Pergamon

SCIENCE DIRECT®

Tetrahedron: *Asymmetry* 14 (2003) 3643–3645

TETRAHEDRON: *ASYMMETRY*

(Salen)Co(II) complex—an efficient catalyst for the high-pressure Friedel–Crafts reaction of 2-methylfuran with alkyl glyoxylates

Piotr Kwiatkowski,[a] Elżbieta Wojaczyńska[a,†] and Janusz Jurczak[a,b,*]

[a]*Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland*
[b]*Department of Chemistry, Warsaw University, Pasteura 1, 02-093 Warsaw, Poland*

Received 26 July 2003; accepted 13 August 2003

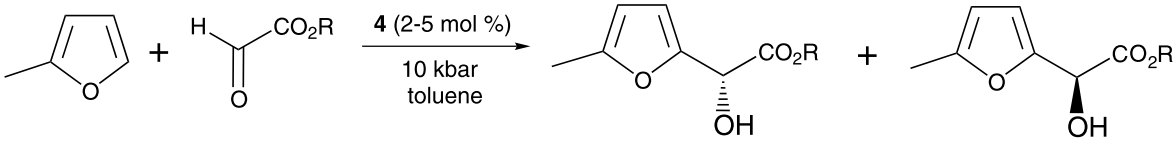
Abstract—The high-pressure (10 kbar) reaction of 2-methylfuran **1** with alkyl glyoxylates **2**, catalyzed by the chiral (Salen)Co(II) complex **4**, afforded the Friedel–Crafts products **3** both in good yield (up to 70%) and enantioselectivity (up to 76% ee).

The Friedel–Crafts reaction of aromatic compounds with aldehydes or ketones is one of the most fundamental reactions in organic chemistry,[1] however, its enantioselective catalytic version is still an unexplored field.[2] We have focused our attention on the reaction of 2-substituted furans, e.g. 2-methylfuran **1**, with simple activated carbonyl compounds such as *n*-butyl **2a** and *iso*-propyl glyoxylate **2b**, leading, under acidic catalytic conditions, to the chiral furfuryl alcohols of type **3** (Scheme 1),[3] providing a broad spectrum of intermediates[4] convenient for further transformation. The diastereoselective variants of this Friedel–Crafts reaction were also studied in our laboratory[5] and justify its potential use in the synthesis of natural products.[6]

Preliminary studies on catalysts for the reaction shown in Scheme 1 have been performed using various cationic Salen complexes of transition metals, such as Ti(IV), Cr(III), Mn(III), Fe(III), Co(III), and Al(III), under thermal conditions (25°C) to give mixtures of enantiomers of **3**[7,8] in good yields (60–80%). Unfortunately, the enantioselectivities were low (<20% ee). Therefore, we decided to test the much less active, commercially available cobalt(II) complex **4a** ($R^1 = R^2 = Bu^t$) (Fig. 1), employed mainly as a catalyst for kinetic resolution of epoxides.[9]

This catalyst promoted the title reaction only moderately (~15% yield), however, the products of type **3** were formed in much better enantioselectivity (>40% ee). This result prompted us to continue the investigations using the high-pressure technique.[10] The results are presented in Table 1.

In the presence of the catalyst (*R*,*R*)-**4a** in toluene, the reaction of **1** and **2** proceeds under atmospheric pres-

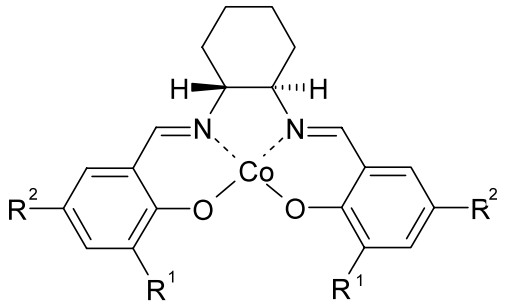


1 **2a** R= Bu^n **2b** R=Pr^i *(R)*-**3a** *(R)*-**3b** *(S)*-**3a** *(S)*-**3b**

Scheme 1.

* Corresponding author. Tel.: +48 22 8230944; fax: +48 22 822599; e-mail: jurczak@icho.edu.pl
† Permanent address: Institute of Organic Chemistry, Biochemistry and Biotechnology, Wroclaw University of Technology, 50-370 Wroclaw, Poland.

0957-4166/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2003.08.012



4 (R^1 and R^2 as defined in Table 2)

Figure 1. (*R*,*R*)-(Salen)Co.

sure, but its yield is negligible (Table 1, entry 1). The increase of pressure clearly accelerates the reaction, resulting at the same time in an increase of enantioselectivity (entries 2–4). We found that enantioselectivity was slightly sensitive to the concentration of glyoxylate **2** (entries 4–6) as well as the concentration of the catalyst (entries 6–11). We observed a clear influence of the solvent on the enantioselectivity (entries 12–15). The best result in this series was obtained for the reaction carried out in toluene (entry 12), whereas the worst result was obtained in CH_2Cl_2 (entry 15).

In turn, we decided to study the influence of the ligand structure of the catalysts (*R*,*R*)-**4** on the title reaction. The results are presented in Table 2. The (*R*)-selectivity was observed for all complexes having R^1 = *tert*-butyl (Table 2, entries 1–5), whereas R^2 practically did not influence the asymmetric induction. The situation changed dramatically when the catalyst having the simplest ligand was used (**4f**, $R^1 = R^2 = H$). In this case, the direction of the induction was reversed, leading to (*S*)-selectivity (entry 6). This tendency was confirmed for three other catalysts having R^1 other than *tert*-butyl (entries 7–9). In all these cases, the inductions were only slightly lower than the previous ones (compare entries 1–5 and 6–9).

Our results present the first example of the enantioselective Friedel–Crafts reaction catalyzed by Salen-type complexes, and open an efficient and economic route to optically active furfuryl alkohols being exceptionally convenient precursors for many natural products, including carbohydrates. At this stage, the rationalization of these results is very difficult.

Table 2. Influence of the ligand structure in the catalyst (*R*,*R*)-**4** on the high-pressure reaction of **1** with **2a**[a]

Entry	Catalyst **4**			Yield (%)	(*R*)-**3**:(*S*)-**3**
	No.	R^1	R^2		
1	**4a**	Bu^t	Bu^t	70	82:18
2	**4b**	Bu^t	Me	60	86:14
3	**4c**	Bu^t	H	49	82:18
4	**4d**	Bu^t	OMe	38	83:17
5	**4e**	Bu^t	Br	28	81:19
6	**4f**[b]	H	H	23	24:76
7	**4g**	H	Bu^t	15	27:73
8	**4h**	Me	Bu^t	30	24:76
9	**4i**[b]	Ph	H	38	19:81

[a] Conditions: **4**—2 mol%, **2a**—0.5 mol/L, **1**—1.5 equiv., toluene, 10 kbar, 25°C, 20 h.
[b] Dissolution of the catalyst was incomplete.

Table 1. Results of the reaction of **2a** or **2b** with **1** in the presence of **4a**[a]

Entry	Glyoxylate **2**		Catalyst **4a** (mol%)	Solvent	Pressure (bar)	Yield (%)	(*R*)-**3**:(*S*)-**3**[b]	E.e. (%)
	R	(mol/L)						
1	Bu^n	0.25	5	Toluene	1	15	72:28	44
2	Bu^n	0.25	5	Toluene	6000	68	74:26	48
3	Bu^n	0.25	5	Toluene	8000	70	76:24	52
4	Bu^n	0.25	5	Toluene	10000	70	86:14	72
5	Bu^n	0.1	5	Toluene	10000	47	88:12	76
6	Bu^n	0.5	5	Toluene	10000	69	83:17	66
7	Bu^n	0.5	2	Toluene	10000	70	81:19	62
8	Bu^n	0.5	1	Toluene	10000	33	78:22	56
9	Bu^n	0.5	0.5	Toluene	10000	31	71:29	42
10	Bu^n	0.5	0.1	Toluene	10000	28	69:31	38
11	Bu^n	0.5	10	Toluene	10000	68	82:18	64
12	Pr^i	0.5	5	Toluene	10000	50	80:20	60
13	Pr^i	0.5	5	Bu^{t}OMe	10000	41	69:31	38
14	Pr^i	0.5	5	MeCN	10000	54	57:43	14
15	Pr^i	0.5	5	CH_2Cl_2	10000	67	52:48	4

[a] Other conditions: 25°C, 20 h.
[b] Enantiomeric excess of **3a** and **3b** was determined by gas chromatography on a capillary chiral column β-dex 120 (permethyl-β-cyclodextrin, 30 m×0.25 mm I.D. Supelco, Bellefonte, USA). Chromatography conditions: carrier gas—argon, 100 kPa; injection temp. 200°C; detector temp. 250°C.

Acknowledgements

Financial support for E.W. from the Polish Science Foundation is gratefully acknowledged.

References

1. (a) Olah, G. A.; Khrisnamurti, R.; Surya Prakash, G. K. *Comprehensive Organic Synthesis*; Pergamon, New York, 1991; Vol. 3, p. 293; (b) Roberts, R. M.; Khalaf, A. A. *Friedel–Crafts Alkylation Chemistry. A Century of Discovery*; Marcel Dekker, New York, 1984.
2. Gathergood, N.; Zhuang, W.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2000**, *122*, 12517.
3. Jenner, G.; Rimmelin, J. *Bull. Soc. Chim. Fr.* **1981**, II-65.
4. (a) Achmatowicz, O.; Burzynska, M. H. *Carbohydr. Res.* **1985**, *141*, 67; (b) Jurczak, J.; Kobrzycka, E.; Raczko, J. *Polish J. Chem.* **1999**, *73*, 29.
5. Pikul, S.; Jurczak, J. *Tetrahedron Lett.* **1985**, *26*, 4145.
6. Pikul, S.; Raczko, J.; Ankner, K.; Jurczak, J. *J. Am. Chem. Soc.* **1987**, *109*, 3981.
7. *Selected data for (R,R)-**3a***: 62% ee; $[\alpha]_D^{25}$ −30.0 (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz) δ 6.24 (d, $J=3.2$ Hz, 1H), 5.94–5.92 (m, 1H), 5.11 (d, $J=6.6$ Hz, 1H), 4.33–4.13 (m, 2H), 3.4 (d, $J=6.6$ Hz, 1H), 2.27 (d, $J=0.9$ Hz, 3H), 1.68–1.54 (m, 2H), 1.39–1.22 (m, 2H), 0.89 (t, $J=7.3$ Hz, 3H); ^{13}C NMR (50 MHz) δ 171.8 (C), 152.8 (C), 149.0 (C), 109.6 (CH), 106.4 (CH), 66.9 (CH), 66.1 (CH_2), 30.4 (CH_2), 18.8 (CH_2), 13.5 (2×CH_3); HRMS $(M+Na)^+$ calcd for $C_{11}H_{16}NaO_4$ 235.0946, found 235.0952; GC (β-dex 120): $T=160$°C, $t_{r(S)}=19.7$ min, $t_{r(R)}=20.1$ min.
8. *Selected data for **3b***: ^1H NMR ($CDCl_3$, 200 MHz) δ 6.22 (d, $J=3.0$ Hz, 1H), 5.93–5.91 (m, 1H), 5.14 (septet, $J=6.3$, 1H), 5.08 (s, 1H), 3.4 (bs, 1H), 2.26 (d, $J=0.8$ Hz, 3H), 1.28 (d, $J=6.3$, 3H), 1.21 (d, $J=6.3$, 3H); ^{13}C NMR (50 MHz) δ 171.2 (C), 153.0 (C), 149.2 (C), 109.4 (CH), 106.4 (CH), 70.4 (CH), 67.0 (CH), 21.6 (CH_3), 21.4 (CH_3), 13.5 (CH_3); HRMS $(M+Na)^+$ calcd for $C_{10}H_{14}NaO_4$ 221.0784, found 221.0800; GC (β-dex 120): $T=150$°C, $t_{r(S)}=11.9$ min, $t_{r(R)}=12.5$ min.
9. (a) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936; (b) Ready, J. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1999**, *121*, 6086.
10. *General procedure for the high-pressure Friedel–Crafts reaction*: To a toluene solution (∼2 mL) of catalyst (*R,R*)-**4**, placed in a Teflon ampoule (5 mL), freshly distilled glyoxylate **2a** or **2b**, and 2-methylfuran **1** were added. Then the ampoule was filled with toluene and placed in a high-pressure vessel, and then pressure was slowly increased to 10 kbar at 25°C. After stabilization of pressure, the reaction mixture was kept under these conditions for 20 h. After decompression, the reaction mixture was purified by chromatography on a silica gel column using hexane/AcOEt 9:1 as an eluent.