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# ACYLCo(III) SALEN

## A NEW UNSYMMETRICAL KETONE SYNTHESIS

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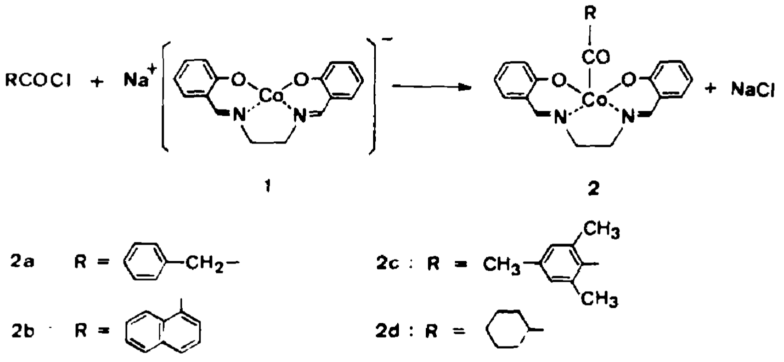
**Abstract**—New acyl complexes of N,N′-ethylenebis(salicylideneiminato)cobalt(III) **2** were prepared and their acyl transfer reactions with several nucleophiles were examined. The reaction with MeMgI at room temp gave unsymmetrical ketones of the type MeCOR in reasonably good yields.

Acyl-transition metal complexes are of special interest in the enzymatic reactions of ferredoxin and vitamin $B_{12}$. A significant role of acyl metal complexes was demonstrated in our synthesis of several amino acids through a biogenetic type reductive $CO_2$ fixation,[1] in which an artificial Fe-S complex was employed as a model of ferredoxin. The fact that the corresponding $\alpha$-keto acid was isolated as the intermediate strongly suggests the acyl-iron complex formation during the course of the reaction. Recently, Collman *et al.*[2] isolated acyl derivatives of momoanionic bi-nuclear Fe–Fe cluster complexes and obtained the corresponding aldehyde in a quantitative yield by protonation on the complex. As for Co ions, vitamin $B_{12}$ was found to contain C–Co linkage. Since that discovery, a large number of other corrinoids or artificial macrocylic ligands to accomodate a Co ion have been found.[3] However their axial ligands are limited mostly to alkyl group and the corresponding acyl complexes were prepared only in a few examples.[4] Thus new acyl complexes of N,N′-ethylenebis(salicylideneiminato)cobalt(III) (hereafter abbreviated as CoSalen) were prepared and their acyl transfer reactions with several nucleophiles were attempted. The reaction with MeMgI gave a new synthetic method of unsymmetrical ketones.

AcylCoSalen's, **2a**–**2d**, were prepared by the reaction of the corresponding acyl chloride with Co(I)Salen **1** which was obtained by the reduction of Co(II)Salen with metallic Na in dry THF.[5] In Table 1 are listed yields, m.ps, elemental analyses and spectroscopic data. PhenylacetylCoSalen (**2a**) is reported[6] to contain three water molecules in the crystal. However, we could not observe the hydration even after washing the crystal with water. Other three complexes are new compounds and exhibit satisfactory analysis.

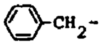
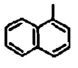
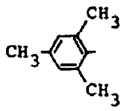
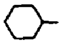
In order to gain insights into the acyl–Co bond, we have examined first the reaction of acylCoSalen with ethanethiol. To a THF solution of **2a** ($3.3 \times 10^{-3}$M, 30 ml), ethanethiol (124 mg, 2.0 mmol) was added under nitrogen and the solution was kept at 60° for 15 hr. Ethyl phenylthiolacetate was formed in 75% yield. A similar reaction with methanol gave methyl phenylacetate in 69% yield. These results suggest that the acyl–Co bond is polarized to $RCO^{\delta+}\ldots Co^{\delta-}$ and that the nucleophilic attack occurs at acyl carbon. The contrasting situation is reported[7] for the alkylCoSalen, in which alkyl group tends to leave as a carbanion by the nucleophilic displacement at the central metal.

The above results are quite interesting in the viewpoints that the appropriate choice of nucelophiles (–Nu) should provide a versatile synthetic method of RCO–Nu. The reaction with Grignard reagent (R′MgX) was found to give unsymmetrical ketones (RCOR′) in moderate yields. AcylCoSalen was dissolved in THF ($3.3 \times 10^{-3}$M, 30 ml) to which MeMgI in ether solution ($8.3 \times 10^{-1}$ M, 6 ml) was added dropwise with stirring at room temperature. After 3 hr, the reaction was quenched by the addition of 1NHCl (50 ml). The aqueous layer was saturated with ammonium sulfate to separate organic layer and extracted with ether (50 ml × 3). The organic layer was combined, dried ($Na_2SO_4$) and concentrated to *ca.* 1 ml. The residual solution was analyzed by vpc. All of the ketone formed were collected through preparative vpc and identified by the comparison of IR and NMR spectra with those of authentic samples. Results were summarized in Table 2. The yields, although they are not



Scheme 1.

Table 1. Synthesis and spectroscopic data of acylCoSalen's 2

| | R | Yield (%) | Color | Mp (°C)[a] | NMR[b] δ (ppm) | IR $\nu_{C=O}$ (cm$^{-1}$) KBr | IR $\nu_{C=O}$ (cm$^{-1}$) $CH_2Cl_2$ |
|---|---|---|---|---|---|---|---|
| **2a** |  | 65 | orange | 177–180 | 3.60(4H,s,$CH_2CH_2$); 4.63(2H, s,$CH_2$); 6.23–7.35(13H,m, aromatic); 7.93(2H,s,=CH) | 1696 | 1722 |
| **2b** |  | 85 | brown | 174–180 | ——[c] | 1689 | 1701 |
| **2c** |  | 75 | green | 185–186 | 1.18(3H,s,$CH_3$); 2.01(6H,s, $CH_3$); 3.79(4H,s,$CH_2CH_2$); 6.24 (2H,s,aromatic); 6.59–7.09(8H, m,aromatic); 7.88(2H,s,=CH) | 1698 | 1710 |
| **2d** |  | 66 | brown | 197–199 | 1.20(11H,br,cyclohexyl); 3.57 (4H,s,$CH_2CH_2$); 6.00–7.50(8H, m,aromatic); 8.00(2H,s,=CH) | 1718 | 1727 |

[a] With decomposition.

[b] In DMSO-$d_6$ for **2a** and **2d** or in $CDCl_3$ for **2c**.

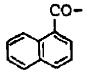
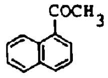
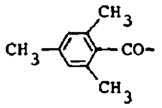
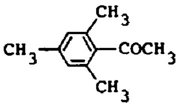
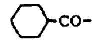
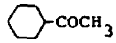
[c] The complex is not soluble in DMSO-$d_6$ or in $CDCl_3$ enouth to allow NMR measurement.

Elemental Analysis of AcylCoSalen 2

| **2** | Formula | Calculated C | Calculated H | Calculated N | Found C | Found H | Found N |
|---|---|---|---|---|---|---|---|
| **2a** | $C_{24}H_{21}O_3N_2Co$ | 64.87 | 4.76 | 6.30 | 64.91 | 4.78 | 6.29 |
| **2b** | $C_{27}H_{21}O_3N_2Co$ | 67.50 | 4.41 | 5.83 | 67.21 | 4.53 | 5.62 |
| **2c** | $C_{26}H_{27}O_4N_2Co$[a] | 63.67 | 5.55 | 5.71 | 63.68 | 5.39 | 5.74 |
| **2d** | $C_{23}H_{25}O_3N_2Co$ | 63.30 | 5.77 | 6.42 | 63.10 | 5.63 | 6.46 |

[a] Calculated as monohydrate.

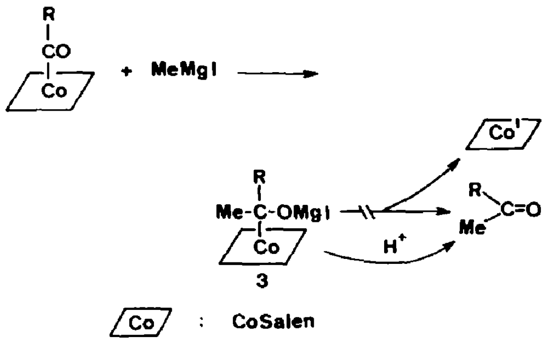
Table 2. Synthesis of unsymmetrical ketones

| | RCO-CoSalen RCO- | Product | Yield[a] (%) |
|---|---|---|---|
| **2a** | $C_6H_5CH_2CO-$ | $C_6H_5CH_2COCH_3$ | 57 |
| **2b** |  |  | 59 |
| **2c** |  |  | 91 |
| **2d** |  |  | 52 |

[a] Based on RCO-CoSalen used.

optimized, are relatively high, especially when such a hindered acyl grouping as 2,4,6-trimethylbenzoyl was employed.

It is interesting to note that the unsymmetrical ketone was obtained even in the presence of a large excess (50 equiv.) of Grignard reagent. In the conventional ketone synthesis from acyl halide and Grignard reagent,[8] the use of excess Grignard reagent should be carefully avoided to supress the further addition to the ketone thus formed. In the present reaction, the leaving group is a strong nucleophile, Co$^I$Salen, so that the initial addition



Scheme 2.

product 3 does not seem to liberate free ketone unless the reaction is quenched by addition of acid. This prevents the side reaction of the carbinol formation.

The present method allows the potential use of other types of Grignard reagents and offers one of the useful snythetic methods of unsymmetrical ketones.

## EXPERIMENTAL

IR spectra were obtained with a Hitachi model 215 spectrophotometer (KBr disc or $CH_2Cl_2$ solution). NMR spectra were recorded with a Varian EM-360 instrument with $Me_4Si$ as internal standard. Electronic spectra were measured with a Hitachi model 340S spectrometer or a Union Giken model MS-401 spectrometer. Vpc. analyses were performed on a Shimadzu 4BT instrument (DC 550 20%, 2.0 m or PEG 20 M 5%, 0.8 m, $H_2$ as a carrier gas).

*General procedure for the synthesis of acylCoSalen's* 2. A suspension of CoSalen (2.5 g, 7.7 mmol) and Na sand (195 mg, 8.4 mg-atom) in THF (40 ml) was stirred overnight at RT under $N_2$. The resulting green soln was filtered through a sintered glass filter and cooled at −70°. To this soln was added dropwise with stirring a THF soln (30 ml) of acyl chloride (7.7 mmol). The mixture was stirred at −70° for further 3 hr and gradually warmed up to RT during 2 hr. The acyl complex ppt was collected on a sintered glass filter and washed successively with water (20 ml × 2) and finally dried *in vacuo* (Table 1).

*Reaction with ethane thiol.* A soln of phenyl-acetylCoSalen (44.4 mg, 0.1 mmol) was bubbled by argon gas for 20 min. Ethane thiol (146 mg, 2.0 mmol) was added to the soln and the mixture was stirred at 60° for 15 hr. The soln was concentrated to *ca.* 1 ml and added by 50 ml ether to precipitate solid material which was centrifuged (3000 rpm, 10 min) and washed with 25 ml ether. The combined ether solns were concentrated and the mixture was analyzed by vpc using diphenylmethane as an internal standard. The yield was 13.4 mg (75%) by the analyses of two different columns (PEG 20M (5%), 0.8 m and DC 550 (20%), 2.0 m). The product was collected through a preparative vpc and identified to ethyl phenylthiolacetate by a comparison of IR spectrum of the authentic sample.

*Reaction with methanol.* PhenylacetylCoSalen (22.2 mg, 0.05 mmol) was treated with MeOH (320 mg, 10 mmol) as described above. The product, methyl phenylacetate, was collected through a preparative vpc and identified by the comparison of IR spectrum of the authentic sample. The yield was 5.2 mg (69%) by two different vpc conditions (DC 550 (20%) 2 m, n-dodecane as an internal standard; PEG 20M (5%), 0.8 m, α-methylnaphthalene as an internal standard).

*Reaction with methylmagnesium iodide.* To a dry THF soln (30 ml) of acylCoSalen ($1.0 \times 10^{-4}$ mol), an ether soln (6 ml) of MeMgI ($5.0 \times 10^{-3}$ mol) was added dropwise with stirring and the mixture was stirred for 3 hr. The reaction was quenched by the addition of 50 ml of 1 N HCl. The aqueous soln was saturated with $(NH_4)_2SO_4$ and extracted with ether (50 ml × 3). The combined ether extracts were dried over $Na_2SO_4$ and concentrated to *ca.* 1 ml. The residual soln was analyzed by vpc using methylnapthalene, diphenylmethane, bibenzyl and tetralin as internal standards for methyl benzyl ketone, methyl α-napthyl ketone, methyl mesityl ketone and methyl cyclohexyl ketone, respectively (DC 550 (20%), 2.0 m). All of the ketone formed were collected through a preparative vpc and identified by the comparison of IR and NMR spectra of the authentic samples.

## REFERENCES

[1a] T. Nakajima, Y. Yabushita and I. Tabushi, *Nature*, **256**, 60 (1975); [b] I. Tabushi, Y. Yabushita and T. Nakajima, *Tetrahedron Letters* 4343 (1976).

[2] J. P. Collman, R. K. Rothrock, R. G. Finke and F. Rose-Munch, *J. Am. Chem. Soc.* **99**, 7381 (1977).

[3] For reviews: [a] D. Dodd and M. D. Johnson, *J. Organometal. Chem.* **52**, 1 (1973); [b] J. M. Pratt and P. J. Craig, *Advan. Organometal. Chem.* **11**, 331 (1973).

[4a] K. Bernhauer and E. Irion, *Biochem. Z.* **339**, 530 (1964); [b] R. Yamada, T. Umetani, S. Shimizu and S. Fukui, *J. Vitaminol.* **14**, 316 (1968).

[5a] G. Costa, G. Mestroni and G. Pellizer, *J. Organometal. Chem.* **11**, 333 (1968); [b] C. Floriani, M. Puppis and F. Calderazzo, *Ibid.* **12**, 209 (1968).

[6] J. Booth, P. J. Craig, B. Doobs, J. M. Pratt, G. L. P. Randall and A. G. Williams, *J. Chem. Soc.* (A), 1964 (1971).

[7] R. M. McAllister and J. H. Weber, *J. Organometal. Chem.* **77**, 91 (1974).

[8] D. A. Shirley, *Org. Reaction* **8**, 28 (1954).