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Reaction of Methyl 1-(2-Bromoisobutyryl)cyclopentanecarboxylate and 3-(1-Bromocyclopentyl)-2,2-dimethyl-3-oxopropionate with Zinc and Aromatic Aldehydes

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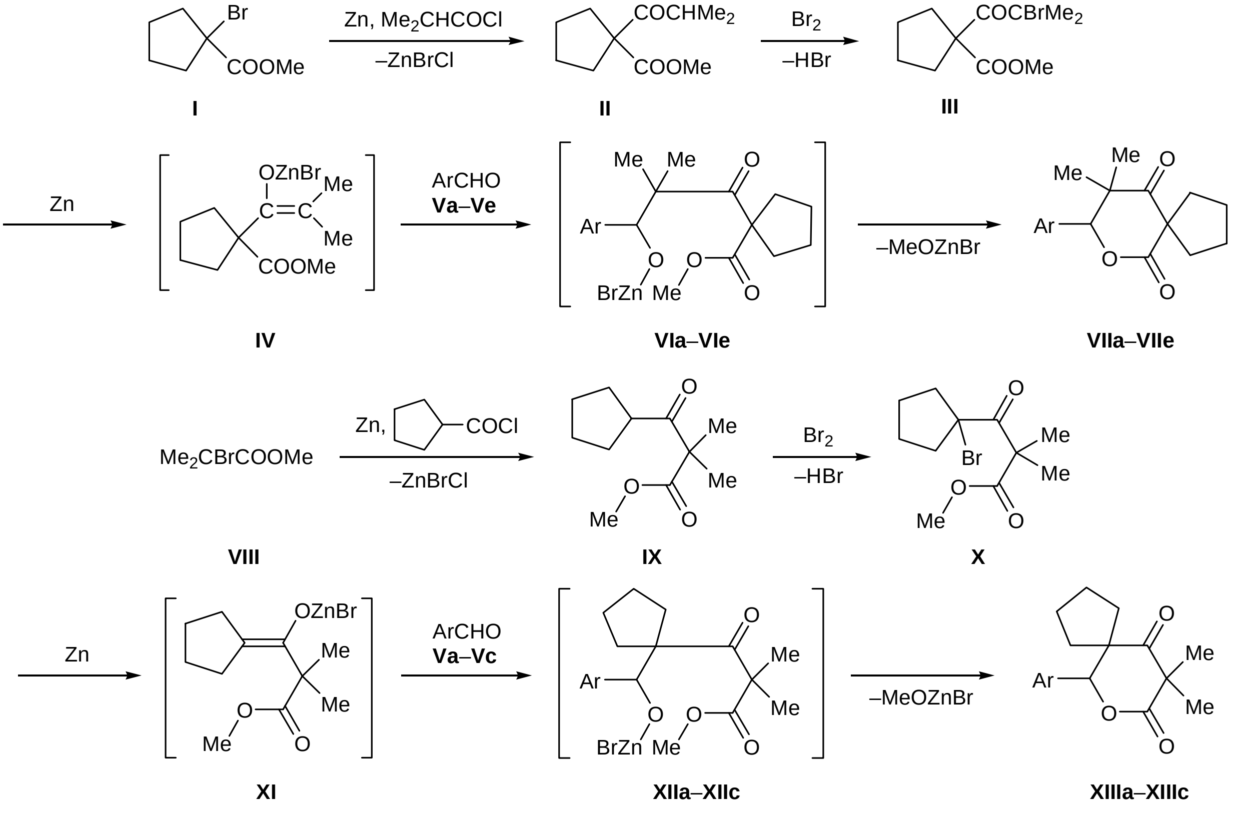
Abstract—Methyl 1-(2-bromoisobutyryl)cyclopentanecarboxylate and 3-(1-bromocyclopentyl)-2,2-dimethyl-3-oxopropionate react with zinc and aromatic aldehydes to afford 8-aryl-9,9-dimethyl-7-oxaspiro[4.5]decane-6,10-diones and 10-aryl-7,7-dimethyl-9-oxaspiro[4.5]decane-6,8-diones, respectively.

In continuation of our studies on the Reformatsky reaction as a method of synthesis of substituted 2,3,5,6-tetrahydropyran-2,4-diones possessing spiro carbon atoms [1, 2], we examined reactions of methyl 1-(2-bromoisobutyryl)cyclopentanecarboxylate (**III**) and methyl 3-(1-bromocyclopentyl)-2,2-dimethyl-3-oxopropionate (**X**) with zinc and aromatic aldehydes **Va**–**Ve**. Initial bromo derivative **III** was synthesized by reaction of methyl 1-bromocyclopentanecarboxylate (**I**) with zinc and isobutyryl chloride and subsequent

Scheme 1.



VII, **XIII**, Ar = Ph (**a**), 4-BrC_6H_4 (**b**), 3-$O_2NC_6H_4$ (**c**), 4-$CH_3OC_6H_4$ (**d**), 4-$(CH_3)_2NC_6H_4$ (**e**).

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bromination of methyl 1-isobutyrylcyclopentanecarboxylate (**II**) thus formed. In a similar way, from methyl α-bromoisobutyrate **VIII**, zinc, and cyclopentanecarbonyl chloride, we obtained methyl 2,2-dimethyl-3-oxo-3-cyclopentylpropionate (**IX**), and bromination of the latter afforded bromo derivative **X**.

We found that methyl 1-(2-bromoisobutyryl)cyclopentanecarboxylate and methyl 3-(1-bromocyclopentyl)-2,2-dimethyl-3-oxopropionate are capable of reacting with zinc in ethyl acetate to give bromozinc enolates **IV** and **IX**, respectively. The latter reacted with aromatic aldehydes **Va**–**Ve** to afford bromozinc alkoxides **VI** and **XII** which underwent spontaneous intramolecular cyclization to substituted tetrahydropyran-2,4-diones possessing a spiro-fused cyclopentane ring in position *3* or *5*, namely 8-aryl-9,9-dimethyl-7-oxaspiro[4.5]decane-6,10-diones **VIIa**–**VIIe** and 10-aryl-7,7-dimethyl-9-oxaspiro[4.5]decane-6,8-diones **XIIIa**–**XIIIc** (Scheme 1, see table).

The yields of the final products were 43–62%. Their structure was proved by the data of elemental analysis and ^{1}H NMR and IR spectroscopy. The ^{1}H NMR spectra of compounds **VII** and **XIII** contain characteristic signals in the δ regions 6.60–8.20, 5.29–5.63, 0.83–1.47, and 0.63–2.53 ppm, which belong, respectively, to protons of the aromatic substituent, CH proton in position *6*, protons of the geminal methyl groups, and cyclopentane ring protons. In the IR spectra we obsered absorption bands due to stretching vibrations of the ketone (1715–1720 cm^{-1}) and lactone carbonyl groups (1750–1760 cm^{-1}).

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer. The ^{1}H NMR spectra of compounds **II**, **III**, **VIIa**–**VIIe**, **IX**, **X**, and **XIIIa**–**XIIIc** were measured on an RYa-2310 spectrometer (60 MHz) using tetramethylsilane as internal reference.

Methyl 1-isobutyrylcyclopentanecarboxylate (II). A solution of 0.1 mol of methyl 1-bromocyclopentanecarboxylate and 0.1 mol of isobutyryl chloride

Yields, melting points, IR and ^{1}H NMR spectral parameters, and elemental analyses of 8-aryl-9,9-dimethyl-7-oxaspiro[4.5]-decane-6,10-diones **VIIa**–**VIIe** and 10-aryl-7,7-dimethyl-9-oxaspiro[4.5]decane-6,8-diones **XIIIa**–**XIIIc**

Comp. no.	Yield, %	mp, °C	IR spectrum, νC=O, cm^{-1}		^{1}H NMR spectrum, δ, ppm			
			ketone	lactam	Ar	Me_2C, s	$(CH_2)_4$, m	CHO, s
VIIa	58	190–191	1720	1760	7.30 s (5H, Ph)	0.87, 0.98	1.37–2.53	5.38
VIIb	52	154–155	1720	1760	7.18 d, 7.50 d (4H, 4-BrC_6H_4)	0.83, 0.97	1.26–2.53	5.37
VIIc	62	178–180	1720	1750	7.67 m, 8.22 m (4H, 3-$O_2NC_6H_4$)	0.90, 1.05	1.55–2.47	5.55
VIId	48	145–146	1715	1750	3.68 s (3H, MeO); 6.87 d, 7.27 d (4H, 4-$MeOC_6H_4$)	0.88, 0.97	1.40–2.47	5.35
VIIe	43	205–206	1715	1750	2.86 s (6H, Me_2N); 6.63 d, 7.15 d (4H, $Me_2NC_6H_4$)	0.87, 0.93	1.45–2.33	5.29
XIIIa	55	151–152	1720	1750	7.33 s (5H, Ph)	1.37, 1.47	0.63–2.40	5.46
XIIIb	60	163–164	1720	1750	7.22 d, 7.51 d (4H, 4-BrC_6H_4)	1.38, 1.43	1.03–1. 85	5.40
XIIIc	56	160–161	1720	1755	7.70 m, 8.23 m (4H, 3-$O_2NC_6H_4$)	1.40, 1.45	0.83–1.85	5.63

Comp. no.	Found, %			Formula	Calculated, %		
	C	H	N (Br)		C	H	N(Br)
VIIa	74.82	7.38	–	$C_{17}H_{20}O_3$	74.97	7.40	–
VIIb	58.03	5.48	(22.68)	$C_{17}H_{19}BrO_3$	58.13	5.45	(22.75)
VIIc	64.25	5.97	4.30	$C_{17}H_{19}NO_5$	64.34	6.04	4.41
VIId	71.58	7.25	–	$C_{18}H_{22}O_4$	71.50	7.33	–
VIIe	72,19	8.06	4.35	$C_{19}H_{25}NO_3$	72.35	7.99	4.44
XIIIa	75.06	7.47	–	$C_{17}H_{20}O_3$	74.97	7.40	–
XIIIb	58.01	5.39	(22.60)	$C_{I7}H_{19}BrO_3$	58.13	5.45	(22.75)
XIIIc	64.27	6.12	4.39	$C_{17}H_{19}NO_5$	64.34	6.04	4.41

in 40 ml of anhydrous benzene was added dropwise to a mixture of 10 g of zinc (prepared as fine turnings) and 10 ml of anhydrous ethyl acetate. The mixture was heated for 1 h under reflux, separated from excess zinc by decanting, and hydrolyzed with water. The organic phase was separated and dried over anhydrous sodium sulfate, the solvent was distilled off, and the residue was twice distilled under reduced pressure. Yield 72%. bp 107–109°C (13 mm), d_4^{20} = 1.0297, n_D^{20} = 1.4528. IR spectrum, ν, cm^{-1}: 1720, 1735, 1750 (C=O). ^1H NMR spectrum, δ, ppm: 0.91 d (6H, CH_3), 1.25–2.21 m [8H, $(CH_2)_4$], 2.61 m (1H, CHCO), 3.54 s (3H, CH_3O). Found, %: C 66.52; H 9.08. $C_{11}H_{18}O_3$. Calculated, %: C 66.64; H 9.15.

Methyl 2,2-dimethyl-3-oxo-3-cyclopentylpropionate (IX) was synthesized as described above for compound **II** from methyl α-bromoisobutyrate and cyclopentanecarbonyl chloride. Yield 64%. bp 94–96°C (6 mm), d_4^{20} = 1.0277, n_D^{20} = 1.4521. IR spectrum, ν, cm^{-1}: 1720, 1735, 1750 (C=O). ^1H NMR spectrum, δ, ppm: 0.85–2.03 m [8H, $(CH_2)_4$], 1.23 s (6H, CH_3), 2.55–2.95 m (1H, CHC=O), 3.62 s (3H, CH_3O). Found, %: C 66.69; H 9.24. $C_{11}H_{18}O_3$. Calculated, %: C 66.64; H 9.15.

Methyl 1-(2-bromoisobutyryl)cyclopentanecarboxylate (III). Bromine, 0.11 mol, was added with stirring to a solution of 0.1 mol of compound **II** in 25 ml of acetic acid. The mixture was heated for 1.5 h on a water bath, the solvent was distilled off, and the residue was distilled under reduced pressure. Yield 86%. bp 127–129°C (7 mm), d_4^{20} = 1.3491, n_D^{20} = 1.4911. IR spectrum, ν, cm^{-1}: 1715, 1735, 1755, 1760 (C=O). ^1H NMR spectrum, δ, ppm: 1.83 s (6H, CH_3), 1.17–2.53 m [8H, $(CH_2)_4$], 3.60 s (3H, CH_3O). Found, %: C 47.51; H 6.02; Br 28.95. $C_{11}H_{17}BrO_3$. Calculated, %: C 47.67; H 6.18; Br 28.83.

Methyl 3-(1-bromocyclopentyl)-2,2-dimethyl-3-oxopropionate (X) was synthesized from ester **IX** as described above for compound **III**. Yield 58%. bp 133–136°C (9 mm), mp 35–36°C (from petroleum ether). IR spectrum, ν, cm^{-1}: 1715, 1740, 1765 (C=O). ^1H NMR spectrum, δ, ppm: 1.45 s (6H, CH_3), 1.55–2.45 m [8H, $(CH_2)_4$], 3.62 s (3H, CH_3O). Found, %: C 47.49; H 6.11; Br 28.78. $C_{11}H_{17}BrO_3$. Calculated, %: C 47.67; H 6.18; Br 28.83.

8-Aryl-9,9-dimethyl-7-oxaspiro[4.5]decane-6,10-diones. *a. Compounds* ***VIIa, VIIb,*** *and* ***VIId***. A mixture of 0.03 mol of compound **III** and 0.023 mol of the corresponding aldehyde in 20 ml of anhydrous ethyl acetate was added dropwise with stirring to a mixture of 6 g of fine zinc turnings, a catalytic amount of $HgCl_2$, and 10 ml of anhydrous ethyl acetate. The mixture was heated for 1 h under reflux and cooled, the liquid phase was separated by decanting and hydrolyzed with 5% hydrochloric acid, the organic layer was separated, and the aqueous layer was extracted with two portions of diethyl ether. The extracts were combined with the organic phase, dried over anhydrous sodium sulfate, and evaporated, and the residue was twice recrystallized from methanol–ethyl acetate.

b. Compounds ***VIIc*** *and* ***VIIe***. A solution of 0.03 mol of compound **III** in 10 ml of ethyl acetate was added with stirring to a mixture of 6 g of activated zinc (prepared as fine turnings) and 10 ml of anhydrous ethyl acetate. The mixture was heated for 30 min under reflux, the liquid phase was separated by decanting, and 0.023 mol of aldehyde **Vc** or **Ve** was added. The subsequent procedure was the same as in *a*.

10-Aryl-7,7-dimethyl-9-oxaspiro[4.5]decane-6,8-diones XIIIa–XIIIc were synthesized from compound **X**, following the procedures described above in *a* (**XIIIa** and **XIIIb**) and *b* (**XIIIc**).

The yields, melting points, IR and ^1H NMR spectral parameters, and elemental analyses of compounds **VIIa**–**VIIe** and **XIIIa**–**XIIIc** are given in table.

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