Rapid Synthesis of α,β-Didehydroaspartic-Acid Derivatives Carrying a β-Substituent

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A convenient preparation of *N*-(alkoxycarbonyl)-2,3-didehydroaspartic acid anhydrides **4** with substitution at the 3-position is reported. The key step is a cobalt-mediated acylation of an acetylene moiety, producing the highly functionalized didehydroamine acid derivative in good yield. Unnatural didehydroaspartates are readily accessible.

Introduction. – The α,β-dehydro-α-amino acids [1] have garnered considerable interest following their discovery in a number of naturally occurring oligopeptides. Furthermore, incorporation of an α,β-didehydro-α-amino acid into a synthetic peptide introduces unique conformational constraints, leading to the application of didehydrooligopeptides as mechanistic probes in studies of enzyme mechanisms and/or binding [2]. Accordingly, ready synthetic access to a variety of natural and unnatural α,β-didehydro-α-amino acids is desirable[1]). In the course of another study, we encountered an unusual rearrangement which we now report as an easy synthetic route to *N*-protected (*E*)-α,β-didehydroaspartic-acid derivatives with substitution at the β-position.

Results and Discussion. – Preparation of alkynyl isocyanates **1** by *Curtius* rearrangement proceeds cleanly without isolation of the intermediate azides if the starting acyl chlorides are carefully purified (*Scheme*). Alkynyl isocyanates have been reported only twice previously [4] and obtained both times *via* a *Curtius* rearrangement. In neither case, however, the compound was isolated or characterized. Alcoholysis of the isocyanates **1** produces a 2 : 1 adduct of the alcohol to the isocyanate from trapping of the ketenimine formed after tautomerization of the initial adduct by a second equivalent of the alcohol. Therefore, **1** is protected with octacarbonyl dicobalt producing a characteristically deep-red cobalt complex **2** in quantitative yield. On alcoholysis, the latter produces the protected alkynylcarbamate **3**, similarly to the protected ynamines reported by *Witulski* and *Stengel* [5], in moderate yield, *i.e.*, 60–65% after purification by column chromatography. The yield of **3** largely depends on the completeness of degassing; the $Co_2(CO)_6$-protected compounds are susceptible to air oxidation. Not only is the yield lower if the solution is not kept O_2-free, but trace amounts of paramagnetic Co^{2+} formed by oxidation prevent the collection of NMR data in some instances.

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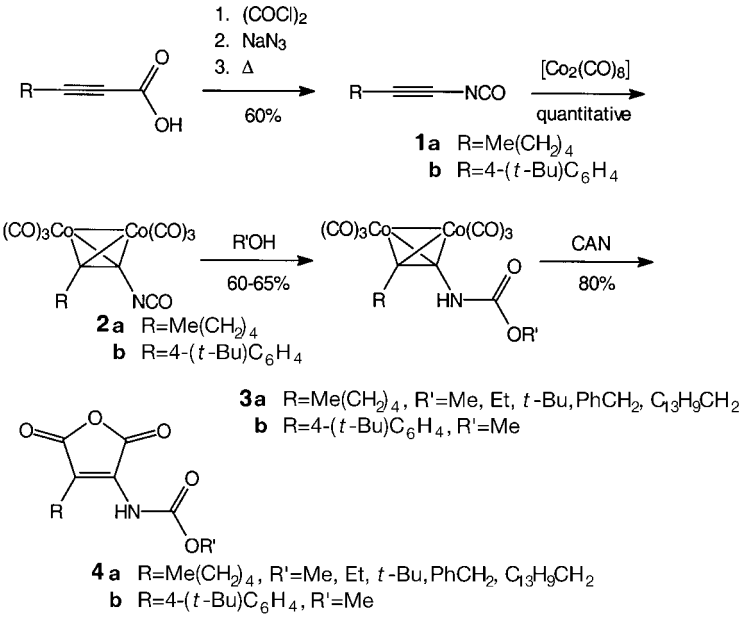
[1]) Several other synthetic routes have been recently reported [3].



Hydrolysis of **2a**,**b** occurs slowly when H_2O is added to solutions of the isocyanates at room temperature. The initial product, a carbamic acid, decarboxylates immediately, and in the IR spectrum, the intensity of both the characteristic vibrational modes of an amino group (3406 cm^{-1}) and of dissolved CO_2 (2336 cm^{-1}) are increasing, while the NCO band (2253 cm^{-1}) of the isocyanate is disappearing and the three characteristic bands of the $Co_2(CO)_6$ group at 2019, 2053, and 2091 cm^{-1} change very little. Although the formed cobalt-protected primary ynamine (see *Exper. Part*) can reversibly be protonated, it shows none of the other characteristic amine reactivity, *e.g.*, no imine formation with either acetone or benzaldehyde, and no phthalimide formation with phthaloyl chloride. Although the point was not further investigated, one can suppose that both electronic and steric considerations play a role.

Surprisingly, attempted oxidative removal of the $Co_2(CO)_6$ protecting group from **3a** or **3b** with ceric ammonium nitrate (CAN) and a conventional workup results not in the regeneration of the triple bond, but rather in the clean production of maleic anhydride derivatives **4a** and **4b**, both previously unreported, which can be immediately recognized as anhydrides of an *N*-protected (*E*)-2,3-didehydroaspartic acid carrying a substituent in 3-position. While further mechanistic work is clearly necessary to clarify the unusual transformation, the similarity between the reaction **3** → **4** and the acylation step in the cobalt-catalyzed amidocarbonylation synthesis of amino acids [6][2]) or a cobalt-promoted conversion of acrylamides to succinimides [8] suggests that the anomalous behavior of **3**, relative to other $Co_2(CO)_6$-protected alkynes, stems from the successive coordination of the urethane carbamate carbonyl O-atom to each metal center, with associated insertion of a coordinated CO into each metal–carbon bond. Moreover, the tolerance of ester, ether, and nitrile functional groups in amidocarbonylations suggests that these groups should not pose problems either in the present reaction. Hydrolysis of **4** presumably produces the diacid, which, upon workup and

[2]) Mechanistic studies have been performed for the acylation step in amidocarbonylations [7].

isolation, however, spontaneously dehydrates to the anhydride. Attempts to hydrolyze **4a** (R' = pentyl, specifically under the conditions described by *Shin et al.* [9], result only in the reisolation of **4a** (R' = pentyl). On the other hand, methanolysis of **4a** (R' = $PhCH_2$) easily produces the two possible methyl esters in a 4 : 1 ratio (see *Exper. Part*).

(*E*)-2,3-Didehydroaspartic acid has been identified as one of the amino acids in the hexapeptide mycotoxin phomopsin A [10]. The (*Z*)-isomer has been found as a constituent of polycyclic cinnamycin and duramycin peptides [11]. Furthermore, the incorporation of (*Z*)-2,3-didehydroaspartate in place of aspartate in Ac–Asp–Glu–OH, a dipeptide for which a role in synaptic processes has been proposed, produces an inhibitor [12] for NAALA dipeptidase (*N*-acetylated α-linked acidic dipeptidase). In the latter study, the defined orientation of the carboxy groups in the didehydroaspartate relative to aspartate itself served to probe the binding site of the enzyme. Accordingly, facile synthetic access to these structures would be useful. While a number of general routes to didehydroamino acids have been described [1], published routes to 2,3-didehydroaspartic-acid derivatives include only 2,3-elimination from 3-hydroxyaspartic-acid esters [9][11] or anhydrides [13] and *Wittig-Horner* olefination after condensation of *N*-acyl-2-[bis(alkyloxy)phosphinyl]glycine esters with an alkyl glyoxylate [12][14][15]. Two Japanese patents [16] claim a synthesis of 3-substituted 2,3-didehydroaspartic-acid esters by Ti-, Sn-, or Zn-mediated coupling reactions, but no further reports on this method have appeared.

As a synthesis of 3-substituted 2,3-didehydroaspartic-acid derivatives, the transformation **1** → **4** presents several advantages. Substituents at position 3 are easily incorporated with the present methodology, the substituent being already present in the starting alkynoic acid. The generation of the (*E*)-isomer is noteworthy, given that the 2,3-elimination route [11] is reported to produce exclusively the (*Z*)-2,3-didehydroaspartate. The *Wittig-Horner* procedure produces a mixture with the (*Z*)-isomer predominating in a ratio of *ca.* 3 : 1. A specific preparation for the (*E*)-isomer has been reported only once [9]; it involves an intermediate aminomaleic anhydride [13]. The present methodology also produces a maleic-anhydride derivative, but with a more versatile substitution. Lastly, the amino group is formed in its carbamate-protected form, which is compatible with current peptide-coupling technologies.

Conclusion. – A curious rearrangement in a $CO_2(CO)_6$-protected alkynylcarbamate leads to a convenient synthesis of 2,3-didehydroaspartic-acid derivatives. Mechanistically, the reaction resembles previously documented acylations in organocobalt compounds, from which coordination of the carbamate carbonyl O-atom to the metal centers may be inferred as the key feature leading to the anomalous behavior.

Support for this project from the *Swiss National Science Foundation* and the ETH-Zürich is acknowledged.

Experimental Part

General. All solvents were of spectroscopic grade or distilled and dried before usage. Column chromatography (CC): Silica gel *60* (40–63 μm; *Fluka*); the eluent was pressed through the column with an approximate pressure of 1.0 bar; TLC monitoring. TLC: precoated silica-gel plates *60 F 254* on glass (*Merck*); visualization by UV light (254 and 366 nm) or aq. $KMnO_4$ soln. IR Spectra: *Perkin-Elmer-FT-IR-Paragon-1000* spectrometer; quantitatively reproducible results were obtained using a 0.05-cm NaCl cell; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Bruker-AMX-500* spectrometer, chemical shifts δ in ppm rel. to the resonance of $CHCl_3$ (7.26

and 77.0 ppm, resp). GC/MS: EI mode; *Fisons MD800* (MS), *GC8000* (GC) equipped with a *DB-5* capillary column. Elemental analyses: Microanalysis Laboratory at the Laboratorium für Organische Chemie, ETH-Zürich.

Oct-2-ynoyl Chloride. A soln. of oct-2-ynoid acid (10.0 g, 71.3 mmol) and oxalyl chloride (19.9 g, 156.8 mmol) in dry benzene (40 ml) was stirred for 4 h at 50°. After filtration and removal of solvent and excess oxalyl chloride, the remaining oil was distilled at 90°/0.1 Torr: 10.3 g (91%) of oct-2-ynoyl chloride. ^{1}H-NMR (500 MHz, $CDCl_3$): 2.41 (*t*, 2 H, CH_2); 1.61 (*m*, 2 H, CH_2); 1.29 (*m*, 4 H, CH_2); 0.92 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 150.4; 98.2; 94.6; 30.2; 26.1; 20.8; 18.2; 13.3.

Oct-2-ynoyl Azide. To NaN_3 (11.86 g, 182.5 mmol) suspended in MeCN/Et_2O 2:1 (300 ml) and a few drops of pyridine, oct-2-ynoyl chloride (15.07 g, 95.0 mmol) in MeCN (40 ml) was added at −5° over 1 h. After stirring for another 3 h at −5°, the slurry was allowed to warm up to 10°, and Et_2O (100 ml) was added. The slurry was washed with cold aq. $NaHCO_3$ soln. and H_2O. After drying (Na_2SO_4) at 3° overnight, the soln. was evaporated: 10.89 g of an oil. Rapid CC (silica gel, petroleum ether/Et_2O 4:1) yielded 9.04 g (58%) of the azide was a colorless oil with a strong fruity smell. Due to its thermal instability, the compound had to be stored at −20°, where it was stable over a period of months. IR (CCl_4): 1684 (C=O), 2148 (N_3), 2237 (C≡C). ^{1}H-NMR (500 MHz, $CDCl_3$): 2.35 (*t*, 2 H, CH_2); 1.57 (*m*, 2 H, CH_2); 1.36 (*m*, 4 H, CH_2); 0.88 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 158.3; 95.5; 74.5; 30.9; 27.1; 22.0; 18.9; 13.8. MS (70 eV): 165 (M^+). Anal. calc. for $C_8H_{11}N_3O$: C 58.17, H 6.71, N 25.44, O 9.69; found: C 58.25, H 6.79, N 25.31, O 9.65.

*3-[4-(*tert*-Butyl)phenyl]prop-2-ynoic Acid.* To a soln. of [4-(*tert*-butyl)phenyl]acetylene (10.0 g, 63.3 mmol) in dry THF (10 ml) at −40°, 1.6M BuLi in hexane (38.5 ml, 61.6 mmol) was added over 90 min. The soln. was allowed to warm up to −20°, and after stirring for another 30 min, CO_2 gas was bubbled vigorously through the soln. until it had warmed up to r.t. The next day, the precipitate was collected and dissolved in H_2O. The aq. phase was acidified with 1M HCl and extracted with CH_2Cl_2. The extract was dried (Na_2SO_4) and evaporated. 11.7 g (92%) of anal. pure [4-(*tert*-butyl)phenyl]prop-2-ynoic acid. ^{1}H-NMR (500 MHz, $CDCl_3$): 9.00 (br. COOH); 7.59 (*dd*, arom. 2 H); 7.44 (*dd*, 2 arom. H); 1.35 (*s*, *t*-Bu). ^{13}C-NMR (125 MHz, $CDCl_3$): 156.2; 152.7; 130.9; 123.4; 113.7; 87.3; 77.4; 32.7; 28.6.

*3-[4-(*tert*-Butyl)phenyl]prop-2-ynoyl Chloride.* A suspension of 3-[4-(*tert*-butyl)phenyl]prop-2-ynoic acid (10.2 g, 50.5 mmol) in H_2O (20 ml) was neutralized with NaOH (2.0 g, 50.5 mmol) dissolved in H_2O (10 ml). The H_2O was removed carefully and the residue powdered and suspended in benzene. After removal of benzene, the salt was dried for several hours under high vacuum. To a suspension of the salt in dry benzene (50 ml), oxalyl chloride (6 ml, 127.0 mmol) was added rapidly at 0° and then the mixture stirred at r.t. overnight. After filtration and removal of solvent and excess oxalyl chloride, the remaining oil was distilled at 103°/0.3 Torr: 8.9 g (80%) of the acyl chloride. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.59 (*dd*, 2 arom. H); 7.46 (*dd*, 2 arom. H); 1.36 (*s*, *t*-Bu). ^{13}C-NMR (125 MHz, $CDCl_3$): 156.0; 149.1; 133.3; 125.6; 114.6; 94.6; 83.6; 34.9; 30.5.

*3-[4-(*tert*-Butyl)phenyl]prop-2-ynoyl Azide.* To NaN_3 (4.0 g, 61.5 mmol) suspended in MeCN/Et_2O 1:1 (150 ml) and a few drops of pyridine acyl chloride (8.9 g, 40.4 mmol) in MeCN (13 ml) was added at −5° over 1 h. After stirring for another 3 h at −5°, the slurry was allowed to warm up to 10°, and Et_2O (75 ml) was added. The slurry was washed with cold aq. $NaHCO_3$ soln. and H_2O. After drying (Na_2SO_4) at 4° overnight, the soln. was evaporated: 9.4 g of an oil. Rapid CC (silica gel, petroleum ether/Et_2O 4:1) yielded 6.3 g (55%) of the azide as a nearly colorless oil that solidified after some time. Due to the thermal instability of the azide, the compound had to be stored at −20°, where it was stable over a period of months. IR (CCl_4): 1685 (C=O), 2135 (N_3), 2220 (C≡C). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.58 (*dd*, 2 arom. H); 7.47 (*dd*, 2 arom. H); 1.36 (*s*, *t*-Bu). ^{13}C-NMR (125 MHz, $CDCl_3$): 153.3; 148.2; 135.1; 125.2; 114.3; 93.6; 81.9; 32.3; 28.8. MS (70 eV): 199 (M^+).

Hept-1-ynyl Isocyanate (**1a**). A typical thermolysis to convert oct-2-ynoyl azide into hept-1-ynyl isocyanate was carried out as follows: A soln. of the azide (100 g, 605 μmol) in dry and degassed hexane (15 ml) was heated at 90° for 28 min. The progress of the reaction was followed by N_2 gas evolution, and the completion was checked by IR. The reaction proceeded well in a variety of solvents, including CCl_4, $CHCl_3$, $CDCl_3$, heptane, and THF. It was not possible to isolate the isocyanate for further purification. Spectroscopic data were obtained from the reaction soln. without further purification. Based on the integrated peak area in the GC/MS trace of the soln. of the isocyanate of **1a** the purity was estimated to be > 95%. IR (hexane): 2262 (C≡C), 2317 (NCO). ^{1}H-NMR (500 MHz, $CDCl_3$): 2.16 (*t*, 2 H, CH_2); 1.48 (*m*, 2 H, CH_2); 1.35 (*m*, 4 H, CH_2); 0.88 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 115.9; 63.0; 56.0; 31.0; 27.7; 22.3; 17.9; 13.9. MS (70 eV): 137 (M^+).

*[4-(*tert*-Butyl)phenyl]ethynyl Isocyanate* (**1b**). As described for **1a**, with the azide (100 mg, 440 μmol) in dry and degassed toluene (20 ml) at 90° for 20 min. The reaction proceeded cleanly in a variety of solvents, including hexane, CCl_4, $CHCl_3$, heptane, but not in THF. It was not possible to isolate the isocyanate for further

purification. Based on the integrated peak area in the GC/MS trace of the soln. of the isocyanate, the purity of **1b** was estimated to be >95%. IR (toluene): 2251 (C≡C), 2304 (NCO). MS (70 eV): 199 (M^+).

*Hexacarbonyl[μ-(1,2-η:1,2-η)hept-1-ynyl Isocyanate]dicobalt(*Co–Co*)* (**2a**). To a freshly prepared soln. of hept-1-ynoyl isocyanate in hexane, [$Co_2(CO)_8$] (1 equiv.) was added. After stirring for 1 h at r.t., no further CO gas evolution was observed. The deep red soln. was characterized without any purification. Several attempts to isolate **2a** neat failed and yielded only uncharacterizable polymeric material. IR (hexane): 2033 (C≡O), 2057 (C≡O), 2092 (C≡O), 2253 (NCO). ^{1}H-NMR (500 MHz, $CDCl_3$): 2.75 (*t*, 2 H, CH_2); 1.63 (*m*, 2 H, CH_2); 1.41 (*m*, 4 H, CH_2); 0.93 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 198.7; 128.9; 98.7; 86.4; 32.5; 31.7; 30.8; 22.4; 13.9.

*{μ-(1,2-η:1,2-η)-2-[4-(*tert*-Butyl)phenyl]ethynyl Isocyanate}hexacarbonyldicobalt(*Co–Co*)* (**2b**). As described for **2a** with a soln. of [4-(*tert*-butyl)phenyl]ethynyl isocyanate in toluene and [$Co_2(CO)_8$] (1 equiv.). An attempt to isolate **2b** neat from the deep red soln. failed and yielded only uncharacterizable polymeric material. IR (toluene): 2033 (C≡O), 2060 (C≡O), 2093 (C≡O), 2250 (NCO).

*Hexacarbonyl{μ-[(1,2-η:1,2-η)hept-1-ynyl]carbamic Acid Alkyl Ester}dicobalt(*Co–Co*) Complexes* **3a**: *General Procedure*. To a freshly prepared soln. of **2a** in hexane, alcohol R′OH (5 equiv.) was added at r.t. After stirring for 30 min and evaporation, the dark residue was chromatographed (degassed silica gel, thoroughly degassed petroleum ether/Et_2O 4:1). After evaporation, compounds **3a** were isolated as deep red oils that solidified after some time.

(Methyl Ester)dicobalt **3a** (R′ = Me): Yield 65%. IR (CCl_4): 1750 (C=O), 2023 (C≡O), 2051 (C≡O), 2091 (C≡O). ^{1}H-NMR (500 MHz, $CDCl_3$): 6.70 (br. NH); 3.79 (*s*, MeO); 2.79 (*t*, 2 H, CH_2); 1.62 (*m*, 2 H, CH_2); 1.38 (*m*, 4 H, CH_2); 0.89 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 199.3; 155.1; 98.9; 90.5; 52.9; 33.2; 31.8; 31.3; 22.4; 13.9.

(Ethyl Ester)dicobalt **3a** (R′ = Et): Yield 61%. IR (CCl_4): 1752 (C=O), 2021 (C≡O), 2052 (C≡O), 2089 (C≡O). ^{1}H-NMR (500 MHz, $CDCl_3$): 6.90 (br. NH); 4.23 (*q*, MeCH_2O); 2.82 (*t*, 2 H, CH_2); 1.63 (*m*, 2 H, CH_2); 1.41 (*m*, 7 H, CH_2, *Me*CH_2O); 0.91 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 199.0; 154.1; 98.6; 90.3; 62.0; 32.8; 31.4; 30.9; 22.0; 13.9; 13.4.

(Benzyl Ester)dicobalt **3a** (R′ = PhCH_2): Yield 60%. IR (CCl_4): 1747 (C=O), 2023 (C≡O), 2051 (C≡O), 2091 (C≡O). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.41 (*m*, 5 arom. H); 6.75 (br. NH); 5.22 (*s*, PhCH_2O); 2.80 (*t*, 2 H, CH_2); 1.61 (*m*, 2 H, CH_2); 1.39 (*m*, 4 H, CH_2); 0.93 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 199.0; 154.0; 135.0; 128.2; 98.2; 90.2; 67.7; 32.8; 31.3; 30.9; 22.0; 13.5.

*(*tert*-Butyl Ester)dicobalt* **3a** (R′ = *t*-Bu): Yield 75%. IR (CCl_4): 1741 (C=O), 2022 (C≡O), 2050 (C≡O), 2089 (C≡O). ^{1}H-NMR (500 MHz, $CDCl_3$): 6.82 (br. NH); 2.85 (*t*, 2 H, CH_2); 1.65 (*m*, 2 H, CH_2); 1.52 (*m*, 13 H, CH_2, *t*-Bu); 0.95 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 197.4; 151.1; 97.3; 89.0; 79.6; 31.1; 29.3; 28.9; 25.6; 20.0; 11.4.

*[(9*H*-Fluoren-9-yl)methyl Ester]dicobalt* **3a** (R′ = $C_{13}H_9CH_2$): Yield 68%. IR (CCl_4): 1747 (C=O), 2023 (C≡O), 2051 (C≡O), 2092 (C≡O). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.79 (*dd*, arom. H); 7.63 (*dd*, 2 arom. H); 7.38 (*m*, 4 arom. H); 6.79 (br. NH); 4.62 (*d*, 2 H, CHCH_2O); 4.31 (*t*, C*H*CH_2); 2.88 (*t*, 2 H, CH_2); 1.71 (*m*, 2 H, CH_2); 1.46 (*m*, 4 H, CH_2); 0.95 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 199.2; 153.8; 143.1; 141.0; 127.4; 126.6; 124.5; 119.7; 98.4; 90.2; 67.0; 46.7; 32.2; 31.9; 31.2; 22.2; 13.8.

*{μ-{(1,2-η:1,2-η)-[4-(*tert*-Butyl)phenyl]ethynyl}carbamic Acid Methyl Ester}hexacarbonyldicobalt(*Co–Co*)* **3b**. According to the *General Procedure* (see **3a**), with a soln. of **2b** in toluene and MeOH (5 equiv.): Yield 68%. Deep red oil. IR (CCl_4): 1739 (C=O), 2025 (C≡O), 2055 (C≡O), 2094 (C≡O). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.50 (br. NH); 7.45 (*m*, 4 arom. H); 3.83 (*s*, MeO); 1.38 (*s*, *t*-Bu). ^{13}C-NMR (125 MHz, $CDCl_3$): 198.6; 155.9; 150.7; 134.2; 128.0; 125.5; 98.1; 80.5; 52.5; 34.3; 30.8.

N-*(Alkoxycarbonyl)-2,3-didehydro-3-pentylaspartic Acid Anhydride* (=*(2,5-Dihydro-2,5-dioxo-4-pentylfuran-3-yl)carbamic Acid Alkyl Ester*; **4a**): *General Procedure*. To a thoroughly degassed soln. of **3a** (500 μmol) in acetone (50 ml), $Ce(NH_4)_2(NO_3)_6$ (3 equiv.) was added at r.t. within 1 h, the soln. changed its color form deep red to purple. After stirring overnight, the acetone was evaporated, and the org. compounds were extracted from H_2O with Et_2O. After drying (Na_2SO_4) and evaporation, the residue was chromatographed or recrystallized.

N-*(Methoxycarbonyl)-3-pentyl Derivative* **4a** (R′ = Me): Yield 70%, after CC (silica gel, petroleum ether/Et_2O 4:1). Colorless oil. IR (CCl_4): 1678 (C=O), 1769 (C=O), 1845 (C=O), 3385 (N–H). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.18 (br. NH); 3.84 (*s*, MeO); 2.74 (*t*, 2 H, CH_2); 1.54 (*m*, 2 H, CH_2); 1.32 (*m*, 4 H, CH_2); 0.88 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 165.8; 163.9; 151.7; 133.7; 122.0; 53.9; 31.8; 28.7; 25.1; 22.3; 13.9. MS (70 eV): 241 (M^+). Anal. calc. for $C_{11}H_{15}NO_5$: C 54.77, H 6.27, N 5.81; O 33.16; found: C 54.56, H 6.33, N 5.92, O 33.17.

N-*(Ethoxycarbonyl)-3-pentyl Derivative* **4a** (R′ = Et): Yield 80%, after CC (silica gel, petroleum ether/Et_2O 4:1). Colorless oil. IR (CCl_4): 1676 (C=O), 1765 (C=O), 1846 (C=O), 3380 (N–H). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.22 (br. NH); 4.25 (*q*, MeCH_2O); 2.75 (*t*, 2 H, CH_2); 1.53 (*m*, 2 H, CH_2); 1.30 (*m*, 7 H, CH_2, *Me*CH_2O); 0.86 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 165.5; 163.5; 150.9; 135.5; 121.5; 62.9; 31.2; 28.0; 24.5; 21.8; 13.8; 13.4. MS (70 eV): 255 (M^+). Anal. calc. for $C_{12}H_{17}NO_5$: C 56.46, H 6.71, N 5.49, O 31.34; found: C 56.33, H 6.71, N 5.43, O 31.53.

N-*[(Benzyloxy)carbonyl]-3-pentyl Derivative* **4a** (R′ = PhCH_2): Yield 50%, after CC (silica gel, petroleum ether/Et_2O 4:1). Colorless oil. IR (CCl_4): 1676 (C=O), 1771 (C=O), 1844 (C=O), 3384 (N–H). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.42 (*m*, 5 arom. H); 7.23 (br., NH); 5.26 (*s*, PhCH_2O); 2.78 (*t*, 2 H, CH_2); 1.58 (*m*, 2 H, CH_2); 1.33 (*m*, 4 H, CH_2); 0.88 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 165.8; 163.8; 151.0; 134.6; 133.6; 129.0; 128.8; 128.6; 122.0; 68.9; 31.6; 28.6; 25.0; 22.3; 13.9. MS (70 eV): 317 (M^+). Anal. calc. for $C_{17}H_{19}NO_5$: C 64.34, H 6.03, N 4.41, O 25.21; found: C 64.13, H 6.26, N 4.41, O 25.20.

N-*[(*tert-*Butoxy)carbonyl]-3-pentyl Derivative* **4a** (R′ = *t*-Bu): Yield 15%, after CC (silica gel, petroleum ether/Et_2O 4:1). Colorless oil. IR (CCl_4): 1682 (C=O), 1771 (C=O), 1849 (C=O), 3380 (N–H). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.27 (br. NH); 2.75 (*t*, 2 H, CH_2); 1.56 (*m*, 2 H, CH_2); 1.52 (*s*, *t*-Bu); 1.32 (*m*, 4 H, CH_2); 0.89 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 166.1; 164.2; 149.9; 134.2; 120.9; 83.5; 31.5; 28.4; 27.9; 24.9; 22.3; 13.9. MS (70 eV): 283 (M^+).

N-*{[(9*H*-Fluoren-9-yl)methoxy]carbonyl}-3-pentyl Derivative* **4a** (R′ = $C_{13}H_9CH_2$): Yield 84%, after recrystallization from EtOH. Colorless crystals. IR (CCl_4): 1675 (C=O), 1773 (C=O), 1840 (C=O), 3389 (N–H). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.78 (*dd*, 2 arom. H); 7.58 (*dd*, 2 arom. H); 7.42 (*dd*, 2 arom. H); 7.35 (*dd*, 2 arom. H); 7.12 (br. H); 4.59 (*d*, CHC*H*O); 4.27 (*t*, C*H*CH_2O); 2.71 (*t*, 2 H, CH_2); 1.50 (*m*, 2 H, CH_2); 1.31 (*m*, 4 H, CH_2); 0.98 (*t*, Me). ^{13}C-NMR (125 MHz, $CDCl_3$): 165.7; 163.9; 151.1; 142.9; 141.4; 133.5; 128.2; 127.3; 124.7; 122.3; 120.3; 68.5; 46.8; 31.8; 28.6; 25.0; 22.3; 13.9. MS (70 eV): 405 (M^+). Anal. calc. for $C_{24}H_{23}NO_5$: C 71.10, H 5.72, N 3.45, O 19.73; found: C 70.89, H 5.62, N 3.51, O 19.98.

*3-[4-(*tert-*Butyl)phenyl]-2,3-didehydro-*N*-(methoxycarbonyl) Acid Anhydride* (*={4-[4-(*tert-*Butyl)phenyl]-2,5-dioxo-2,5-dihydrofuran-3-yl}carbamic Acid Methyl Ester*; **4b**). According to the *General Procedure* (see **4a**), with a thoroughly degassed soln. of **3b** (287 mg, 592 μmol) in acetone (50 ml) and $Ce(NH_4)_2(NO_3)_6$ (974 mg, 1.78 mmol). CC (silica gel, Et_2O/MeOH/AcOH 30:1:1) gave **4b** in 87% yield. IR (CCl_4): 1682 (C=O), 1771 (C=O), 1846 (C=O), 3380 (N–H). ^{1}H-NMR (500 MHz, $CDCl_3$): 7.55 (br. NH); 7.46 (*m*, 4 arom. H); 3.61 (*s*, MeO); 1.34 (*s*, *t*-Bu). ^{13}C-NMR (125 MHz, $CDCl_3$): 164.5; 163.4; 154.1; 151.7; 132.5; 129.3; 125.4; 125.1; 122.0; 53.8; 35.0; 31.1. MS (70 eV): 303 (M^+).

Attempted Hydrolysis of **4a** (R′ = pentyl). To a soln. of anhydride **4a** (R′ = pentyl) **4a** (253 mg, 798 μmol), 1M LiOH (15 ml) was slowly added at r.t. After stirring overnight, H_2O (50 ml) was added and the soln. washed twice with AcOEt. The aq. phase was brought to pH 1 with 1M HCl and extracted twice with AcOEt. After drying ($MgSO_4$), evaporation yielded 227 mg of a slightly yellow solid. With or without purification by CC (silica gel, Et_2O), spectra (NMR, IR, MS) and elemental analysis were identical with those of **4a**.

Methanolysis of **4a** (R′ = PhCH_2): N-*[(Benzyloxy)carbonyl]-2,3-didehydroaspartic Acid Monomethyl Ester*. To a soln. of anhydride **4a** (R′ = PhCH_2; 219 mg, 691 μmol) in dry MeOH (10 ml), Et_3N (105 mg, 1.04 mmol) in MeOH (1 ml) was slowly added at 0°. After stirring overnight at r.t., the mixture was evaporated and the oil (286 mg) submitted to CC (silica gel, Et_2O/MeOH/AcOH 30:1:1): two isomeric esters (4:1) with identical retention times. ^{1}H-NMR (500 MHz, $CDCl_3$): 9.18 (br. 1 H, NH); 7.35 (*s*, 5 arom. H); 6.80 (br., 1 H, COOH); 5.15 (*s*, 2 H, CH_2O); 3.78 (*s*, 3 H, MeO); 2.38 (*t*, 2 H, CH_2); 1.40 (*m*, 2 H, CH_2); 1.25 (*m*, 4 H, CH_2); 0.83 (*t*, 3 H, Me); minor isomer: 9.18 (br., 1 H, NH); 7.40 (*s*, 5 arom. H); 6.80 (br., 1 H, COOH); 5.22 (*s*, 2 H, CH_2O); 3.78 (*s*, 3 HMeO); 2.75 (*t*, 2 H, CH_2); 1.59 (*m*, 2 H, CH_2); 1.25 (*m*, 4 H, CH_2); 0.83 (*t*, 3 H, Me). MS (70 eV): 349 (M^+). Anal. calc. for $C_{18}H_{23}NO_6$: C 61.88, H 6.64, N 4.01, O 27.48; found: C 62.88, H 6.88, N 4.03, O 26.21.

*Hexacarbonyl[μ-(1,2-η:1,2-η)-hept-1-yn-1-amine]dicobalt(*Co–Co*)*. To a freshly prepared soln. of **2a** (605 μmol) in dry CCl_4 (10 ml) containing 1% of THF, H_2O (1 equiv.) was added. The reaction was followed over several hours by IR. The NCO band at 2253 cm^{-1} gradually disappeared, and new bands appeared at 2336 (dissolved CO_2, identified by comparison with an authentic sample) and 3406 cm^{-1} (NH_2 of ynamine). The three characteristic bands of the $Co_2(CO)_6$ moiety at 2019, 2053, and 2091 cm^{-1} remained virtually unchanged. Attempts to isolate the ynaminedicobalt neat for further characterization gave only uncharacterizable polymeric material.

Attempted Condensation of the Hexacarbonylheptynaminedicobalt with Carbonyl Compounds. To a freshly prepared soln. of the heptynaminedicobalt (see above; 605 μmol) in CCl_4 (10 ml) containing 1% THF (from **2a**, see above) more THF (10 ml), acetone (10 ml), and cat. amounts of NaOAc and AcOH were added. After 3 h

stirring at r.t. under Ar, no deep red product was detectable by TLC (petroleum ether/Et_2O 4:1) and after stirring overnight, most of the starting material had decomposed. The mixture was evaporated and the residue (139 mg) dissolved in acetone (20 ml) and treated with $Ce(NH_4)_2(NO_3)_6$ (320 mg, 584 μmol). After 2 h, stirring, the mixture was evaporated and the org. compounds were extracted from H_2O with CH_2Cl_2. The org. phase was dried (Na_2SO_4) and evaporated: 113 mg of material. None of the products could be identified by GC/MS as being derived from unprotected ynamine.

A second condensation attempt proceeded as follows: To a freshly prepared soln. of ynaminedicobalt (605 μmol) in CCl_4 (10 ml) containing 1% THF (see above), benzophenone (1 equiv.) and a cat. amount of CF_3COOH were added. There was no deep red product detectable by TLC (petroleum ether/Et_2O 4:1) after stirring for 1 h at r.t., for 30 min at 50°, and for 30 min at 80°.

*{μ-(1,2-η:1,2-η)-2-[4-(*tert*-Butyl)phenyl]ethyn-1-amine}hexacarbonyldicobalt (*Co–Co*)*. To a freshly prepared soln. of **2b** (880 μmol) in toluene (40 ml), H_2O (1 equiv.) was added. The soln. was heated at 40°, and the reaction was followed over several minutes by IR. The NCO band at 2250 cm^{-1} gradually disappeared, and new bands appeared at 2335 (dissolved CO_2, identified by comparison with an authentic sample) and 3345 cm^{-1} (NH_2 of ynamine). The three characteristic bands of the $Co_2(CO_6)$ moiety at 2033, 2060, and 2093 cm^{-1} remained virtually unchanged. Attempts to isolate the ynaminedicobalt **5b** neat for further characterization gave only uncharacterizable polymeric material.

*Attempted Phthalimide Formation with the {[(*tert*-Butyl)phenyl]ethynamine}hexacarbonyldicobalt*. To a freshly prepared soln. of the ethynaminedicobalt (see above, 800 μmol) in toluene (40 ml) phthaloyl chloride (179 mg, 880 μmol) and 4-(dimethylamino)pyridine (215 mg, 1.76 mmol) were added. After 3 h stirring at r.t. under Ar no deep red product was detectable by TLC (petroleum ether/Et_2O 4:1).

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Received September 21, 1998