sites for anionic guests. The possibility that they can also act as catalytic sites is being explored.

References and Notes

(1) This work was supported by the U.S. Public Health Service Research Grant No. GM12640-10 from the Department of Health, Education and Welfare, and by a grant from the National Science Foundation, GP33533X.
(2) J. M. Timko, R. C. Helgeson, M. Newcomb, G. W. Gokel, and D. J. Cram, *J. Am. Chem. Soc.*, **96**, 7097 (1974).
(3) (a) Carbon and hydrogen analyses were within 0.30% of theory; (b) mass spectra exhibited the molecular ion; (c) ^{1}H NMR spectra were consistent with the assigned structures.
(4) The authors are indebted to Dr. Kenji Koga who first prepared these compounds.
(5) H. L. Goering, T. Rubin, and M. S. Newman, *J. Am. Chem. Soc.*, **76**, 787 (1954).
(6) Treatment of **15** in carbon tetrachloride with 2.2 equiv of NBS gave **16.**
(7) (a) F. Vögtle, *Chem. Ber.*, **102**, 1784 (1969); (b) *ibid.*, **105**, 2955 (1972).
(8) The mixture was stirred at 25° (12 hr). The methyl ester of **20** was prepared similarly. The crude isolated diesters were treated with excess diazomethane. All cycles were purified by chromatography first on silica gel and then by gel permeation (Bio Beads SX-8). Analytical samples were obtained by GLPC. Acids **5–8** and **20** were prepared from their esters by hydrolysis with sodium hydroxide–ethanol. Reduction of ester **2** with LAH gave **9**, methylation of which with sodium hydride and methyl iodide in THF gave **10.** Compounds **1–20** were oils except the following: **5**, mp 106–112°; **6**, mp 100–101°; **7**, mp 86–95°; **10**, mp 70–71°; **11**, mp 44–46°; **16**, mp 77–79°; **17**, mp 84–88°; **18**, mp 101–103°; **19**, not purified; **20**, mp 54–62°.
(9) Acid (0.1 mmol) in 20–30 ml of water was neutralized with LiOH and titrated (pH-metric) with 0.10 *N* HCl and 0.10 *N* LiOH.
(10) (a) An X-ray structure of **6** reveals the carboxyl to be hydrogen-bonded to the oxygen on the C_2 axis of the molecule (I. Goldberg and K. N. Trueblood, private communication). (b) The X-ray structure determination of this complex is being undertaken by I. Goldberg and K. N. Trueblood (private communication).
(11) Footnote 4 of ref 2 describes the method. Scale C was used.
(12) Reference 2 erroneously reported the K_a of **11** at 22° to be 1500. In addition, the K_a of **11** at 0° is 1800 rather than the 2000 reported in ref 2.
(13) A mixture was shaken of 2 ml of dichloromethane containing **0**.05 mmol of acid and 1 ml of aqueous salt solution of μ = 2.0 (2.0 *M* LiCl, NaCl, KCl or 0.67 *M* $CaCl_2$) and 2 drops of 2 *N* LiOH, NaOH, or KOH (for Ca, solid $Ca(OH)_2$ was added), respectively. The aqueous phase had pH >11. The dichloromethane phase after filtering through glass wool was evaporated. The residue was dissolved in 50 μl of $CDCl_3$ contalning 0.0147 mmol of toluene, the ^{1}H NMR spectrum was taken (60 MHz), and the area of the host's methylene or methyl protons was compared (±10%) to that of the toluene's methyl protons.
(14) A 0.5 *M* solution of the acid host in 0.10 ml of $CDCl_3$ was made 0.7 *M* in $(CH_3)_3CNH_2$, and the resulting solution was shaken with 0.10 ml of D_2O. The layers were separated, and the protons of the host and guest (plus free amine) were counted in their ^{1}H NMR spectra in each layer under identical conditions for each complex. Values of K_d were calculated from the relative amounts of host in each layer. Excess $(CH_3)_3CNH_2$ was observed in each layer.
(15) NOTE ADDED IN PROOF. A second possible complex locates the $(CH_3)_3C$ group on the side of the macroring opposite the tilted benzene ring, whose CO_2^- group hydrogen bonds one NH, and alternate distant ether oxygens hydrogen bond NH_2 (CPK molecular models).

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Chromatographic Optical Resolution through Chiral Complexation of Amino Ester Salts by a Host Covalently Bound to Silica Gel[1]

Sir:

Previous papers demonstrated that optically active host **1** exhibited chiral recognition in complexation in solution of the enantiomers of primary amines and amino ester salts as guests.[2a,b] Total optical resolutions of primary amine salts were realized by liquid-liquid chromatography in which salts in stationary aqueous phases absorbed on silica gel were eluted fractionally with chloroform solutions of (*RR*)-**1**.[2c,d] We report here the covalent attachment of (*RR*)-**1**[2a] to silica gel and use of the designed chiral host

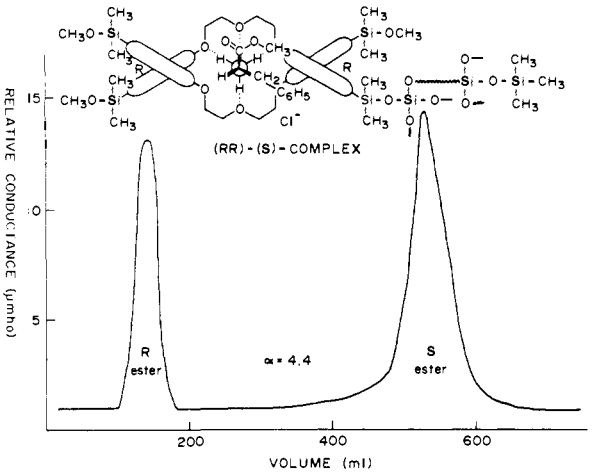
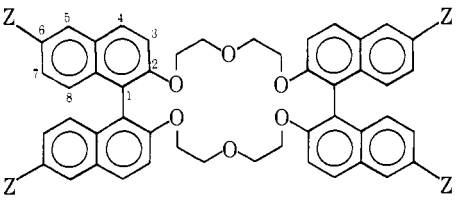


Figure 1. Chromatographic optical resolution by host-bound silica gel of methyl phenylalaninate hydrochloride salt.

sites to totally resolve amine (especially amino ester) salts as guests by solid-liquid chromatography.

Bromination (7 mol of Br_2 in CH_2Cl_2 added at −5° over 1 hr) of the isomers of **1** (1 mol) gave **2** whose four bromine



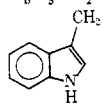
(*RR*)(*SS*)-**1**, Z = H;[2a] (*RR*)-**1**, Z = H;[2a] (*RS*)-**1**, Z = H[2a]

Compd no.	Z	Mp, °C	Yld, %
(*RR*)(*SS*)-**2**[3a,b]	Br	299–300	80
(*RR*)-**2**[3a]	Br	189–191	91
(*RS*)-**2**[3]	Br	334–335	90
(*RS*)-**3**[3a,c]	$Si(CH_3)_2OCH_3$	95–96	84

atoms were substituted in the 6-positions.[4] Addition of (*RS*)-**2** to butyllithium in dry glyme under nitrogen at −75° followed by dichlorodimethylsilane at −75° (mixture then refluxed) followed (after evaporation) by dry methanol gave (*RS*)-**3.** Treatment of the tetrakis(dimethylchlorosilyl) compound (similarly prepared from optically pure (*RR*)-**2**)[5] with dry carbon-free silica gel followed by methanol gave after washing and drying, host-bound silica gel, 3.94% by weight carbon by combustion. If each cycle is covalently bound at only one site, and the other three are capped with CH_3O groups, the silica gel is 0.059 mmol per gram in host residues, or each host site has an average molecular weight of 17,000. Further treatment of this silica gel with excess trimethylsilyl chloride to cap the more hindered SiOH groups gave (*RR*)-**4**[5] (H), 4.65% by weight carbon by combustion, or 0.20 mmol/g in $(CH_3)_3Si$ groups.

Table I reports the results of chromatograms run[6] on racemic α-phenylethylammonium hexafluorophosphate, the methyl or isopropyl esters of phenylglycine hexafluorophosphate or hydrochloride salts, and the methyl esters of the hydrochloride salts of valine, phenylalanine, and tryptophan. The configurational identities of the enantiomers in the bands eluted were established by their signs of rotation (e.g., in runs 1, 3, 4, and 6) or by comparisons of their retention volumes with those of pure enantiomers put through the same column under the same conditions as their racemates (runs 7, 8, and 9). Plots of the relative conductance vs. milliliters of eluate gave curves for each run from which the

Table I. Optical Resolution by Solid–Liquid Chromatography at 25°

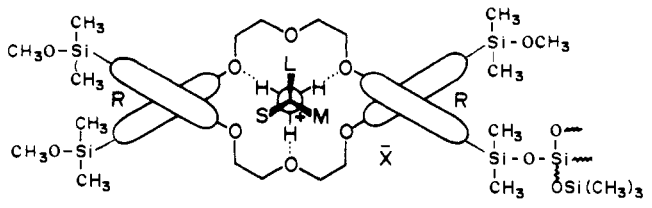
Run no.	$RR'CHNH_3^+\bar{X}$: R	R′	X^-	Molar ratio, H[a]/G	Mobile phase	Carrier[b] concn, M	Separat factor α	Configur better bound enantiomer
1	C_6H_5	CH_3	PF_6	21	CH_2Cl_2	4.4×10^{-5}	1.47	*S*
2	C_6H_5	CH_3	PF_6	84	$CHCl_3$	2.0×10^{-4}	1.67	*S*
3	C_6H_5	CO_2CH_3	Cl	20	CH_2Cl_2	4.4×10^{-6}	1.20	*R* or *D*
4	C_6H_5	CO_2CH_3	PF_6	50	$CHCl_3$	2×10^{-4}	1.40	*R* or *D*
5	C_6H_5	CO_2CH_3	PF_6	128	$CHCl_3$	0.8%(v/v)[c]	1.52	*R* or *D*
6	C_6H_5	$CO_2CH(CH_3)_2$	Cl	80	CH_2Cl_2	5%(v/v)[d]	2.93	*R* or *D*
7	$(CH_3)_2CH$	CO_2CH_3	Cl	23	$CHCl_3$	1×10^{-2}	1.73	*S* or *L*
8	$C_6H_5CH_2$	CO_2CH_3	Cl	23	$CHCl_3$	5×10^{-3}	4.4	*S* or *L*
9		CO_2CH_3	Cl	70	$CHCl_3$	2×10^{-4}	6.4	*R* or *D*

[a] Column contained 0.82 mmol of host. [b] 18-crown-6. [c] Ethanol was carrier. [d] Isopropyl alcohol was carrier.

separation factors, α, were calculated.[7] Figure 1 records the plot for run 8. Good base-line separation was observed for the enantiomers of the ester salts of phenylalanine and tryptophan, but the minima between the two peaks did not come to base line in the other runs. Host-bound silica gel noncapped with $(CH_3)_3Si$ groups gave poorer curves, and bad tailing was observed. With capped material (*RR*)-**4** tailing was observed for the less hindered alkylammonium salts, but little for the more hindered. These facts suggest that even with capped material SiOH groups are still available for complexing less hindered RNH_3^+ guests (G) and cause band overlap. Although dichloromethane as the mobile phase gave less tailing, it also gave lower separation factors.

In liquid-liquid (chloroform-water) chromatography with (*RR*)-**1** as host and amine salts as guest, $\alpha \sim (D_A/D_B)$, where D_A is the distribution coefficient of the more and D_B that of the less complexed enantiomer in the chloroform phase.[2b,c] The results obtained with complexation at the silica gel-chloroform interface qualitatively resemble those observed in chloroform. The formula of Figure 1 illustrates the structure visualized for the complex of the ester salt of phenylalanine, and illustrates the *four-point binding model* as the more stable diastereomeric complex. This model also explains the results with valine. The *three-point binding model* **5** is illustrated by the results obtained with the salts of α-phenylethylamine, of the phenylglycine esters, and of the tryptophan ester. Similar models applied in chloroform solution, but only to the *hexafluorophosphate salts* of α-phenylethylamine and the methyl esters of valine, phenylalanine, and phenylglycine.[2] The hydrochloride salts failed to extract, or if they did, no chiral recognition was observed.[8] Possibly at the silica interface, the chloride ion is in a more polar environment, and does not destructure the host-guest complex by hydrogen bonding the alkylammonium ion as in chloroform.[8] Another difference between complexation at the interface and in solution is that chiral recognition on the three-point model side is lower and on the four-point model side is higher at the interface than in solution.

These results demonstrate that, by rational design of host compounds covalently bound at a remote site to silica gel, complete optical resolution by highly structured complexation of guest compounds at the solid-liquid interface can be accomplished. We anticipate that covalent binding of **1** and its derivatives to macroreticular polystyrene resins will produce higher concentrations of host per unit weight and a chromatographic support free of unwanted binding sites.



5, three-point binding model

L = C_6H_5 or $C_8H_6NCH_2$; M = CH_3, CO_2CH_3, or $CO_2CH(CH_3)_2$; S = H

References and Notes

(1) This work was supported by U.S. Public Health Service Research Grant No. GM12640-10 from the Department of Health, Education, and Welfare and by a grant from the National Science Foundation, GP33533X.

(2) (a) E. P. Kyba, K. Koga, L. R. Sousa, M. G. Siegel, and D. J. Cram, *J. Am. Chem. Soc.*, **95**, 2692 (1973); (b) R. C. Helgeson, J. M. Timko, P. Moreau, S. C. Peacock, J. M. Mayer, and D. J. Cram, *ibid.*, **96**, 6762 (1974); (c) L. R. Sousa, D. H. Hoffman, L. Kaplan, and D. J. Cram, *ibid.*, **96**, 7100 (1974); (d) in the synthesis of (*S*)- and (*R*)-**4** of ref 2c, 2-(2′-chloroethoxy)ethyl 2′-tetrahydropyranyl ether was treated with (*S*)- or (*R*)-**1** of ref 2c in sodium hydride–DMF at 70°, not sodium hydroxide–butanol as erroneously reported.

(3) (a) Carbon and hydrogen analyses were within 0.30% of theory. (b) ^1H NMR spectra in $CDCl_3$ were consistent with assigned structures. (c) Mass spectra exhibited molecular ions.

(4) The structural assignments depend on the 100-MHz ^1H NMR first-order spectrum ($CDCl_3$) of (*RR*)(*SS*)-**2**, δ 3.17 (m, CH_2OCH_2, 16 H), 3.81 (m, $ArOCH_2$, 8 H), 6.85 (d, ArH-8, $J_{7,8}$ = 9 Hz, 4 H), 7.20 (d of d, ArH-7, $J_{7,8}$ = 9 Hz, $J_{5,7}$ = 2 Hz, 4H), 7.25 (d, ArH-3, $J_{3,4}$ = 9 Hz, 4 H), 7,80 (d, ArH-4, $J_{3,4}$ = 9 Hz, 4 H), 7.97 (d, ArH-5, $J_{5,7}$ = 2 Hz, 4 H). ArH-8 is shielded by the naphthalene ring bound at the 1-position and split by ArH-7; ArH-7 is split by both ArH-8 and ArH-5; ArH-5 is deshielded by its ortho bromine and peri interaction; ArH-3 and ArH-4 split one another; ArH-3 is shielded by its ortho RO group; ArH-4 is deshielded by its peri interaction. We thank M. S. Siegel for first preparing (*RR*)(*SS*)-**2** and assigning its structure.

(5) To 2.11 g of optically pure (*RR*)-**2** in 200 ml of dry glyme stirred under pure nitrogen at −75° was added a trace of triphenylmethane indicator and dropwise 10 ml of butyllithium (2.2 *M* in hexane). After 2 hr of stirring the reaction mixture was added to 12 g of dichlorodimethylsilane stirred under nitrogen at −75°. The reaction mixture was stirred at 25° for 4 hr, heated at reflux for 12 hr, cooled, and filtered, and the solids were washed with dry glyme. Volatile materials were removed (ultimately at 0.1 mm), and the residue was dissolved in dry (P_2O_5) chloroform (15 ml) and filtered into a stirred slurry of 40.0 g of dry (constant weight at 300°) Davidson No.56 Silica Gel (200–325 mesh, pore volume 1.20 ml/g, surface area 285 m^2/g, average pore diameter 168 Å) and 250 ml of dry (P_2O_5) chloroform under nitrogen. The mixture was stirred for 10 hr (while the evolved HCl was purged with pure nitrogen) and filtered, and the filtrate was washed successively with dry chloroform, methanol, benzene, and chloroform. The material was dried at 90° at 0.01 mm pressure for 18 hr to constant weight, ~41.6 g. From the washings was obtained 0.10 g of optically pure (*RR*)-**1**. Treatment of the host-bound silica gel with 10 g of $(CH_3)_3SiCl$ gave by a similar procedure ~41.7 g of trimethylsilyl-capped final useful solid phase host, (*RR*)-**4**. This material absorbs little water, a little methanol, but 2.6 g absorbs 6.6 g of chloroform before looking wet. The dry material (14.0 g) packed (tamping) into a stainless steel column (0.75 i.d. by 56 cm) provided a mobile phase volume of chloroform of 23 ml.

(6) Chromatograms were run at constant flow rates that ranged in different runs from 0.60 to 1 ml/min with pressure drops of 300–975 psi. Amine salts (1–8 mg) dissolved in 2 ml of the mobile phase were injected at the top of the column. The mobile phase of chloroform or dichloromethane contained low concentrations of 18-crown-6 (G. W. Gokel, D. J. Cram, C. L. Liotta, H. P. Harris, and F. L. Cook, *J. Org. Chem.*, **39**, 2445 (1974)) to act as a salt carrier. The column eluate was passed through a conductivity cell (ref 2c) to detect eluted salt. Between runs, the column was washed with methanol and was unchanged over a period of months.

(7) L. R. Snyder and J. J. Kirkland, "Introduction to Modern Liquid Chromatography", Wiley, New York, N.Y., 1974, pp 25–29, 35–37.
(8) J. M. Timko, F. de Jong, and D. J. Cram, unpublished results.
(9) African-American Institute, AFGRAD, Fellow.

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S-Alkylation and S-Acylation of the Thiocarbonyl Ligand in Metal Complexes

Sir:

We recently reported the formation of stable sulfur-bound adducts of an electron-rich metal thiocarbonyl complex with metal-containing Lewis acids.[1] We now wish to communicate the results of some reactions of electron-rich metal thiocarbonyl complexes with organic electrophiles.

Methyl fluorosulfonate (eq 1) and triethyloxonium tetrafluoroborate react rapidly with a CH_2Cl_2 suspension of

$$W(CO)(CS)(DPE)_2 + CH_3SO_3F \longrightarrow [(DPE)_2(CO)W(CSCH_3)]SO_3F \quad (1)$$

cis-$W(CO)(CS)(DPE)_2$[1] (**1**) (DPE = ethylenebis(diphenylphosphine)) to give the S-alkylated derivatives. Crystallization by addition of hexane and cooling gives excellent yields (>90%) of the orange methylated product[2] and the red ethylated analog.[3] The former exhibits a singlet in its proton NMR spectrum at τ 7.90 assignable to the methyl group and is a two-ion conductor in nitrobenzene (Table I). Its infrared spectrum shows a band near 1260 cm^{-1} which is attributed to the fluorosulfonate anion; there are no other new absorptions in the region of 1160–1400 cm^{-1}. The thiocarbonyl band has apparently shifted to lower frequency and appears overlapped with a DPE ligand absorption, as occurred with the metal complex adducts.[1] The ethylated derivative exhibits no new infrared absorptions from 1160 to 1400 cm^{-1}, suggesting that the thiocarbonyl ν(CS) frequency is lowered in this complex also; unfortunately the 1100-cm^{-1} region is further obscured by absorption of the tetrafluoroborate anion. The NMR spectrum exhibits a quartet at τ 7.90 and a triplet at τ 9.25 (J = 7 Hz), characteristic of an ethyl group. Both complexes are air-stable and can be crystallized from solution repeatedly without decomposition. These derivatives are the first known complexes of the *S*-alkylthiocarbonylium ligand, $CS\text{-}R^+$.

For comparison, the carbonyl analog of **1**, *cis*-$W(CO)_2(DPE)_2$[4] (**2**) was stirred in CH_2Cl_2 with 1 equiv of $(Et_3O)BF_4$ under N_2 for 3 hr. A yellow complex crystallized upon addition of diethyl ether; residual solvent was removed by heating the solid at 100° under vacuum. The air-stable, ionic product contains two terminal carbonyl groups in a nearly trans configuration, as suggested by the intensities of the two ν(CO) absorptions in its ir spectrum (Table I). The same arrangement of two CO groups was seen in the related complexes $[W(CO)_2(DPE)_2HgX]HgX_3$[5] and *trans*-$W(CO)_2(DPE)_2^{2+}$.[6] The presence of an ethyl group in the complex is confirmed by the NMR spectrum which has a quartet at τ 6.51 and a triplet at τ 8.79 (J = 7 Hz). This product is therefore formulated as a seven-coordinate W(II) alkyl complex, $[(C_2H_5)W(CO)_2(DPE)_2]BF_4$.

A similar product, $[HW(CO)_2(DPE)_2]CF_3SO_3$, is obtained when **2** is treated with CF_3SO_3H in CH_2Cl_2 under N_2. The yellow, ionic product crystallizes on addition of ether; heating at 100° under vacuum removes the CH_2Cl_2 of solvation to give the pure product. The NMR spectrum of this complex gives definite proof that the metal is the site of protonation. The proton appears as a triplet of triplets (J_{PMH} = 74 Hz, $J_{P'MH}$ = 13 Hz) centered at 4.91 ppm upfield from TMS. This splitting pattern was previously seen for $[HMo(CO)_2(Me_2PCH_2CH_2PMe_2)_2]HCl_2$[7] and is evidence that the carbonyl groups are trans to each other with the proton coordinating through an octahedral face.

The thiocarbonyl complex **1** also is protonated by CF_3SO_3H, but, in contrast to its reactions with Et_3O^+ and $MeSO_3F$, the addition occurs at the metal. The infrared spectrum of this product shows that *both* the carbonyl ν(CO) and thiocarbonyl ν(CS) frequencies have increased; the thiocarbonyl absorption appears as a strong, distinctive band at 1207 cm^{-1}. Further evidence that the metal is protonated is provided by the NMR spectrum. The proton again appears as a triplet of triplets (J_{PMH} = 72 Hz, $J_{P'MH}$ = 13 Hz) centered at 2.79 ppm upfield from TMS. This pattern indicates that the complex has rearranged to the geometry in which the CO and CS groups are trans to each other and the proton occupies an octahedral face, as suggested for $HW(CO)_2(DPE)_2^+$. The difference in chemical shifts of the metal protons in the two metal hydride complexes is an indication of a substantial decrease in electron density at the metal caused by replacing CO with CS.

Just as metal-containing Lewis acids were found to be unreactive toward them, $W(CO)_5(CS)$,[8] $W(CO)_4(CS)(PPh_3)$,[8] and $W(CO)_3(CS)(DPE)$[1] (having ν(CS) frequencies of 1258, 1247, and 1215 cm^{-1}, respectively) also do not react with the triethyloxonium ion. The metal thiocarbonyl anion, *trans*-$IW(CO)_4(CS)^-$ (**3**), however, does react with alkylating agents. This thiocarbonyl derivative was prepared in good yield (>80%) by heating a tetrahydrofuran solution of $W(CO)_5(CS)$ and equimolar tetra-*n*-butylammonium iodide at 50° for 2 hr; it crystal-

Table I. Infrared and Conductivity Measurements

Compound	ν(CO),[a] cm^{-1}	ν(CS),[a] cm^{-1}	Λ,[b] ohm^{-1} cm^2 mol^{-1}
$W(CO)(CS)(DPE)_2$	1838 s	1161 s	
$[W(CO)(DPE)_2(CSCH_3)]FSO_3$	1898 s	*c*	21.6
$[W(CO)(DPE)_2(CSC_2H_5)]BF_4$	1898 s	*c*	25.6
$[HW(CO)(CS)(DPE)_2]CF_3SO_3$	1958 s	1207 s	19.8
$W(CO)_2(DPE)_2$	1846 s, 1781 s		
$[(C_2H_5)W(CO)_2(DPE)_2]BF_4$	1970 vw, 1864 vs		24.0
$[HW(CO)_2(DPE)_2]CF_3SO_3$	1968 w, 1862 vs		19.8
$(n\text{-}C_4H_9)_4N[IW(CO)_4(CS)]$	2062 w, 1947 vs	1195 s	25.6
$IW(CO)_4(CSCH_3)$	2115 w, 2033 vs[d]	1118 m[d]	
$IW(CO)_4[CSC(O)CH_3]$	2124 w, 2049 vs, 2040 vs[d,e]	1081 m[d]	
$IW(CO)_4[CSC(O)CF_3]$	2137 w, 2057 vs, 2052 vs[d,f]	*g*	

[a] Recorded in CH_2Cl_2 solvent unless specified otherwise. [b] Approximately 10^{-3} M in nitrobenzene. [c] This peak overlaps a DPE ligand absorption near 1095 cm^{-1}. [d] Pentane solution. [e] Also ν(C=O) at 1753 cm^{-1}. [f] Also ν (C=O) at 1737 cm^{-1}. [g] Obscured by C–F absorption.