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SEPARATION OF DIASTEREOMERS, STRUCTURAL ISOMERS, AND HOMOLOGS OF η^5-CYCLOPENTADIENYLCOBALT AND DINUCLEAR MOLYBDENUM COMPLEXES BY REVERSE PHASE HIGH PERFORMANCE LIQUID CHROMATOGRAPHY USING DEOXYGENATED SOLVENTS

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Summary

High performance liquid chromatography (HPLC) is being used as an analytical and preparative tool for the characterization and isolation of a series of air-sensitive organometallic compounds. Reversed phase chromatography with octadecylsilyl-modified silica (ODS) as a stationary phase and polar mobile phases saturated with argon are employed in the separation of products.

High performance (pressure) liquid chromatography (HPLC) has recently been applied to the separation of complex organometallic mixtures. It has been employed in the separation of products from the reaction of $Fe_2(CO)_9$ with di-t-butyl-sulfurdiimine [1], manganese, chromium, iron, and cobalt carbonyl derivatives [2], metallacarboranes [3], metal clusters [4], metal chelates [5], 2,2′-bipyridylruthenium diacid/ester mixtures [6], the two 2,3-dimethylnaphthalenechromium tricarbonyl isomers [7], *cis*/*trans*-isomers of substituted butadieneiron tricarbonyl complexes [8] and hydrogen shift isomers of phenylcycloheptatrieneiron tricarbonyl [9]. In this paper we report that reversed phase HPLC may be readily applied to the preparative separation of isomeric η^5-cyclopentadienyl-η^4-cyclobutadienecobalt complexes and of structurally analogous dinuclear molybdenum derivatives. Some of the components in the mixtures are moderately to strongly air-sensitive. Nevertheless, quantitative isolation is possible by the use of deoxygenated and argon saturated solvents.

Experimental

Apparatus

A slightly modified Altex Model 330 Isocratic liquid chromatographic system was used. The instrumentation consisted of a Model 110A single-piston

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pump equipped with a pulse dampener and preparative head (maximum pressure: 6000 psi), a UV detector with wavelength detectors of 254 nm and/or 280 nm (sensitivity 0.005 AU full scale), a preparative (Altex) flow cell (path length: 0.5 mm, volume 2 μl), and a variable-volume universal injector (sample loop: 20 μl, 1.0 ml, or 2.0 ml). All separations were accomplished using Altex Ultrasphere-ODS reverse phase columns (250 mm length with 10 mm I.D.; 5 μm particle size; column volume 12.9 ml). Occasionally, for particularly difficult separations, two such columns were used in series.

Chemicals and materials

Generally the eluent used contained MCB Omnisolv grade acetonitrile or methanol. Dichloromethane and dioxane were both Mallinckrodt reagent grade solvents filtered through a 5 μm Millipore filter. The water employed was de-ionized and filtered through a 2 μm Millipore filter. The following chemicals were purchased: $[Co(CO)_2(\eta^5\text{-}C_5H_5)]$ (Strem); $[(Mo(CO)_3(\eta^5\text{-}C_5H_4R)_2]$ (R = H, Me) (Alfa Ventron); 5-hexene-1-yne (Farchan), while bis(trimethylsilyl)-acetylene (BTMSA) was available from PCR Research Chemicals. The alkyne 3-phenyl-but-1-yne was prepared according to the literature [10] and 3-(2-propynyl)cyclopentene by the addition of 3-chlorocyclopentene to a stirred solution of dilithiopropyne in tetrahydrofuran at —78° C.

Procedures

All new compounds gave satisfactory spectral (*m/e*, ^{1}H and ^{13}C NMR, IR) and/or analytical data, reported elsewhere [15—17]. The reaction of η^5-cyclopentadienylcobalt dicarbonyl with alkynes was typically carried out by adding a deoxygenated mixture of BTMSA and equimolar quantities of other reagents to a refluxing solution of deoxygenated BTMSA over 48 h using a syringe pump The reaction was worked up by vacuum transfer of the solvent and chromatography on neutral alumina (activity II). Elution with pentane gave $CpCo(CO)_2$ and other minor products followed by the primary product mixture.

The mixtures of dinuclear molybdenum compounds were prepared following literature procedures [11]. The η^5-CpMo carbonyl compounds were purified by gravity flow column chromatography on Florisil eluting with benzene. The mixture of XVIII—XX was generated by irradiating XVIII and XX dissolved in benzene at 25° C in a closed system. The mixture of XXI—XXIII was prepared by mixing XVIII and XX in toluene and refluxing the solution with a nitrogen purge. Preliminary purification of the reaction products was accomplished by gravity flow column chromatography on Florisil eluting with benzene/hexane (25/75). This procedure separates the XVIII—XX series of compounds from the XXI—XXIII series but will give no separation within either set.

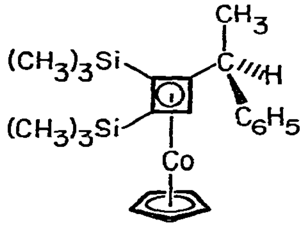
After extended preparative use of the HPLC system an apparent accretion of organometallic decomposition products greatly increases the column back pressure and noticeably reduces the sample resolution. At this point the column can be completely regenerated by eluting with the following series of solvents (all filtered through 2 μm Millipore filter): i) ten column volumes of a saturated solution of EDTA in dioxane/water (20/80), ii) five to ten column volumes of distilled water, iii) five column volumes of acetone, iv) ten column volumes of dichloromethane, v) reequilibration of the column with the solvent to be used in subsequent separations.

Results and discussion

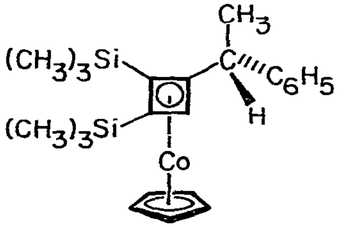
The compounds separated by HPLC described in this study were all prepared as part of current mechanistic and synthetic projects in organometallic chemistry. Some of these complexes are highly air-sensitive and subject to rapid ligand decomplexation in the presence of protic acids or moderately basic solutions. These complexes are frequently unstable to normal phase chromatography on silica and tend to elute with the solvent front on activity II—III neutral alumina with pentane as eluent. In the case of molybdenum, the triply bonded species XXI—XXIII are unstable to either basic alumina or silica gel and inseparable on Florisil when eluting with a benzene/hexane mixture. The strongly hydrophobic nature of the above solutes makes their separation a formidable challenge to the synthetic chemist.

After some experimentation, a highly loaded octadecyl-modified silica gel column (Ultrasphere C-18) was chosen for the separation of the compounds described. On an analytical scale Ultrasphere C-2 and C-8 columns are less efficient for separating the reaction products under our conditions. The polarity of the solvent systems was adjusted to obtain the best solubility-polarity properties. For the molybdenum complexes, protic solvents may be used. Thus, in this series, a much higher solvent polarity is attainable and a correspondingly higher degree of resolution is possible. Both cobalt and molybdenum compound mixtures contain air-sensitive components and as such were eluted with solvents deoxygenated by argon purge. The columns were equilibrated with the argon-saturated solvents by preeluting ten to twenty column volumes of solvent before use.

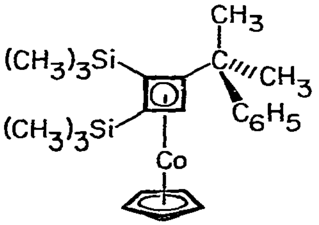
The reaction of BTMSA with 3-phenyl-but-1-yne and CpCo(Co)$_2$ [12] provides after initial normal gradient chromatography an inseparable mixture (one spot by TLC) of the diastereomeric complexes I and II (stereochemistry assigned arbitrarily) and the homolog III (derived from an impurity in the starting alkyne).



I



II



III

Despite the close structural similarity of the products, convenient separation is achieved by HPLC using acetonitrile/water (9/1). The results of this separation are shown in Fig. 1.

A more difficult separation problem presents itself in the mixture obtained when 1-trimethylsilyl-3-phenyl-but-1-yne is employed in the above reaction.

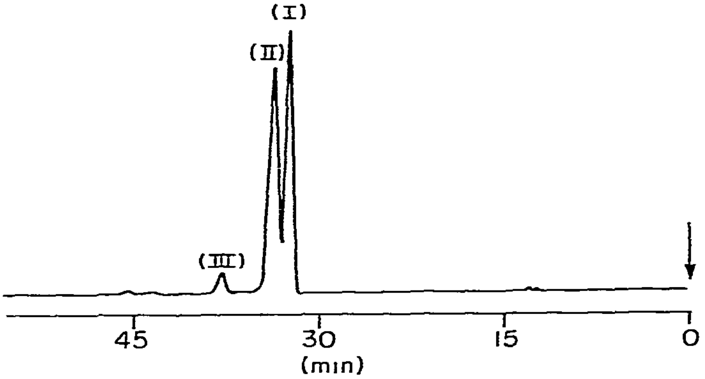
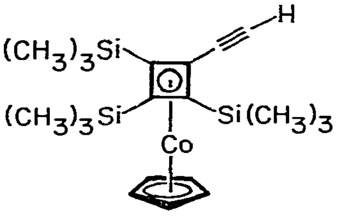
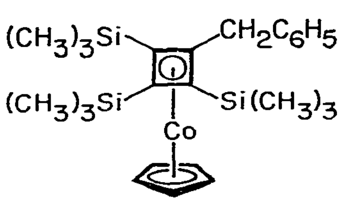


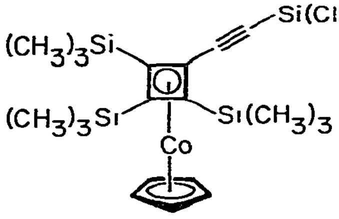
Fig. 1. Chromatogram of a sample of a mixture of I—III; flow 1.3 ml/min; pressure 1420 psig; CH_3CN/H_2O, 9/1; 75 mg in 5 ml solvent; 1 ml sample loop.



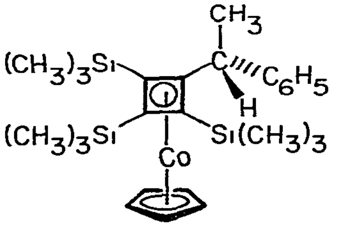
(IV)



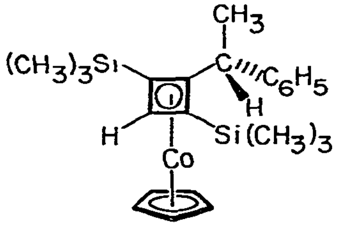
(V)



(VI)



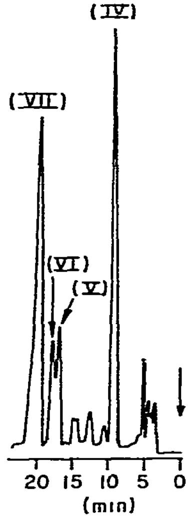
(VII)



(VIII)

Highly silylated products from reactions of this type are exceedingly nonpolar and ordinarily inseparable unless rendered less hydrophobic by (partial) desilylation [13]. Indeed, gravity flow column chromatography (alumina) gave an inseparable mixture (pentane eluent). The resolution of these reaction products by HPLC is shown in Fig. 2. Compounds IV—VII were isolated and fully characterized. Compound V is the product of the reaction of BTMSA with 1-trimethylsilyl-3-phenylpropyne, an impurity in 1-trimethylsilyl-3-phenyl-but-1-yne, whereas IV and VI are derived from mono- and bistrimethylsilylated 1,3-butadiyne formed from BTMSA by apparent silyl-acetylide metathesis [14].

Compound VII was of interest to us as a potential precusor to VIII, an isomer to I and II. This potential is borne out in practice, VII being selectively protodesilylated to VIII. Mixtures of I, II, and VIII required separation in con-



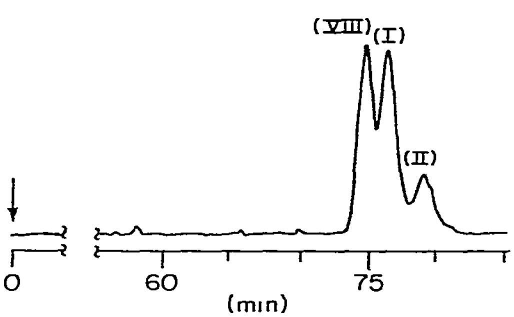
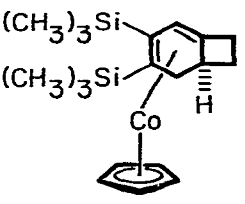


Fig. 2. Chromatogram of a sample of a mixture of IV—VII in addition to other compounds. flow 2.8 ml/min; pressure 4000 psig; CH_3OH/H_2O, 19/1; 75 mg in 5 ml solvent; 1 ml sample loop.

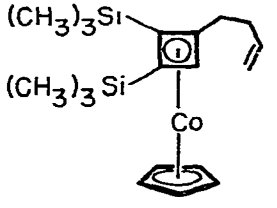
Fig. 3. Chromatogram of a sample of a mixture of I, II and VIII; flow 3 ml/min. pressure 4000 psig; CH_3OH/H_2O, 9/1; 50 mg in 5 ml solvent; 1 ml sample loop. This separation necessitated the coupling of two preparative columns in series

nection with other work [12]. This is currently only possible by the use of HPLC and demonstrated by Fig. 3. To achieve the observed resolution in this case two preparative columns had to be coupled in series.

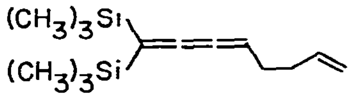
Another application of HPLC, this time to the separation of isomers IX and X, is shown in Fig. 4. These compounds are formed in the cobalt mediated



(IX)



(X)



(XI)

intermolecular [2+2+2] cycloaddition of 5-hexen-1-yne with BTMSA [15]. The widely differing retention volumes allow for ready quantitative separation. A variation on this reaction utilizes 3-(2-propynyl)cyclopentene and BTMSA. This experiment was performed in an effort to determine the feasibility of tricyclic ring synthesis of the type XII. Initial GC-MS data indicated the presence of four compounds with the molecular weight expected for XII. However, HPLC indicated that none of the desired XII compound had been formed; the isolation of the major components allowed the structural identification [15,17] of seven compounds (Fig. 5), XIII—XVII, and VI. Evidently, under the reaction conditions, double bond isomerization is rapid leading to a kinetic double bond redistribution as evidenced by the formation of XIII—XV. The

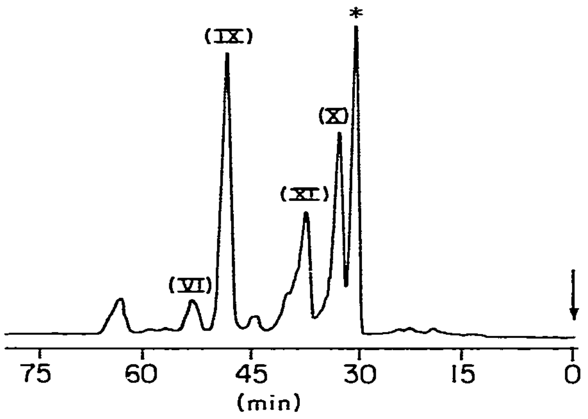
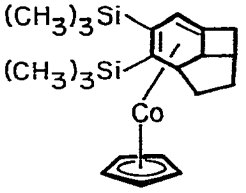
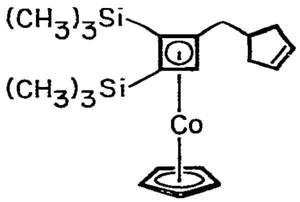


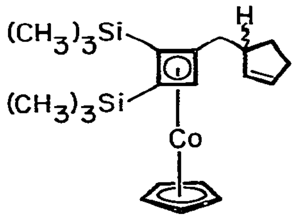
Fig. 4. Chromatogram of the reaction product of 5-hexene-1-yne and BTMSA in the presence of 1-equivalent of $CpCo(CO)_2$ after initial gravity flow chromatographic purification (neutral alumina). The peak marked by an asterisk is the free diene ligand of X, isolated and fully characterized in addition to VI, and IX—XI: flow 0.5 ml/min; pressure 200 psig; CH_3CN/CH_2Cl_2, 94/6; 100 mg in 5 ml solvent; 1 ml sample loop.



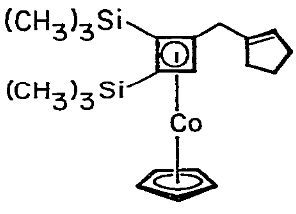
(XII)



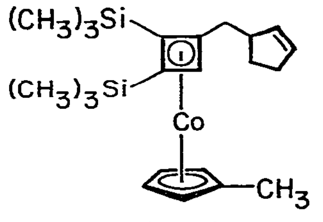
(XIII)



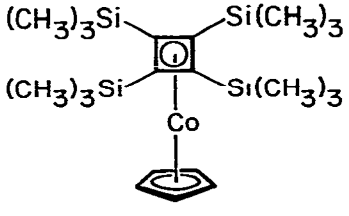
(XIV)
2-diastereomers



(XV)



(XVI)



(XVII)

two diastereomers of XIV could be characterized by NMR spectroscopy but were not separable.

The generation of methylated analog XVI in this reaction is curious. We have seen similar Cp-methylated derivatives in other work connected with the interaction of alkynes with $CpCo(CO)_2$. Although the origin of the methyl group is unknown, trimethylsilyl groups appear unnecessary for its formation, methylated compounds being observed with other alkynes as well [16]. The detection and clean separation of XVI serves to further illustrate the power of HPLC in the separation of organometallic compounds of this type.

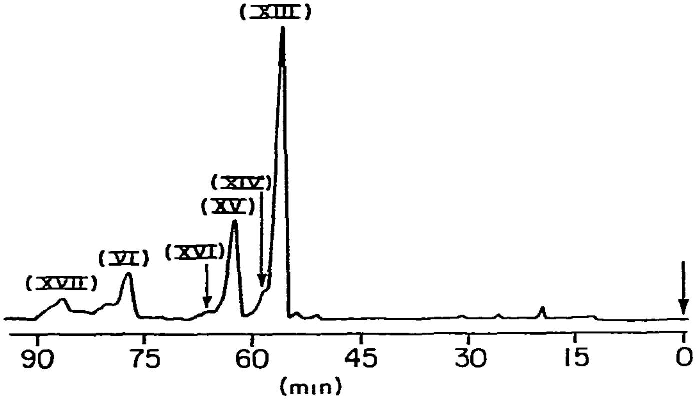
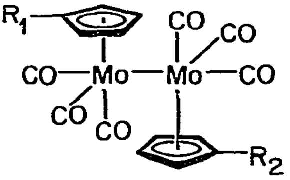
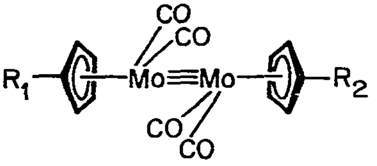


Fig. 5. Chromatogram of the pentane components from neutral alumina chromatography of the products from the reaction of 3-(2-propynyl)cyclopentene, BTMSA, and CpCo(CO)$_2$. The indicated compounds were isolated and structurally identified. Flow 1.25 ml/min; pressure 600 psig; CH$_3$CN/CH$_2$Cl$_2$, 94/5; 100 mg in 5 ml solvent. 1 ml sample loop.

Finally, we would like to demonstrate the facile separation of six dinuclear molybdenum complexes using HPLC. These compounds were synthesized as part of a mechanistic study and their unambiguous analytical differentiation



(XVIII) $R_1 = R_2 = H$
(XIX) $R_1 = CH_3$, $R_2 = H$
(XX) $R_1 = R_2 = CH_3$



(XXI) $R_1 = R_2 = H$
(XXII) $R_1 = CH_3$, $R_2 = H$
(XXIII) $R_1 = R_2 = CH_3$

was necessary. Fig. 6 depicts the clean separation of a mixture of XVIII—XXIII. It is interesting to note that within each series (singly versus triply

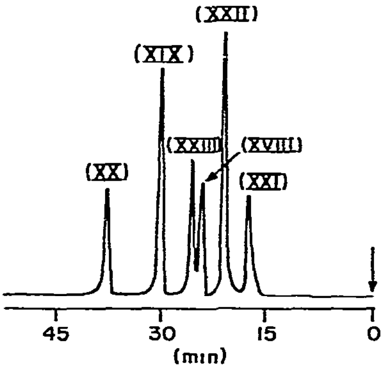


Fig. 6. Chromatogram of a mixture of XVIII—XXIII; flow 0.5 ml/min; pressure 200 psig. CH$_3$CN/H$_2$O, 5/1; 20 mg in 3 ml; 1 ml sample loop.

bound Mo—Mo) the increase in hydrophobicity with increasing methyl substitution is clearly reflected in the retention volumes. Moreover, the less carbonylated series is also relatively more polar.

Conclusion

The use of reversed phase HPLC for the purification and identification of structurally very similar organometallic compounds, for which the application of normal phase chromatography is inadequate, has been demonstrated. Because of its mildness, speed and separation efficiency, HPLC can provide a valuable means of purification for previously inseparable organometallic mixtures.

Acknowledgments

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