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Reaction of Reformatsky Reagent Prepared from Methyl 1-Bromocyclohexanecarboxylate and Zinc with Substituted Chalcones

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Abstract— Methyl 1-bromocyclohexanecarboxylate reacts with zinc and substituted chalcones yielding the corresponding spiro-3,4-dihydropyran-2-one derivatives, 3- aryl-5- aryl-2-oxaspiro[5.5]undec-3-en-1-ones.

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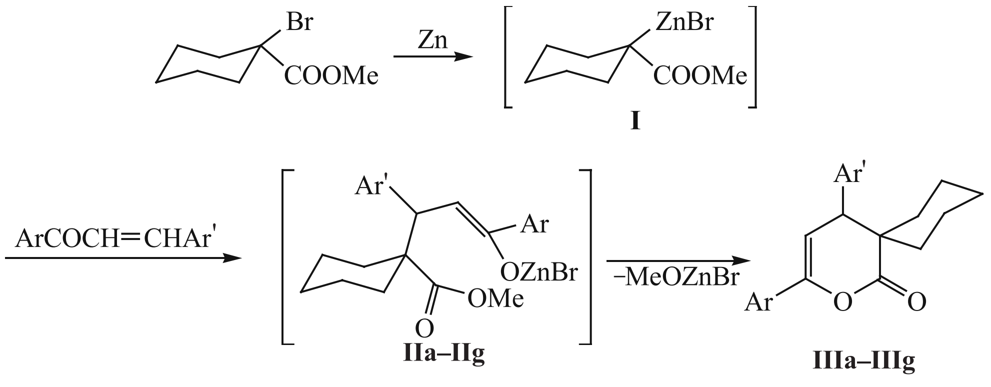
Reformatsky reagents reacting with α,β-unsaturated ketones add either in position *1*,*2* of the conjugated system or in position *1*,*4*; therewith the products of the 1,4-addition undergo cyclization with the formation of unsaturated lactones, derivatives of dihydropyran-2-one (see scheme) [1].

In order to prepare similar compounds with a spiro carbon atom we carried out a reaction of methyl 1-bromocyclohexanecarboxylate with zinc and substituted chalcones. In the first stage a Reformatsky reagent **I** was formed that further added to 1,3-diaryl-2-propen-1-ones giving intermediate compounds **IIa–IIg**. The latter by an attack of a nucleophilic oxygen on the carbonyl carbon of the ester group underwent cyclization with liberation of zinc methylate bromide to form substituted spiro-3,4-dihydropyran-2-ones, namely, 3,5-diaryl-2-oxaspiro[5.5]-undec-3-en-1-ones **IIIa–IIIg**.

Yields of reaction products attain 39–50%. The composition and structure of compounds obtained were proved by elemental analysis, IR and ^{1}H NMR spectra. In the IR spectra the characteristic absorption bands of the carbonyl group appeared in the region 1735–1760 cm^{-1}, and those of the C=C bond, at 1645–1665 cm^{-1}. The ^{1}H NMR spectra contained signals of protons of aryl substituents in the region 6.70–7.72 ppm, doublets of protons at the double bond in the region 5.74–6.17 ppm, methine protons doublets at 3.45–3.51 ppm, and the signals from protons of the cyclohexane ring in the range 0.91–2.25 ppm.

Scheme.



Ar = Ph, Ar' = Ph (**a**), 4-BrC$_6$H$_4$ (**b**), 4-ClC$_6$H$_4$ (**c**), 4-MeOC$_6$H$_4$ (**d**); Ar = 4-MeC$_6$H$_4$, Ar' = 4-BrC$_6$H$_4$ (**e**); Ar = 4-MeOC$_6$H$_4$, Ar' = 4-BrC$_6$H$_4$ (**f**); Ar = Ar' = 4-ClC$_6$H$_4$ (**g**).

1-Phenyl-3-(3-nitrophenyl)-2-propen-1-one did not react with Reformatsky reagent **I**: From the reaction mixture the initial chalcone was recovered.

EXPERIMENTAL

IR spectra of compounds **IIIa–IIIg** were recorded on a spectrophotometer Specord 75IR from mulls in mineral oil. ^{1}H NMR spectra of solutions of these compounds in $CDCl_3$ were registered on a spectrometer Tesla BS-576A (100 MHz), internal reference HMDS.

3,5-Diaryl-2-oxaspiro[5.5]undec-3-en-1-ones IIIa–IIIg. To a mixture of 1.5 g of fine zinc turnings, catalytic quantity of mercuric chloride, 1 ml of HMPA, and 10 ml of anhydrous ethyl acetate was added dropwise at stirring a mixture of 11 mmol of methyl 1-bromocyclohexanecarboxylate and 10 mmol of an appropriate chalcone in 20 ml of anhydrous benzene. The reaction mixture was boiled for 2 h, cooled, decanted from excess zinc, and hydrolyzed with 5% solution of acetic acid. The organic layer was separated, the reaction products were twice extracted from the water layer into ethyl acetate. The combined organic solution was dried with anhydrous sodium sulfate, ethyl acetate was distilled off, and compounds **IIIa–IIIg** were recrystallized from ethyl acetate.

3,5-Diphenyl-2-oxaspiro[5.5]undec-3-en-1-one (IIIa). Yield 1.50 g (47%), mp 140–141°C. IR spectrum, ν, cm^{-1}: 1645 (C=C), 1735 (C=O). ^{1}H NMR spectrum, δ, ppm: 6.87–7.66 m (10H, 2Ph), 5.83 d (1H, =CH, *J* 6.5 Hz), 3.49 d (1H, ArCH, *J* 6.5 Hz), 0.98– 2.22 m [10H, $(CH_2)_5$]. Found, %: C 83.12; H 7.06. $C_{22}H_{22}O_2$. Calculated, %: C 82.99; H 6.96.

5-(4-Bromophenyl)-3-phenyl-2-oxaspiro[5.5]-undec-3-en-1-one (IIIb). Yield 1.67 g (42%), mp 126–127°C. IR spectrum, ν, cm^{-1}: 1655 (C=C), 1745 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.08–7.65 m, 6.92 d (9H, Ph, 4-BrC_6H_4, *J* 8.4 Hz), 5.78 d (1H, =CH, *J* 6.5 Hz), 3.47 d (1H, ArCH, *J* 6.5 Hz), 0.93–2.23 m [10H, $(CH_2)_5$]. Found, %: C 66.37; H 5.45; Br 19.98. $C_{22}H_{21}BrO_2$. Calculated, %: C 66.51; H 5.33; Br 20.11.

3-Phenyl-5-(4-chlorophenyl)-2-oxaspiro[5.5]-undec-3-en-1-one (IIIc). Yield 1.52 g (43%), mp 150–151°C. IR spectrum, ν, cm^{-1}: 1660 (C=C), 1740 (C=O). ^{1}H NMR spectrum, δ, ppm: 6.87–7.72 m (9H, Ph, 4-ClC_6H_4), 5.79 d (1H, =CH, *J* 6.5 Hz), 3.46 d (1H, ArCH, *J* 6.5 Hz), 0.96–2.21 m [10H, $(CH_2)_5$]. Found, %: C 75.03; H 5.87; Cl 9.91. $C_{22}H_{21}ClO_2$. Calculated, %: C 74.89; H 6.00; Cl 10.05.

5-(4-Methoxyphenyl)-3-phenyl-2-oxaspiro[5.5]-undec-3-en-1-one (IIId). Yield 1.60 g (46%), mp 140–141°C. IR spectrum, ν, cm^{-1}: 1665 (C=C), 1735 (C=O). ^{1}H NMR spectrum, δ, ppm: 6.76–7.69 m (9H, Ph, 4-$MeOC_6H_4$), 5.86 d (1H, =CH, *J* 6.5 Hz), 3.75 s (3H, MeO), 3.49 d (1H, ArCH, *J* 6.5 Hz), 1.02–2.21 m [10H, $(CH_2)_5$]. Found, %: C 79.12; H 7.03. $C_{23}H_{24}O_3$. Calculated, %: C 79.28; H 6.94.

5-(4-Bromophenyl)-3-(4-methylphenyl)-2-oxaspiro[5.5]undec-3-en-1-one (IIIe). Yield 2.06 g (50%), mp 142–143°C. IR spectrum, ν, cm^{-1}: 1665 (C=C), 1740 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.46 d, 7.31 d, 7.10 d, 6.92 d (8H, 4-MeC_6H_4, 4-BrC_6H_4, *J* 8.4 Hz), 5.74 d (1H, =CH, *J* 6.5 Hz), 3.45 d (1H, ArCH, *J* 6.5 Hz), 2.34 s (3H, Me), 1.01–2.18 m [10H, $(CH_2)_5$]. Found, %: C 67.01; H 5.55; Br 19.71. $C_{23}H_{23}BrO_2$. Calculated, %: C 67.16; H 5.64; Br 19.43.

5-(4-Bromophenyl)-3-(4-methoxyphenyl)-2-oxaspiro[5.5]undec-3-en-1-one (IIIf). Yield 1.67 g (39%), mp 129–130°C. IR spectrum, ν, cm^{-1}: 1645 (C=C), 1750 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.38–7.62 m, 6.98 d, 6.79 d (8H, 4-$MeOC_6H_4$, 4-BrC_6H_4, *J* 8.5 Hz), 6.17 d (1H, =CH, *J* 6.5 Hz), 3.69 d (1H, ArCH, *J* 6.5 Hz), 3.67 s (3H, MeO), 1.00–2.20 m [10H, $(CH_2)_5$]. Found, %: C 64.50; H 5.61; Br 18.59. $C_{23}H_{23}BrO_3$. Calculated, %: C 64.64; H 5.42; Br 18.70.

3,5-Bis(4-chlorophenyl)-2-oxaspiro[5.5]undec-3-en-1-one (IIIg). Yield 1.70 g (44%), mp 134–135°C. IR spectrum, ν, cm^{-1}: 1660 (C=C), 1760 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.50 d, 7.23 d, 7.15 d, 6.93 d (8H, 4-ClC_6H_4, 4-ClC_6H_4, *J* 8.5 Hz), 5.74 d (1H, =CH, *J* 6.5 Hz), 3.48 d (1H, ArCH, *J* 6.5 Hz), 0.91–2.25 m [10H, $(CH_2)_5$]. Found, %: C 68.41; H 5.08; Cl 18.56. $C_{22}H_{20}Cl_2O_2$. Calculated, %: C 68.23; H 5.20; Cl 18.31.

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