Reactions between Furyl Ketones and Grignard Reagents. III. Suppression of 1,4-Addition of Benzylmagnesium Chloride to Alkyl 2-Furyl Ketones by Voluminous Alkyl Groups at the Carbonyl Carbon *

RAINER SJÖHOLM and AGNETA LUNDQVIST

Institutionen för organisk kemi, Åbo Akademi, SF-20500 Åbo 50, Finland

When alkyl 2-furyl ketones react with alkylmagnesium halides the amount of conjugate addition increases at the expense of 1,2-addition when the size of the alkyl group of the ketone or that of the reagent is increased.[2,3]

However, in our studies of the title reaction, we observed a trend opposing that observed for alkyl reagents.

Results. When benzylmagnesium chloride was allowed to react with alkyl 2-furyl ketones (R = Et, i-Pr or *t*-Bu) 1,2- and 1,4-additions (*cis* and *trans*) were observed (Scheme 1). The 1,4-addition products were oxidized by air during the work-up procedure. The oxidations, which have been dealt with in detail previously,[2-5] resulted in the formation of compounds *3* and *4*. No 1,6-additions were observed.

The results are presented in Table 1. For comparison, results from Refs. 2 and 5 are included. The yields are normalized and "1,4-addition" includes all 1,4-addition products. The data in Table 1 show that the amount of 1,4-addition decreases drastically when the size of the group at the carbonyl carbon of the ketone is increased.

Table 1. Normalized[a] and total yields of products from the reaction of benzylmagnesium chloride with alkyl 2-furylketones and furfural (2-FurCOR). Yields are given in mol-% of reacted substrate.

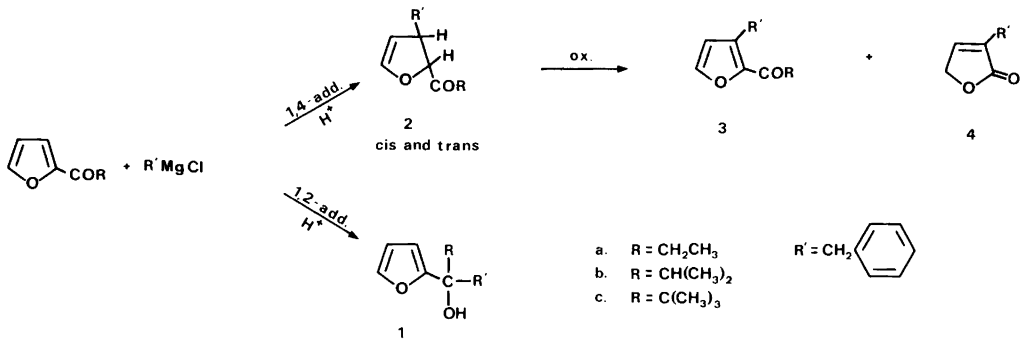
Substrate R	Products 1,2-addn	1,4-addn[b]	Total yield
H[d]	17	83	–[f]
Me[e]	33	67	54
Et	55	45	65
i-Pr	97	3	78
t-Bu	>99	<1	80

[a] 100 % = % 1,2-addn + % 1,4-addn. [b] Oxidation products included. [d] Data from Ref. 5. [e] Data from Ref. 2. [f] Tot. yield not determined.

The observed effect is opposed to the one observed with i-propyl and *t*-butyl Grignard reagents.

Discussion. The explanation of the difference between alkyl- and benzylmagnesium chlorides in reactions with alkyl 2-furyl ketones, is probably to be found in the possibility of the substrate occupying two different conformations. One hypothesis, presented previously,[3] is based on the assumption that the ketones, in their reactions with benzylmagnesium chloride, are forced into the less favourable *syn* conformation as a results of coordination of the Mg-atom of the reagent to both oxygen atoms of the substrate. This would then bring a bulky group at the carbonyl carbon very close to C-3 in the furan ring, thus preventing 1,4-addition.

* *Cf.* Ref. 1; For Part II, see Ref. 3.



Scheme 1.

0302-4369/80/060446-03$02.50

At this stage, no evidence for this hypothesis can be presented. A closer study of the mechanisms involved in the reactions of alkyl and benzyl Grignard reagents with alkyl 2-furyl ketones is now in progress.

Experimental. 1-(2-Furyl)-propan-1-one, 1-(2-furyl)-2-methylpropan-1-one and 1-(2-furyl)-2,2-dimethylpropan-1-one were prepared by methods described previously.[3]

The reactions between the ketones and benzylmagnesium chloride and the qualitative and quantitative analyses were performed as described previously,[3] except that benzophenone and benzyl benzoate were used as internal GLC-standards.

Compounds *2b*, *2c*, *3b* and *3c* could not be isolated. However, comparison of their mass spectra with those of similar compounds, isolated previously[2,5] and identified by ^{1}H NMR spectroscopy, confirmed the structures.

The ^{1}H NMR spectra of the furfuryl alcohols (*1*) displayed ABX spin systems for the furan ring protons, the shifts ranging from δ 5.91 to 6.28 ppm for H_3 and H_4 and from δ 7.39 to 7.41 ppm for H_5. The spin systems were not completely analyzed and the exact shifts and couplings are omitted. The shifts of the OH protons are concentration dependant and are also omitted.

2-(2-Furyl)-1-phenylbutan-2-ol (1a). ^{1}H NMR (60 MHz, $CDCl_3$): δ 0.87 (CH_3CH_2-, t, J 7.8 Hz), 1.88 (CH_3CH_2-, q, J 7.8 Hz), 3.00 and 3.24 (PhCH_2-, AB-syst., J_{AB} 13.4 Hz), 6.73 to 7.34 (PhH, m). MS [IP 70 eV; *m/e* (% rel. int.)]: 216 (2, M), 198 (22, M$-H_2O$), 183 (5, M$-H_2O-CH_3$), 169 (9, M$-H_2O-CH_3CH_2$), 125 (100, M$-$PhCH$_2$), 105 (7), 95 (9, FurCO), 91 (17, PhCH$_2$), 43 (15), 29 (10, CH_3CH_2).

2-(2-Furyl)-3-methyl-1-phenylbutan-2-ol (1b). ^{1}H NMR (60 MHz, $CDCl_3$): δ 0.91 and 1.02 [$(CH_3)_2CH-$, dd, J 6.7 Hz], 2.13 [$(CH_3)_2CH-$, sept, J 6.7 Hz], 3.00 and 3.36 (PhCH_2-, AB-syst., J_{AB} 12.7 Hz), 6.7 to 7.3 (PhH, m). MS [IP 70 eV; *m/e* (% rel. int.)]: 230 (1, M), 212 (12, M$-H_2O$), 197 (5, M$-H_2O-CH_3$), 187 [17, M$-(CH_3)_2CH$], 169 [6, M$-H_2O-(CH_3)_2CH$], 139 (100, M$-$PhCH$_2$), 105 (17) 97 (34), 95 (17, FurCO), 91 (23, PhCH$_2$), 43 [36, $(CH_3)_2CH$].

2-(2-Furyl)-3,3-dimethyl-1-phenylbutan-2-ol (1c). ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.05 [$(CH_3)_3C-$, s], 2.98 and 3.45 (PhCH_2-, AB-syst., J_{AB} 12.9 Hz), 6.7 to 7.2 (PhH, m). MS [IP 70 eV; *m/e* (% rel. int.)]: 244 (3, M), 226 (2, M$-H_2O$), 211 (2, M$-H_2O-CH_3$), 187 [100, M$-(CH_3)_3C$], 111 (25), 105 (42), 95 (24, FurCO) 91 (42, PhCH$_2$), 57 [13, $(CH_3)_3C$], 43 (45).

In all reaction mixtures two isomers of the 2,3-dihydrofuryl ketones formed by 1,4-addition of the reagent to the ketones were detected. These were identified as *cis* and *trans* isomers, respectively, based on arguments presented previously.[2] However, only one of the 1,4-addition products (*2a*), shown to be *trans* by ^{1}H NMR spectroscopy,[5] could be isolated. The mass spectra of the isomers were very similar and only the MS data of the more abundant isomer (believed to be *trans*) are given below.

trans - *1 - (3 - Benzyl - 2,3 - dihydro - 2 - furyl) - propan - 1 - one* (2a). ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.20 (CH_3CH_2-, t, J 7.8 Hz), 2.27 (CH_3CH_2-, q, J 7.8 Hz), ~2.5–3.7 (PhCH_2- and H'_3, poorly resolved ABX-system), 4.48 (H'_2, d, J 5.4 Hz), 4.91 (H'_4, t, J 2.6 Hz), 6.38 (H'_5, dd, J 2.6 and 1.6 Hz). MS [IP 70 eV; *m/e* (% rel. int.)]: 216 (2, M) 214 (1, M$-$2H), 187 (3, M$-CH_3CH_2$), 148 (5, M$-$68), 159 (10, M$-CH_3CH_2CO$), 125 (5, M$-$PhCH$_2$), 95 (1, FurCO), 91 (63, PhCH$_2$), 68 (4, C_4H_4O), 57 (100, CH_3CH_2CO).

1 - (3 - Benzyl - 2,3 - dihydro - 2 - furyl) - 2 - methylpropan-1-one (2b). MS [IP 70 eV; *m/e* (% rel. int.)]: 230 (1, M), 228 (<1, M$-$2H), 187 [7, M$-(CH_3)_2CH$], 162 (4, M$-$68), 159 [7, M$-(CH_3)_2CHCO$], 139 (8, M$-$PhCH$_2$), 95 (3, FurCO), 91 (100, PhCH$_2$), 71 (71, $(CH_3)_2$ CHCO], 43 [59, $(CH_3)_2CH$].

1 - (3 - Benzyl - 2,3 - dihydro - 2 - furyl) - 2,2 - dimethylpropan-1-one (2c). MS [IP 70 eV; *m/e* (% rel. int.)]: 244 (2, M), 242 (2, M$-$2H), 187 [77, M$-(CH_3)_3C$], 176 (4, M$-$68), 159 [6, M$-(CH_3)_3CCO$], 153 (17, M$-$PhCH$_2$), 95 (13, FurCO), 91 (97, PhCH$_2$), 85 [43, $(CH_3)_3CCO$], 68 (8, C_4H_4O), 57 [100, $(CH_3)_3C$].

Only one of the substituted furyl ketones, formed by oxidation of the primary 1,4-addition products, could be isolated and the structure confirmed by ^{1}H NMR spectroscopy. The other two were identified by their mass spectra.

1-(3-Benzyl-2-furyl)-propan-1-one (3a). ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.19 (CH_3CH_2-, t, J 7.5 Hz), 2.91 (CH_3CH_2-, q, J 7.5 Hz), 4.22 (PhCH_2-, s), 7.26 (PhH, s), 6.30 (H'_4, d, J 1.9 Hz), 7.36 (H'_5, d, J 1.9 Hz). MS [IP 70 eV; *m/e* (% rel. int.)]: 214 (100, M), 199 (4, M$-CH_3$), 185 (100, M$-CH_3CH_2$), 181 (13), 157 (77, M$-CH_3CH_2CO$), 129 (47, M$-CH_3CH_2CO-$CO), 128 (60, M$-CH_3CH_2CO-$CHO), 91 (22, PhCH$_2$), 77 (27, Ph), 57 (18, CH_3CH_2CO).

1 - (3 - Benzyl - 2 - furyl) - 2 - methylpropan - 1 - one (3b). MS [IP 70 eV; *m/e* (% rel. int.)]: 228 (53, M), 213 (6, M$-CH_3$), 195 (6), 185 [100, M$-(CH_3)_2CH$], 157 [44, M$-(CH_3)_2CHCO$], 129 [23, M$-(CH_3)_2CHCO-$CO], 128 [26, M$-(CH_3)_2CHCO-$CHO], 91 (19, PhCH$_2$), 77 (11, Ph), 71 [6, $(CH_3)_2CHCO$], 43 [13, $(CH_3)_2CH$].

1-(3-Benzyl-2-furyl)-2,2-dimethylpropan-1-one (3c). MS [IP 70 eV; *m/e* (% rel. int.)]: 242 (25, M), 217 (3, M$-CH_3$), 186 (30), 185 [100, M$-(CH_3)_3C$], 157 [11, M$-(CH_3)_3CCO$], 129 [7, M

$-(CH_3)_3CCO-CO]$, 128 [19, $M-(CH_3)_3CCO-CHO]$, 91 (21, $PhCH_2$), 77 (7, Ph), 57 [39, $(CH_3)_3C$].

3-Benzyl-2-(5H)-furanone(4). The ^1H NMR and mass spectral data were found to be identical with those reported previously for this compound.[5]

Acknowledgements. Financial support of this work by *Stiftelsens för Åbo Akademi Forskningsinstitut* and *Magnus Ehrnrooths stiftelse* is gratefully acknowledged.

1. Results presented in part at *Ninth International Conference on Organometallic Chemistry*, Dijon, France 1979 and at *Third International Symposium of Furan Chemistry*, Smolenice, Czechoslovakia 1979.
2. Sjöholm, R. and Aura, P.-E. *Acta Acad. Abo. Ser. B 38* (1978) No. 1.
3. Sjöholm, R. and Wörlund, K. *Acta Chem. Scand. B 34* (1980) 435.
4. Sjöholm, R. *Acta Chem. Scand. B 31* (1977) 278.
5. Sjöholm, R. *Acta Chem. Scand. B 32* (1978) 105.

Received April 25, 1980.