8250 *J. Am. Chem. Soc.* **1988**, *110*, 8250–8252

$Ph_3P{=}CH_2$, DBU, and pyridine) also react with **1**, but tractable products have thus far not been isolated from these reactions. A strong band at 1670 cm^{-1} is observed in the IR spectrum of **2** and is assignable as $\nu(C{=}N)$ of the allylideneamido ligand. The salient feature of the ^1H NMR spectrum of **2** is the appearance of a doublet at 4.91 δ for the azomethine proton. The only literature precedent for the formation of an alkylideneamido ligand from an organoimido ligand in a mononuclear complex concerns a group of alkylimido rhenium(V) species of the general formula $RCH_2N{\equiv}ReCl_3(PR'_3)_2$ (R = H, Me, Et);[15] interestingly, the ^1H NMR resonances for the α-methylene protons in these complexes are found to be shifted to high field (between ca. 0.5 and −0.5 δ). The formation of alkylideneamido ligands in this manner cannot be considered a general reaction type: modifying the coordination sphere of the above rhenium complexes by the introduction of dialkyldithiocarbamate ligands renders the alkylimido ligands inert to the abstraction reaction.[16] The dehydrohalogenation reaction of **1** can be reversed by treating benzene solutions of **2** with ethereal anhydrous HCl at room temperature.

In summary, the synthesis of **1** and its conversion to **2** via allylic hydrogen abstraction provide two complexes which feature ligands of presumed relevance to the ammoxidation of propylene and provide support for a crucial step in the proposed mechanism of acrylonitrile synthesis. Work is underway to extend these studies to the further modelling of ammoxidation chemistry.

Acknowledgment. We are grateful to the National Science Foundation (Grant No. CHE-8604359) for support of this research.

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(14) ^1H NMR (400 MHz, $CDCl_3$, 298 K) δ 5.81 (m, 1 H, —C*H*=), 4.91 (d, *J* = 4.9 Hz, 1 H, N=C*H*), 5.49 (d, *J* = 16.9 Hz, 1 H, =CH_2 trans), 5.30 (d, *J* = 9.9 Hz, 1 H, =CH_2 cis), 3.87 (br, 8 H, —OCH_2CH_2—), 1.92 (br, 8 H, —OCH_2CH_2—); ^{13}C NMR (100.1 MHz, C_6D_6, 298 K) 134.6 (d, N=*C*H), 129.7 (d, —*C*H=), 118.2 (t, =*C*H_2), 68.5 (t, —O*C*H_2CH_2—), 25.1 (t, —OCH_2*C*H_2—); IR (Nujol, cm^{-1}) 1670, $\nu(C{=}N)$, 1632, $\nu(C{=}C)$.

(15) (a) Chatt, J.; Dosser, R. J.; King, F.; Leigh, G. J. *J. Chem. Soc., Dalton Trans.* **1976**, 2435. (b) Bakir, M.; Fanwick, P. E.; Walton, R. A. *Inorg. Chem.* **1988**, *27*, 2016.

(16) Goeden, G. V.; Haymore, B. L. *Inorg. Chem.* **1983**, *22*, 157.

Synthetic Studies of the Cyclopropyl Iminium Ion Rearrangement. 3. Application of the Cyclopropyl Acyliminium Ion Rearrangement to a Concise and Highly Convergent Synthesis of (±)-Lycorine

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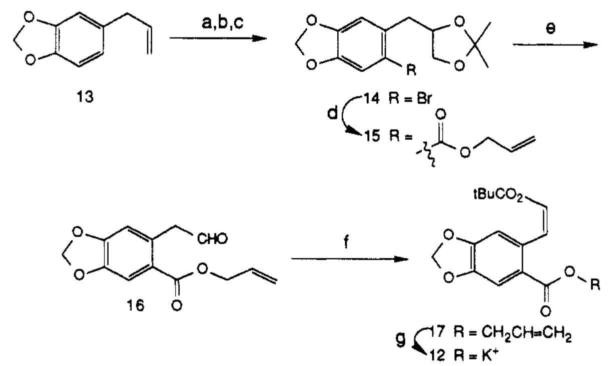
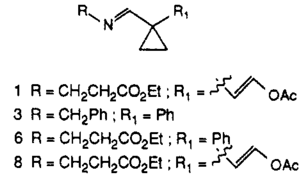
Received August 12, 1988

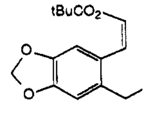
Previous studies of the cyclopropyl iminium ion rearrangement in our laboratores have demonstrated its utility for the synthesis of Δ^2-pyrrolines, particularly acid-sensitive dienamine systems which are unavailable by other methods.[1,2] Such a process would appear to provide an exceptionally concise approach to *Amaryllidaceae* alkaloids of the lycorine class.[2] Employing this approach obviates the lengthy sequences required to manipulate the stereochemistry and oxidation state of the ring C substituents by developing the correct stereochemical relationships and oxidation state directly early in the sequence.[3,4] However, a significant limitation was encountered in the application to cyclopropyl imines such as **1** which bear electronegative α substituents. The markedly reduced nucleophilicity of **1** rendered it unreactive to even highly activated alkyl halides such as **2**, mesylates, and even triflates.[5,6]

Scheme I[a]



[a] Reagents: (a) OsO_4 (catalytic), NMO (1.1 equiv), acetone/H_2O, 23 °C, 15 h; (b) acetone, TsOH (catalytic), 23 °C, 15 h; (c) NBS (1 equiv), DMF, 23 °C, 20 h; (d) *n*BuLi (1.1 equiv), THF, −78 °C, 30 min, then $ClCO_2CH_2CH{=}CH_2$ (1.1 equiv), THF, −78 °C (1 h) → 23 °C (1 h); (e) H_5IO_6 (1.2 equiv), 1 N HCl/THF (1:1), 23 °C, 3.5 h; (f) $((CH_3)_3CCO)_2O$ (1.1 equiv), Et_3N (1.3 equiv), DMF, 23 °C, 15 h; (g) $Pd(C_6H_5)_3P)_4$ (catalytic), $C_5H_{11}C(C_2H_5)CO_2K$, EtOAc/CH_2Cl_2 (1:1), 23 °C, 15 h.





2

In order to successfully implement our iminium ion approach to lycorine, the low nucleophilicity of imines such as **1** had to be overcome. We anticipated that the required enhanced reactivity could be achieved by generation and rearrangement of the related cyclopropyl acyliminium ions which should result from the reaction of cyclopropyl imines with acid halides. The chemistry of the *N*-acylcyclopropyliminium ions was expected to parallel the chemistry of the *N*-dialkylcyclopropyliminium ions as is observed for their acyclic counterparts.[7] Additionally, advantage could be taken of the greater stability and ease of purification of the resulting *N*-acyl enamides and dienamides relative to enammonium salts however at the expense of requiring an additional operation to effect deblocking and ring closure to the Δ^2-pyrroline.

The feasibility of the desired rearrangement was established by treatment of imine **3** (available via the Staudinger reaction of benzyl azide and 1-phenylcyclopropane carboxaldehyde (**4**)) with acetyl chloride in CH_2Cl_2 or CH_3CN at room temperature

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(1) Boeckman, R. K., Jr.; Jackson, P. F.; Sabatucci, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 2191.

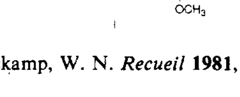
(2) Boeckman, R. K., Jr.; Sabatucci, J. P.; Goldstein, S. W.; Springer, D. M.; Jackson, P. F. *J. Org. Chem.* **1986**, *51*, 3740.

(3) (a) Tsuda, Y.; Sano, T.; Taga, J.; Isobe, K.; Toda, J.; Takagi, S.; Yamaki, M.; Murata, M.; Irie, H.; Tanaka, H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1358. (b) Sano, T.; Kashiwaba, N.; Toda, J.; Tsuda, Y.; Irie, H. *Heterocycles* **1980**, *14*, 1097. (c) Moller, O.; Steinberg, E.-M.; Torssell, K. *Acta Chem. Scand., Ser. B.* **1978**, *32*, 98. See also ref 2.

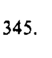
(4) (a) For an excellent recent review on the *Amaryllidaceae* alkaloids, see: Martin, S. F. In *The Alkaloids*; Academic Press, In.: 1987; Vol. 30, pp 251–376. (b) For a comprehensive survey of previous synthetic work directed toward the galanthan ring system, lycorine, and lycorine derivatives, see: Martin, S. F.; Tu, C.; Kimura, M.; Simonsen, S. H. *J. Org. Chem.* **1982**, *47*, 3634. (c) Stork, G.; Morgans, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 7110.

(5) A number of α substituents including vinyl and phenyl render the resulting imines (including *N*-alkyl and *N*-benzyl derivatives) unreactive to alkylation. For example, treatment of **1** with benzyl triflate followed by *n*Bu_4NCl resulted in recovery of **1** unchanged.

(6) Efforts to prepare the iminium ion by condensation of i and ii were thwarted by competing intramolecular reactions involving the enol ester.



i

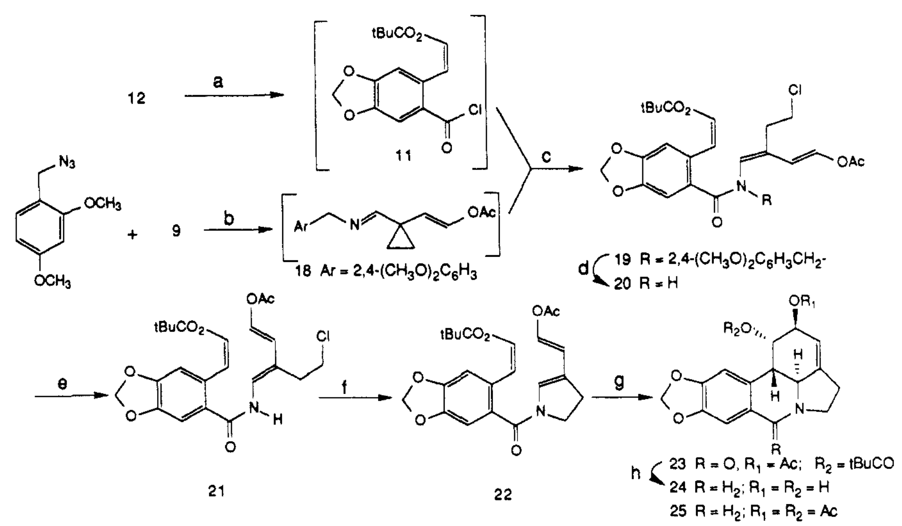


ii

(7) Speckamp, W. N. *Recueil* **1981**, *100*, 345.

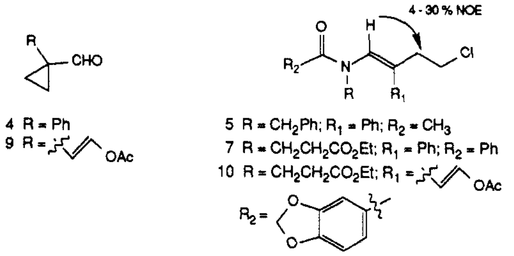
0002-7863/88/1510-8250$01.50/0

Scheme II[a]



[a] Reagents: (a) $(COCl)_2$ (3 equiv), PhH, Δ, 12 h; (b) Ph_3P (1.0 equiv), Et_2O, 23 °C, 4 h; (c) CH_3CN, 23 °C, 15 h; (d) 40% TFA/CH_2Cl_2 (0.25 M), 23 °C, 40 min; (e) $Pd(CH_3CN)_2Cl_2$ (0.25 equiv), $PhCH_3$, (0.1 M), 23 °C, 5 h; (f) DBU (1 equiv), $CHCl_3$, 23 °C, 2 h; (g) 2-ClPhCH$_3$, Δ, 56 h; (h) LAH (xs), THF, Δ, 2 h.

which afforded after workup a single *N*-acetyl enamide **5** in 90% yield.[8,9] The geometry of the enamide double bond was established as *Z* based upon NOE measurements. The process was confirmed to be general for a variety of imines and acid halides; for example, imine **6** obtained as above from ethyl 3-azidopropionate upon treatment with benzoyl chloride afforded the (*Z*)-enamide **7** in 72% yield. Most importantly, treatment of imine **8** obtained from aldehyde **9**[10] with piperonyl chloride provided the (*Z*,*E*)-enamide **10** in 55% yield. *The stereochemical outcome of the acyliminium ion rearrangement is surprising in light of the results for the related cyclopropyl iminium ion cases which underwent spontaneous cyclization to enammonium salts,*[1] *a result which, in the latter, most probably arises by isomerization of the intermediate enamines and dienamines subsequent to rearrangement.*[11]



With the feasibility of the key rearrangement established (albeit requiring subsequent isomerization to the (*E*,*E*)-dienamide), we embarked on the synthesis of acid halide **11** required for conversion to (±)lycorine. The potassium salt **12** (the expected precursor of **11**) was prepared from readily available materials in seven steps as shown in Scheme I. Safrole (**13**) was converted to the crystalline bromide **14** (mp 48–49 °C) in 74% yield (from safrole) with standard manipulations.[12,13] Treatment of **14** with *n*BuLi in THF and inverse addition to a −78 °C solution of $ClCO_2CH_2CH{=}CH_2$ provided allyl ester **15** in 80% yield. Oxidative cleavage of **15** with H_5IO_6 in 1 N HCl/THF afforded the unstable aldehyde **16** which was directly converted stereoselectively to the (*Z*)-enol pivalate **17** (9:1) with pivalic anhydride in Et_3N/DMF in 94% total yield (from **15**).[14] Potassium salt **12** was then obtained in 89% yield by palladium-catalyzed deallylation of **16**.[15]

The key coupling/rearrangement was effected (Scheme II) by slow addition of 1.1 equiv of an 0.25 M solution of **11** (prepared from **12**) in dry CH_3CN to 1 equiv of imine **18** (from 2,4-dimethoxybenzylazide and cyclopropyl aldehyde **9**) in dry CH_3CN (0.7 M) at room temperature. After 15 h, workup and purification by flash chromatography gave the (*Z*,*E*)-dienamide **19** (56% yield based on **9**). The expected *Z* geometry of the enamide double bond was confirmed by NOE on the deblocked amide **20** obtained from **19** upon treatment with 40% TFA/CH_2Cl_2 (76% yield). The required isomerization to (*E*,*E*)-dienamide **21** was effected by treatment of **20** with $Pd(CH_3CN)_2Cl_2$ in $PhCH_3$ at room temperature which afforded a mixture of **20** and **21** (1:1, 90%) plus a trace of other isomer(s). Separation and recycling of **20** was readily accomplished after conversion of **21** to pyrrolide **22** with DBU in $CHCl_3$ (70% overall yield of **22** from **20**).[16] Thermolysis of **22** in 2-chlorotoluene under reflux provided a single isolable cycloadduct, the blocked oxylycorine **23**, in 50–60% yield.[2,4c] Conversion of **23** to (±)lycorine (**24**) was effected as previously described by concomitant LAH reduction of the B-ring lactam and unmasking of the D-ring diol.[3a] Synthetic (±)lycorine (**24**) and the derived diacetate **25** were identical with a sample of authentic materials in all respects including TLC behavior (**24**: R_f 0.35, $EtOAc/CHCl_3/CH_3OH$ (2:2:1)) and ^1H NMR spectroscopy.[3,17]

Thus, the cyclopropylacyliminium ion rearrangement has been demonstrated to be a general process leading completely stereoselectively to *trans*-β-chloroethyl enamides which is applicable

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(8) Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635.

(9) All new substances had spectroscopic data (IR, NMR (300 MHz), MS) consistent with the assigned structure and had satisfactory combustion or high resolution mass spectral analytical data.

(10) Available in six steps from commercially available cyclopropyl cyanide, see ref 1.

(11) Since the formation of enamides is most likely under kinetic control, the stereochemical outcome of the rearrangement step is probably similar for the related cyclopropyliminium ions. However, we were unable to verify this result experimentally since the intermediate dienamines could not be isolated in those cases. In the alkyl iminium ion cases, cyclization ensues presumably after enamine isomerization.

(12) Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

(13) Guthrie, A. E.; Semple, J. E.; Jouille, M. M. *J. Org. Chem.* **1982**, *47*, 2374.

(14) The observed selectivity (9:1 (*Z*:*E*)) is likely the result of kinetic control during deprotonation of an acyloxonium ion intermediate. The stereoelectronically favored conformation for proton transfer to afford the *Z* isomer is structurally similar to the probable major ground-state conformation of the acyloxonium intermediate based on dipole considerations although the observed ground-state conformational preference is lower in one case (3:1 (*Z*:*E*)): Karabatsos, G. J.; Bushman, D. W. *Tetrahedron* **1975**, *31*, 1471.

(15) Jeffrey, P. D.; McCombie, S. W. *J. Org. Chem.* **1983**, *48*, 587.

(16) Amide **21** was also converted to pyrrolide **22** in 70% yield by treatment with BSA in benzene under reflux. This conversion was not consistently reproducible when applied to the mixture of diene isomers.

(17) Spectroscopic and TLC comparison were made with an authentic samples of natural (−)-lycorine (**24**) and **25**. We thank Professor Gilbert Stork for providing us with a sample of **24**. Authentic diacetate **25** was prepared according to a literature procedure.[3a]

to imines of low inherent nucleophilicity and has led to an extremely concise synthesis of (±)lycorine (13 steps from safrole).

Acknowledgment. We are grateful to the National Institute of General Medical Sciences of the National Institutes of Health for a grant (GM-29290) in support of these studies. We also acknowledge support in the form of NRSA fellowships to S.W.G. (GM-09624) and M.A.W. (GM-10641).

Supplementary Material Available: Spectroscopic and selected analytical data for compounds **5**, **7**, **12**, **14**, **15**, **17**, and **19–23** (3 pages). Ordering information is given on any current masthead page.

Thermal Encapsulation and Photochemical Deencapsulation of Ag(I) by $[Ir_2(dimen)_4](PF_6)_2$ (dimen = 1,8-Diisocyanomenthane). X-ray Crystal Structure of $[AgIr_2(dimen)_4](PF_6)_3{\cdot}2DMSO$

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Received May 16, 1988

During the past few years, our group has been studying the electrochemical properties of d^8–d^8 metal complexes of Rh(I) and Ir(I).[1-4] These complexes undergo either two one-electron oxidation processes or a single two-electron process that results in the formation of a metal–metal bond. We were surprised that our attempts to generate stable d^8d^7 radical species[3] from compounds with long (4.45 Å) metal–metal distances ($[M_2(dimen)_4](PF_6)_2$ (M = Rh,[5] Ir,[6,7] dimen[8,9] = 1,8-diisocyanomenthane)), via the addition of the one-electron oxidant Ag^+, gave Ag^+ adducts instead.[10] We report here our preliminary observations regarding the formation, structure, and properties of the more stable adduct with M = Ir. This remarkable adduct features an encapsulated, two-coordinate Ag^+ ion that deencapsulates on exposure to near ultraviolet light.

The sequential addition of $AgPF_6$ to CH_3CN solutions of $[Ir_2(dimen)_4](PF_6)_2$ results in UV–vis spectral changes consistent with the clean conversion to a single new species. The end point of the spectral changes are reached when 1.0 ± 0.1 equiv of $AgPF_6$ are added. Rotary evaporation of a similarly prepared acetone solution gives a pale yellow, microcrystalline powder. Elemental analysis indicates that the powder has the composition $[AgIr_2(dimen)_4](PF_6)_3{\cdot}1acetone$.[7] Slow recrystallization of the powder from DMSO/ether gave yellow crystals that were the subject of an X-ray structural characterization.[11,12] An ORTEP illustration of the $[AgIr_2(dimen)_4(DMSO)_2]^{3+}$ cation is shown in Figure 1.

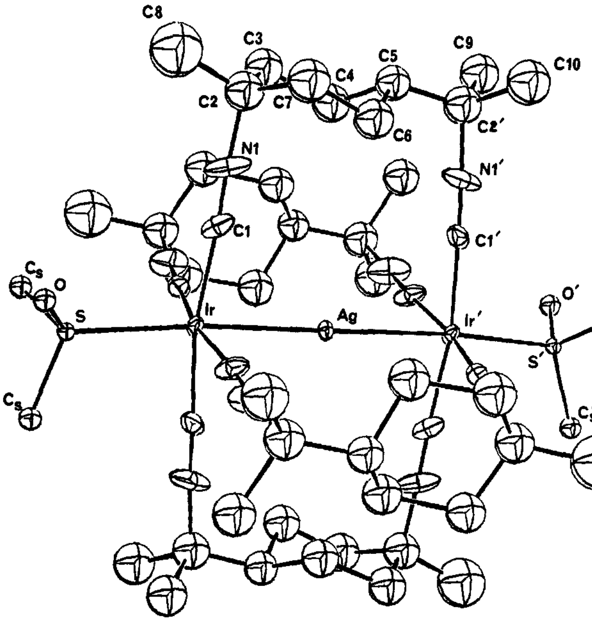

Figure 1. ORTEP view of the $AgIr_2(dimen)_4(DMSO)_2^{3+}$ cation.

The structure reveals that the Ag^+ ion has been encapsulated by the Ir_2^{2+} complex to form a linear $Ir–Ag–Ir^{3+}$ unit. The Ir–Ag distances are 2.642 (1) Å and require an Ir–Ir distance of 5.284 Å. No other atoms are within reasonable bonding distances of the Ag^+, suggesting that the encapsulation reaction is driven by the formation of the Ir^+–Ag^+ interactions and the accompanying solvation changes.

In solution, the $[AgIr_2(dimen)_4]^{3+}$ cation exhibits a pronounced ability to coordinate ligands in the Ir axial positions. Axial coordination shifts the intense electronic transition that is characteristic of the linear arrangement of metal atoms in $[AgIr_2(dimen)_4]^{3+}$. For example, solutions of $[AgIr_2(dimen)_4]^{3+}$ in CH_2Cl_2 exhibit this transition at 390 nm. Addition of acetone, acetonitrile, pyridine, or triphenylphosphine to the solution results in a shift of the absorption band to higher energy. In the cases of pyridine[7] and triphenylphosphine,[7] the bis adducts $[AgIr_2(dimen)_4(L)_2]^{3+}$ have been isolated and characterized.

Several of our preliminary measurements and observations suggest a rich and interesting chemistry for the encapsulated Ag^+ adduct. One point of immediate interest is the magnitude of the Ag^+ encapsulation equilibrium constant. A potentiometric titration[13] (Figure 2) of a $AgPF_6$/DMSO solution with $[Ir_2(dimen)_4]^{2+}$ that utilized a Ag metal electrode to monitor $[Ag^+]$ gives

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(1) Rhodes, M. R.; Mann, K. R. *Inorg. Chem.* **1984**, *23*, 2053.

(2) Boyd, D. C.; Rodman, G. S.; Mann, K. R. *J. Am. Chem. Soc.* **1986**, *108*, 1779.

(3) Boyd, D. C.; Matsch, P. A.; Mixa, M. M.; Mann, K. R. *Inorg. Chem.* **1986**, *25*, 3331.

(4) Bullock, J. P.; Boyd, D. C.; Mann, K. R. *Inorg. Chem.* **1987**, *26*, 3084.

(5) (a) Mann, K. R. *Crystal Struct. Commun.* **1981**, *10*, 451. (b) Che, C.-M.; Herbstein, F. H.; Schaefer, W. P.; Marsh, R. E.; Gray, H. B. *Inorg. Chem.* **1984**, *23*, 2572. (c) Gladfelter, W. L.; Lynch, M. W.; Schaefer, W. P.; Hendrickson, D. N.; Gray, H. B. *Inorg. Chem.* **1981**, *20*, 2390. (d) Gladfelter, W. L.; Gray, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 5910.

(6) Smith, T. P. Ph.D. Thesis, California Institute of Technology, **1982**.

(7) New compounds were characterized by ^1H and $^{13}C\{^1H\}$ NMR, IR, UV-vis, FAB mass spectrometry, and C, H, N elemental analyses. Complete data appear in the microfiche addition as Supplementary Material.

(8) Liptak, A.; Kusiak, J. W.; Pitha, J. *J. Med. Chem.* **1985**, *28*, 1699.

(9) Prepared by a standard method, see: Weber, W. P.; Gokel, G. W.; Ugi, I. K. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 530.

(10) A variety of Ag^+ adducts of transition-metal complexes have been reported: (a) Connelly, N. G.; Lucy, A. R.; Galas, A. M. R. *J. Chem. Soc., Chem. Commun.* **1981**, 43. (b) Connelly, N. G.; Lucy, A. R.; Payne, J. D.; Galas, A. M. R.; Geiger, W. E. *J. Chem. Soc., Dalton Trans.* **1983**, 1879. (c) Ladd, J. A.; Hope, H.; Balch, A. L. *Organometallics* **1984**, *3*, 1838. (d) Rhodes, L. F.; Huffman, J. C.; Caulton, K. G. *J. Am. Chem. Soc.* **1984**, *106*, 6874. (e) Rhodes, M. R. Ph.D. Thesis, University of Minnesota, **1984**. (f) Ciriano, M. A.; Oro, L. A.; Pêrez-Torrente, J. J.; Tiripicchio, A.; Tiripicchio-Camellini, M. *J. Chem. Soc., Chem. Commun.* **1986**, 1737. (g) Liston, D. J.; Reed, C. A.; Eigenbrot, C. W.; Scheidt, W. R. *Inorg. Chem.* **1987**, *26*, 2740. (h) Balch, A. L.; Ghedini, M.; Oram, D. E.; Reedy, P. E. *Inorg. Chem.* **1987**, *26*, 1223. (i) Uson, R.; Fornies, J.; Thomas, M.; Casas, J. M.; Cotton, F. A.; Falvello, L. R. *Inorg. Chem.* **1987**, *26*, 3482.

(11) Crystallographic data for $[IrAg(dimen)_4(PF_6)_3{\cdot}2DMSO$: MW = 1814.52; orthorhombic; space group no. 71, *Immma* = 14.42 (7) Å, b = 24.50 (4) Å, c = 11.72 (8) Å, V = 4140 Å^3, Z = 2, p(calcd) = 1.455 g cm^{-3}, crystal dimensions 0.05 × 0.07 × 0.32 mm; Mo Kα radiation, λ = 0.71073 Å; Enraf-Nonius SPD-CAD4 diffractometer; R = 0.0883, R_w = 0.0995 for 2312 observed reflections $F_o^2 > \sigma^2(F_o^2)$. An empirical absorption correction was applied. All calculations were carried out on PDP 8A and 11/34 computers with the Enraf-Nonius CAD 4-SDP programs as described previously: Bohling, D. B.; Gill, T. P.; Mann, K. R. *Inorg. Chem.* **1981**, *20*, 194. The dimen ligands in this structure were disordered,[5] in a manner similar to that previously found.[5a]

(12) Positional parameters are available as Supplementary Material. The full details of this structure will be published elsewhere.

(13) A very weak, second end point corresponding to a $Ag^+:Ir_2^{2+}$ ratio of 2:1 is also apparent in the titration curve (Figure 2). The equilibrium constant for the formation of this species is small and was ignored in our data analysis.

0002-7863/88/1510-8252$01.50/0