CONDITIONS OF THE DIECKMANN CONDENSATION OF ALKYL 2-(N-METHYL-N-(ALKOXYCARBONYLMETHYL)SULFAMOYL)-BENZOATES

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The Dieckmann condensation of alkyl 2-(N-methyl-N-(alkoxycarbonylmethyl)sulfamoyl)benzoates *IIIa*—*IIIe* with various bases affords alkyl 4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate 1,1-dioxides *IVa*—*IVe* which are intermediates in the synthesis of antiinflammatory drug piroxicam. The yields of benzothiazines *IVa*—*IVe* depend mostly on the nature of a base, reaction temperature and solvent used for these condensations. Hitherto undescribed esters *IIIb*—*IIIe* were synthesized and their structures were confirmed by ^{1}H and ^{13}C NMR, and mass spectra.

In connection with the study of preparation of highly effective antiinflammatory drug piroxicam (4-hydroxy-2-methyl-N-(2-pyridyl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide) we wish to report our results on the construction of the benzothiazine skeleton *IV*. The synthetic route, shown in Scheme 1, was chosen for the preparation of esters *IV*. These synthetic steps have already been described in literature, but only for methyl ester *IVa* (refs[1,2]). However, from the point of view of the target product it would be advantageous if the preparation were carried out with other esters *IV*, preferentially the alkoxyethyl esters *IVd* and *IVe* (ref.[3]). This is due to the fact that azeotropic aminolysis of *IVa* in xylene using 2-aminopyridine affords highly coloured piroxicam in low yield. In order to obtain convenient piroxicam intermediates, we decided to check the effects of various bases and solvents on the yields of the required esters *IV*. As a model substance we chose methyl ester *IIIa* because of its easy preparation. It was prepared under mild conditions by addition of *Ia* to a methanolic solution of sodium hydroxide and subsequent methylation[1]. Similarly, other starting esters *IIIb*—*IIIe* (and *IIIa* for comparison) were prepared from alkyl-2*H*-1,2-benzothiazolin-3-one-2-acetate 1,1-dioxides *Ib*—*Ie*. In these cases, however, the compounds *Ib*—*Ie* were treated with 1·1 equivalents of sodium alkoxide in the corresponding absolute alcohol affording dialkyl dicarboxylates *IIb*—*IIe*, which

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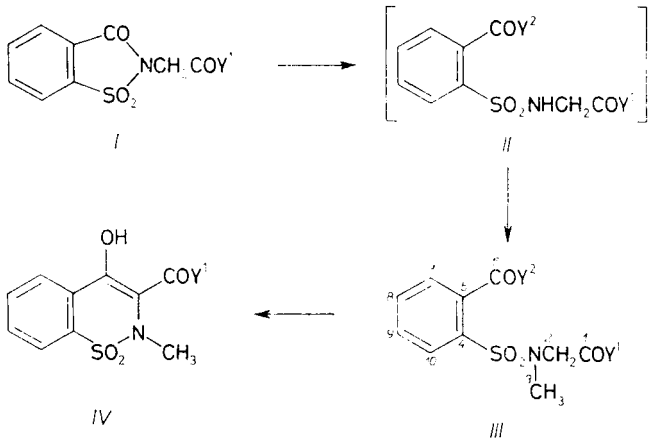
were in situ methylated on nitrogen atom to give esters *IIIb–IIIe*. As methylating agents, dimethyl sulfate or methyl *p*-toluenesulfonate were used.



In formulae *I–IV*: *a*, $Y^1 = Y^2 = OCH_3$ *b*, $Y^1 = Y^2 = OC_2H_5$ *c*, $Y^1 = Y^2 = OCH(CH_3)_2$ *d*, $Y^1 = Y^2 = OCH_2CH_2OCH_3$ *e*, $Y^1 = Y^2 = OCH_2CH_2OC_2H_5$ *f*, $Y^1 = NH$–  ; $Y^2 = OCH_3$

SCHEME 1

The structure determinations of the new compounds *IIIb–IIIe* were based on elemental analyses, ^{1}H NMR, ^{13}C NMR and mass spectral data, which were in full agreement with the proposed structures (Tables I–IV).

In 1976, Lombardino reported[4] that the Dieckmann condensation of *IIIf* in the presence of sodium hydride in tetrahydrofuran (THF) affords desired product in 2% yield. This reaction was carried out under reflux for nine days. Quite recently, Binder et al.[5] have described the Dieckmann condensation of esters of the type *IIIa*. In this case, sodium methoxide in methanol was used as catalyst and an ester of the type *IVa* was obtained in 20% yield at room temperature. We assumed that the use of strong base at a higher temperature would lead to degradation of sulfamoyl framework and consequently to lower yield of desired product. Therefore we decided to perform the reactions at the lowest possible temperature when a strong base was used. The results obtained by using sodium hydride in different solvents are summarized in Table V. Good yields were obtained in the solvents of higher polarity and at lowest possible temperatures. Because of the relatively high freezing point of dimethyl sulfoxide (DMSO), it was not possible to perform the reaction at lower temperatures. In this case, low yields of *IVa* were obtained. Furthermore, we examined the use of lithium diisopropylamide (LDA) for deprotonation of esters

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TABLE I

Data for compounds *IIIa*—*IIIe*

Compound[a] (Yield, %)	M.p., °C (solvent)	Formula (M.w.)	Calculated/Found				Mass spectra, *m/z* (rel. int., %)
			% C	% H	% N	% S	
IIIa (82)	63—64[b] (2-propanol)	$C_{12}H_{15}NO_6S$ (301·3)	47·83 —	5·02 —	4·65 —	10·64 —	302 (M + 1, 0·5); 270 (1·8); 242 (1·9); 199 (100); 178 (2·8); 135 (6·7); 105 (1·7)
IIIb (78)	73—75 (2-propanol)	$C_{13}H_{19}NO_6S$ (329·3)	51·06 50·74	5·82 5·66	4·25 4·30	9·73 9·75	331 (M + 2, 0·1); 284 (1·8); 256 (1·2); 213 (11·6); 192 (2·9); 185 (100); 116 (6·2); 105 (1·9)
IIIc (77)[c]	63—66 (hexane–ether)	$C_{16}H_{23}NO_6S$ (357·4)	53·77 53·49	6·49 6·34	3·92 3·96	8·97 9·10	358 (M + 1, 0·2); 298 (1·5); 270 (1·0); 227 (6·0); 206 (2·8); 185 (100); 130 (5·2); 121 (1·5); 105 (1·0)
IIId (62)	63—65 (ethanol)	$C_{16}H_{23}NO_8S$ (389·4)	49·35 49·11	5·95 5·81	3·60 3·63	8·23 8·37	390 (M + 1, 0·4); 314 (0·3); 286 (0·2); 243 (2·9); 222 (1·7); 185 (0·2); 146 (3·8); 105 (1·3); 59 (100)
IIIe (75)	oil	$C_{18}H_{27}NO_8S$ (417·4)	51·79 51·52	6·52 6·32	3·36 3·52	7·68 7·95	418 (M + 1, 6·9); 372 (3·5); 328 (1·2); 300 (0·3); 236 (3·5); 160 (7·1); 105 (4·1); 73 (100)

[a] Dimethyl sulfate as methylating agent, procedure *A*; [b] ref.[1]: m.p. 62—64°C; [c] reaction was carried out at 70°C.

TABLE II

^{1}H NMR parameters (δ, ppm; ^3J(H, H), Hz) of compounds *IIIa*–*IIIe*

Compound	NCH_3	NCH_2	Arom.	Other signals
IIIa	2·99 s	4·11 s	7·60–7·92 m	3·62 s, 3 H ($CH_2CO_2CH_3$); 3·92 s, 3 H ($ArCO_2CH_3$)
IIIb	3·00 s	4·11 s	7·49–7·95 m	1·19 t, 3 H ($CH_2CO_2CH_2CH_3$, J = 7·1); 1·39 t, 3 H ($ArCO_2CH_2CH_3$, J = 7·1); 4·10 q, 2 H ($CH_2CO_2CH_2$, J = 7·2); 4·41 q, 2 H ($ArCO_2CH_2$, J = 7·2)
IIIc	3·00 s	4·10 s	7·46–7·96 m	1·18 d, 6 H ($CH_2CO_2CH(CH_3)_2$, J = 6·3); 1·39 d, 6 H ($ArCO_2CH(CH_3)_2$, J = 6·3); 4·98 hept, 1 H (CH_2CO_2CH, J = 6·3); 5·29 hept, 1 H ($ArCO_2CH$, J = 6·3)
IIId	2·99 s	4·18 s	7·53–7·95 m	3·36 s, 3 H ($CH_2CO_2CH_2CH_2OCH_3$); 3·40 s, 3 H ($ArCO_2CH_2CH_2OCH_3$); 3·52 m, 2 H ($CH_2CO_2CH_2CH_2$); 3·72 m, 2 H ($ArCO_2CH_2CH_2$); 4·21 m, 2 H ($CH_2CO_2CH_2$); 4·29 m, 2 H ($ArCO_2CH_2$)
IIIe	2·98 s	4·17 s	7·53–7·95 m	1·20 t, 3 H ($CH_2CO_2CH_2CH_2OCH_2CH_3$, J = 7·0); 1·21 t, 3 H ($ArCO_2CH_2CH_2OCH_2CH_3$, J = 6·9); 3·50 q, 2 H ($CH_2CO_2CH_2CH_2OCH_2$, J = 7·0); 3·55 q, 2 H ($ArCO_2CH_2CH_2OCH_2$, J = 6·9); 3·56 m, 2 H ($CH_2CO_2CH_2CH_2$); 3·75 m, 2 H ($ArCO_2CH_2CH_2$); 4·20 m, 2 H ($CH_2CO_2CH_2$); 4·49 m, 2 H ($ArCO_2CH_2$)

TABLE III

^{13}C NMR parameters (δ, ppm; J, Hz) of compound *IIIa*

Carbon	δ	^1J(C, H)	^3J(C, H)
C(Y-1)	52·03 q	J(C(Y-1), H(Y-1)) = 147·5	
C-1	168·30 s		
C-2	50·83 tq	J(C-2, H-2) = 141·0	J(C-2, H-3) = 4·0
C-3	35·74 qt	J(C-3, H-3) = 140·4	J(C-3, H-2) = 4·0
C-4	136·85 t		J(C-4, H-9) = J(C-4, H-7) = 7·1
C-5	132·87 t		J(C-5, H-8) = J(C-5, H-10) = 7·0
C-6	169·13 s		
C(Y-2)	52·04 q	J(C(Y-2), H(Y-2)) = 147·8	
C-7	130·37 dd	J(C-7, H-7) = 164·9	J(C-7, H-9) = 7·7
C-8	129·08 dm	J(C-8, H-8) = 164·9	
C-9	128·51 dm	J(C-9, H-9) = 164·8	
C-10	132·44 dd	J(C-10, H-10) = 164·7	J(C-10, H-8) = 7·7

TABLE IV

Proton-decoupled ^{13}C NMR spectra (δ, ppm) of compounds *IIIb* – *IIIe*

Compound	C-1	C-2	C-3	C-6	C-arom.		Other signals
IIIb	167·91	51·03	35·72	168·72	128·49 130·11 133·41	129·11 132·29 137·00	14·02 (CH_3); 14·05 CH_3); 61·23 (CH_2); 62·34 (CH_2)
IIIc	167·40	51·19	35·68	168·25	128·46 129·94 133·85	129·09 132·19 137·17	21·68 (CH_3); 69·00 (CH); 70·05 (CH)
IIId	167·53	50·92	35·64	168·80	128·63 130·24 132·67	129·14 132·29 136·92	58·92 (CH_3); 64·12 (CH_2); 65·17 (CH_2); 70·13 (CH_2)
IIIe	167·50	50·99	35·62	168·81	128·64 130·23 132·66	129·15 132·28 136·90	15·09 (CH_3); 64·32 (CH_2); 65·36 CH_2); 66·60 (CH_2); 68·00 (CH_2)

IIIa–*IIIe* and the consequent Dieckmann condensation. Up to now, the best results have been obtained just with this reagent in THF at −78°C (Table V). Deprotonation in the presence of hexamethylphosphoramide (HMPA) gave more coloured solution and lower yield of product. Further, diisopropylaminomagnesium bromide was also examined as a known powerful condensating agent[6]. However, the magnesium complex with ester *IIIa* exhibited low solubility in organic solvents and lower yields of *IVa* were obtained. No reaction was observed with calcium hydride, which is probably due to the low basicity and low solubility of calcium hydride in DMSO. The ratios of CaH_2 to CH_3OH (mol/mol) were 2 : 1 and 1 : 1, respectively. The reactions were carried out at 120°C for 3 h.

As shown in Table VI we used some of the alkali-metal and alkaline-earth-metal alkoxides for reactions mentioned above. Magnesium methoxide was found to be the best reagent for condensation because of its solubility in methanol, and sufficient basicity. On the other hand, magnesium 2-alkoxyethoxides which are also soluble,

TABLE V

Results of the Dieckmann condensation of esters *IIIa*–*IIIe* using sodium hydride, lithium diisopropylamide, and diisopropylaminomagnesium bromide as base catalysts

Base[a]	R in *III*	Solvent	*T*, °C	Time, min	Yield, %
NaH	CH_3	toluene	−10	50	34
NaH	CH_3	ether	20	60	32[c]
NaH	CH_3	diglyme	−50	210	69
NaH	CH_3	DMSO[b]	20	6	8
NaH	CH_3	DMSO/THF (1 : 9)	−15	45	46
NaH	CH_3	THF	−60	210	66
NaH	CH_3	THF/HMPA (4 : 1)	−60	210	74
LDA	CH_3	THF/HMPA (4 : 1)	−78	330	73
LDA	CH_3	THF	−78	330	87
LDA	C_2H_5	THF	−78	330	76
LDA	$CH(CH_3)_2$	THF	−78	330	66
LDA	$CH_3OCH_2CH_2$	THF	−78	330	77
LDA	$C_2H_5OCH_2CH_2$	THF	−78	330	51[c]
i-Pr_2NMgBr	CH_3	THF/ether (1 : 1)	20	120	31

[a] With NaH, 4·2 eq. was used and concentration of methanol in solvents was 3 vol. %; [b] without addition of methanol; [c] suspension of *III* in solvent.

showed only weak inclination for condensation. We conclude that the poor chemical yields found with these bases are attributable to the decrease of the basicity of the alkoxyethoxides, due to strong complexation ability of the 2-alkoxyethanols. Recently, Svoboda and co-workers[7] showed that basicity of calcium methoxyethoxide is unsufficient for the formation of the carbanion indispensable for the subsequent cyclization of the intermediate *IId*. We observed that calcium methoxide reacted with the ester *IIIa* to give *IVa* in 38% yield. In the next experiment we examined the effect of lithium methoxide on the yield of ester *IVa*. As we have found by the comparison of lithium methoxide and LDA in THF at −78°C, the former is not a condensating agent by itself under these conditions. The reaction of *IIIa* with lithium methoxide in THF started at about 10°C as it was found by warming the reaction mixture to room temperature. The start of the reaction is indicated by yellow colourization of the solution. Reaction of *IIIa* with sodium methoxide in methanol afforded *IVa* in poor yield and large amounts of by-products were formed. Decreasing the temperature below 20°C caused freezing of the mixture. Condensation of *IIIa* in the presence of potassium tert-butoxide in THF also gave a poor yield. This fact is probably due to an extremely high basicity of tert-butoxide anion.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. NMR spectra were recorded on a Bruker AM-400 instrument (^{1}H at 400·13 MHz, ^{13}C at 100·61 MHz) in deuterio-

TABLE VI

Results of the Dieckmann condensation of esters *IIIa*—*IIIe* using alkali-metal (MOR) and alkaline-earth-metal ($M(OR)_2$) alkoxides as base catalyst

Compound	M	R	Solvent	*T*, °C	Time, h	Yield, %
IIIa	Mg	CH_3	ROH	reflux	2	79[a,c]
IIIb	Mg	C_2H_5	ROH	reflux	3	62[a,c]
IIIc	Mg	$CH(CH_3)_2$	ROH	reflux	3	0[a,d]
IIId	Mg	$CH_3OCH_2CH_2$	ROH	120	1	24[b,d]
IIIe	Mg	$C_2H_5OCH_2CH_2$	ROH	100	3	36[a,d]
IIIa	Ca	CH_3	ROH	reflux	7	38[c,e]
IIIa	Li	CH_3	THF	20	2	54[f]
IIIa	Na	CH_3	ROH	20	2	21[g]
IIIa	K	$C(CH_3)_3$	THF	−78	2	9[h]

[a] 2M-$M(OR)_2$; [b] 4M-$M(OR)_2$; [c] molar ratio $M(OR)_2$/*III* = 1·2; [d] molar ratio $M(OR)_2$/*III* = 2·2; [e] 1M-$Ca(OCH_3)_2$; [f] 1·1 eq. of base; [g] 6 eq. of base; [h] 2·1 eq. of base.

chloroform with tetramethylsilane as internal standard. Mass spectra were measured on a Jeol JMS-D 300 spectrometer (electron energy 70 eV).

Alcohols, toluene, and diethylenglykol-dimethylether (diglyme) were distilled from sodium; diisopropylamine, DMSO, HMPA from calcium hydride, and stored over 3A molecular sieves. Diethylether and THF were freshly distilled from sodium benzophenone ketyl under nitrogen. Solution of butyllithium was titrated by 2-propanol with 1,10-phenanthroline as indicator[8].

Sodium hydride (powder) and calcium hydride (40 mesh) were purchased from Croft Laboratories and Aldrich, respectively. The esters *Ia*—*Ie* were prepared according to literature procedures[9]. All compounds were checked for purity by TLC on silica gel (Silufol UV 254-Kavalier, Czechoslovakia) in toluene–ethanol–acetic acid (80 : 5 : 3).

Alkyl 2-(N-Methyl-N-(alkoxycarbonylmethyl)sulfamoyl)benzoates (*IIIa*—*IIIe*)

Procedure A. A solution of sodium alkoxide (0·21 mol) in the corresponding alcohol (100 ml) was added to a finely ground esters *Ia*—*Ie* (0·20 mol) at room temperature. After stirring for 7—10 min, the methylating agent (0·21 mol) was added (dimethyl sulfate over 20 min, methyl *p*-toluenesulfonate all at once) to the clear solution. The solution was stirred at room temperature for 2 h and then cold water (250 ml) was added. The separated solid was filtered off, washed with water and recrystallized. With *IIIe*, the oily product was extracted with dichloromethane, dried over $MgSO_4$ and the solvent was removed under reduced pressure to give pure ester *IIIe*.

Procedure B. A solution of sodium hydroxide (8·80 g, 0·22 mol) in methanol (250 ml) was added to a finely ground ester *Ia* (51·04 g, 0·20 mol) at room temperature. After stirring for 7—10 min, the methylating agent (0·22 mol) was added (dimethyl sulfate over 5 min, methyl *p*-toluenesulfonate all at once). The reaction time and workup as with Procedure *A*.

The analytical data and yields are given in Table I and Table VII.

Influence of the Base Nature on the Dieckmann Condensation of Esters *IIIa*—*IIIe*

Sodium Hydride (General Procedure)

The ester *IIIa* (1·00 g, 3·3 mmol) and sodium hydride (0·34 g, 14 mmol) were suspended by stirring in dry solvent (10 ml) under nitrogen, and then methanol (0·3 ml, 7·4 mmol) was added.

Table VII

Preparation of the compound *IIIa*

Procedure	Base system	M.p.[a], °C	Yield, %
A	CH_3ONa–CH_3OH	63—64	82[b]
B	NaOH–CH_3OH	63—65	82[b]
A	CH_3ONa–CH_3OH	63—65	72[c]
B	NaOH–CH_3OH	64—66	37[c]

[a] Crystallized from 2-propanol; [b] dimethyl sulfate as methylating agent; [c] methyl *p*-toluenesulfonate as methylating agent.

The reaction temperatures and times are given in Table V. After the reaction had been complete (the disappearance of *Ia* was controlled by TLC), the mixture was quenched with 18% HCl (10 ml) and then water (10 ml) under cooling was added. Reaction product was extracted twice with dichloromethane, the combined organic phases washed with water and dried over $MgSO_4$. After removal of the solvent, the residue was crystallized from ethanol. The yields are given in Table V.

Lithium Diisopropylamide

A solution of diisopropylamine (1·01 ml, 7·3 mmol) in THF (15 ml) was cooled to −78°C. To this solution butyllithium (4·8 ml, 7·3 mmol) in hexane was added under nitrogen, it was stirred for 10 min at about −10°C and then cooled to −78°C. A solution of ester *IIIa* (1·00 g, 3·3 mmol) in THF (5 ml) was then added all at once and stirred for 330 min. Before quenching, the solution was warmed to 0°C and then 18% HCl (10 ml) and water (20 ml) were added and the mixture was stirred for 10 min at 0°C. Reaction product was extracted twice with dichloromethane, the combined organic phases washed with water and dried over $MgSO_4$. After removal of the solvent, the residue was crystallized from ethanol to give *IVa* (0·77 g; 87%), m.p. 167—168°C (ref.[7] 168—170°C). Mass spectrum, *m/z* (% rel. int.): 269 (M, 8·7), 237 (3·8), 168 (2·3), 117 (10·3), 104 (100), 76 (4·5). Similarly were prepared esters *IVb*—*IVe*.

IVb: m.p. 141—143°C (ref.[10] 136—138°C). Mass spectrum, *m/z* (% rel. int.): 283 (M, 8·6), 237 (4·4), 168 (2·9), 117 (9·3), 104 (100), 76 (3·2).

IVc: m.p. 107—108°C. Mass spectrum, *m/z* (% rel. int.): 297 (M, 3·7), 255 (7·6), 237 (7·6), 168 (3·4), 117 (100), 104 (9·5), 76 (2·9). For $C_{13}H_{15}NO_5S$ (297·3) calculated: 52·52% C, 5·09% H, 4·71% N, 10·78% S; found: 52·15% C, 5·16% H, 4·72% N, 10·82% S.

IVd: m.p. 109—110°C (ref.[7] 107—109°C). Mass spectrum, *m/z* (% rel. int.): 313 (M, 8·7), 255 (0·3), 237 (5·2), 168 (2·7), 117 (9·6), 104 (9·7), 76 (2·8), 59 (100).

IVe: m.p. 109—111°C (ref.[7] 108—111°C). Mass spectrum, *m/z* (% rel. int.): 327 (M, 10·2), 282 (0·1), 237 (5·1), 168 (3·1), 117 (9·1), 104 (9·4), 76 (2·4), 73 (100).

Diisopropylaminomagnesium Bromide

A Grignard solution was prepared under nitrogen from Mg (0·18 g, 7·3 mmol) and ethylbromide (0·80 g, 7·3 mmol) in anhydrous ether (10 ml). To this solution diisopropylamine (0·74 g, 7·3 mmol) was added and the mixture was stirred at 20°C for 30 min. To this solution *IIIa* (1·00 g, 3·3 mmol) in THF (10 ml) was added and the resulting suspension was stirred for 2 h. After that, 18% HCl (10 ml) and water (10 ml) were added and the reaction product was extracted twice with dichloromethane, the combined organic phases washed with water and dried over $MgSO_4$. After removal of the solvent, the residue was crystallized from ethanol to give *IVa* (0·28 g; 31%).

Magnesium Alkoxides $Mg(OR)_2$

R = CH_3. A mixture of Mg (0·10 g, 4·1 mmol) and dry methanol (2·1 ml) was refluxed up to complete solution (1 h). To this solution ester *IIIa* (1·00 g, 3·3 mmol) was added and boiling was continued. The mixture became a clear yellow solution and after 45 min a suspension was formed. After boiling for 2 h, the reaction mixture was cooled, 18% HCl (10 ml) and water (10 ml) were added and the separated solid was filtered off, washed with water and ethanol to afford *IVa* (0·70 g, 79%).

R = C_2H_5. Similarly as for R = CH_3, but $Mg(OC_2H_5)_2$ was prepared as a suspension in ethanol.

R = $CH(CH_3)_2$. Similarly as for R = CH_3, but $Mg(OCH(CH_3)_2)_2$ was entirely insoluble in 2-propanol.

R = $CH_3OCH_2CH_2$. Similarly as for R = CH_3. In the course of the reaction the mixture was a clear red solution.

R = $C_2H_5OCH_2CH_2$. Similarly as for R = $CH_3OCH_2CH_2$. The yields, reaction temperatures and times are given in Table VI.

Calcium Methoxide

A mixture of calcium hydride (0·17 g, 4·1 mmol) and dry methanol (4·0 ml) was refluxed for 4 h. Ester *IIIa* (1·00 g, 3·3 mmol) was added to the suspension and boiling was continued for 7 h. Then the mixture was worked up as described for $Mg(OR)_2$-promoted condensations to give *IVa* (0·34 g; 38%).

Lithium Methoxide

A solution of methanol (0·15 ml, 3·6 mmol) in THF (15 ml) was cooled to 0°C. To this solution butyllithium (2·4 ml, 3·6 mmol; in hexane) was added, the solution was warmed to room temperature and then a solution of *IIIa* (1·00 g, 3·3 mmol) in THF (5 ml) was added and the mixture was stirred for 2 h. After that, 18% HCl (10 ml) and water (20 ml) were added, reaction product was extracted twice with dichloromethane, the combined organic phases washed with water and dried over $MgSO_4$. After removal of the solvent, the residue was crystallized from ethanol to give *IVa* (0·48 g; 54%).

Sodium Methoxide

A solution of sodium methoxide (19·8 mmol) in the dry methanol (9·9 ml) was added to a finely ground *IIIa* (1·00 g; 3·3 mmol) at 20°C. After stirring for 2 h, the reaction mixture was cooled, 18% HCl (10 ml) and water (10 ml) were added and the separated solid was filtered off, washed with water and ethanol to give *IVa* (0·19 g; 21%).

Potassium tert-Butoxide

A solution of potassium tert-butoxide (0·82 g, 7·3 mmol) in THF (15 ml) was cooled to −78°C. To this solution a solution of *IIIa* (1·00 g, 3·3 mmol) in THF (5 ml) was added and the mixture was stirred for 2 h. The reaction mixture was worked up as described for the preparation of *IVa* with lithium methoxide to give *IVa* (0·08 g; 9%).

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