Acta Chemica Scandinavica B 31 (1977) 278—280

Reactions between 2-Furanaldehyde and Grignard Reagents. I. 1,4- and 1,6-Additions of *t*-Butylmagnesium Chloride

RAINER SJÖHOLM

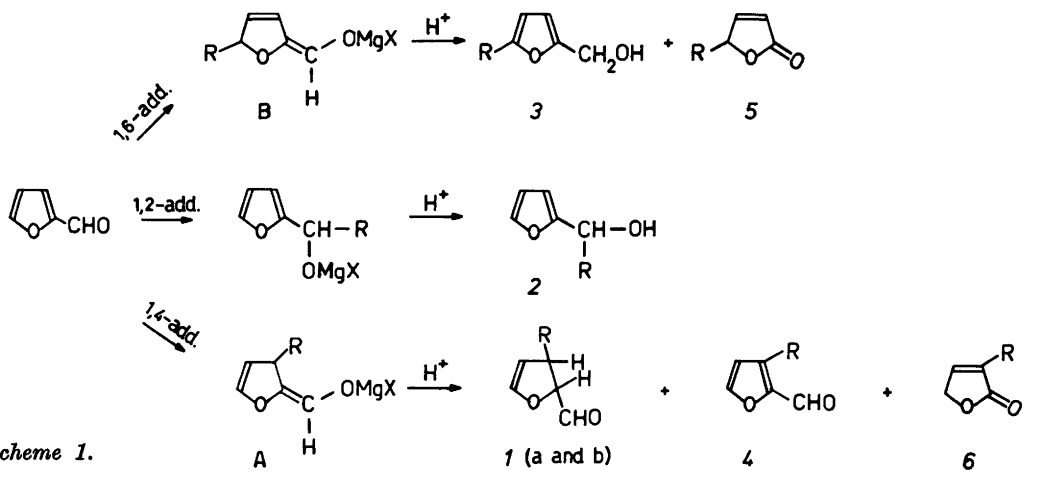
Institutionen för organisk kemi, Åbo Akademi, SF-20500 Åbo 50, Finland

When methylmagnesium iodide, ethylmagnesium bromide, isopropylmagnesium chloride, and isobutylmagnesium chloride react with 2-furanaldehyde, only 1,2-addition products are formed. *t*-Butylmagnesium chloride gives 1,4- and 1,6-addition products besides 1,2-addition. The 1,6-addition product rearranged easily and was isolated as 5-*t*-butylfurfuryl alcohol. Two lactones, 5-*t*-butyl-2-(5*H*)-furanone and 3-*t*-butyl-2-(5*H*)-furanone, were also isolated from the reaction mixture. The formation of the various products is discussed.

1,2-Addition of Grignard reagents to 2-furanaldehyde is a well-known reaction, which has been widely used for the preparation of various secondary furfuryl alcohols.[1]

Conjugate addition of Grignard reagents to the furan nucleus in 2-furanaldehyde, however, has not been previously reported. Gocmen *et al.*[2] could not detect any reaction products arising from conjugate addition, when they studied the reactions between 2-furanaldehyde and various Grignard reagents (methyl-, ethyl-, butyl- and phenylMgX). Fuson *et al.*[3,4] have shown that phenylmagnesium bromide adds in the 1,4-mode to furyl and benzofuryl ketones in which the carbonyl group is highly sterically hindered. They ascribed the 1,4-addition mainly to the steric effect. Berreby *et al.*,[5] however, reported a 30 % yield of conjugate addition in the reaction between 2-acetylfuran and benzylmagnesium chloride. In this case steric hindrance should be less important.

The 1,6- and 1,8-additions of *t*-butyl and benzyl Grignard reagents to diethyl furfurylidenemalonates [6–9] definitely show that steric hindrance cannot be the only factor determining whether addition of Grignard reagents to furan rings happens or not. These results seemed to justify a reinvestigation of the reactions between 2-furanaldehyde and Grignard reagents. Methylmagnesium iodide, ethylmagnesium bromide, isopropylmagnesium chloride, isobutylmagnesium chloride, and *t*-butylmagnesium chloride were chosen as the reagents. Except for the *t*-butyl reagent, the alkyl Grignard reagents gave only 1,2-adducts [*2*, R = CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$] (*cf.* Ref. 2). In addition to the 1,2-adduct *2*, which was the major product, the *t*-butyl reagent gave six products. The products were separated and purified by preparative gas chromatography. The identifications were performed by NMR and mass spectroscopy. The compound with the shortest retention time (*1a*) proved to be 3-*t*-butyl-2,3-dihydro-2-furanaldehyde formed by 1,4-addition of *t*-butylmagnesium chloride to 2-furanaldehyde. The ^1H NMR spectrum of *1a* showed that the *t*-butyl group is *trans* to the aldehyde group. The gas chromatogram showed a rather small peak on the slope of the peak of compound *1a*. This component (*1b*) was not isolated, but the mass spectrum was very similar to that of compound *1a*. On these presumptions, it seems possible that *1b* is the *cis* form of 3-*t*-butyl-2,3-dihydro-2-furanaldehyde. The preferential formation of the *trans* form is expected on steric grounds, assuming that both *1a* and *1b* are formed from the same precursor, namely the enolate A (Scheme 1) primarily formed in the 1,4-addition of *t*-butylmagnesium chloride to 2-furanaldehyde. However, no definite proof on the structure of 1b can be presented.



Scheme 1.

Compound *2* [R = C(CH$_3$)$_3$] was identified as 1-(2-furyl)-2,2-dimethylpropan-1-ol. This product is the result of 1,2-addition of the reagent to 2-furanaldehyde.

The formation of compound *3* represents a rather interesting 1,6-addition of *t*-butylmagnesium chloride to 2-furanaldehyde. In this case the primary product probably is the enolate B (Scheme 1). During the work-up of the reaction mixture the enol formed from this salt easily rearranges prototropically to the energetically more favourable structure, giving 5-*t*-butylfurfuryl alcohol. The mechanism is analogous to the one presented by Holmberg *et al.*[6] for the rearrangement of diethyl 2,3-dihydro-2-furylidenemethylmalonates under acidic conditions. The corresponding dihydro compound could not be detected by GLC.

The next compound on GLC proved to be 3-*t*-butyl-2-furanaldehyde (*4*). This compound is probably formed from *1* by some kind of oxidation.

The remaining compounds (*5* and *6*) proved to be lactones, namely 5-*t*-butyl-2-(5*H*)-furanone and 3-*t*-butyl-2-(5*H*)-furanone. Fuson *et al.*[3] have shown that lactones are formed when highly hindered benzofuryl ketones react with Grignard reagents under conditions not rigidly excluding air. In this work exclusion of air during the reaction did not reduce the amounts of lactones formed. Fuson also showed that a stream of oxygen passed through the reaction mixture after interruption of the reaction, increased the yield of lactones by oxidation of the enol formed when the reaction mixture was acidified. In the present work the mentioned procedure had no effect on the product distribution. This shows that in this case probably no enols are present after the interruption of the reaction as they immediately rearrange when formed. This indicates that the lactones are formed directly from the enolates.

When a great excess of Grignard reagent was used (10:1), the molar ratios of compounds *1* (*1a*+*1b*), *2*, *3*, *4*, *5*, and *6* were 29:63:2:2.5:0.5:3 (by GLC). It should be noted that compounds *5* and *6* probably are, at least primarily, 1,6- and 1,4-addition products and thus the molar ratios between 1,2-, 1,4- and 1,6-addition products are 63:34.5:2.5.

It may seem strange that no 3-*t*-butylfurfuryl alcohol, formed analogously to the formation of compound *3*, was detected. However, this could be explained by the steric strain that would be present in this compound (*cf.* Ref. 9). This steric strain arises from the proximity of the two bulky substituents in positions 2 and 3 in the furan ring. This and the fact that *1* represents a vinyl ether which is resonance stabilized explain the preferential formation of 3-*t*-butyl-2,3-dihydro-2-furanaldehyde.

Corresponding formation of 5-*t*-butyl-2,5-dihydro-2-furanaldehyde from the enolate B is not expected as the formation of *3* is accompanied by a considerable gain in resonance energy. Moreover, the rearrangement would lead to the formation of an energetically unfavourable structure.

EXPERIMENTAL

2-Furanaldehyde. Commercial 2-furanaldehyde was used (Riedel-de Haën, BRD) after purification by distillation (161 – 162 °C).

The reactions of 2-furanaldehyde with methylmagnesium iodide, ethylmagnesium bromide, isopropylmagnesium chloride and isobutylmagnesium chloride were performed by adding 2-furanaldehyde (20 mmol) dissolved in absolute diethyl ether (100 ml) to a stirred solution of 100 ml of 1 M (by titration) Grignard reagent. Stirring was continued for 1 h. The reaction mixture was worked up in the usual way using NH_4Cl solution. Each reaction gave only one product (by GLC and NMR), namely the α-substituted furfuryl alcohol [*2*, R = CH_3, CH_2CH_3, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$]. The structures were confirmed by NMR and mass spectra.

The reaction between 2-furanaldehyde and t-butylmagnesium chloride was performed in the described way with one exception, the excess of Grignard reagent was greater (10:1). One reaction was performed under nitrogen and the ether used was distilled from benzophenone ketyl. However, the gas chromatogram (glass column 3 mm × 3 m; stationary phase 3 % OV-17 on Gas-Chrom Q; N_2 30 ml/min) of the resulting reaction mixture was identical with that of the reaction mixture from an experiment where no attempts to exclude air were made. In one experiment (under N_2) the reaction mixture was divided into two parts which were worked up separately. A stream of oxygen was passed through one of the ether solutions for 0.5 h. The gas chromatograms of the two solutions were identical.

The reaction products were separated and purified by preparative GLC (column 9.5 mm × 6.1 m; stationary phase 30 % SE-30 on Chromosorb W; He 200 ml/min).

3-t-Butyl-2,3-dihydro-2-furanaldehyde (1). The NMR spectrum clearly shows that *1* is a dihydrofuran aldehyde. The magnitude of the coupling between H-2 and H-3, assuming envelope conformation,[10] is in agreement with the value obtained for the *trans* form by the Karplus' rule. ^1H NMR (60 MHz, CCl_4): δ 4.3 (H-2, dd, *J* 4.3 and 1.4 Hz), 2.7 (H-3, ddd, *J* 4.3, 2.6 and 1.9 Hz), 4.8 (H-4, dd, *J* 2.7 and 2.6 Hz). 6.3 (H-5, dd, *J* 2.7 and 1.9 Hz), 9.5 (C*H*O, *J* 1.4 Hz), 0.9 [C(CH_3)$_3$, s].

MS[IP 70 eV; *m/e* (% rel. int.)]: 154 (15, M), 125 (2.5 [M – CHO]), 98 (16.8), 97 (7.5), 69 (43.8), 57 (100).

1-(-2-Furyl-)-2,2-dimethylpropan-1-ol [*2*, *R* = *C*(CH_3)$_3$]. This well-known substance was easily identified from NMR and mass spectra.

5-t-Butyl furfuryl alcohol (3). The NMR and mass spectra were compared with spectra of a synthesized sample[7] and were found to be identical.

3-t-Butyl-2-furanaldehyde(4). The NMR spectrum confirmed the aldehyde structure by showing a one-proton signal at δ 9.4. The substituent position was confirmed by the existence of an AB-system arising from H-4 and H-5. ^1H NMR (60 MHz, CCl_4): δ 6.1 (H-4, d, *J* 3.6 Hz), 7.0 (H-5, d, *J* 3.6), 9.4 (C*H*O), 1.3 [C(CH_3)$_3$, s].

MS [IP 70 eV; *m/e* (% rel. int.)]: 152 (26.3, M), 137 (100, M – CH_3), 123 (4.7, M – CHO), 109 (14.1), 95 (9.1).

5-t-Butyl-2-(5H)-furanone (5). This compound was synthesized by a method described in Ref. 11. Compound *5* and the synthesized compound gave identical NMR and mass spectra. ^1H NMR (60 MHz, CCl_4): δ 6.1 (H-3, dd, *J* 5.7 and 2.0 Hz) 7.6 (H-4, dd, *J* 5.7 and 1.3 Hz), 4.7 (H-5, dd, *J* 2.0 and 1.3 Hz), 1.1 [C(CH_3)$_3$, s].

MS [IP 70 eV; *m/e* (% rel. int.)]: 140 (1.5, M), 125 (4.0, M – CH_3), 97 (6.3), 84 (16.0), 57 (100).

3-t-Butyl-2-(5H)-furanone (6). ^1H NMR (60 MHz, CCl_4): δ 6.9 (H-4, t, *J* 1.8 Hz), 4.6 (H-5, d, *J* 1.8 Hz), 1.2 [C(CH_3)$_3$, s].

MS [IP 70 eV; *m/e* (% rel. int.)]: 140 (47.9, M), 125 (42.3, M – CH_3), 122 (13.4, M – H_2O), 111 (9.9, M – CHO), 107 (6.4), 97 (67.4), 95 (34.7), 79 (49.4), 57 (17.5), 41 (100).

REFERENCES

1. Dunlop, A. P. and Peters, F. N. *The Furans*, Reinhold, New York 1953, p. 253.
2. Gocmen, M., Soussan, G. and Fréon, P. *Bull. Soc. Chim. Fr.* (1973) 1310.
3. Fuson, R. C., Kaiser, E. W. and Speck, S. B. *J. Org. Chem. 6* (1941) 845.
4. Fuson, R. C. and Wallingford, H. P., *J. Am. Chem. Soc. 75* (1953) 5951.
5. Berreby, E., Morizur, J.-P. and Wiemann, J. *Bull. Soc. Chim. Fr.* (1967) 3529.
6. Holmberg, G.-A., Karlsson, M., Ulfstedt, O. and Olli, M. *Acta Chem. Scand. 26* (1972) 3483.
7. Holmberg, G.-A., Olli, M., Strand, U. and Jalonen, H. *Acta Chem. Scand. 27* (1973) 1219.
8. Holmberg, G.-A., Jalander, L., Norrgård, H. and Pettersson, B. *Acta Chem. Scand. B 28* (1974) 909.
9. Holmberg, G.-A., Wennström, M. and Grönlund, M. *Acta Chem. Scand. B 29* (1975) 728.
10. Taskinen, E. Diss., *Ann. Acad. Sci. Fenn. Ser. A 2 163* (1972).
11. Hill, G. A., Salvin, V. and O'Brien, Jr., W. T. M. *J. Am. Chem. Soc. 59* (1937) 2385.

Received, October 19, 1976.