment with sodium methoxide in methanol¹¹. We prepared methyl 2,3-epoxy-3-arylpropanoates *V* and

TABLE II
Yields and physico-chemical characteristics of epoxy nitriles *IV*

Compound	Yield, % (<i>Z/E</i>)		B.p., °C/kPa (m.p., °C)	Formula (mol. w.)	Calculated/found		
	method <i>A</i>	method <i>B</i>			H C	% H	% N
<i>IVa</i>	41 (56/44)	55 (50/50)	120–127/0.27 ^a	C ₁₁ H ₁₁ NO ₂ (189.2)	—	—	—
<i>IVc</i>	35 (50/50)	58 (52/48)	<i>Z</i> : 136–140/2.27 <i>E</i> : 142–146/2.27	C ₁₁ H ₁₁ NO (173.2)	76.28 76.16	6.40 6.58	8.09 7.84
<i>IVd</i>	40 (52/48)	50 (45/55)	<i>Z</i> : 153–156/2.40 <i>E</i> : 158–162/2.40	C ₁₃ H ₁₅ NO (201.3)	77.58 77.36	7.51 7.72	6.96 6.74
<i>IVe</i>	37 (56/44)	39 (42/58)	117–121/0.09	C ₁₄ H ₁₇ NO (215.3)	78.10 77.89	7.96 8.03	6.51 6.45
<i>IVf</i>	55 (30/70)	60 (36/64)	130–135/2.67 ^b	C ₁₀ H ₉ NO (159.2)	75.45 75.41	5.70 5.83	8.80 8.68
<i>IVg</i>	39 (36/64)	70 (60/40)	<i>Z</i> : 86.5–88, <i>E</i> : 104–105	C ₁₆ H ₁₃ NO (235.3)	81.67 81.43	5.57 5.59	5.95 6.11
<i>IVi</i>	85 (47/53)	59 (40/60)	<i>Z</i> : 160–165/0.27 <i>E</i> : 162–167/0.27	C ₁₀ H ₈ BrNO (238.1)	50.45 50.36	3.39 3.48	5.88 5.66
<i>IVj</i>	45 (54/56)	50 (50/50)	150–156/0.24	C ₁₁ H ₈ N ₂ O (184.2)	71.73 71.68	4.38 4.49	15.21 15.09
<i>IVk</i>	73 (47/53)	61 (50/50)	<i>Z</i> : 160–163/0.2 <i>E</i> : 162–164/0.2	C ₁₀ H ₈ N ₂ O ₃ (204.2)	58.82 58.49	3.95 3.77	13.72 13.57

^a Partial decomposition; ^b reported²⁴ b.p. 114°C/2.5 kPa.

TABLE III
Proton NMR spectra of epoxy nitriles III and IV

Compound	(Z)-isomer		(E)-isomer		Other signals
	H-n ^a	H-2	H-n ^a	H-2	
IIIa	3.75	4.20	3.40	4.24	3.81 s (3 H, OCH ₃); 6.92 d and 7.20 d (4 H, arom. ^b); 6.95 d and 7.35 d (4 H, arom. ^c)
IIIb	3.76	4.24	3.43	4.25	1.30 s (9 H, CH ₃); 7.38 dd (4 H, arom.)
IIIc	3.75	4.23	3.40	4.26	2.19 s (3 H, CH ₃); 7.17 d and 7.34 d (4 H, arom.)
III _f	3.72	4.20	3.35	4.23	7.20–7.40 m (5 H, arom.)
III _g	3.77	4.26	3.41	4.30	7.26–7.64 m (9 H, arom.)
III _h	3.74	4.19	3.39	4.27	7.22 d and 7.39 d (4 H, arom. ^b); 7.36 dd (4 H, arom. ^c)
III _k	3.93	4.42	3.52	4.45	7.64 d and 8.32 d (4 H, arom. ^b); 7.51 d and 8.28 d (4 H, arom. ^c)
IVa	1.76	3.58	1.96	3.35	3.84 s (3 H, OCH ₃); 7.20–7.45 m (4 H, arom.)
IVc	1.74	3.58	1.94	3.33	2.37 s (3 H, CH ₃); 7.10–7.34 m (4 H, arom.)
IVd	1.77	3.59	1.96	3.35	0.94 t (3 H, CH ₃); 1.64 m (2 H, CH ₂); 2.63 t (2 H, CH ₂); 7.25 m (4 H, arom.)
IVe	1.74	3.55	1.96	3.36	0.88 d (6 H, CH ₃); 1.88 m (1 H, CH); 2.26 d (2 H, CH ₂); 7.15 dd (4 H, arom. ^b); 7.15 d and 7.32 d (4 H, arom. ^c)
IV _f	1.74	3.57	1.96	3.33	7.38 m (5 H, arom.)
IV _g	1.66	3.43	1.87	3.20	7.10–7.49 m (9 H, arom.)
IV _i	1.78	3.60	1.95	3.35	7.36 d and 7.51 d (4 H, arom. ^b); 7.29 d and 7.56 d (4 H, arom. ^c)
IV _j	1.84	3.71	2.00	3.41	7.43–7.73 m (4 H, arom.)
IV _k	1.86	3.72	2.01	3.42	7.45 d and 8.28 d (4 H, arom. ^b); 7.66 d and 8.32 d (4 H, arom. ^c)

^a For compounds IIIa–IIIk n = 3, for IVa–IVk n = 4; ^b aromatic protons of (E)-isomer; ^c aromatic protons of (Z)-isomer.

methyl 2,3-epoxy-3-arylbutanoates *VI* by an alternative method, using the reaction with anhydrous methanol in the presence of potassium carbonate and subsequent hydrolysis. The physico-chemical data of the esters *V* and *VI* are given in Tables IV and V. As seen from their $^1\text{H NMR}$ spectra, the isomer populations in *V* and *VI* correspond to those in the starting epoxy nitriles *III* and *IV*. For (*Z*)-isomers of compounds *V* the signals of oxirane ring protons H-2 and H-3 appear at 4.15–4.35 ppm and 3.70–3.92 ppm, respectively ($J = 4.5\text{--}4.7$ Hz) and the ester methoxyl signal at 3.53–3.62 ppm. For (*E*)-isomers the respective chemical shifts for H-2 and H-3 are 4.05–4.23 ppm and 3.49–3.54 ppm ($J = 1.7$ Hz) and the methoxyl signal is located at 3.78–3.86 ppm. The chemical shifts of H-2 and H-4 signals in (*Z*)-isomers of compounds *VI* (Table VI) are 3.68–3.69 ppm and 1.73–1.81 ppm, respectively, and the signal of the ester methoxyl appears at 3.42–3.50 ppm. Analogously, the (*E*)-isomers have the H-2 and H-4 signals at 3.44–3.47 ppm and 1.75–1.83 ppm and the methoxyl signal at 3.81–3.86 ppm.

The mass spectral fragmentation pattern for compounds *V* and *VI* (Table VII) are compatible with the suggested structure and with the published data for unsubstituted epoxy esters¹².

TABLE IV
Results of conversion of epoxy nitriles *III* into epoxy esters *V*

Compound	Yield, % (<i>Z/E</i>)	B.p., °C/Pa (m.p., °C)	Formula (mol. w.)	Calculated/found	
				% C	% H
<i>Va</i>	60 (46/54)	104–106/40	$\text{C}_{11}\text{H}_{12}\text{O}_4$ (208.2)	63.45 63.27	5.81 5.77
<i>Vb</i>	90 (52/48)	94–97/40	$\text{C}_{11}\text{H}_{18}\text{O}_3$ (234.3)	71.77 71.84	7.74 7.66
<i>Vc</i>	60 (55/45)	92–94/80	$\text{C}_{11}\text{H}_{12}\text{O}_3$ (192.2)	68.74 68.58	6.29 6.19
<i>Vf</i>	61 (47/53)	74–75/27 ^a	$\text{C}_{10}\text{H}_{10}\text{O}_3$ (178.2)	67.41 67.38	5.65 5.73
<i>Vg</i>	92 (48/52)	(94–112)	$\text{C}_{16}\text{H}_{14}\text{O}_3$ (254.3)	75.58 75.46	5.55 5.47
<i>Vh</i>	80 (44/56)	89–92/13	$\text{C}_{10}\text{H}_9\text{ClO}_3$ (212.6)	56.49 56.63	4.27 4.12
<i>Vk</i>	93 (50/50)	(<i>Z</i> : 94–98, <i>E</i> : 138–141)	$\text{C}_{10}\text{H}_9\text{NO}_5$ (223.2)	53.82 53.66	4.06 3.87

^a Reported²⁴ b.p. 84°C/70 Pa.

EXPERIMENTAL

The melting points were determined on a Boetius block (Zeiss, Jena) and are uncorrected. Infrared spectra were taken on a Perkin-Elmer 325 spectrometer in chloroform. ^1H NMR spectra were measured on a Varian XL-100-15 instrument in deuteriochloroform with tetramethylsilane as internal standard. Mass spectra were obtained with a Jeol DX 300 spectrometer (electron energy 70 eV). Gas-liquid chromatography was performed on a Chrom 5 chromatograph (Laboratorní přístroje, Prague); flame-ionization detector, 5% OV-17 on Gaschrom Q, column diameter 3 mm.

Chemicals: 4-Methoxybenzaldehyde (*Ia*, b.p. 120–123°C/2.4 kPa), 4-tert-butylbenzaldehyde (*Ib*, b.p. 113–116°C/2 kPa), and 4-methylbenzaldehyde (*Ic*, b.p. 82–85°C/2.26 kPa) were prepared according to ref.¹³, 4-phenylbenzaldehyde (*Ig*, b.p. 135–138°C/0.11 kPa) according to ref.¹⁴, 4-chlorobenzaldehyde (*Ih*, m.p. 45–46°C) and 4-nitrobenzaldehyde (*Ik*, m.p. 105 to 106°C) according to ref.¹⁵. 4-Methoxyacetophenone (*Iia*, b.p. 138–140°C/2.5 kPa), 4-methylacetophenone (*Iic*, b.p. 98–100°C/2.7 kPa), 4-propylacetophenone (*Iid*, b.p. 145–147°C/3.46 kPa), 4-isobutylacetophenone (*Iie*, b.p. 145–148°C/2.7 kPa), 4-phenylacetophenone (*Iig*,

TABLE V
Results of conversion of epoxy nitriles *IV* into epoxy esters *VI*

Compound	Yield, % (<i>Z/E</i>)	B.p., °C/Pa (m.p., °C)	Formula (mol. w.)	Calculated/found	
				% C	H H
<i>VIc</i>	46 (46/54)	85–88/100	$\text{C}_{12}\text{H}_{14}\text{O}_3$ (206.2)	69.81 69.67	6.84 6.75
<i>VIId</i>	46 (53/47)	96–99/13	$\text{C}_{14}\text{H}_{18}\text{O}_3$ (234.3)	71.77 71.59	7.74 7.48
<i>VIe</i>	63 (42/58)	93–96/13	$\text{C}_{15}\text{H}_{20}\text{O}_3$ (248.3)	72.55 72.34	8.12 8.11
<i>VIIf</i>	56 (44/56)	82–84/100 ^a	$\text{C}_{11}\text{H}_{12}\text{O}_3$ (192.2)	68.74 68.88	6.29 6.35
<i>VIg</i>	84 (40/60)	(50–75)	$\text{C}_{17}\text{H}_{16}\text{O}_3$ (268.3)	76.10 76.04	6.01 5.89
<i>VIi</i>	74 (49/51)	129–130/199	$\text{C}_{11}\text{H}_{11}\text{BrO}_3$ (271.1)	48.73 48.41	4.09 3.87
<i>VIj</i>	44 (48/52)	107–108/20	$\text{C}_{12}\text{H}_{11}\text{NO}_3$ (207.2)	69.55 69.11	5.35 4.94
<i>VIk</i>	84 (52/48)	114–115/13	$\text{C}_{11}\text{H}_{11}\text{NO}_5$ (237.2)	55.70 55.36	4.67 4.52

^a Reported⁷ b.p. 75–77°C/27 Pa.

TABLE VI
Proton NMR spectra of epoxy esters *V* and *VI*

Compound	(Z)-isomer			(E)-isomer			Other signals
	H-n ^a	H-2	OCH ₃	H-n ^a	H-2	OCH ₃	
<i>Va</i>	3.70	4.21	3.57	3.51	4.05	3.77	3.79 s (3 H, OCH ₃ ^b); 3.80 s (3 H, OCH ₃ ^c); 6.84–7.34 m (4 H, arom.)
<i>Vb</i>	3.71	4.23	3.62	3.52	4.08	3.80	1.29 s (9 H, CH ₃ ^b); 1.31 s (9 H, CH ₃ ^c); 7.19–7.40 m (4 H, arom.)
<i>Vc</i>	3.71	4.20	3.53	3.49	4.05	3.78	2.31 s (3 H, CH ₃ ^b); 2.33 s (3 H, CH ₃ ^c); 7.10–7.29 m (4 H, arom.)
<i>Vf</i>	3.73	4.25	3.54	3.52	4.09	3.82	7.26–7.42 m (5 H, arom.)
<i>Vg</i>	3.74	4.15	3.57	3.54	4.11	3.84	7.32–7.65 m (9 H, arom.)
<i>Vh</i>	3.71	4.20	3.54	3.52	4.09	3.79	7.19–7.35 m (4 H, arom.)
<i>Vk</i>	3.92	4.35	3.54	3.51	4.23	3.86	7.49 d and 8.25 d (4 H, arom. ^b); 7.63 d and 8.22 d (4 H, arom. ^c)
<i>Vlc</i>	1.73	3.68	3.47	1.75	3.46	3.83	2.35 s (3 H, CH ₃); 7.11–7.36 m (4 H, arom.)
<i>Vld</i>	1.73	3.68	3.45	1.75	3.47	3.82	0.92 t (3 H, CH ₃); 1.59–1.67 m (2 H, CH ₂); 2.56 t (2 H, CH ₂), 7.11–7.30 m (4 H, arom.)
<i>Vle</i>	1.73	3.67	3.42	1.75	3.47	3.81	0.88 d (6 H, CH ₃); 1.85 m (1 H, CH); 2.44 d (2 H, CH ₂); 7.06–7.29 m (4 H, arom.)
<i>Vlf</i>	1.74	3.69	3.46	1.76	3.43	3.82	7.28–7.39 m (5 H, arom.)
<i>Vlg</i>	1.73	3.68	3.48	1.75	3.45	3.82	7.25–7.65 m (9 H, arom.)
<i>Vli</i>	1.73	3.69	3.49	1.74	3.43	3.84	7.25 d and 7.49 d (4 H, arom. ^b); 7.28 d and 7.45 d (4 H, arom. ^c)
<i>Vlj</i>	1.76	3.67	3.49	1.78	3.44	3.84	7.29 d and 7.60 d (4 H, arom. ^b); 7.36 d and 7.54 d (4 H, arom. ^c)
<i>Vlk</i>	1.81	3.67	3.50	1.83	3.47	3.86	7.58 d and 8.23 d (4 H, arom. ^b); 7.62 d and 8.20 d (4 H, arom. ^c)

^a For compounds *Va*–*V/k* n = 3, for compounds *Vlc*–*Vlk* n = 4; ^b aromatic protons of (*Z*)-isomer; ^c aromatic protons of (*E*)-isomer.

b.p. 204–210°C/1.6 kPa), and 4-bromoacetophenone (*IIIi*, b.p. 130–132°C/2.67 kPa) were obtained as described¹⁶. 4-Cyanoacetophenone (*IIj*, b.p. 122–125°C/0.4 kPa) was obtained according to ref.¹⁷ and 4-nitroacetophenone (*IIIk*, m.p. 80°C) according to ref.¹⁸. Chloroacetonitrile (b.p. 122–124°C) was prepared as described in ref.¹⁹.

TABLE VII
Mass spectra of epoxy esters *V* and *VI*

Compound	m/z /relative intensity, % ^a
<i>Va</i>	209/3, 208/16 (M^+), 192/14, 152/11, 151/100, 149/16, 148/15, 136/10, 135/12, 121/29, 91/11, 77/11
<i>Vb</i>	235/11, 234/59 (M^+), 220/38, 219/60, 208/13, 204/15, 192/13, 179/53, 177/100, 176/16, 175/34, 164/20, 163/76, 159/39, 147/60, 145/18, 132/26, 131/66, 117/28, 115/45, 91/54, 57/36
<i>Vc</i>	192/8 (M^+), 136/10, 135/100, 132/16, 119/10, 105/51, 104/23, 103/24, 91/18, 78/16, 77/16
<i>Vf</i>	178/8 (M^+), 162/10, 122/28, 121/100, 119/17, 118/28, 106/12, 105/14, 91/86, 90/76, 89/57, 79/24, 77/33
<i>Vg</i>	254/24 (M^+), 198/17, 197/100, 194/31, 181/8, 167/45, 165/66
<i>Vh</i>	214/2, 212/6 (M^+), 157/35, 155/100, 152/11, 139/7, 125/28, 124/13, 89/44
<i>Vk</i>	223/3 (M^+), 166/100, 150/3, 136/5, 120/10, 89/20
<i>VIc</i>	206/13 (M^+), 178/29, 149/8, 147/23, 146/28, 118/42, 117/93, 115/37, 91/41, 43/11
<i>VI d</i>	234/10 (M^+), 206/37, 177/13, 175/26, 174/41, 147/100, 145/86, 117/33, 115/26, 105/18, 91/23, 43/27
<i>VIe</i>	249/6, 248/32 (M^+), 247/25, 232/49, 224/20, 205/19, 191/92, 189/33, 188/100, 176/47, 145/31, 133/15, 117/63, 115/28, 91/19, 43/8
<i>VI f</i>	192/13 (M^+), 177/9, 164/41, 135/10, 133/59, 132/50, 105/100, 104/43, 103/79, 79/16, 78/15, 77/46, 51/19, 43/11
<i>VI g</i>	268/25 (M^+), 267/20, 252/26, 236/20, 211/29, 209/31, 208/100, 196/23, 181/31, 180/48, 179/48, 178/48, 165/28, 152/26, 43/10
<i>VI i</i>	272/14 (M^+), 270/14 (M^+), 256/22, 254/26, 215/52, 213/69, 212/98, 210/100, 200/21, 198/23, 185/20, 184/45, 183/36, 182/46, 157/9, 155/9, 132/52, 103/88, 102/39, 77/47, 43/17
<i>VI j</i>	218/8, 217/10 (M^+), 201/23, 185/8, 161/13, 160/100, 158/26, 157/79, 146/49, 130/42, 129/70, 128/40, 103/31, 102/40, 43/19
<i>VI k</i>	238/3, 237/7 (M^+), 221/17, 220/23, 190/17, 181/11, 180/100, 178/13, 177/71, 165/14, 131/12, 119/27, 103/36, 91/22, 77/34, 43/10

^a Diagnostically important ion species of relative intensity higher than 10%.

Condensation of Substituted Benzaldehydes *I* or Acetophenones *II* with Chloroacetonitrile

A) Two-phase catalysis. A mixture of the carbonyl compound (20 mmol), chloroacetonitrile (1.51 g; 20 mmol), and the solvent (15 ml; benzene or dichloromethane for *Ih, Ik*) was added dropwise at 5–10°C to a vigorously stirred mixture of 50% sodium hydroxide solution (10 ml) and benzyltriethylammonium chloride (0.3 g). After stirring for 1 h the mixture was diluted with ether (50 ml), washed with ice-cold water (2 × 30 ml), brine (30 ml), dried over magnesium sulfate and taken down. Liquid products were distilled, crystalline compounds were purified by flash chromatography on silica gel (benzene–light petroleum 9 : 1), see Tables I and II.

B) Homogeneous catalysts. A solution of potassium tert-butoxide in tert-butyl alcohol (1.5 mol l⁻¹; 13 ml) was added dropwise under nitrogen at 5–10°C to a stirred mixture of the carbonyl compound (20 mmol), chloroacetonitrile (1.51 g; 20 mmol), and dichloromethane (15 ml). After stirring for 1 h the mixture was diluted with ice-cold water (100 ml) and extracted with ether (3 × 30 ml). The ethereal solution was washed with ice-cold water (2 × 30 ml) and brine (30 ml) and dried over magnesium sulfate. The solvent was removed and the products were isolated as described under *A* (Tables I and II).

2-Arylpropanals *VIIc*, *VII f*, and *VIII i*

A) A mixture of epoxy nitrile *IVc* (3.07 g; 17.7 mmol), ethanol (23 ml), and 10% potassium hydroxide solution (17 ml) was refluxed for 10 h. After evaporation to dryness, the residue was diluted with water and washed with ether. The aqueous portion was adjusted to pH 2 with hydrochloric acid and refluxed for 3 h. The mixture was cooled and extracted with ether (20 ml), the ethereal solution was washed with sodium hydrogen carbonate solution (5 ml) and water (5 ml) and dried over magnesium sulfate. Distillation afforded 0.36 g (2.4 mmol) of 2-(4-methylphenyl)propanal (*VIIc*), b.p. 84–85°C/2.66 kPa (reported²⁰ b.p. 222–223°C); yield 14%. IR spectrum (CHCl₃, cm⁻¹): 1 690 s (C=O). ¹H NMR spectrum: 1.42 d, 3 H (CH₃); 2.34 s, 3 H (CH₃); 3.59 q, 1 H (CH); 7.02 d and 7.15 d, 4 H (arom.); 9.65 s, 1 H (CHO).

B) Using the same procedure as described under *A*, nitrile *IVf* (2.82 g; 17.7 mmol) afforded 0.9 g (38%) of 2-phenylpropanal (*VII f*), b.p. 88°C/3.7 kPa (reported²¹ b.p. 84–86°C/1.33 kPa). IR spectrum (CHCl₃, cm⁻¹): 1 690 s (C=O). ¹H NMR spectrum: 1.43 d, 3 H (CH₃); 3.62 q, 1 H (CH); 7.19–7.39 m, 5 H (arom.); 9.67 s, 1 H (CHO).

C) The nitrile *IVi* (1.47 g; 6.2 mmol) was converted into 2-(4-bromophenyl)propanal (*VIII i*; 0.45 g; 34%) using the same procedure as described under *A*; b.p. 65–68°C/0.09 kPa (reported²² b.p. 98–100°C/0.26 kPa). IR spectrum (CHCl₃, cm⁻¹): 1 690 s (C=O). ¹H NMR spectrum: 1.43 d, 3 H (CH₃); 3.60 q, 1 H (CH); 7.09 d and 7.47 d, 4 H (arom.); 9.65 s, 1 H (CHO).

Methyl 2,3-Epoxy-3-arylpropanoates *V* and Butanoates *VI*

A mixture of the epoxy nitrile (10 mmol), freshly calcined potassium carbonate (1.38 g; 1 mmol), and dry methanol (5 ml) was stirred at 20°C for 3 h, acidified with hydrochloric acid (0.85 ml of conc. HCl in 15 ml of water) and stirred at 0–5°C for 2 h. After extraction with benzene (2 × 15 ml), the organic layer was washed with water (3 × 10 ml) and brine (10 ml) and dried over magnesium sulfate. Liquid esters were distilled, crystalline products were purified by flash chromatography on silica gel in benzene. The results are summarized in Tables III and IV.

Elemental analyses were carried out in the Laboratory of Organic Analysis (Dr L. Helešić, Head), IR spectra were measured in the Laboratory of Absorption Spectroscopy (Dr A. Kohoutová, Head), NMR spectra were taken in the Laboratory of NMR Spectroscopy (Dr P. Trška, Head) and mass

spectra were determined in the Laboratory of Mass Spectrometry (Dr V. Kubelka, Head), all of the Prague Institute of Chemical Technology. The authors thank all of them.

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