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Synthesis of dienic α-Ketoesters by Friedel-Crafts Reaction of Ethyl Oxalyl Chloride with Tricarbonyl Iron Complexes of E- and Z- Substituted Acyclic Dienes.

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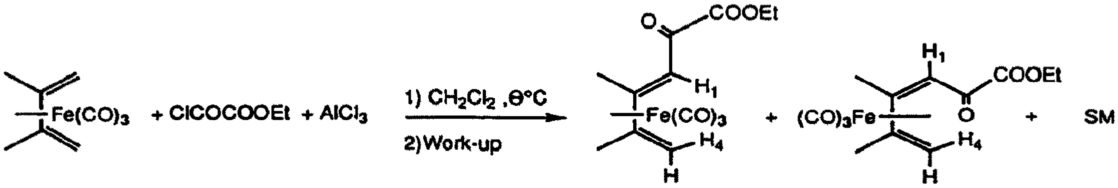
Key Words : *Iron tricarbonyl complexes, Friedel-Crafts acylation, 1,3-dienes, ethyl oxalyl chloride, aluminium chloride, α-ketoesters, decomplexation, cerium ammonium nitrate, E → Z isomerization.*

Abstract : *Tricarbonyl iron coordinated acyclic dienes react with ethyl oxalyl chloride/*$AlCl_3$ *to E- dienic α-ketoester complexes. This allows a rapid synthesis of such dienes by decomplexation. Not only E- alkyl-substituted but also Z-substituted dienes can be functionalized this way, whereas Z-dienic α-ketoester complexes can be obtained by acid catalyzed E → Z isomerization.*

Friedel-Crafts type acylation is an easy way to functionalize conjugated dienes as tricarbonyl iron complexes[1]. This reaction leads in general primarily to complexes of Z-dienones as a result of the mechanism by an endo attack, with coordinative saturation of the positively charged iron in the intermediate π-allyl complex being achieved by coordination of the oxygen of the entering carbonyl group[1a,2]. Functionalized acid chlorides can be used, but the choice is rather limited due to problems of intramolecular reactions, particularly under the conditions of the Friedel-Crafts reaction. Acid chlorides of hemiesters of ω-diacids have been successfully employed, with chains of 3 to 6 CH_2-units between the two functions[1d,1e,3], leading also primarily to complexes of Z-dienones.

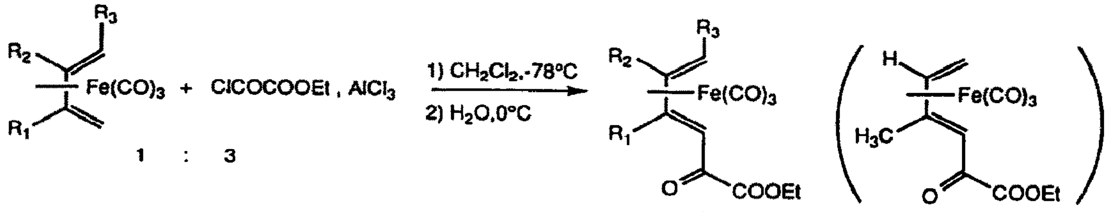
We were now interested in the possibility of using the acid chloride of the simplest hemiester, ethyl oxalyl chloride[4], where the proximity of the ketone and the ester-functions could induce a different evolution of the reaction. In fact the Friedel-Crafts reaction seems now to lead directly with complexes of simple acyclic dienes to complexes of E-dienones.

The reaction of the tricarbonyl iron complex of 2,3-dimethyl butadiene with ethyl oxalyl chloride and aluminium trichloride in methylene chloride, followed by simple work-up with water, showed a marked dependence on the reaction conditions (temperature, stoichiometry). With one equivalent of the 1:1 $RCOCl/AlCl_3$ complex (Perrier complex), the reaction is rapid but incomplete, being however non destructive (total mass balance 90 %). An easily separable[5] mixture of the Z- and E-dienone complexes[6] 1 and 2 along with ca 50 % recovered starting material (SM) was obtained after simple aqueous work-up. An excess of the Perrier complex improves the yield in favour of the E-dienone complex and with 2.5 equivalents, even at -78°C, the E-dienone complex is virtually obtained alone, nearly 90 % of the starting complex being converted. The addition of a base before aqueous work-up enhances the proportion of the Z-dienone complex, specially if $AlCl_3$ is used in excess (Et_3N, Z/E ratio 3:2)[7].



Complex	ClCOR	$AlCl_3$	θ°C	Work-Up	1	2	SM
1	1	1	0	H_2O,0° C	21 %	17 %	51 %
1	1.25	1.25	-20	H_2O,0° C	44 %	15 %	35 %
1	2.5	2.5	-78	H_2O,0° C	69 %	traces	11 %
1	2	2	-78	1) NEt_3,-78° C 2)H_2O,0° C	37 %	25 %	19 %
1	2	4	-78	ibid.	29 %	45 %	-

Without basic work-up and with a greater excess of the Perrier complex at low temperature, the reaction becomes complete and E-dienones are obtained alone in the general case (complexes 1, 3, 4 and 5 + 6 starting from isoprene) :

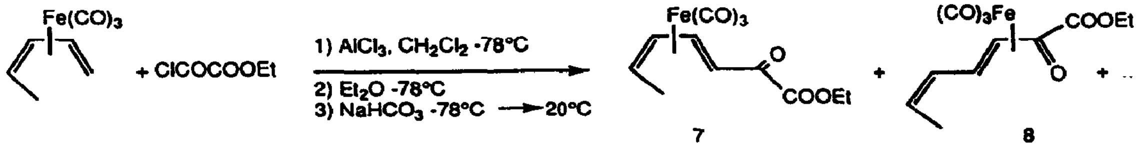


1,3,4,5

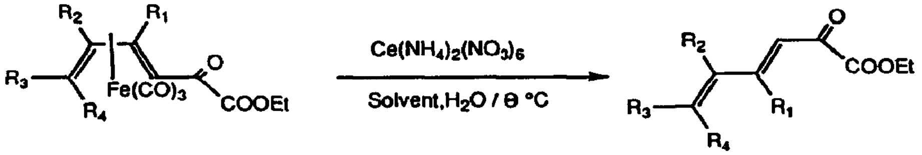
6

R_1= R_2= CH_3, R_3= H	70%	1		
R_1= R_2= R_3= H	70%	3		
R_1= R_2= H, R_3= CH_3	70%	4		
R_1= R_3= H, R_2= CH_3	60%	5	2:1	6

That complexes of E-dienones are obtained under the present Friedel-Crafts acylation and work-up conditions indicates that the coordinative saturation of the iron in the cationic π-allyl complex must not necessarily be achieved here by the carbonyl oxygen of the ketonic function. The formation of the E rather than the Z-dienone complex may therefore result from the direct coordination with an oxygen of the alkoxycarbonyl group or from a subsequent *unusually facile* Z → E isomerization. Such Z → E isomerizations are known to proceed by base or acid catalysis[1a,1c,8] and we found that acid chlorides alone can promote it too[1c]. This holds true also in the present case and even the preformed Perrier complex $EtO_2CCOCl/AlCl_3$ achieves partially this isomerization, if present in excess. The direct formation of the E-dienone complex is however suppported by the fact that the complex of Z-piperylene could be rapidly acylated with ethyl oxalyl chloride / $AlCl_3$ to the Z,E–dienone complex 7[9] isolated beside the haptotropic isomer 8[10] *even in the case when the acylation with simple acid chlorides fails with tricarbonyl iron complexes of Z-1-substituted dienes*[11].

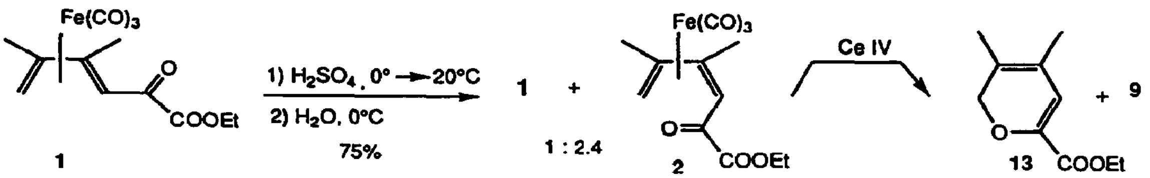


The Friedel-Crafts acylation of acyclic diene complexes with ethyl oxalyl chloride leads in consequence in general to complexes of E-dienic ketoesters. Since such dienes seem not to be easily available otherwise[12], we tried to obtain them by decomplexation of their complexes. This could be achieved with cerium^{IV} ammonium nitrate. With 5 equivalents, below -20°C in EtOH/H_2O an incomplete transformation led to the free ligands, separable from the partially recovered starting complexes by simple SiO_2 chromatography (→ dienes 11-12, mass balance ca. 80-90 %). With a greather excess of Ce^{IV} reagent (8-10 equivalents) at -5° C in THF/H_2O the reactions became complete, and dienic α-ketoesters were obtained in high yield[13]. The crude products are formed quantitatively and are almost pure, containing only traces of THF. They seem however to be chemically labile, since attempts of higher purification by chromatography on SiO_2 resulted in loss of material. They are also prone to polymerization, even slowly in the refrigerator. It is therefore preferable to use them as crude products, soon after the high yield decomplexation[14].



1 $R_1=R_2=CH_3$, $R_3=R_4=H$	THF	-5° C	9 quantitative
3 $R_1=R_2=R_3=R_4=H$	THF	-5° C	10 quantitative
4 $R_1=R_2=R_4=H$, $R_3=CH_3$	EtOH	-20° C	11 (78 %) + 4 (11 %)
7 $R_1=R_2=R_3=H$, $R_4=CH_3$	EtOH	-20° C	12 (64 %) + 7 (4 %) + 11 (9 %)

As mentioned above, complexes of Z-dienic ketoesters can be obtained if the Friedel-Crafts reaction is performed with the stoichiometry 1 : 1 : 1 for complex / ethyl oxalyl chloride / $AlCl_3$ or by work-up with Et_3N. Another way to get such Z-substituted complexes results however from the easy E → Z isomerization which can be achieved by treatment with concentrated H_2SO_4[15]. However, by decomplexation, chemically relatively labile 2H-dihydropyranes are obtained as major components instead of free Z-dienones (ca 65 %) :



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5. All products were isolated after usual work-up by column chromatography on silica gel (Merck Si60), with hexane/ether mixtures as eluent. TLC : Merck plates Art. 5715, eluent hexane/ethyl acetate (4:1) : **1** ($R_f = 0.47$), **2** ($R_f = 0.39$).
6. The given structures for complexed dienic keto-esters are in good agreement with C,H-analysis and the relevant spectroscopic data [IR (CCl_4) : υ (C≡O) 1965-2060 cm^{-1} ; (C=O) 1727 cm^{-1} (strong, ketoester, s-trans), 1750 cm^{-1} (weak, ketoester, s-cis) and 1680-1685 cm^{-1} (ketoester, E dienone) or 1670 cm^{-1} (ketoester, Z-dienone). ^1H-NMR ($CDCl_3$, 200 MHz) : easy distinction between Z- and E-substituted complexes, owing to the chemical shifts difference of more than 2ppm for the terminal H_1-protons, the values being markedly higher than those of the corresponding protons of simple dienone complexes (**1** : H_1 1.49 ppm (s), H_4 0.94 ppm (d) ; **2** : H_1 3.79 ppm (s), H_4 1.04 ppm (d)).
7. Once isolated, the complexes of the E and Z-dienones are unaffected by treatment with triethylamine, while $AlCl_3$ alone promotes a partial E → Z isomerization.
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9. **7** : $C_{12}H_{12}FeO_6$, yellow oil isolated 30 % ; IR (CCl_4) : υ (C≡O) 2063, 2005 and 1990 (vs) cm^{-1} ; (C=O) 1754 (w), 1728 (s) and 1685 (s) cm^{-1} ; ^1H-NMR ($CDCl_3$, 200 MHz) : $\delta = 1.32$ (d, 3H, J = 7.1 Hz), 1.38 (t, 3H, J = 7.1 Hz), 3.10 (quint., 1H, J ~ 7 Hz), 3.17 (d, 1H, J = 8.9 Hz), 4.23-4.46 (m, 2H), 5.42 (dd, 1H, J = 7.8 and 5.2 Hz), 6.18 (dd, 1H, J = 8.9 and 5.2 Hz).
10. Beside **7** (30 %) and **8** (ca 20 %), the E,E-complex **4** and decomplexed dienones were also formed. Even under the careful work-up conditions indicated, the formation of the E,E-dienone, as tricarbonyl iron complex (ca. 5 %) or as free ligand, could not be avoided. This may however be due to the presence of about the same amount of E-piperylene complex in the starting material, the complexation of Z-piperylene without any isomerization being difficult.
11. In fact, these complexes are readily attacked by Friedel-Crafts electrophiles such as AcCl, $AlCl_3$ but after aqueous work-up, even with neutralization in situ ($NaHCO_3$), only very small amounts of dienone complexes are present among other products. We found that after very basic work-up (tBuOK in tBuOH), some dienone complexes can nevertheless be isolated (Z,E and E,E-hepta-2,4-dien-6-ones, respectively 6 % and 3 %).
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13. THF was the solvent of choice, the otherwise used alcohols, EtOH and mainly MeOH, leading here to more polar compounds, resulting apparently from rapid Michaël additions to these very electrophilic dienes.
14. Selected data : **11** : IR (CCl_4) : υ (C=O) 1728 (s), 1692 (s) and 1668 (m) cm^{-1}, υ (C=C) 1633 (s) and 1594 (s) cm^{-1} ; UV (CH_3CN) λ max 292 nm ($\epsilon = 17600$) ; ^1H-NMR (C_6D_6, 200 MHz) : $\delta = 1.30$ (d, 3H, J = 6.0 Hz), 5.60 (dq, 1H, J = 15.0 and 6.0 Hz), 5.76 (dd, 1H, J = 15.0 and 10.5 Hz), 6.61 (d, 1H, J = 15.5 Hz), 7.38 (dd, 1H, J = 15.5 and 10.5 Hz) + EtO_2C-group.
    12 : IR (CCl_4) : υ (C=O) 1728 (s), 1691 (s) and 1670 (m) cm^{-1}, υ (C=C) 1619 (m) and 1587 (s) cm^{-1} ; UV (CH_3CN) λ max 295 nm ($\epsilon = 13300$) ; ^1H-NMR (C_6D_6, 200 MHz) : $\delta = 1.32$ (dd, 3H, J = 7.3 and 1.6 Hz), 5.53 (dq, 1H, J = 11.5 and 7.3 Hz), 5.81 (t, 1H, J = 11.5 Hz), 6.71 (d, 1H, J = 15.4 Hz), 7.88 (dd, 1H, J = 15.4 and 11.5 Hz) + EtO_2C-group.
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