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Migratory Insertion of Isonitriles into Titanacyclobutane Complexes. A Novel Stereocontrolled Synthesis of Substituted Cyclobutanimines

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Summary: Isonitrile migratory insertion into substituted titanacyclobutane complexes provides for the stereocontrolled synthesis of synthetically valuable organic cyclobutanimines. Using the sterically crowded permethyltitanocene system, the intermediate iminoacyl complex is isolable and can be diverted by carbonylation to yield five-membered-ring enamidolate complexes.

The development of titanacyclobutane formation by radical alkylation of (η^3-allyl)titanium complexes has raised considerable potential for generating new organic methodology based on this reactivity pattern.[1] The conversion of titanacyclobutane complexes to organic products can, in principle, be accomplished in a number of ways, exploiting the polarized titanium−carbon bonds to elaborate a range of stereochemically defined, highly functionalized products. The most direct titanacyclobutane transformations involve the migratory insertion of unsaturated small molecules: we recently reported that carbonylation of titanacyclobutanes can be controlled to provide organic cyclobutanones[2] and cyclopentenediolate complexes,[3,4] respectively, by single and double insertions of carbon monoxide. The titanium cyclopentenediolate intermediates can be further converted to various functionalized cyclopentanone derivatives.[3]

Isonitrile migratory insertion, complementary to the carbonylation reaction, potentially provides for the direct introduction of nitrogen functionality into the derived organic products.[5] Although isoelectronic with carbon monoxide, isonitriles can be modulated both sterically and electronically via the nitrogen substituent, raising the possibility for greater control of post-insertion reactivity. The synthesis of iminoacyl complexes by isonitrile insertion in group 4 metal complexes is well-precedented,[5,6] including isolated examples of insertions into the titanacyclobutane structural class.[7] In this communication, isonitrile insertion and subsequent transformations in two series of titanacyclobutane complexes are reported, culminating in a general synthesis of stereochemically defined organic cyclobutanimines.

Exploratory reactions were conducted in the permethyltitanocene series. The addition of 1 equiv of either *tert*-butyl isocyanide or cyclohexyl isocyanide to 3-isopropylbis(pentamethylcyclopentadienyl)titanacyclobutane (**1**)[1a] at low temperature yields the iminoacyl complexes **2a** and **2b**, respectively, in high yield (Scheme 1).[8] Both complexes were isolated as thermally stable, analytically pure brownish green cubes after recrystallization from cold hexane. Although both iminoacyl moieties are assigned as η^1-coordinated on the basis of infrared spectroscopy,[9] the ν_{CN} band for the *tert*-butyl complex **2a** appears at 1588 cm^{-1}, more than 20 cm^{-1} higher in energy than the corresponding band for the

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[1] (a) Casty, G. L.; Stryker, J. M. *J. Am. Chem. Soc.* **1995**, *117*, 7814. (b) Ogoshi, S.; Stryker, J. M. *J. Am. Chem. Soc.* **1998**, *120*, 3514. (c) Carter, C. A. G.; McDonald, R.; Stryker, J. M. *Organometallics* **1999**, *18*, 820. (d) Greidanus, G.; McDonald, R.; Stryker, J. M. *Organometallics* **2001**, *20*, 2492.

[2] Carter, C. A. G.; Greidanus, G.; Chen, J.-X.; Stryker, J. M. *J. Am. Chem. Soc.* **2001**, *123*, 8872.

[3] Carter, C. A. G.; Casty, G. L.; Stryker, J. M. *Synlett* **2001**, 1046 (Special Issue).

[4] Enediolate formation by reductive double carbonylation of metallacyclobutane complexes is well-known: (a) Brown-Wensley, K. A.; Buchwald, S. L.; Cannizzo, L.; Clawson, L.; Ho, S.; Meinhardt, D.; Stille, J. R.; Straus, D.; Grubbs, R. H. *Pure Appl. Chem.* **1983**, *55*, 1733. (b) Petersen, J. L.; Egan, J. W., Jr. *Organometallics* **1987**, *6*, 2007. (c) Dennehy, R. D.; Whitby, R. J. *J. Chem. Soc., Chem. Commun.* **1990**, 1060. (d) Beckhaus, R.; Wilbrandt, D.; Flatau, S.; Bohmer, W.-H. *J. Organomet. Chem.* **1992**, *423*, 211. (e) Tjaden, E.; Stryker, J. M. *J. Am. Chem. Soc.* **1993**, *115*, 2083.

[5] Reviews: (a) Durfee, L. D.; Rothwell, I. P. *Chem. Rev.* **1988**, *88*, 1059. (b) Carnahan, E. M.; Protasiewicz, J. D.; Lippard, S. J. *Acc. Chem. Res.* **1993**, *26*, 90.

[6] Recent and leading references for group 4 metal isonitrile insertions: (a) Santamaría, C.; Beckhaus, R.; Haase, D.; Koch, R.; Saak, W.; Strauss, I. *Organometallics* **2001**, *20*, 1354. (b) Antiñolo, A.; Carrillo-Hermosilla, F.; Corrochano, A.; Fernández-Baeza, J.; Lara-Sanchez, A.; Ribeiro, M. R.; Lanfranchi, M.; Otero, A.; Pellinghelli, M. A.; Portela, M. F.; Santos, J. V. *Organometallics* **2000**, *19*, 2837. (c) Bashall, A.; Collier, P. E.; Gade, L. H.; McPartlin, M.; Mountford, P.; Pugh, S. M.; Radojevic, S.; Schubart, M.; Scowen, I. J.; Trösch, D. J. M. *Organometallics* **2000**, *19*, 4784. (d) Kuroda, S.; Sato, Y.; Mori, M. *J. Organomet. Chem.* **2000**, *611*, 304. (e) Segerer, U.; Blaurock, S.; Sieler, J.; Hey-Hawkens, E. *J. Organomet. Chem.* **2000**, *608*, 21. (f) Thorn, M. G.; Fanwick, P. E.; Rothwell, I. P. *Organometallics* **1999**, *18*, 4442. (g) Cadierno, V.; Zablocka, M.; Donnadieu, B.; Igau, A.; Majoral, J.-P.; Skowronska, A. *J. Am. Chem. Soc.* **1999**, *121*, 11086. (h) Tomaszewski, R.; Arif, A. M.; Ernst, R. D. *J. Chem. Soc., Dalton Trans.* **1999**, 1883. (i) Ahlers, W.; Erker, G.; Fröhlich, R. *J. Organomet. Chem.* **1998**, *571*, 83. (j) Andrés, R.; Galakhov, M.; Gómez-Sal, M. P.; Martín, A.; Mena, M.; Santamaría, C. *Chem. Eur. J.* **1998**, *4*, 1206. (k) Scott, M. J.; Lippard, S. J. *Organometallics* **1997**, *16*, 5857. (l) Rietveld, M. H. P.; Hagen, H.; van de Water, L.; Grove, D. M.; Kooijman, H.; Veldman, N.; Spek, A. L.; van Koten, G. *Organometallics* **1997**, *16*, 168. (m) Giannini, L.; Caselli, A.; Solari, E.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C.; Re, N.; Sgamellotti, A. *J. Am. Chem. Soc.* **1997**, *119*, 9709.

[7] Two reports of insertion into α-methylenetitanacyclobutane complexes have appeared: (a) See ref 4c. (b) Beckhaus, R.; Wagner, T.; Zimmermann, C.; Herdweck, E. *J. Organomet. Chem.* **1993**, *460*, 181.

[8] Complete experimental, spectroscopic, and analytical data are included as Supporting Information.

[9] See ref 5a and the following: (a) Carmona, E.; Palma, P.; Paneque, M.; Poveda, M. L. *Organometallics* **1990**, *9*, 583. (b) Bochmann, M.; Wilson, L. M.; Hursthouse, M. B.; Short, R. *Organometallics* **1987**, *6*, 2556.

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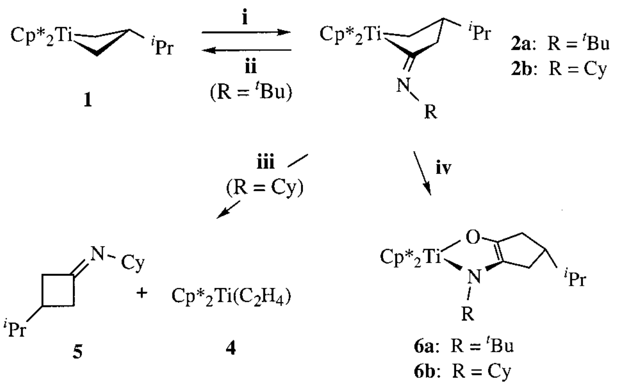
Scheme 1[a]

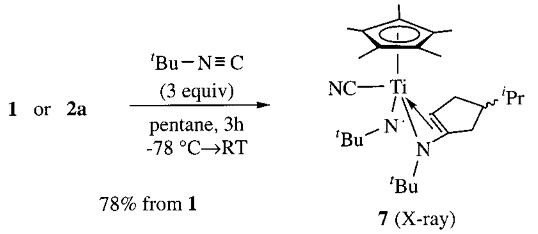


[a] Conditions: (**i**) RN≡C, toluene, −78 °C → room temperature, 1 h, yield 92% (**2a**), 90% (**2b**); (**ii**) 65 °C, toluene, 23 h, quantitative; (**iii**) C_2H_4 (10 psi), 65 °C, toluene, 12 h, yield 90% (**4**), 94% (**5**); (**iv**) CO (60 psig), toluene, −78 °C → room temperature, 10 h, yield 93% (**6a**), 85% (**6b**).

cyclohexyl complex **2b** (ν_{CN} 1567 cm^{-1}). In the structurally similar complexes reported by Beckhaus, iminoacyl complexes derived from both *tert*-butyl isocyanide and cyclohexyl isocyanide show nearly identical infrared absorptions (1564 and 1567 cm^{-1}, respectively), with the coordination mode of the cyclohexyl derivative in the solid state definitively determined to be η^1 by X-ray crystallography.[7b] The large difference in infrared absorptions observed for complexes **2a** and **2b** is unusual: iminoacyl infrared absorptions are generally insensitive to the identity of the alkyl substituent.[9]

Consistent with this difference in imine functionality, thermolysis of the two complexes results in dramatically different reactivities. Thus, heating the cyclohexyl isocyanide adduct **2b** to 65 °C induces reductive cyclization,[10] affording the strained cyclobutanimine **5**[8,11] as the exclusive organic product, isolated in 72% yield. Under these conditions, the titanium fragment largely decomposes to intractable materials.[12] In the presence of ethylene, however, the reaction is considerably cleaner, producing the cyclobutanimine in higher yield and returning the titanium exclusively as the known ethylene adduct $Cp^*_2Ti(C_2H_4)$[13] ($Cp^* = \eta^5\text{-}C_5Me_5$). In contrast, thermolysis of the *tert*-butyl isocyanide adduct **2a**, in either the presence or absence of added ethylene, leads to exclusive *deinsertion* of the isonitrile, returning titanacyclobutane complex **1** quantitatively. No *tert*-butyl isocyanide is observed in the ^1H NMR spectrum of the crude product, suggesting that the deinsertion may proceed by a complex decomposition mechanism. Migratory deinsertion of isonitriles from iminoacyl complexes is comparatively rare.[14]

At low temperature, both iminoacyl complexes **2a** and **2b** evidence similar reactivities. Carbonylation proceeds cleanly in both cases, affording titanium cyclopentenamidolates **6a** and **6b** in high yield as exclusive products (Scheme 1).[8] Although each complex is obtained in crystalline form, neither provides consistent combustion analysis. High-resolution mass spectrometry, however, was used to confirm the elemental composition; spectroscopic analysis was consistent both with the assigned structures and with known examples of this structural class.[15] The insertion of a second isonitrile equivalent into iminoacyl complexes **2a** and **2b** proved to be illuminating, if ultimately less successful. While the reactions of titanacyclobutane complex **1** and cyclohexyl iminoacyl complex **2b** with excess cyclohexyl isocyanide return only intractable mixtures, the corresponding reactions in the *tert*-butyl isocyanide series indeed produce an enediamidate complex by double isonitrile insertion (eq 1).[15,16] In the event, however, the permethyltitanocene complex undergoes an unprecedented fragmentation, ejecting one pentamethylcyclopentadienyl ligand and one *tert*-butyl fragment, producing the half-sandwich enediamidate complex **7**[8] bearing an ancillary cyanide ligand![17] This product is obtained as a 1:1 mixture of diastereomers; the structure was confirmed by X-ray crystallography (Figure 1) of the syn isomer obtained by recrystallization from cold hexane.[18] While the sterically crowded coordination sphere clearly plays a role in this unique transformation, the mechanism remains entirely obscure.



(1)

The synthesis of substituted cyclobutanimines can be generalized using the bis(2-(dimethylamino)indenyl)titanium template, which tolerates the synthesis of stereochemically pure disubstituted titanacyclobutane complexes by free radical alkylation.[1d] Thus, addition of 2,6-dimethylphenyl isocyanide[19] (3 equiv) to titanacyclobutane complexes **8** at low temperature leads to clean production of 2,3-disubstituted cyclobutanimines

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(10) (a) Probert, G. D.; Witby, R. J.; Coote, S. J. *Tetrahedron Lett.* **1995**, *36*, 4113. (b) Davis, J. M.; Witby, R. J.; Jaxa-Chamiec, A. *Tetrahedron Lett.* **1994**, *35*, 1445 and references therein.

(11) Cyclobutanimines are known but are relatively rare: (a) Logothetis, A. L. *J. Am. Chem. Soc.* **1965**, *87*, 749. (b) Newcomb, M.; Williams, W. G. *Tetrahedron Lett.* **1984**, *25*, 2723. (c) Betz, J.; Heushmann, M. *Tetrahedron Lett.* **1995**, *36*, 4043. (d) Stevens, C.; DeKimpe, N. *J. Org. Chem.* **1996**, *61*, 2174. (e) Bisel, P.; Breitling, E.; Frahm, A. W. *Eur. J. Org. Chem.* **1998**, 729.

(12) A minor portion (5% isolated yield) of the titanium is recovered from this reaction as the known double "tuck-in" complex, (η^3:η^4-1,2,3-trimethyl-4,5-dimethylenecyclopentadienyl)titanium: Pattiasina, J. W.; Hissink, C. E.; de Boer, J. L.; Meetsma, A.; Teuben, J. H.; Spek, A. *J. Am. Chem. Soc.* **1985**, *107*, 7758.

(13) Cohen, S. A.; Auburn, P. R.; Bercaw, J. E. *J. Am. Chem. Soc.* **1983**, *105*, 1136.

(14) The conversion of aldimines to isonitriles by migratory deinsertion of an intermediate iminoacyl complex has been recently reported using *trans*-$[Mo(N_2)_2(dppe)_2]$: Seino, H.; Arita, C.; Nonokawa, D.; Nakamura, G.; Harada, Y.; Mizobe, Y.; Hidai, M. *Organometallics* **1999**, *18*, 4165.

(15) Enamidolate and enediamide complexes of the $(ArO)_2Ti$ fragment: Chamberlain, L. R.; Durfee, L. D.; Fanwick, P. E.; Kobriger, L. M.; Latesky, S. L.; McMullen, A. K.; Steffey, B. D.; Rothwell, I. P.; Folting, K.; Huffman, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 6068.

(16) Enediamide complexes of zirconocene and hafnocene systems: Kloppenburg, L.; Petersen, J. L. *Organometallics* **1997**, *16*, 3548 and references therein.

(17) We have as yet been unable to determine the fate of the organic fragment(s) produced during this reaction.

(18) Crystal data for complex **7** ($C_{27}H_{45}N_3Ti$, −60 °C): monoclinic, $P2_1/c$ (No. 14), $a = 16.4949(4)$ Å, $b = 9.4610(3)$ Å, $c = 17.5737(9)$ Å, $\beta = 94.381(3)°$, $V = 2734.5(2)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.116$ g cm^{-3}, $\mu = 2.761$ mm^{-1}, R1 = 0.0524, wR2 = 0.1374 ($F_o^2 > -3\sigma(F_o^2)$). Details of the structure determination are included as Supporting Information.

(19) The use of alkyl isocyanides in this reaction leads to low selectivity in the insertion reaction and poor recovery of the titanium fragment.

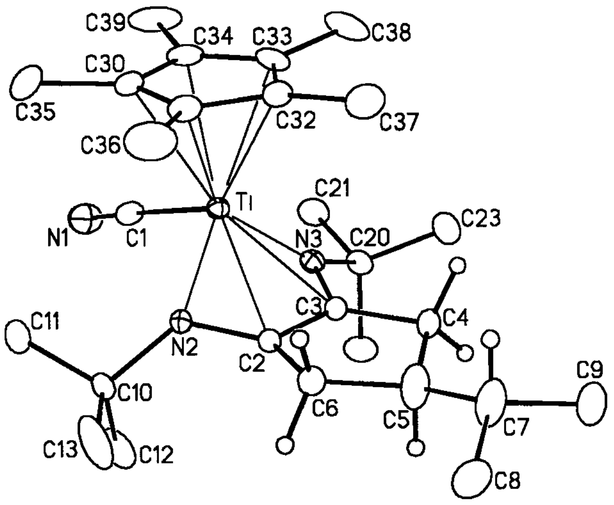
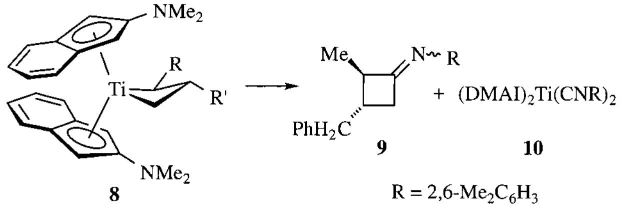


Figure 1. ORTEP drawing of complex **7**. Selected bond distances (Å) and angles (deg): Ti−N2, 1.915(2); Ti−N3, 1.922(3), Ti−C1, 2.177(4); Ti−C2, 2.361(3); Ti−C3, 2.361(3); N1−C1, 1.141(4); N2−C2, 1.384(4); N3−C3, 1.381(4); C2−C3, 1.389(4), Ti−C1−N1, 177.3(3); N2−Ti−N3, 91.4(1); Ti−N2−C2, 89.2(2); Ti−N2−C10, 145.8(2); C2−N2−C10, 124.2(3).

9 and, importantly, recovery of the titanium as the bis(isonitrile) complex **10** in high yield (Table 1).[8] The latter is separated from the cyclobutanimine by crystallization from pentane at low temperature; isolation of the cyclobutanimine is accomplished after exposure to air and filtration of any insoluble titanium-derived residues.[20] In this system, however, we have been unable to isolate (or intercept) the putative iminoacyl intermediates, even upon reaction at low temperature in the presence of 1 equiv of isonitrile.

Isonitrile insertion into titanacyclobutane complexes thus provides a rich and potentially exploitable reactivity manifold, sensitive to both the nature of the isonitrile substituent[21] and the titanocene ancillary ligands. The efficient synthesis of strained, functionalized, and highly substituted four-membered rings by migratory cyclization is particularly noteworthy; current efforts are underway to extend and generalize this interesting reactivity pattern.

Table 1. Cyclobutanimine Synthesis by Isonitrile Insertion into Complex 8[a]



complex	R	R′	isonitrile complex	yield (%)	product	yield (%)	*E*:*Z* ratio
8a	CH_3	Bn	**10**	quant	**9a**	quant	6:1
8b	CH_3	^{i}Pr	**10**	84	**9b**	90	>99:<1
8c	Ph	Bn	**10**	83	**9c**	quant	6:1
8d	Ph	^{i}Pr	**10**	78	**9d**	86	10:1

[a] Conditions: 3 equiv of 2,6-dimethylphenyl isocyanide, −35 °C → room temperature, THF, 3 h.

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Supporting Information Available: Text giving experimental procedures and complete spectroscopic and analytical data for all new compounds and tables giving details of the crystal structure determination of complex **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) The cyclobutanimines are recovered in reasonable purity, containing only minor amounts (≤5%) of unidentified impurities by spectroscopic analysis. Further purification, however, is precluded by competitive hydrolysis during column chromatography.

(21) The variability of isonitrile reactivity as a function of substituent has been noted in other contexts. See, for example, refs 15 and 17 and: Kloppenburg, L.; Petersen, J. L. *Polyhedron* **1995**, *14*, 69.