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

John M. Huggins, Joseph A. King, Jr.,
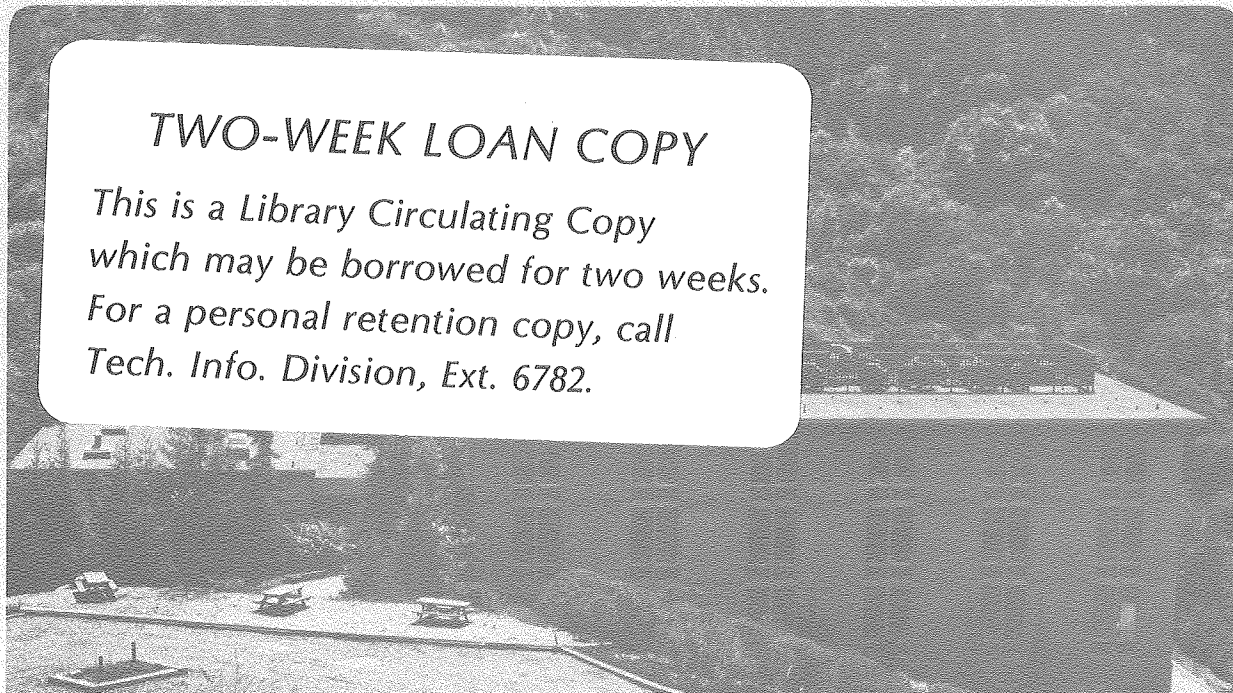K. Peter C. Vollhardt, and Mark J. Winter

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Separation of Diastereomers, Structural Isomers, and Homologs of η^5-Cyclopentadienyl Cobalt and Dinuclear Molybdenum Complexes by Reverse Phase High Performance Liquid Chromatography Using Deoxygenated Solvents

John M. Huggins, Joseph A. King, Jr.*, K. Peter C. Vollhardt* and Mark J. Winter

Department of Chemistry, University of California and the Materials

and Molecular Research Division, Lawrence Berkeley Laboratory, Berkeley,

California 94720 (U.S.A.)

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. Reverse 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-dimethylnaphthalene chromium tricarbonyl isomers [7], cis-trans-isomers of substituted butadiene iron tricarbonyl complexes [8] and hydrogen shift isomers of phenylcyclohepta-triene iron tricarbonyl [9]. In this paper we report that reverse phase HPLC may be readily applied to the preparative separation of isomeric η^5-cyclopenta-dienyl-η^4-cyclobutadiene cobalt 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.

Apparatus

A slightly modified Altex Model 330 Isocratic Liquid Chromatographic system
was used. The instrumentation consisted of a Model 110A single-piston pump
equipped with a pulse dampener and preparative head (maximum pressure: 6000 psi),
a U.V. 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 2μℓ),
and a Variable-Volume Universal Injector (sample loop: 20μℓ, 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: $[Co(CO)_2(\eta^5-C_5H_5)]$ (Strem); $[(Mo(CO)_3(\eta^5-C_5H_4R)_2]$
(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-cyclopentadienyl cobalt 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 48h 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 2μm 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
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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 de-oxygenated 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).
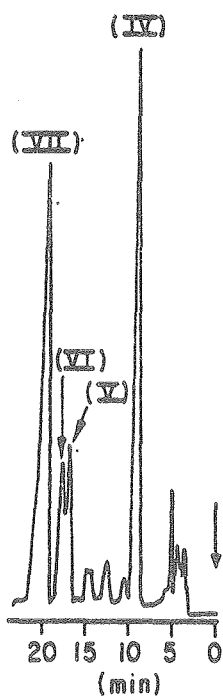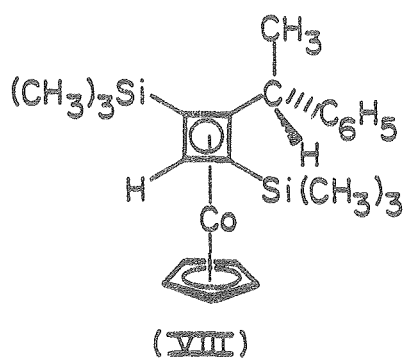
I   II   III

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.

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.

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 of pentane eluants. The resolution of these reaction products by HPLC

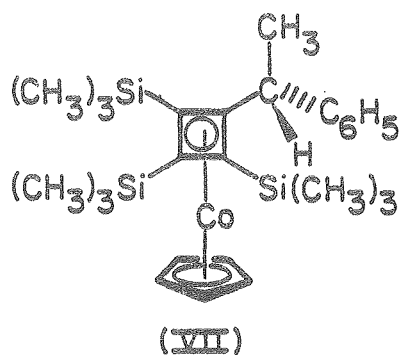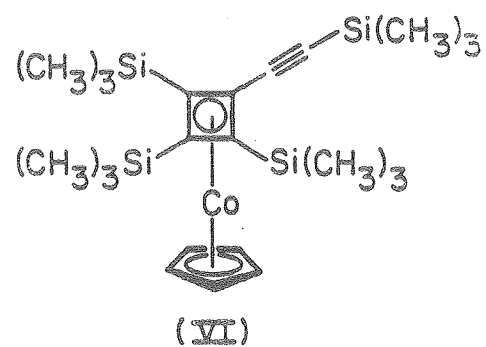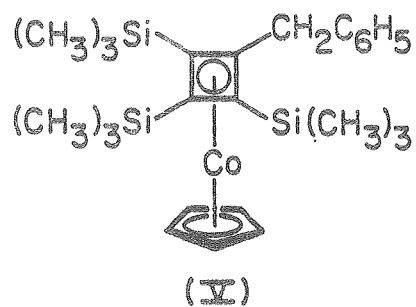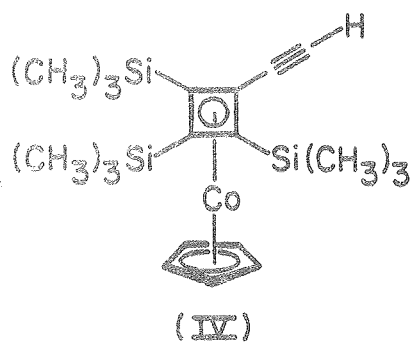is shown in Fig. 2. Compounds (IV)-(VII) were isolated and fully characterized.

Fig. 2

Compound (V) is the product of the reaction of BTMSA with 1-trimethylsilyl-3-phenyl-propyne, 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 precursor 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 connection 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.
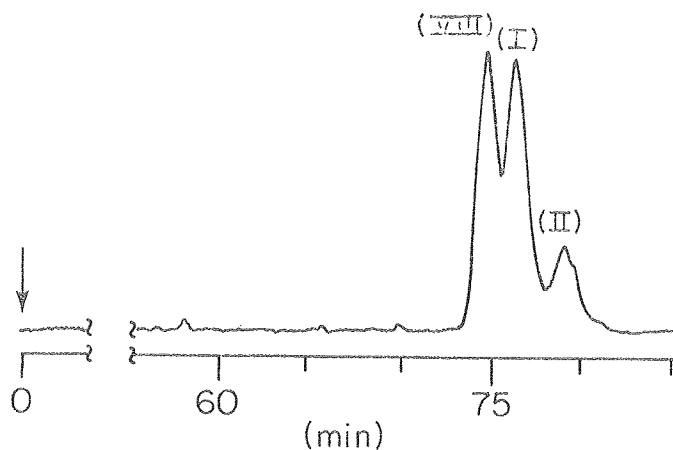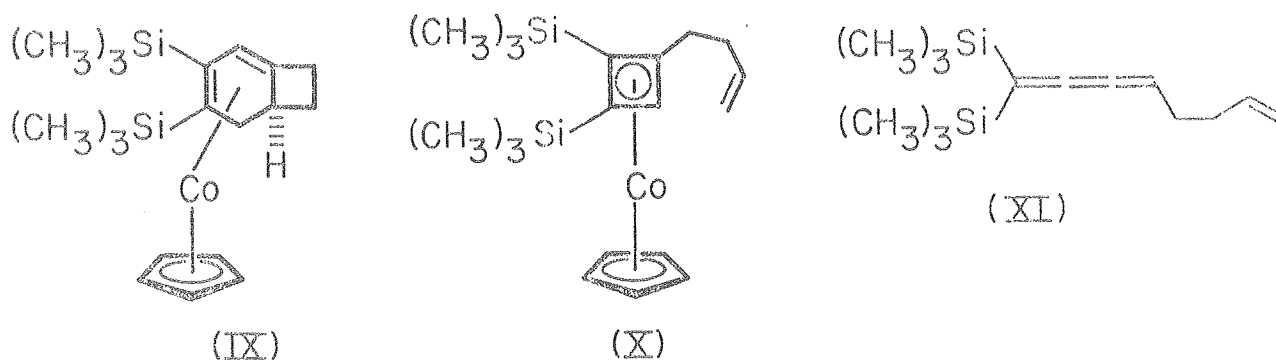

Fig. 3

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

intermolecular [2+2+2] cycloaddition of 5-hexen-1-yne with BTMSA [15]. The

widely differing retention volumes allow for ready quantitative separation.
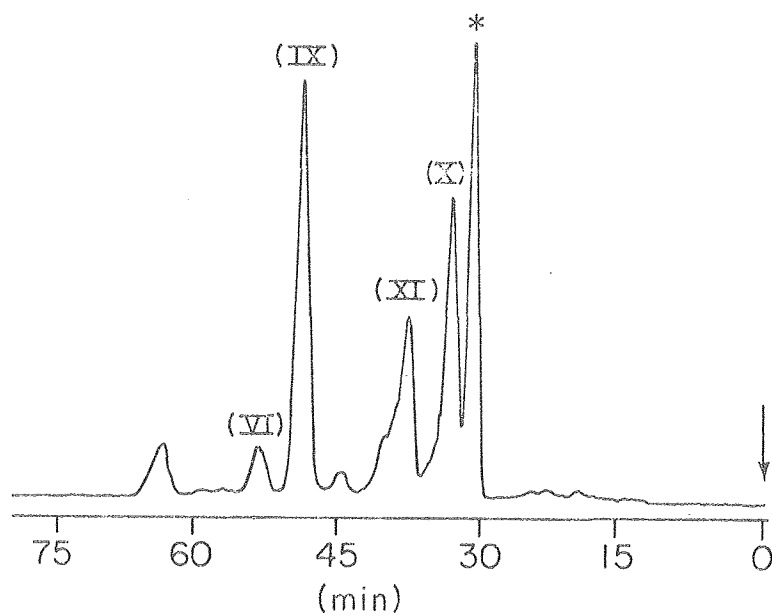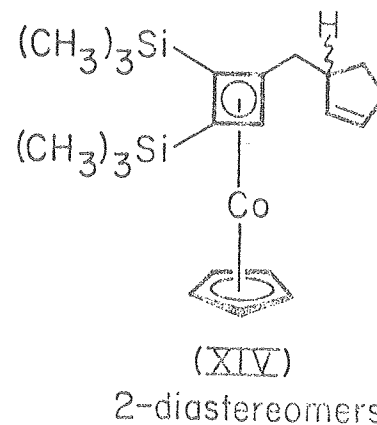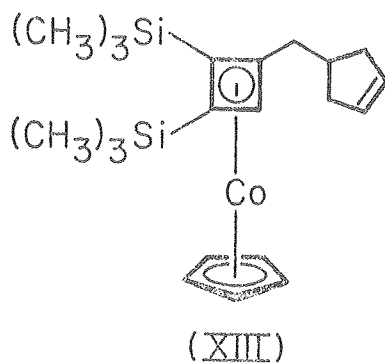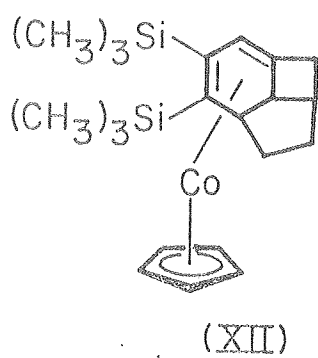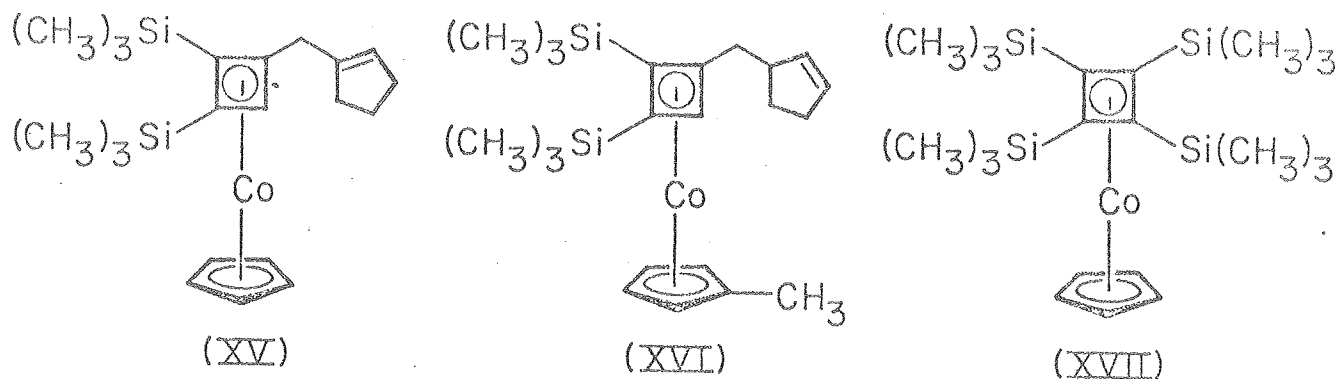

Fig. 4

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 g.c. mass spectrometry data

(XII)   (XIII)   (XIV)

2-diastereomers

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

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

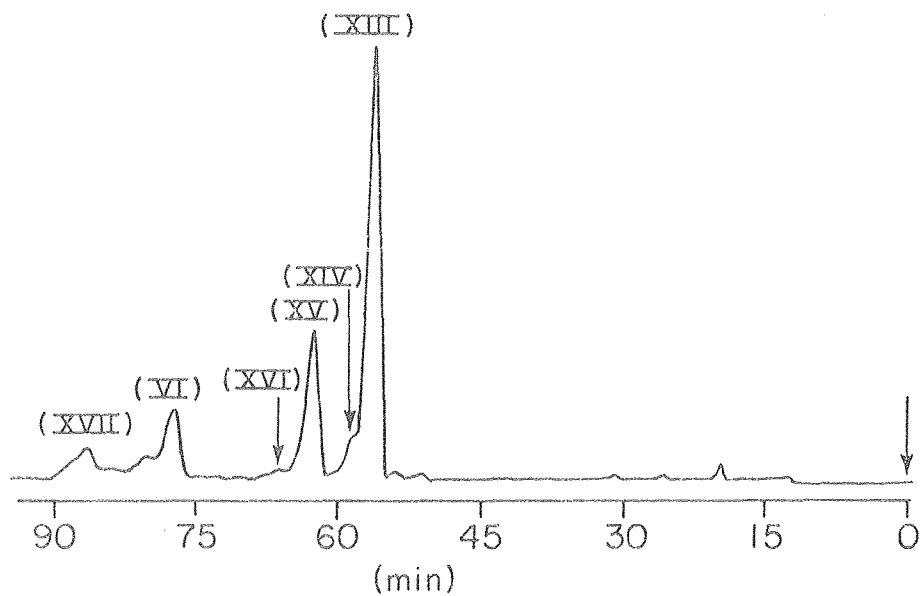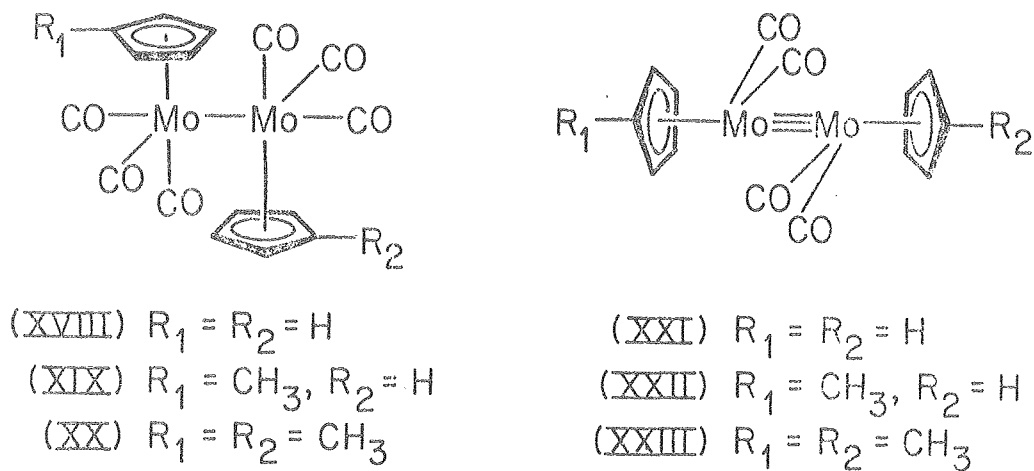of HPLC in the separation of organometallic compounds of this type.

Fig. 5

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 was necessary. Fig. 6 depicts the clean separation of a mixture of (XVIII)-(XXIII).

(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) $R_1 = R_2 = CH_3$

(XXII)

(XIX)

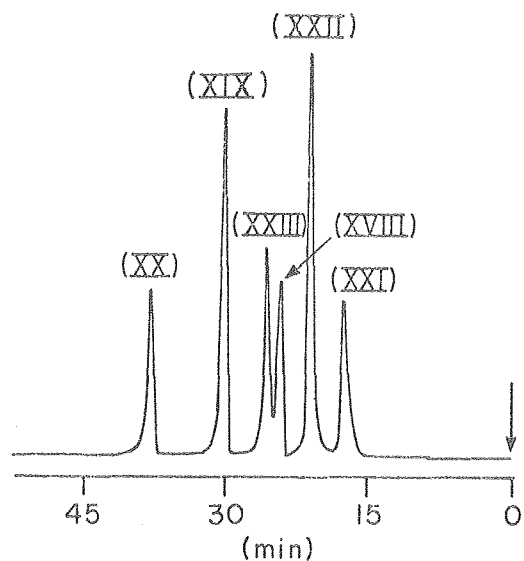(XXIII) (XVIII)

(XX) (XXI)

45   30   I5   0

(min)

Fig. 6

It is interesting to note that within each series (singly versus triply 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 reverse 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 aptly demonstrated. Because of its mildness, speed and separation efficiency, HPLC can provide a valuable means of purification for previously inseparable organometallic mixtures.

Acknowledgments

The authors would like to thank Altex Corp. for the use of the analytical Ultrasphere C-2 and C-8 columns and in particular Ms. Peggy Doyle for her helpful suggestions in the preparation and regeneration of the reverse phase

References
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1. C. H. Gast, F. Nooitgedacht and J. C. Kraak, J. Organometal. Chem.,
    184 (1980) 221.

2. R. Eberhardt, H. Lehner and K. Schlögl, Monatsh. Chem. 104 (1973) 1409;
    D. T. Haworth and T. Liu, J. Chromatogr. Sci., 14 (1976) 519.

3. Z. Plzák, J. Plesek and B. Stibr, J. Chromatogr., 168 (1979) 280;
    W. J. Evans and M. F. Hawthorne, ibid., 88 (1974) 187.

4. C. T. Enos, G. L. Geoffroy and T. H. Risby, J. Chromatogr. Sci., 15
    (1977) 83.

5. J.F.K. Huber, J. C. Kraak and H. Veening, Anal. Chem., 44 (1972) 1554;
    P. C. Uden and I. E. Bigley, Anal. Chim. Acta, 94 (1977) 29.

6. S. J. Valenty and P. E. Behnken, Anal. Chem., 50 (1978) 834.

7. J. M. Greenwood, H. Veening and B. R. Willeford, J. Organometal. Chem.,
    38 (1972) 345.

8. D. G. Gresham, C. P. Lillya, P. C. Uden and F. H. Walters, J. Organometal.
    Chem., 142 (1977) 123; R. E. Graf and C. P. Lillya, ibid., 47 (1973) 413.

9. A. Pryde, J. Chromatogr., 152 (1978) 123.

10. J. Y. Becker, S. Brenner and J. Klein, Isr. J. Chem., 10 (1972) 827.

11. D. S. Ginley, C. R. Bock and M. S. Wrighton, Inorg. Chim. Acta, 23 (1977) 85;
    M. D. Curtis and R. J. Klingler, J. Organometal. Chem., 161 (1978) 23.

12. K.P.C. Vollhardt and M. J. Winter, submitted for publication.

13. See J. R. Fritch and K.P.C. Vollhardt, J. Am. Chem. Soc., 100 (1978) 3643.

14. J. R. Fritch and K.P.C. Vollhardt, J. Am. Chem. Soc., 101 (1979) 2768.

15. C. Chang, C. G. Francisco, T. R. Gadek, J. A. King, Jr., E. D. Sternberg,
    and K.P.C. Vollhardt, Pure Appl. Chem., in press.

16. N. T. Allison, J. R. Fritch and K.P.C. Vollhardt, in preparation.

17. C. Chang, J. A. King, Jr., and K.P.C. Vollhardt, submitted.

Figure captions

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.

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.

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.

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; $CH_3CN-CH_2Cl_2$, 94:5; 100 mg
in 5 ml solvent; 1 ml sample loop.

Fig. 6   Chromatogram of a mixture of (XVIII)-(XXIII); flow 0.5 ml/min;
pressure 200 psig; CH_3CN-H_2O, 5:1; 20 mg in 3 ml; 1 ml sample loop.