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Aldol Condensation Reactions of (Dienone) Tricarbonyliron Complexes. 4[1]. Enantioselective Total Synthesis of 3-Deoxypentoses from (-)-Myrtenal.

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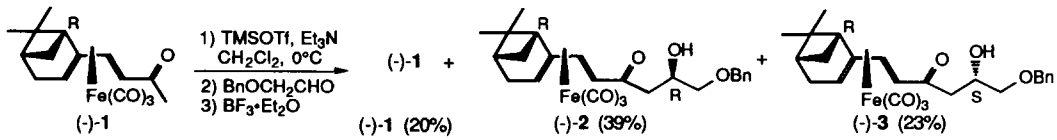
Abstract : The trimethylsilyl enol ether of the tricarbonyliron complex **(-)-1** deriving from (R)-(-)-myrtenal undergoes highly stereoselective cross aldol reactions with $TiCl_4$-coordinated β-alkoxyaldehydes. With BF_3,Et_2O as Lewis acid the reaction is only poorly stereoselective, allowing the synthesis of pairs of easily separable diastereomeric optically active ketols. These features are useful to have access to chiral polyols, as illustrated here by the synthesis of the protected deoxypentoses **(+)-10** and **(-)-11**. © 1997 Elsevier Science Ltd.

In our previous communications[1] on aldol condensation reactions of (1-acetyl diene) tricarbonyliron complexes, we have shown that polyols of known absolute configurations can be obtained in good yields and high e.e. by the use of enantiomerically pure complexes. This was achieved by resolution of the starting complex or by resolution during the aldol condensation step with an optically active protected α-hydroxyaldehyde. Another possibility requiring no resolution step, would be to use an optically pure starting complex obtained by the highly stereoselective complexation of a readily available chiral diene. One such compound is acetylnopadiene (from the reaction of the natural (-)-myrtenal with acetone, 96 %), a dienone which reacts exclusively with iron carbonyl by the least hindered π-face, as described by Salzer et coll.[2]. We first verified that the particularly crowded acetyl-diene complex **(-)-1** could still undergo aldol condensation reactions[3] and that the potential diastereomeric ketols were easily separated by silica gel column chromatography. The reaction was carried out via the silyl enol ether with benzaldehyde and $TiCl_4$. Two easily separable diastereomeric ketols were obtained in excellent overall yield, the reaction being highly diastereselective (less polar, 85 %, more polar, 12 %). By reaction with the preformed (S)-(-)-benzyloxylactaldehyde-$TiCl_4$ complex[4], only one diastereomer was formed, as expected, isolated in 53 % yield. The only other product isolated was the dienone complex **(-)-1** (42 %) resulting from an incomplete reaction under our conditions (CH_2Cl_2, -78° C). Using a reaction sequence similar to that used previously[1], protected colitose can thus be obtained via a very direct route.

With a non chelating Lewis acid such as $BF_3•Et_2O$, no, or at least a reduced diastereofacial selectivity should be observed. We used this feature, combined with the easy separation of the diastereomeric ketols to achieve the synthesis of two 3-deoxypentoses.



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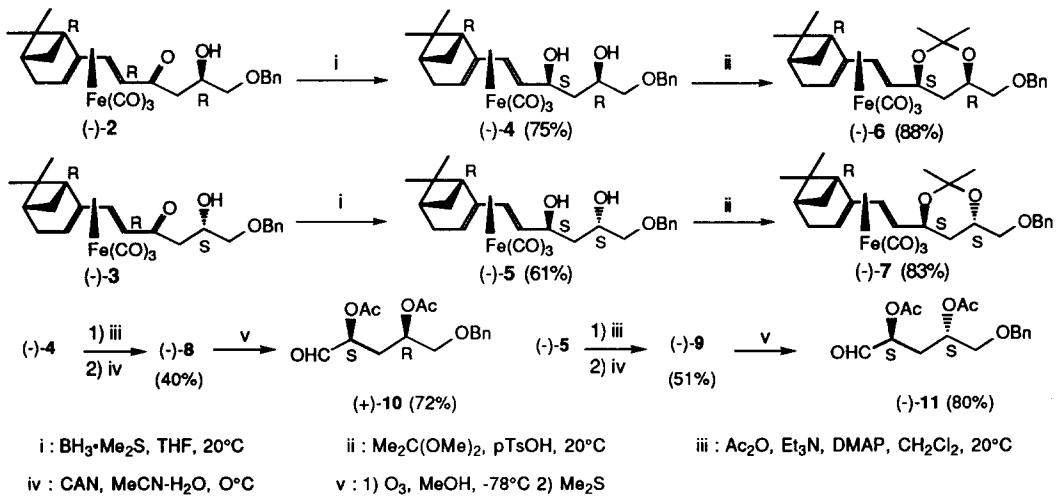
Two diastereomeric ketols (-)-**2** and (-)-**3** were obtained when the aldol condensation reaction was performed with benzyloxyacetaldehyde[5] (crude ratio 1.7:1 ; isolated yields 39 % and 23 %). They were reduced completely stereoselectively to the 1,3-diols (-)-**4** and (-)-**5** (BH_3•Me_2S) and transformed into the acetonides (-)-**6** and (-)-**7** in order to attribute by ^{13}C-NMR[6] the relative configurations of the hydroxyl groups [(-)-**6**, syn, Δδ gem di Me 9.4 ppm, (-)-**7**, anti, Δδ gem di Me 0.4 ppm].

After transformation of the diols into diacetates and decomplexation with cerium^{IV} ammonium nitrate (CAN), the substituted nopadienes (-)-**8** and (-)-**9** were oxidized with ozone in MeOH followed by reduction with Me_2S to yield respectively the protected L-3-deoxy-erythro-pentose (+)-**10** and D-3-deoxy-threo-pentose (-)-**11**. Neither product was contaminated by the other, indicating that no epimerization had occurred during the last steps[7]. The enantiomeric excess of the (-)-myrtenal used (Fluka puriss) was at least 90 % ($[\alpha]_D$ = -14.8). We can therefore expect same ees for the final products.



Acknowledgments : we thank the BASF AG, Ludwigshafen, for repeated gifts of pentacarbonyliron.

References and Notes :

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3. For instance, we could not achieve Friedel-Crafts acylations of nopadiene-Fe(CO)$_3$ (P. Bissinger, These de Doctorat de l'ULP, Strasbourg 1996), a fact which was also reported by Salzer et coll.[2]. The synthesis of acylnopadiene complexes by acylation of the parent complex was very attractive, since nopadiene is readily prepared from the very cheap nopol[8].
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6. Rychnovsky, S.D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, *58*, 3511.
7. (+)-**10** : $C_{16}H_{20}O_6$ (C,H), colorless liquid ; $[\alpha]_D$ = +8 (c=1, $CHCl_3$) : IR (CCl_4, cm^{-1}) ν (C=O) 1746 ; ^{1}H-NMR (C_6D_6, 200 MHz, ppm/TMS, Hz) : δ = 1.64 (s, 3H), 1.66 (s, 3H), 1.83-2.03 (m, 2H), 3.26 (d, 2H, J = 4.8), 4.18 (d, 1H, J = 12.1), 4.26 (d, 1H, J = 12.1), 4.94 (t, 1H, J = 5.8), 5.25 (dq, 1H, J = 8.1 and 4.8), 7.05-7.23 (m, 5H, arom), 9.09 (s, 1H)
(-)-**11** : $C_{16}H_{20}O_6$ (C,H), colorless liquid ; $[\alpha]_D$ = -29 (c=1, $CHCl_3$) : IR (CCl_4, cm^{-1}) ν (C=O) 1745 ; ^{1}H-NMR (C_6D_6, 200 MHz, ppm/TMS, Hz) : δ = 1.67 (s, 3H), 1.72 (s, 3H), 1.56-2.08 (m, 2H), 3.22 (dd, 2H, J = 5.2 and 0.9), 4.18 (d, 1H, J = 12.1), 4.25 (d, 1H, J = 12.1), 5.05 (dd, 1H, J = 10.7 and 3.5), 5.26 (m, 1H), 7.04-7.21 (m, 5H, arom), 9.06 (s, 1H).
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