[16] It is interesting to note that a doubling of the signals in both the ^{1}H and ^{13}C spectra was observed in the NMR spectra of the diphosphate compounds. This result was found to be concentration and substrate dependent, and is thought to reflect slow rotation about the vinylogous carbamate bonds. The doubling of signals was especially prevalent in the farnesyl derivative **2**, and was observed, although to a less degree (ca. 10–15%), in the intermediates that lead up to the farnesyl diphosphate derivative (**5b** and **6b**). The doubling of the NMR signals however, was not observed for the geranyl intermediates (**5a** and **6a**).

[17] K. Alexandrov, E. Rostkova, A. J. Scheidig, R. S. Goody, D. Owen, H. Waldmann, unpublished results.

[18] Standard prenylation assay: 50 µl of the assay contained: 120 pmol Rab 7, 120 pmol REP-1, 120 pmol RabGGTase, and 2.4 nmol of either **1** or **2**. Buffer: 20 mM Hepes pH 7.2, 20 mM NaCl, 5 mM 2-sulfanylethanol (BME), 1 mM NP-40. The mixture was incubated at 37 °C for 20 minutes and the reaction stopped by diluting the samples with cold H_2O and precipitating the protein with 10% trichloroacetic acid. The protein pellet was washed with cold acetone and re-suspended in SDS-PAGE loading buffer. Proteins were resolved on the 15% SDS-PAGE gel and the prenylated proteins were visualized with a Fluor 100 (BioRad) fluorescence scanner.

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[21] For the expression and purification of REP-1, see K. Alexandrov, I. Simon, A. Iakovenko, B. Holz, R. S. Goody, A. Scheidig *FEBS Lett.* **1998**, *425*, 460. RabGGTase baculoviral expression vectors pVL-RabGGTalpha and pVL-RabGGTbeta were obtained from the American Type Culture Collection (order numbers 87154 and 87155, respectively). Baculoviruses were generated and RabGGTase was expressed and purified as described previously: F. P. Cremers, S. A. Armstrong, M. C. Seabra, M. C. Brown, J. L. Goldstein *J. Biol. Chem.* **1994**, *269*, 2111.

Tetravalent Tellurium Ligands

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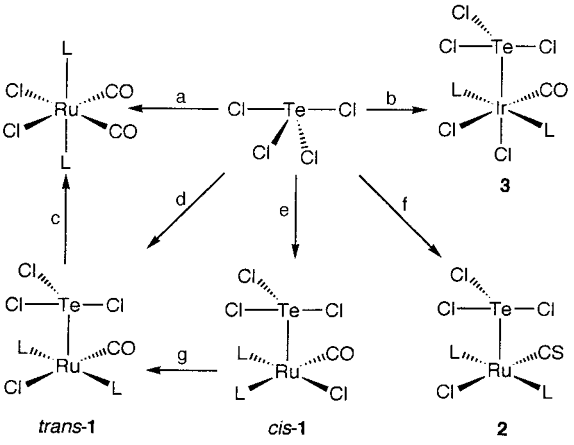
Andrew J. P. White, and David J. Williams

The comparatively sparse chemistry of tellurium-donor ligands typically involves the chalcogen being formally in the divalent state, that is, telluroethers and tellurolates. In recent times, a substantial group of compounds involving "naked" (i.e., substituent-free) tellurium has emerged,[1] heralded by the unsurpassed elegance of the complex [Te{Mn(CO)$_2$(η-C$_5$H$_5$)}$_3$] discovered by Herberhold et. al.[2] Clearly, oxidation states are however of limited use in describing such compounds. Well-defined ligands based on dative tellurium in higher oxidation states are however unknown, although Whitmire and Eveland have recently reported the Zintl cluster [Fe$_2$(CO)$_6$(η^2:μ_2,μ_2-Te$_4$)(μ-TeCl$_2$)], wherein the "TeCl$_2$" bridge might be described as based on either di- or tetravalent tellurium.[3] Tetravalent sulfur ligands are of course well known in the form of sulfoxides, sulfur dioxide, sulfines, sulfur diimides, and iminooxosulfuranes,[4] however such compounds based on tellurium are either transient or oligomeric in nature. Complexes of the SF$_3$ and Se(=O)Cl ligands have been previously reported from the oxidative addition of SF$_4$ or O=SeCl$_2$ to [IrCl(CO)(PEt$_3$)$_2$][5] or [IrCl(CO)(PPh$_3$)$_2$],[6] respectively. A Lewis base adduct of TeCl$_4$ with the pentacarbonyl manganate anion has also been described very recently.[5b] Herein we report the first mononuclear transition metal complexes ligated by the tetravalent trichlorotelluronium group. These result from the reactions of [IrCl(CO)(PPh$_3$)$_2$] or [Ru(CH=CH$_2$)Cl(CA)(PPh$_3$)$_2$] (A = O, S) with tellurium tetrachloride.

We encountered the first trichlorotelluronium ligand in the product of the reaction of [Ru(CH=CH$_2$)Cl(CO)(PPh$_3$)$_2$][7] with TeCl$_4$. In addition to polyvinylchloride, a bright yellow complex formulated as [Ru(TeCl$_3$)Cl(CO)(PPh$_3$)$_2$] (**1**) is obtained in 37% yield after recrystallization (Scheme 1). If the preparation is carried out at room temperature a 1:1 mixture of *cis/trans*-bis(phosphane) isomers results; however, at 50 °C the *trans*-bis(phosphane) arrangement is formed exclusively. The same reaction with [Ru(CH=CH$_2$)Cl(CS)(PPh$_3$)$_2$] however provides only the isomer of [RuCl(TeCl$_3$)(CS)(PPh$_3$)$_2$] (**2**) with *trans*-coordinated phosphanes. It is noteworthy that whilst the TeCl$_3$ ligand in **1** rotates freely at room temperature (singlet ^{31}P resonance), an apparently static structure is adopted for **2** (^{31}P$_A$^{31}P$_B$ system, *trans*-^2J(AB) = 335 Hz). This is consistent with the enhancement of a (presumably weak) π-dative component to the Te–Ru interaction to the more π-acidic but isosteric ruthenium center in **2**. The subsequent chemistry of complexes **1** and **2** has so far proven disappointing in that all attempts to introduce phosphanes, isocyanides, or even CO(!) as a sixth ligand (and thereby coordinative saturation) at ruthenium resulted in deposition of elemental tellurium. Similar deposition of tellurium occurs on treatment with amines or alcohols.



Scheme 1. Reagents and conditions (25 °C unless otherwise indicated, L = PPh$_3$): a) [Ru(CO)$_2$L$_3$], C$_6$H$_6$; b) [IrCl(CO)L$_2$], THF; c) CO, CH$_2$Cl$_2$; d) [Ru(CH=CH$_2$)Cl(CO)(PPh$_3$)$_2$], C$_6$H$_6$, 50 °C; e) [Ru(CH=CH$_2$)Cl(CO)(PPh$_3$)$_2$], C$_6$H$_6$; f) [Ru(CH=CH$_2$)Cl(CS)(PPh$_3$)$_2$], C$_6$H$_6$; g) CDCl$_3$, seven days.

This apparent lack of synthetic utility, coupled with our failure to obtain crystallographic grade crystals of **1** or **2**, led us to explore alternative examples of this ligand. As noted above, the complexes [IrCl(CO)(PR$_3$)$_2$] (R = Et, Ph) oxida-

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tively add tetravalent halides of sulfur and selenium. Accordingly the reaction of Vaska's complex with $TeCl_4$ was investigated: one major product $[IrCl_2(TeCl_3)(CO)(PPh_3)_2]$ (**3**) can be isolated (52%), in addition to small amounts of $[IrCl_3(CO)(PPh_3)_2]$ and $[IrHCl_2(CO)(PPh_3)_2]$. The formulation of the orange compound follows from spectroscopic data (see Experimental Section) and was confirmed by a crystallographic study (Figure 1).[8] The geometry at the iridium center is essentially octahedral with *cis* interligand angles in the range 82.5(5) – 100.70(8)°. The geometry of the "$IrCl_2(CO)(PPh_3)_2$" unit is generally unremarkable other than to note that the two *cis* Ir–Cl bond lengths (Ir–Cl(1) 2.414(3), Ir–Cl(2) 2.372(3) Å) reflect a lesser *trans* influence for the carbonyl than the trichlorotelluronium ligand (14σ). The ligand of interest is the "$TeCl_3$" group and it is reassuring that the geometry at tellurium is entirely as expected based on VSEPR considerations. Thus a virtual trigonal bipyramid is apparent with the two bulkiest substituents (iridium and a lone pair of electrons) occupying equatorial sites; the two "axial" chlorides (Te–Cl(4) 2.609(6), Te–Cl(5) 2.429(6) Å)[9] are folded away from the iridium center (Cl(4)-Te-Cl(5) 163.1(2)°). The "equatorial" Te–Cl(3) bond length at 2.322(4) Å is substantially shorter than those to the axial chlorides. The plane containing Ir, P(1), P(2), and Te is steeply inclined (73°) to that defined by Ir, Te, Cl(4), and Cl(5). If any substantial π-component contributed to the Ir–Te interaction, a value of 0 or 90° might be expected. The iridium–tellurium bond length of 2.656(1) Å is significantly longer (41σ) than that found in the only other structurally characterized mononuclear complex containing an Ir–Te bond, $[Ir(Te\text{-}2,4,6\text{-}tBu_3C_6H_2)(CO)(PPh_3)_2]$ (2.615(1) Å).[10]

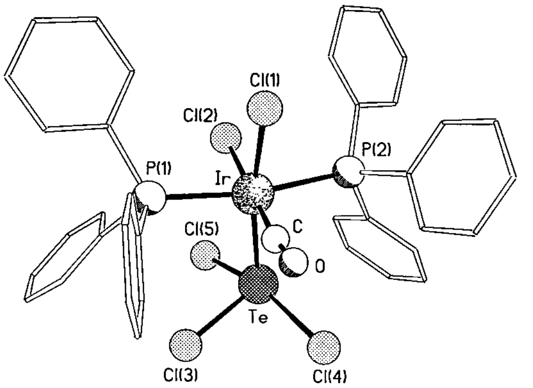

Figure 1. Molecular Structure of **3**. Phenyl groups simplified for clarity.

Although the $TeCl_3$ ligand is unprecedented in transition metal chemistry, the structural features of **3** are entirely as expected. This begs the question of generality for the synthetic approach. Preliminary studies do not however bode well. In the other low-valent systems so far investigated, $TeCl_4$ serves *ultimately* as a mild chlorinating agent rather than simply as an electrophile: $[Fe(CO)_5]$ and $[Fe(CO)_3(PPh_3)_2]$ react with $TeCl_4$ to cleanly provide (albeit conveniently) $[FeCl_2(CO)_4]$ and *cis,cis,trans*-$[FeCl_2(CO)_2(PPh_3)_2]$. The quantitative reaction of $[Ru(CO)_2(PPh_3)_3]$ with $TeCl_4$ is solvent dependent: in benzene, the product *cis,cis,trans*-$[RuCl_2(CO)_2(PPh_3)_2]$ is obtained, whilst in THF the all-*trans* isomer is obtained. It seems reasonable that these reactions fail to provide trichlorotelluronium complexes because in each case one or more ligands can be liberated, which, as shown in the case of **1**, are capable of reducing the intermediate tetravalent tellurium species. This problem is clearly obviated in the case of **3**.

Experimental Section

trans-**1:** $[Ru(CH{=}CH_2)Cl(CO)(PPh_3)_2]$ (0.25 g, 0.35 mmol) was added to a solution of $TeCl_4$ (0.10 g, 0.37 mmol) in benzene (35 mL) which was held at 50 °C. The resulting yellow solution was stirred for 15 min, filtered, concentrated to 10 mL, and the crude product isolated by precipitation with diethyl ether (30 mL). The precipitate was recrystallised three times from a mixture of dichloromethane and diethyl ether. Yield 0.12 g(37%). IR (CH_2Cl_2): $\tilde{\nu} = 1972\ cm^{-1}$ (CO); (Nujol): $\tilde{\nu} = 1972$ (CO), 333, 302 cm^{-1} (TeCl/RuCl); ^{31}P NMR ($CDCl_3$, 25 °C): $\delta = 27.4$; FAB-MS: m/z: 1411 $[Ru_2Cl_3(CO)_2(PPh_3)_4]^+$, 1185 $[M{+}PPh_3]^+$, 717 $[M - TeCl_3{+}CO]^+$, 689 $[M - TeCl_3]^+$; m.p. 174 – 176 °C(decomp); elemental analysis calcd for $C_{37}H_{30}Cl_4OP_2RuTe$ (%): C 48.1, H 3.3%; found: C 48.5, H 3.3.

cis-**1** (spectroscopically observed when the above procedure was carried out at room temperature) IR Nujol: $\tilde{\nu} = 1961$ [$\tilde{\nu}$(CO)] cm^{-1}; ^{31}P NMR ($CDCl_3$, 25 °C): $\delta = 30.4$, 45.9 (AB, $J(AB) = 19.7$ Hz). The *cis* isomer converts to the *trans* isomer slowly on standing in solution.

3: $[IrCl(CO)(PPh_3)_2]$ (0.20 g, 0.26 mmol) in THF (15 mL) was treated with $TeCl_4$ (0.070g, 0.26 mmol). The resulting orange/yellow solution was stirred for 25 min and then diluted with diethyl ether (20 cm^3). The filtered solution was then further diluted with hexane (10 mL) and then concentrated under reduced pressure to provide yellow crystals of the bis(thf) solvate. Yield 0.16 g (52%). IR (Nujol): $\tilde{\nu} = 2090$ (CO), 345, 297, 271 cm^{-1} (TeCl/IrCl); ^{31}P NMR ($CDCl_3$, 25 °C): $\delta = -20.5$; FAB-MS (3-nitrobenzyl alcohol (nba) matrix): m/z: 1246 $[M{+}2\,nba - 3\,HCl]^+$, 815 $[M - TeCl_3]^+$, 787 $[M - PPh_3]^+$, 780 $[M - TeCl_4]^+$, 752 $[M - PPh_3 - HCl]+$, 715 $[M - PPh_3 - 2\,HCl]^+$; elemental analysis calcd for $C_{37}H_{30}Cl_5IrOP_2Te \cdot 2\,C_4H_8O$ (%): C 45.3, H 3.88; found: C 45.70, H 4.00. The complex was also characterised crystallographically.[8]

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Keywords: iridium · oxidative addition · tellurium

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[8] Crystal data for **3**: $C_{37}H_{30}Cl_5IrOP_2Te \cdot C_4H_8O$, $M_r = 1121.7$, triclinic, space group $P\bar{1}$ (no. 2), $a = 12.345(1)$, $b = 12.820(1)$, $c = 15.147(2)$ Å, $\alpha = 95.62(1)$ $\beta = 96.18(1)$, $\gamma =$ 99.76(1)° $V = 2332.1(4)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.60\ g\,cm^{-3}$, $\mu(Cu_{K\alpha}) = 139\ cm^{-1}$, $F(000) = 1088$. A yellow prism

of dimensions 0.28 × 0.13 × 0.07 mm was used. A total of 6403 independent reflections were measured on a Siemens P4/PC diffractometer with graphite-monochromated $Cu_{K\alpha}$ radiation using ω scans. The structure was solved by the heavy atom (Patterson) method and all the major occupancy non-hydrogen atoms were refined anisotropically with absorption corrected (lamina [100]) data using full-matrix least-squares based on F^2 to give $R_1 = 0.071$, $wR_2 = 0.190$ for 5193 independent observed reflections ($|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 120°$) and 443 parameters. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-102341. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[9] An examination of contacts does not reveal any obvious reason for this difference in bond lengths. There is however an intermolecular contact between Cl(5) and its symmetry-related counterpart (3.51 Å).

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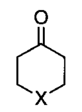
Hydrolysis of Amides Catalyzed by 4-Heterocyclohexanones: Small Molecule Mimics of Serine Proteases**

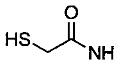
Mousumi Ghosh, Jeffrey L. Conroy, and Christopher T. Seto*

One of the long-standing problems in bioorganic chemistry is the design of catalysts that hydrolyze amide bonds under mild conditions.[1, 2] Amides are stable species; the half-life for peptide hydrolysis under neutral conditions at 25 °C has been estimated to be seven years.[3] However, nature has been able to develop four different classes of proteases that are capable of sequence-specific hydrolysis of peptides with tremendous rate accelerations. Therefore, the design of artificial catalysts that begin to approach the activity and specificity of protein-based catalysts is a fascinating and challenging problem. Here we report that the cyclohexanone **1** and the 4-heterocyclohexanones **2**–**4** are efficient catalysts for the base-promoted hydrolysis of amides.

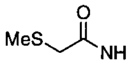
We have shown previously that 4-heterocyclohexanones can be used to synthesize inhibitors of cysteine proteases.[4] These compounds inhibit the protease by reaction of the 4-heterocyclohexanone carbonyl group with the active-site cysteine nucleophile of the enzyme with reversible formation of a hemithioacetal adduct.[5] In our current studies we are interested in developing catalysts of amide hydrolysis, and we reasoned that the amide substrates **5**–**7** could be anchored reversibly to a 4-heterocyclohexanone catalyst to form similar hemithioacetal adducts. Hydrolysis of the amide could then occur through a series of reactions that mimic the mechanism used by serine proteases to catalyze hydrolysis of peptides, as discussed below. These reactions serve as a model for hydrolysis of peptides specifically on the C-terminal side of cysteine residues.



1: X = CH_2
2: X = NH
3: X = S
4: X = O



5: R = C_6H_4-4-CF_3
6: R = C_6H_4-4-OMe
7: R = $CH_2C_6H_4$-4-F



8: R = C_6H_4-4-CF_3

We have monitored the hydrolysis of **5**–**7** catalyzed by 4-heterocyclohexanones by ^1H or ^{19}F NMR spectroscopy, or reverse-phase HPLC.[6] The reactions were performed under pseudo-first-order conditions, and they showed an exponential decrease in the substrate concentration as a function of time. Table 1 shows the observed rate constants for several reactions with a variety of substrates and catalysts. The most efficient catalysis that we have measured is shown in entry 5. In this reaction the hydrolysis of **5** is accelerated by more than four orders of magnitude relative to the background reaction when it is carried out in the presence of 600 mM tetrahydropyranone (THP, **4**).

Table 1. Observed rate constants for hydrolysis of amides catalyzed by 4-heterocyclohexanones.[a]

Entry	Catalyst	Substrate	k_{obs} [s^{-1}]	k_{rel}[b]
1	none	**5**	1.5×10^{-8}	
2	**1**	**5**	2.5×10^{-8}	2
3	**2**	**5**	5.9×10^{-8}	4
4	**3**[c]	**5**	3.7×10^{-8}	2
5	**4**	**5**	2.2×10^{-4}	14700
6	**4**	**6**	1.5×10^{-4}	10000
7	none	**6**	1.5×10^{-8}	
8	**4**	**7**	1.2×10^{-4}	3900
9	none	**7**	3.1×10^{-8}	
10	**4**[c]	**8**	1.0×10^{-7}	

[a] All reactions were performed at 25 °C with 20 mM substrate, 200 mM NaOD, and 600 mM catalyst (where present) D_2O/CD_3OD (4/1) unless otherwise specified. [b] Rate constant relative to the background reaction (no catalyst) with the same substrate. [c] Reaction was performed in D_2O/CD_3OD (1/1) because of low solubility of the catalyst or substrate in aqueous solution.

The efficiency of the hydrolysis reaction is highly dependent on the heteroatom in the 4-heterocyclohexanone catalyst (compare entries 2–5, Table 1). The reactivity of the carbonyl group in the catalyst is controlled by a through-space electrostatic repulsion between the dipoles of the ketone and the heteroatom. We have demonstrated previously that the equilibrium constant for addition of a thiol to 4-heterocyclo-

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