Russian Journal of General Chemistry, Vol. 73, No. 4, 2003, pp. 596–602. Translated from Zhurnal Obshchei Khimii, Vol. 73, No. 4, 2003, pp. 630–636.

Reaction of Zinc Enolates of Alkyl Esters of Substituted 4-Bromo-3-Oxoalkanoic Acids with Aldehydes

V. V. Shchepin, Yu. Kh. Sazhneva, and D. N. Litvinov

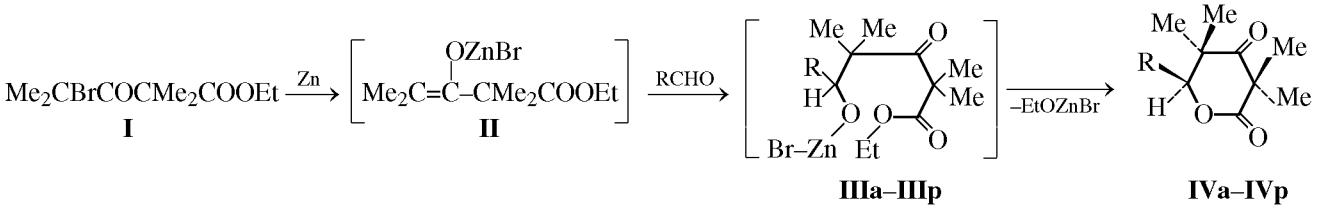
Perm State University, Perm, Russia

Received April 18, 2001

Abstract — Zinc enolates formed from ethyl 4-bromo-2,2,4-trimethyl-3-oxopentanoate react under the conditions of one- of two-stage synthesis with aliphatic, unsaturated, or aromatic aldehydes to form 6-R-2,2,4,4-tetramethyl-2,3,5,6-tetrahydropyran-2,4-diones. Zinc enolates obtained from ethyl 4-bromo-2,2-dimethyl-3-oxopentanoate, -hexanoate, and -2,2,5-trimethyl-3-oxohexanoate under the similar conditions react with aliphatic or aromatic aldehydes to give mainly 5-R^1-6-R^2-3,3-dimethyl-2,3,5,6-tetrahydropyran-2,4-diones as *E* or *Z* isomers or their mixtures. Zinc enolates generated from the ethyl 4-bromo-2,2-diethyl- or 2-benzyl-2-ethyl-3-oxobutanoates react with aromatic aldehydes to give ethyl 5-R-2-R-2-ethyl-3-oxo-4-pentenoates as *E* isomers.

We have briefly reported previously [1] that the reaction of ethyl 4-bromo-2,2,4-trimethyl-3-oxopentanoate with zinc and aldehydes yields substituted 2,3,5,6-tetrahydropyran-2,4-diones. In view of the fact that compounds with the structural fragment of tetrahydropyran-2,4-dione exhibit a pronounced biological activity [2–4] and with the aim to develop a new route to such compounds, we studied systematically the reactions between aldehydes and zinc enolates formed from alkyl esters of substituted 4-bromo-3-oxoalkanoic acids.

We found that zinc enolate **II** formed from ethyl 4-bromo-2,2,4-trimethyl-3-oxopentanoate **I** reacts in ether–ethyl acetate with aliphatic, unsaturated, and aromatic aldehydes as shown below.



I **II** **IIIa–IIIp** **IVa–IVp**

III, IV, R = Pr (**a**), *i*-Pr (**b**), Me–CH≡CH (**c**), PhCH=CBr (**d**), 2-FC_6H_4 (**e**), 2,4-$Cl_2C_6H_3$ (**f**), 3-BrC_6H_4 (**g**), 2-IC_6H_4 (**h**), 4-$MeOC_6H_4$ (**i**), 3,4-$(MeO)_2C_6H_3$ (**j**), 2-HO-5-BrC_6H_3 (**k**), 4-$Me_2NC_6H_4$ (**l**), 2-$NO_2C_6H_4$ (**m**), 3-$NO_2C_6H_4$ (**n**), 4-$NO_2C_6H_4$ (**o**), $C_{14}H_9$ (**p**).

The intermediate bromozinc alcoholate **III** spontaneously cyclizes to form the target products, 6-R-2,2,4,4-tetramethyl-2,3,5,6-tetrahydropyran-2,4-diones **IV**, in the yields of 50–90% (Table 1). The process can be performed both under the conditions of the Reformatsky reaction, i.e., with simultaneous addition of the two components to zinc, and in stages. In the latter case, first zinc enolate **II** is obtained from bromo derivative **I** and zinc, and then the enolate is brought into the reaction with aldehydes. The second alternative appeared to be appropriate with aldehydes containing nitro or amino groups, since the first stage of the reaction, the formation of zink enolate **II**, does not take place if bromo derivative **I** and the above aldehydes are added to zinc simultaneously.

1070-3632/03/7304-0596 $25.00

Table 1. Yields, melting points, ^{1}H NMR spectra, and elemental analyses of 6-R-3,3,5,5-tetramethyl-2,3,5,6-tetrahydropyran-2,4-diones **IVa**–**IVp**

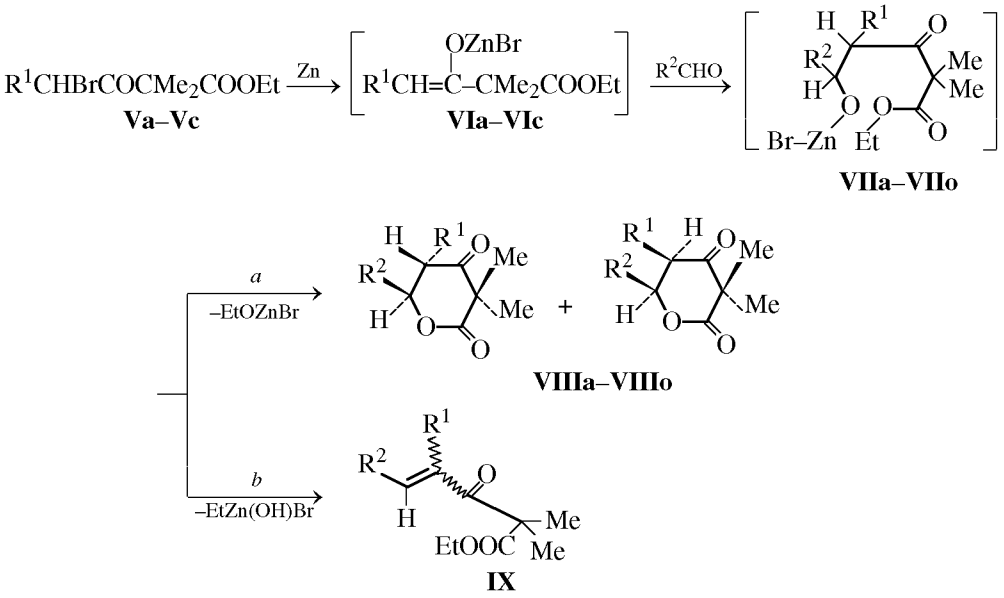
Comp. no.	Yield, %	mp, °C	^{1}H NMR spectrum, δ, ppm			Found, %		Formula	Calculated, %	
			Me_4	CHO	R	C	H		C	H
IVa	68	–	0.93 s, 1.04 s, 1.23 s	4.12 m	0.96–2.00 m (Pr)	67.78	9.43	$C_{12}H_{20}O_3$	67.89	9.50
IVb	62	34	1.06 s, 1.15 s, 1.35 s	4.10 d	1.10 d, ~1.75 m (*i*-Pr)	67.79	9.42	$C_{12}H_{20}O_3$	67.89	9.50
IVc	50	66	0.96 s, 1.03 s, 1.30 s	4.57 d	1.75 d, 5.65 m (Me-CH=CH)	68.45	8.55	$C_{12}H_{18}O_3$	68.54	8.63
IVd	52	97–98	1.20 s, 1.27 s, 1.40 s, 1.47 s	5.58 s	7.35–7.49 m, 7.50 s, 7.64 d (PhCH=CBr)	58.00	5.34	$C_{17}H_{19}BrO_3$	58.12	5.41
IVe	71	96–97	0.97 s, 0.98 s, 1.40 s, 1.50 s	6.00 s	7.20–7.37 m, 7.43–7.60 m (2-FC_6H_4)	68.15	6.40	$C_{15}H_{17}FO_3$	68.18	6.44
IVf	86	121–122	1.00 s, 1.03 s, 1.40 s, 1.50 s	6.04 s	7.55 d, 7.62 d, 7.64 s (2,4-$Cl_2C_6H_3$)	57.12	5.07	$C_{15}H_{16}Cl_2O_3$	57.16	5.12
IVg	85	130–131	0.93 s, 0.98 s, 1.40 s, 1.50 s	5.89 s	7.35–7.48 m, 7.60 d, 7.61 s (3-BrC_6H_4)	55.30	5.18	$C_{15}H_{17}BrO_3$	55.38	5.23
IVh	70	109–110	1.00 s, 1.41 s, 1.53 s	5.90 s	~7.18 m, ~7.52 m, 7.95 d (2-IC_6H_4)	48.28	4.50	$C_{15}H_{17}IO_3$	48.39	4.57
IVi	74	106–107	0.91 s, 1.36 s, 1.47 s	5.75 s	3.80 s (Me), 6.97 d, 7.33 d (4-$MeOC_6H_4$)	69.42	7.23	$C_{16}H_{20}O_4$	69.54	7.30
IVj	76	162–163	0.90 s, 1.37 s, 1.40 s	5.30 s	3.77 s (MeO), 6.82 s [3,4-$(MeO)_2C_6H_3$]	66.58	7.11	$C_{17}H_{22}O_5$	66.67	7.19
IVk	51	232–233	1.00 s, 1.40 s, 1.48 s	5.93 s	10.03 s (HO), 6.87 d, 7.30 d, 7.40 s (2-HO-5-BrC_6H_3)	52.68	4.90	$C_{15}H_{17}BrO_4$	52.79	4.99
IVl	55	180–181	0.93 s, 0.95 s, 1.37 s, 1.46 s	5.60 s	6.70 d, 7.20 d (4-$Me_2NC_6H_4$)	70.47	7.89	$C_{17}H_{23}NO_3$	70.59	7.96
IVm[a]	70	90–91	0.89 s, 1.00 s, 1.40 s, 1.50 s	6.49 s	7.69–7.77 m, 7.80–7.91 m, 8.05 d (2-$NO_2C_6H_4$)	61.77	5.78	$C_{15}H_{17}NO_5$	61.86	5.84
IVn[a]	78	165–166	0.92 s, 0.98 s, 1.40 s, 1.43 s	5.50 s	7.30–7.77 m, 7.95–8.30 m (3-$NO_2C_6H_4$)	61.75	5.76	$C_{15}H_{17}NO_5$	61.86	5.84
IVo[a]	89	203–204	0.93 s, 1.00 s, 1.41 s, 1.53 s	6.06 s	7.73 d, 8.29 d (4-$NO_2C_6H_4$)	61.76	5.79	$C_{15}H_{17}NO_5$	61.86	5.84
IVp	90	195–197	0.78 s, 1.15 s, 1.57 s, 1.73 s	7.30 s	7.48–7.63 m, 8.07–8.19 m, 8.52 d, 8.70 s, 8.78 d ($C_{14}H_9$)	79.18	6.30	$C_{23}H_{22}O_3$	79.77	6.36

[a] The compound was prepared by procedure *b*.

The composition and structure of **IVa**–**IVp** was determined by elemental analysis and ^{1}H NMR and IR spectroscopy. The ^{1}H NMR spectra of **IVa**–**IVp** contain characteristic signals in the regions 0.78–1.73 and 4.10–7.30 ppm, belonging to the methyl and methine (CHO) protons, respectively. The IR spectra contain characteristic absorption bands in the regions 1720–1730 and 1745–1765 cm^{-1}, belonging to the ketone carbonyl and lactone groups, respectively.

Then we studied the reaction of zinc enolates formed from ethyl 4-bromo-2,2-dimethyl-3-oxopentanoate **Va**, 4-bromo-2,2-dimethyl-3-oxohexanoate **Vb**, and 4-bromo-2,2,5-trimethyl-3-oxohexanoate **Vc** with aldehydes. The reaction can proceed by parthway *a* yielding pyrandiones **VIII** and by pathway *b* yielding unsaturated oxo acid esters **IX**.

We found that the major reaction pathway was cyclization of bromozinc alcoholates **VIIa**–**VIIo** by

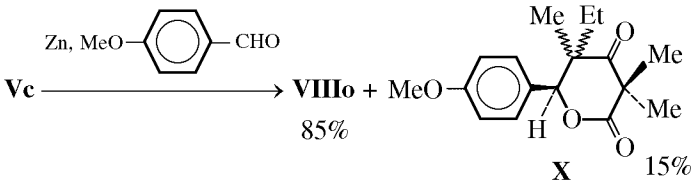


V, VI, R^1 = Me (**a**), Et (**b**), *i*-Pr (**c**). **VII, VIII,** R^1 = Me, R^2 = 3,4-$(MeO)_2C_6H_3$ (**a**), 4-$NO_2C_6H_4$ (**b**); R^1 = Et, R^2 = Pr (**c**), Ph (**d**), 2-FC_6H_4 (**e**), 4-ClC_6H_4 (**f**), 2,4-$Cl_2C_6H_3$ (**g**), 3-BrC_6H_4 (**h**), 4-BrC_6H_4 (**i**), 2-IC_6H_4 (**j**), 2-$NO_2C_6H_4$ (**k**), 3-$NO_2 \cdot C_6H_4$ (**l**), 4-$NO_2C_6H_4$ (**m**); R^1 = *i*-Pr, R^2 = 2,4-$Cl_2C_6H_3$ (**n**), 4-$MeOC_6H_4$ (**o**). **IX,** R^1 = Et, R^2 = 4-ClC_6H_4.

pathway *a*, affording 5-R^1-6-R^2-3,3-dimethyl-2,3,5,6-tetrahydropyran-2,4-diones **VIIIa**–**VIIo** in 42–85% yields (Table 2).

Pathway *b* is realized to only a minor extent. For example, after separation of crystalline pyrandione **VIIIf**, the product of the reaction between ethyl 4-bromo-2,2-dimethyl-3-oxohexanoate, zinc, and 4-chlorobenzaldehyde, the remaining liquid was vacuum-distilled. As a result, we isolated ethyl 2,2-dimethyl-3-oxo-5-(4-chlorophenyl)-4-ethyl-2-pentenoate **IX**; its amount was 15% relative to that of the corresponding pyrandione **VIIIf**.

We also found that, in the reaction of ethyl 4-bromo-2,2,5-trimethyl-3-oxohexanoate **Vc** with zinc and anisaldehyde, along with pyrandione **VIIIo** as the major product, the product of rearrangement of the isopropyl radical, 6-(4-methoxyphenyl)-3,3,5-trimethyl-5-ethyl-2,3,5,6-tetrahydropyran-2,4-dione (**X**, 15%) was also formed.



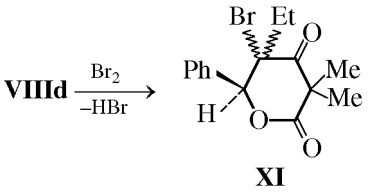
The similar rearrangement was noted previously in [5].

The mechanism of the above rearrangement is yet unclear.

The composition and structure of pyrandiones **VIIIa**–**VIIIo** were determined by elemental analyses and ^{1}H NMR and IR spectroscopy. The ^{1}H NMR spectra of **VIIIa**–**VIIIo** contain characteristic signals in the regions 1.29–1.55 and 5.19–6.56 ppm, belonging to the methyl and methine (CHO) protons, respectively. The IR spectra contain characteristic absorption bands in the regions 1705–1720 and 1745–1760 cm^{-1}, belonging to the ketone carbonyl and lactone groups, respectively.

The ^{1}H NMR data show that compounds **VIIIa**–**VIIIo** are obtained as single (*E* or *Z*) geometric isomers or as their mixtures. The quantum-chemical calculations of the molecular geometry of the two isomers show that the dihedral angle HC^5C^6H in the *E* isomer is 127.8°, and in the *Z* isomer it is 52.7°. This allows the signal assignment in the ^{1}H NMR spectra of the products to *E* or *Z* isomers on the basis of the spin–spin coupling constant of HC^5C^6H protons, taking into account that the stronger the dihedral angle HC^5C^6H deviates from 0° or 180°, the smaller the spin–spin coupling constant. It can be thus concluded that the isomer with the higher constant (12 Hz) has the *E* configuration, while that with the lower constant (1–4 Hz) has the *Z* configuration (Table 2).

With 3,3-dimethyl-6-phenyl-5-ethyl-2,3,5,6-tetrahydropyran-2,4-dione (**VIIId**) as an example, it was shown that bromination of the pyrandiones obtained occurs at the 5-position of the heteroring, yielding 5-bromo-3,3-dimethyl-6-phenyl-5-ethyl-2,3,5,6-tetrahydropyran-2,4-dione (**XI**).



XI

Table 2. Yields, melting points, ^{1}H NMR spectra, and elemental analyses of 5-R^1-6-R^2-3,3-dimethyl-2,3,5,6-tetrahydropyran-2,4-diones **VIIIa**–**VIIIo**

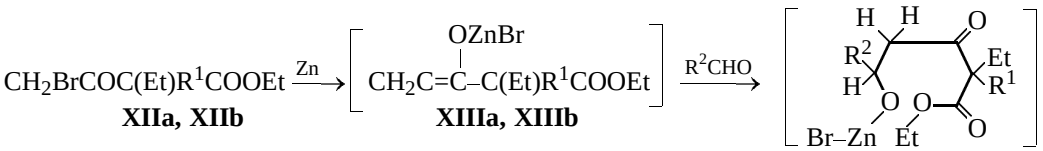
Comp. no.	Yield, %	mp, °C (solvent)	Content, %		*E*				
			E	*Z*	CMe_2	CHR^1	CHR^2	R^1	R^2
VIIIa	42	133–134 (MeCOOEt/MeCN)	100	0	1.38 s, 1.45 s	~3.25 m	5.38 d (*J* 11 Hz)	0.80 d (Me)	3.83 s (MeO), 6.96 d, 6.98 d, 7.12 s [(3,4-$(MeO)_2C_6H_3$]
VIIIb[a]	80	205–207 (MeCN)	5	95					
VIIIc[b]	43	55–56 (C_6H_{14})							
VIIId	71	86–87 (C_6H_{14})	100	0	1.31 s, 1.37 s	2.45–2.91 m	5.20 d (*J* 11 Hz)	0.73 t, 1.09–1.60 m (Et)	7.47 s (Ph)
VIIIe	85	67–68 (Et_2O/C_6H_{14})	35	65	1.41 s, 1.45 s	3.23–3.33 m	5.80 d (*J* 11 Hz)	0.77 t, 1.23–1.40 m (Et)	7.69 t, 7.20–7.38 m, 7.38–7.54 m (2-FC_6H_4)
VIIIf	74	112–113 (CCl_4/C_6H_{14})	100	0	1.30 s, 1.36 s	2.43–2.90 m	5.19 d (*J* 11 Hz)	0.72 t, 1.03–1.63 m (Et)	6.97 d, 6.57 d (4-ClC_6H_4)
VIIIg	80	118–119 (CCl_4)	100	0	1.44 s, 1.46 s		5.88 d (*J* 11 Hz)	0.75 t, 1.18–1.78 m (Et)	7.40–7.54 m (2,4-$Cl_2C_6H_3$)
VIIIh	75	77–78 (CCl_4/C_6H_{14})	45	55	1.39 s, 1.43 s	3.19–3.29 m	5.68 d (*J* 11 Hz)	0.73 t, 1.20–1.40 m (Et)	7.81 s, 7.33–7.45 m, 7.50–7.60 m (3-BrC_6H_4)
VIIIi	75	111–112 (CCl_4/C_6H_{14})	100	0	1.40 s, 1.44 s	3.00–3.19 m	5.60 d (*J* 11 Hz)	0.75 t, 1.26–1.41 m (Et)	7.50 d, 7.60 d (4-BrC_6H_4)
VIIIj	74	115–116 (CCl_4)	100	0	1.41 s, 1.46 s	3.31–3.42 m	5.70 d (*J* 11 Hz)	0.75 t, 1.35–1.50 m (Et)	7.20 t, 7.53 t, 7.69 d, 7.95 d (2-IC_6H_4)
VIIIk[a]	63	124–125 (Et_2O/MeCOOEt)	0	100					
VIIIl[a]	61	141–142 (Et_2O/MeCOOEt)	0	100					
VIIIm[a]	70	147–149 (MeCN)	0	100					
VIIIn	67	133–134 (CCl_4)	100	0	1.38 s, 1.46 s	~3.30 m	6.00 d (*J* 11 Hz)	0.80 d, 1.05 d, 1.73 m (*i*-Pr)	7.58 s, 7.53 d, 7.80 d (2,4-$Cl_2C_6H_3$)
VIIIo[c]	62	85–86 (MeCOOEt)	100	0	1.29 s, 1.41 s	~3.04 m	5.65 d (*J* 11 Hz)	0.77 d, 1.09 d, 1.79 m (*i*-Pr)	3.83 s (MeO), 6.96 d, 7.43 d (4-$MeOC_6H_4$)

Table 2. (Contd.)

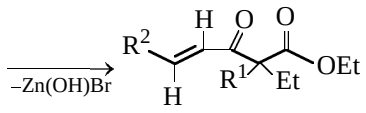
Comp. no.	*Z*					Found, %		Formula	Calculated, %	
	CMe_2	CHR^1	CHR^2	R^1	R^2	C	H		C	H
VIIIa						65.60	6.80	$C_{16}H_{20}O_5$	65.75	6.85
VIIIb[a]	1.40 s, 1.55 s	~3.20 m	6.32 d (*J* ~3 Hz)	0.80 d (Me)	7.69 d, 8.30 d (4-$NO_2C_6H_4$)	60.51	5.35	$C_{14}H_{15}NO_5$	60.65	5.42
VIIIc[b]						67.72	9.41	$C_{12}H_{20}O_3$	67.89	9.50
VIIId						72.98	7.31	$C_{15}H_{18}O_3$	73.15	7.37
VIIIe	1.39 s, 1.54 s	2.97–3.07 m	6.20 d (*J* ~4 Hz)	0.79 t, 1.23–1.40 m (Et)	7.20–7.38 m, 7.38–7.54 m (2-FC_6H_4)	68.03	6.39	$C_{15}H_{17}FO_3$	68.18	6.44
VIIIf						64.01	6.03	$C_{15}H_{17}ClO_3$	64.17	6.10
VIIIg						53.97	5.05	$C_{15}H_{16}Cl_2O_3$	57.16	5.12
VIIIh	1.37 s, 1.50 s	2.88–2.99 m	6.12 d (*J* ~1–2 Hz)	0.76 t, 1.20–1.40 m (Et)	7.33–7.45 m, 7.50–7.60 m (3-BrC_6H_4)	55.25	5.18	$C_{15}H_{17}BrO_3$	55.38	5.23
VIIIi						55.23	5.17	$C_{15}H_{17}BrO_3$	55.38	5.23
VIIIj						48.19	4.49	$C_{15}H_{17}IO_3$	48.39	4.57
VIIIk[a]	1.39 s, 1.52 s	2.92–3.02 m	6.56 d (*J* ~1–2 Hz)	0.76 t, 1.39–1.52 m (Et)	7.70 t, 7.78–7.96 m, 8.20 d (2-$NO_2C_6H_4$)	61.67	5.75	$C_{15}H_{17}NO_5$	61.86	5.84
VIIIl[a]	1.38 s, 1.44 s	2.86–2.98 m	6.32 d (*J* ~1–2 Hz)	0.77 t, 1.23–1.42 m (Et)	7.30–7.77 m, 7.95–8.30 m (3-$NO_2C_6H_4$)	61.70	5.77	$C_{15}H_{17}NO_5$	61.86	5.84
VIIIm[a]	1.39 s, 1.53 s	2.87–2.99 m	6.29 d (*J* ~1–3 Hz)	0.76 t, 1.20–1.40 m (Et)	7.71 d, 8.30 d (4-$NO_2C_6H_4$)	61.69	5.76	$C_{15}H_{17}NO_5$	61.86	5.84
VIIIn						58.20	5.45	$C_{16}H_{18}Cl_2O_3$	58.37	5.51
VIIIo[c]						70.18	7.58	$C_{17}H_{22}O_4$	70.32	7.64

[a] The compounds were prepared by pathway *b*. [b] ^{1}H NMR spectrum of compound **VIIIc** ($CDCl_3$), δ, ppm: 1.36 s, 1.41 s (6H, CMe_2), 0.96 t, 1.28–1.62 m (5H, Et), 1.28–1.62 m (7H, Pr), ~2.69 m (1H, C*H*Et), ~4.64 m (1H, C*H*Pr), does not allow unambiguous assignment to *E* or *Z* isomer. [c] Isolated as a mixture with 6-(4-methoxyphenyl)-3,3,5-trimethyl-5-ethyl-2,3,5,6-tetrahydropyran-2,4-dione (**X**, 15%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.55 t, ~1.25 m, ~1.65 m (5H, Et), 0.90 s (3H, Me), 1.35 s, 1.50 s (6H, CMe_2), 5.70 s (1H, CH), 6.96 d, 7.35 d (4H, C_6H_4).

Then we studied the reaction of zinc enolates formed from ethyl 4-bromo-2-ethyl-3-oxobutanoate **XIIIa** and 4-bromo-2-benzyl-2-ethyl-3-oxobutanoate **XIIIb** with aldehydes in order to synthesize pyrandiones containing no substituents in position 5 of the heteroring. It was reported previously that the reaction of ethyl 4-bromo-2,2-diethyl-3-oxobutanoate with zinc and aldehydes in ether–ethyl acetate yields only the products of linear structure, namely, ethyl 2,2-diethyl-3-oxo-5-R-4-pentenoates [6]. Similarly, in



XIIa, XIIb **XIIIa, XIIIb** **XIVa**–**XIVd**



XVa–**XVd**

XII, XIII, R^1 = Et (**a**), CH_2Ph (**b**); **XIV, XV**, R^1 = Et, R^2 = 3-BrC_6H_4 (**a**), 4-$Me_2NC_6H_4$ (**b**); R^1 = CH_2Ph, R^2 = Ph (**c**), 4-BrC_6H_4 (**d**).

Table 3. Yields, melting points, elemental analyses, and ^{1}H NMR spectra of ethyl 5-R-2-R-2-ethyl-3-oxo-4-pentenoates

Comp. no.	Yield, %	mp, °C or bp, °C (*p*, mm)	^{1}H NMR spectrum, δ, ppm					
			R^2	CH=	=CHCO	Et	R^1	OEt
XVa	73	93–94	7.35 t, 7.52 s, 7.65 d, 7.93 s (3-BrC_6H_4)	7.52 d (*J* 16 Hz)	7.04 d (*J* 16 Hz)	1.93 q (CH_2), 0.76 t (Me)	1.93 q (CH_2), 0.76 t (Me)	4.18 q (CH_2), 1.20 t (Me)
XVb	45	117–119	6.69 d, 7.45 d (4-$Me_2NC_6H_4$)	7.50 d (*J* 16 Hz)	6.61 d (*J* 16 Hz)	1.90 q (CH_2), 0.75 t (Me)	1.90 q (CH_2), 0.75 t (Me)	4.15 q (CH_2), 1.20 t (Me)
XVc	68	210–215 (2–3)	7.23 m (Ph)	7.57 d (*J* 16 Hz)	6.67 d (*J* 16 Hz)	1.80 q (CH_2), 0.77 t (Me)	3.10 s (CH_2), 7.00 s (Ph)	4.03 q (CH_2), 1.10 t (Me)
XVd	72	80–81	7.33 s (4-BrC_6H_4)	7.47 d (*J* 16 Hz)	6.57 d (*J* 16 Hz)	1.80 q (CH_2), 0.77 t (Me)	3.10 s (CH_2), 7.03 s (Ph)	4.07 q (CH_2), 1.10 t (Me)

Table 3. (Contd.)

Comp. no.	Found, %		Formula	Calculated, %	
	C	H		C	H
XVa	57.65	5.80	$C_{17}H_{21}BrO_3$	57.79	5.94
XVb	71.80	8.43	$C_{19}H_{27}NO_3$	71.92	8.52
XVc	78.65	7.08	$C_{22}H_{24}O_3$	78.57	7.14
XVd	63.50	5.49	$C_{22}H_{23}BrO_3$	63.61	5.54

our case, due to the absence of substituents in position 4 of bromozinc alcoholate **XIV**, the major reaction pathway is elimination of the zinc subsalt from intermediate **XIV** and formation of ethyl 5-R-2-R-2-ethyl-3-oxo-4-pentenoates **XV** as the only products in the yields of 45–73% (Table 3), regardless of the solvent (ether–HMPA) and the radical in position 2.

The composition and structure of **XVa**–**XVd** were determined by elemental analysis and ^{1}H NMR and IR spectroscopy. The ^{1}H NMR spectra of **XVa**–**XVd** contain typical doublet signals of protons at the double bond in the regions 6.57–7.04 and 7.47–7.57 ppm. The spin–spin coupling constant of the olefin protons (16 Hz) is indicative of the *E* conformation of the above compounds. Their IR spectra contain characteristic absorption bands in the regions 1600–1610, 1680–1690, and 1720–1725 cm^{-1} belonging to the double bond and the ketone and lactone carbonyl groups, respectively.

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrophotometer using neat samples. The ^{1}H NMR spectra were recorded for solutions in CCl_4 (**IVa**–**IVc, VIIIf, XVc, XVd**) or $CDCl_3$ (**VIIIc**, **VIIIg**) on an RYa-2310 (60 MHz) instrument or in DMSO-d_6 (**IVd**–**IVo, VIIIa, VIIIb, VIIIe, VIIIh**–**VIIIk, VIIIm**–**VIIIo, XVa, XVb**) on a Bruker AM-300 spectrometer.

The quantum-chemical calculation was carried out by the SCF MO LCAO method in the MNDO approximation [7] included in the MOPAC 6.0 program package.

6-R-2,2,4,4-Tetramethyl-2,3,5,6-tetrahydropyran-2,4-diones IVa–IVl and IVp. *a*. A mixture of 0.05 mol of ethyl 4-bromo-2,2,4-trimethyl-3-oxopentanoate and 0.045 mol of an aldehyde was added to 10 g of fine zinc chips in 10 ml of ether and 30 ml of ethyl acetate. After adding the whole amount of the reactants, the mixture was refluxed for 30 min. After cooling, it was hydrolyzed with 10% HCl and extracted with ether. The organic layer was separated, washed to the neutral reaction, and dried with sodium sulfate; the solvent was distilled off. The products were purified by double recrystallization from hexane. Compound **IVa** was purified by vacuum distillation.

b. Compounds **IVm**–**IVo**. A 0.05-mol portion of ethyl 4-bromo-2,2,4-trimethyl-3-oxopentanoate was added to 10 g of activated fine zinc chips in 20 ml of ether and 20 ml of ethyl acetate. The reaction mixture was refluxed for 30 min and separated from zinc by decanting; 0.035 mol of an aldehyde was added. Further work-up was similar to procedure *a*. The products were purified by double recrystallization from methanol.

5-R^1-6-R^2-3,3-Dimethyl-2,3,5,6-tetrahydropyran-2,4-diones. Compounds **VIIIa**, **VIIIc**, **VIIIj**, **VIIIn**, and **VIIIo** were prepared similarly to procedure *a* starting from ethyl 4-bromo-4-R^1-3-oxoalkanoates.

Compounds **VIIIb** and **VIIIk**–**VIIIm** were prepared similarly to procedure *b* starting from ethyl 4-bromo-4-R^1-3-oxoalkanoates.

Ethyl 2,2-dimethyl-3-oxo-5-(4-chlorophenyl)-4-ethyl-4-pentenoate IX. The liquid residue after separation of crystalline pyrandione **VIIIf** was vacuum-distilled. Yield 11%, bp 151–153°C (4 mm), n_D^{20} 1.5552. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: ~7.09 m, 7.25 m (CH=), 1.49 s (CMe_2), 1.10 t (3H, Me), 4.16 q (2H, CH_2). Found, %: C 66.01; H 6.76. $C_{17}H_{21}ClO_3$. Calculated, %: C 66.13; H 6.81.

5-Bromo-3,3-dimethyl-6-phenyl-5-ethyl-2,3,5,6-tetrahydropyran-2,4-dione XI. A 0.06-mol portion of bromine was added dropwise with stirring to a solution of 0.05 mol of 3,3-dimethyl-6-phenyl-5-ethyl-2,3,5,6-tetrahydropyran-2,4-dione in 15 ml of CCl_4. The mixture was heated on a water bath to the end of decolorization. After removal of the solvent, the product was recrystallized twice from hexane–carbon tetrachloride. Yield 77%, mp 123–124°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 t, 1.98 q (5H, Et), 1.25 s, 1.43 s (6H, Me_2), 5.28 s (1H, CH), 7.33 s (5H, Ph). Found, %: C 55.27; H 5.18. $C_{15}H_{17}BrO_3$. Calculated, %: H 55.38; C 5.23.

Ethyl 5-R-2-R-2-ethyl-3-oxo-4-pentenoates. Compound **XVa** was prepared similarly to procedure *a* in 20 ml of ether and 20 ml of HMPA; compounds **XVc** and **XVd** were prepared in 20 ml of ether and 20 ml of ethyl acetate starting from ethyl 4-bromo-2-*R*-3-oxobutanoates.

Compound **XVb** was prepared similarly to procedure *b* starting from 0.075 mol of ethyl 4-bromo-2,2-diethyl-3-oxobutanoate and 0.05 mol of 4-*N*,*N*-dimethylaminobenzaldehyde.

REFERENCES

1. Shchepin, V.V. and Gladkova, G.E., *Zh. Org. Khim.*, 1995, vol. 31, no. 7, p. 1094.
2. US Patent 4544399, 1985, *Ref. Zh. Khim.*, 1986, 13O467P.
3. US Patent 4544399, 1985, *Ref. Zh. Khim.*, 1986, 5O40P.
4. Australian Patent 560716, 1987, *Ref. Zh. Khim.*, 1988, 11O433P.
5. Shchepin, V.V. and Gladkova, G.E., *Zh. Org. Khim.*, 1993, vol. 29, no. 3, p. 474.
6. Shchepin, V.V., Litvinov, D.N., Russkikh, N.Yu., and Vakhrin, M.I., *Zh. Org. Khim.*, 2000, vol. 36, no. 2, p. 192.
7. Dewar, M.J.S. and Thiel, W., *J. Am. Chem. Soc.*, 1977, vol. 99, no. 15, p. 4899.