mode for the reductively activated naphthalene in 6^- does not unambiguously establish η^4 coordination for the reductively activated benzene ligands in 3^- and 2^{2-}, but, given the similarities in the course of protonation of 6^-, 3^-, 2^{2-}, and 7^{2-}, the proof of η^4 coordination for the naphthalene ligand in 6^- strongly supports our hypothesis of η^4-coordination in 2^{2-} and 3^-.

Acknowledgment. We thank the National Science Foundation for financial support through Grant No. CHE-8722424.

Note Added in Proof. Wey and Butenschön have recently reported that the ^{13}C NMR spectrum of 3^- confirms η^4 coordination of the benzene ligand.[21]

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(21) Wey, H. G.; Butenschön, H. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1444.

Nonorganometallic Pathway of the Passerini Reaction Assisted by $TiCl_4$

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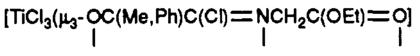
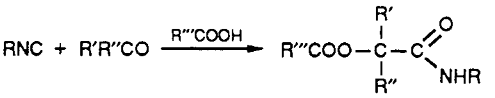
Summary: The reaction of $TiCl_4$ with different isocyanides did not lead to any insertion of the isocyanide functionality into the Ti–Cl bond but to simple adducts such as $\{[TiCl_3(2,6\text{-}Me_2C_6H_3NC)]_2(\mu_2\text{-}Cl)_2\}$, $[(TiCl_4)_2(\mu_2\text{-}O{=}P(OEt_2CH_2NC)_2]$, and $[(TiCl_4)_2(\mu_2\text{-}O{=}C(OEt)CH_2NC)_2]$. This ruled out any organometallic pathway in the Passerini reaction assisted by $TiCl_4$. The present mechanism is proposed on the basis of the isolation and structural characterization of the key intermediate



$$[TiCl_3(\mu_3\text{-}OC(Me,Ph)C(Cl){=}NCH_2C(OEt){=}O]$$

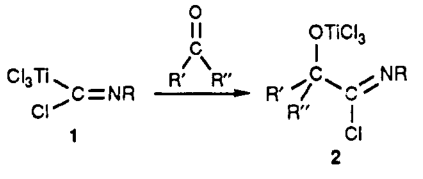
derived from the reaction of $PhCOCH_3$ and $CNCH_2COOEt$ assisted by $TiCl_4$.

Several mechanisms[1] have been proposed for the reaction of a carbonyl compound with an isocyanide assisted by a carboxylic acid, known as the Passerini[2] reaction, which produces the ester of an α-acyloxy amide (eq 1).



$$RNC + R'R''CO \xrightarrow{R'''COOH} R'''COO{-}C(R')(R''){-}C({=}O)NHR \quad (1)$$

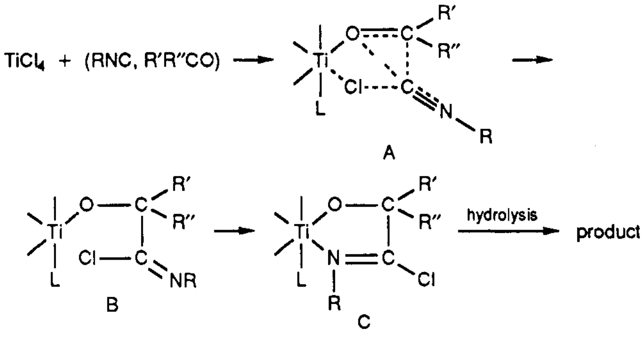
In a variation of the Passerini reaction the acid employed was $TiCl_4$.[3] For such a version the organometallic pathway (2) has been proposed.[3]



(2)

The mechanism proposed in reaction 2 is essentially based on the intermediacy of an organometallic derivative from a nonorganometallic precursor[3,4] (complex 1) and the formation of an intermediate (complex 2) by the insertion of a carbonyl function into a Ti–C σ bond.[3] Studying the reaction of $TiCl_4$ and isocyanides, we found, in contrast to reports in the literature,[4] that, independent of the stoichiometry, the solvent, and the nature of the substituent at the isocyanide ligand, simple adducts are formed rather than insertion products such as 1.[5] This is exemplified by the isolation and structural characterization of $[TiCl_4(CNBu^t)_2]$[5] (3), $\{[TiCl_3(2,6\text{-}Me_2C_6H_3NC)]_2(\mu_2\text{-}Cl)_2\}$[6] (4), $[(TiCl_4)_2(\mu_2\text{-}O{=}P(OEt)_2CH_2NC)_2]$[6] (5), and $[(TiCl_4)_2(\mu_2\text{-}O{=}C(OEt)CH_2NC)_2]$[6] (6). The insertion of the isonitrile into the Ti–Cl bond was mainly supported by an IR spectrum showing, when taken in air, a strong band at around 1625 cm^{-1}.[5] This band belongs, however, to the formamide derived from the hydrolysis of RNC. In accord with the adduct formation, metal-bonded isocyanides in 3–6 have a C–N stretching higher than that

Scheme I



L = RNC, R'R''CO, μ-Cl, donor atom on R

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(1) (a) Baker, R. H.; Stanonis, D. *J. Am. Chem. Soc.* **1951**, *73*, 699. (b) Ugi, I.; Meyer, R. *Chem. Ber.* **1961**, *94*, 2229. (c) Hagedorn, I.; Eholzer, U. *Chem. Ber.* **1965**, *98*, 936. (d) Saegusa, T.; Taka-Ishi, N.; Fujii, H. *Tetrahedron* **1968**, *24*, 3795.

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(6) Details are reported for the preparation of 6 only: The slow addition of $TiCl_4$ (2.0 mL, 3.47 g, 18.3 mmol) to a CH_2Cl_2 (100 mL) solution of $CNCH_2COOEt$ (2.0 mL, 2.07 g, 18.3 mmol) gave a yellow solid (93%). ^{1}H NMR (200 MHz, CD_2Cl_2): δ 4.64 (s, 2 H, CH_2), 4.33 (q, 2 H, Et), 1.33 (t, 3 H, Et). ν(CN) (Nujol): 2254 cm^{-1} (2165 cm^{-1} in the free isocyanide). Complex 4: ν(CN) (CH_2Cl_2 solution) 2200 cm^{-1} (vs 2123 cm^{-1} in the free ligand). Complex 5: ν(CN) (Nujol) 2245 cm^{-1} (vs 2153 cm^{-1} in the free ligand). The structures of 3,[5] 4, and 5 have been determined by an X-ray analysis (Carofiglio, T.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C., unpublished results).

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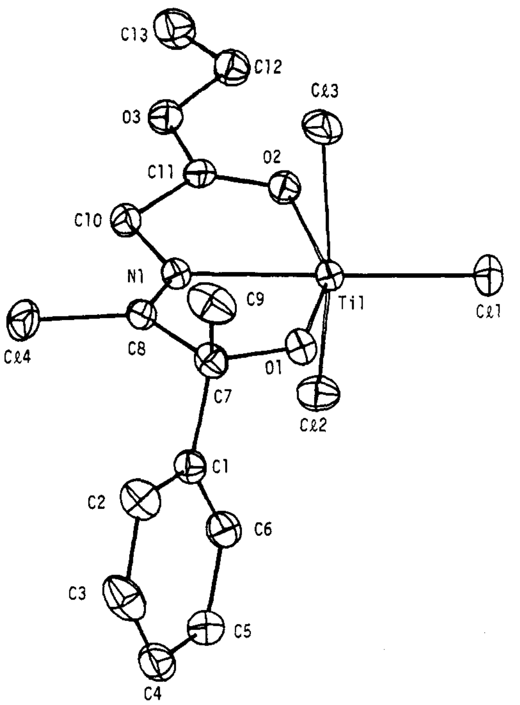
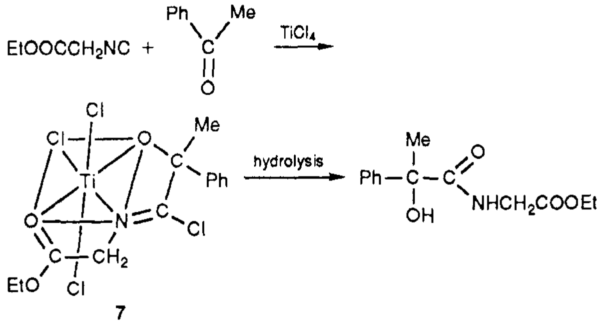


Figure 1. ORTEP drawing for complex 7, $C_{13}H_{15}Cl_4NO_3Ti$ (30% probability ellipsoids). Bond distances (Å) and angles (deg) are as follows: Ti–Cl1 = 2.259 (1), Ti–Cl2 = 2.311 (1), Ti–Cl3 = 2.340 (1), Ti–O1 = 1.779 (2), Ti–O2 = 2.131 (2), Ti–N1 = 2.174 (2), O1–C7 = 1.430 (4), O2–C11 = 1.232 (4), N1–C8 = 1.254 (3), N1–C10 = 1.441 (4), C7–C8 = 1.528 (4), C10–C11 = 1.449 (4), C8–Cl4 = 1.719 (3); O1–Ti–O2 = 148.9 (1), Ni–Ti–Cl1 = 178.1 (1), Cl2–Ti–Cl3 = 161.4 (1), O1–Ti–N1 = 75.6 (1), O2–Ti–N1 = 73.3 (1).

of the corresponding free ligand.[6]

Therefore, we were back to the hypothesis of the Lewis acid serving to enhance the electrophilicity of the carbonyl compound. The preformed isocyanide complexes, such as 3–6, have the sole function of making available the free isocyanide so that it can be replaced by the added carbonyl compound. Then the addition of the isocyanide to the >CO group can proceed as proposed in Scheme I. In order to prove this, we isolated and crystallized in 76% yield complex 7, formed from the reaction of 6 with acetophenone.[7]



(3)

Complex 7 was hydrolyzed to the corresponding α-hydroxy amide. An ORTEP view of 7[8] is given in Figure 1 along with selected bond distances and angles. The three donor atoms O,N,O are arranged in the *mer* configuration. Complexes analogous to 7 have been identified in the reaction of 6 with PhCHO and 2,4,6-$Me_3C_6H_2CHO$ and by the use of other isocyanides, and they do not derive from any insertion of the carbonyl group into a Ti–C bond. The results cited so far allow us to propose Scheme I for the Passerini reaction assisted by $TiCl_4$.

We considered titanium to be constantly hexacoordinate. The simultaneous addition of an electrophile and a nucleophile to the carbon of an isocyanide (A) is well documented.[9] In reaction 3 the substituent (R) at the isocyanide has an oxygen donor atom that can play the role of L or, at a certain time of the reaction, replace L in Scheme I. The isolation of the more stable *mer* isomer for 7 is not conclusive for the stereochemical role played by titanium, because of its kinetic lability.

Acknowledgment. We thank the Swiss National Foundation for Scientific Research (Grant No. 20-28470.90) for financial support.

Supplementary Material Available: Tables of crystal data, data collection, and solution and refinement parameters, atomic coordinates, hydrogen coordinates, thermal parameters, and bond distances and angles for complex 7 (5 pages); a table of observed and calculated structure factors for complex 7 (18 pages). Ordering information is given on any current masthead page.

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[7] Procedure for 7: Acetophenone (0.45 mL, 0.46 g, 3.9 mmol) was added to a toluene (50 mL) suspension of 6 (1.17 g, 1.93 mmol). The resulting deep yellow solution gave on standing a light yellow crystalline solid (76%). Suitable crystals for X-ray analysis were obtained by crystallization from hot toluene. The synthesis of 7 can be carried out equally well by adding the isocyanide to a CH_2Cl_2 solution containing $TiCl_4$ and acetophenone. ^1H NMR (200 MHz, CD_2Cl_2): δ 1.51 (t, 3 H, Et), 2.24 (s, 3 H, Me), 4.73 (q, 2 H, Et), 4.77 (s, 2 H, CH_2), 7.45 (m, 3 H, Ph), 7.80 (m, 2 H, Ph).

[8] Structure of 7: $C_{13}H_{15}Cl_4NO_3Ti$, M_r = 423.0, triclinic, space group $P\bar{1}$, a = 9.731 (2) Å, b = 10.552 (3) Å, c = 8.978 (2) Å, α = 96.66 (2)°, β = 101.86 (2)°, γ = 95.30 (2)°, V = 889.7 (4) Å^3, Z = 2, ρ_{calcd} = 1.579 g cm^{-3}, λ(Mo Kα) = 0.71069 Å, μ(Mo Kα) = 10.90 cm^{-1}, crystal dimensions 0.39 × 0.41 × 0.55 mm^3; 3200 unique observed structure amplitudes ($I > 2\sigma(I)$) collected at room temperature on a Philips PW 1100 diffractometer in the range 6° < 2θ < 60°. The structure was solved with use of SHELX-86 and anisotropically refined by full-matrix least squares; the model converged to R = 0.042 (R_w = 0.052). The hydrogen atoms were directly located from a difference map and introduced in calculations as fixed contributors. All calculations were carried out with use of SHELX-76.

[9] March, J. *Advanced Organic Chemistry*; Academic: New York, 1985; p 869.