Supporting Information

A Short And Diverse Route Towards Complex Natural Product-Like Macrocycles

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General. Proton and Carbon nmr spectra were obtained in CDCl₃ or CD₃OD and determined with a Mercury 400 spectrometer. Chemical shifts are expressed in ppm (δ) with respect to TMS as an internal standard. Electrospray ionisation mass spectra (ESI) were obtained using a MSD (Hewlett-Packards HPLC 1100 driven electrospray MS instrument). Products were purified by preparative chromatography with silica gel and ethylacetate as eluent. The purity was determined utilizing a Hewlett-Packard LC 1100 system using a YMC column, 2 mm x 50 mm, 2 μ m ODSA, detection wave length at 220 and 254 nm; flow: 0,6 ml/min., with a 6 min. gradient from 90 % H₂O to 10 % H₂O (0,5% CH₃COOH) vs. CH₃CN. Preparative HPLC was performed on a Labomatic System, using a Grom Sil 120 ODS-4 HE column (10 μ M, 100 x 30 mm) with a 30 min. methanol/water gradient (40-100% MeOH) with single wavelength detection at 254 nm, flow 50 ml.

Experimental Procedures

General procedure for the preparation of carboxylic acids (No: **1** – **6**) with terminal double bound from carboxylic acid anhydrides with amines or alcohol's: To 4 mmol carboxylic acid anhydride, 4 mmol DMAP and 4 mmol pyridine in 10 ml THF (dry) and 4 mmol of the amine or hydroxy compound were added and refluxed for 2 hours at 78 °C. The reaction mixture is quenched with 10 ml 2N HCl at 0°C and stirred for 5 min. The aqueous layer is transferred to a separation funnel and extracted for three times with 10 ml ethylacetate. The organic layer was dried over Na₂SO₄ and concentrated in vacuum. The product could be crystallized or otherwise purified by column chromatography.

Biphenyl-2,2'-dicarboxylic acid 2-(2,4-dimethyl-hepta-2,6-dienyl) ester (**2**): 1,40g (95%) C₂₃H₂₄O₄ MW 364,45 g/mol; ; **HPLC-MS (ESI-TOF)**: t_R = 4,149 min.; m/z = 363 [M-H]⁻; **¹H-NMR (CD₃OD, 400 MHz)**: δ = 0,92 (d, 3H, CH₃CH); 1,40 (s, 3H, CH₃C); 1,99 (t, 2H, CH₂CH=CH₂); 2,44 (m, 1H, CH₃CH); 4,37 (s, 2H, OCH₂); 4,97-5,13 (m, 2H, H₂C=CHCH₂); 5,67-5,78 (m, 1H, H₂C=CHCH₂); 7,16-7,21 (m, 2H, Ar-CH); 7,41-7,56 (m, 4H, Ar-CH); 7,97 (m, 2H, Ar-CH). **¹³C-NMR (CD₃OD, 100 MHz)**: δ = 14,27 (CH₃); 20,59 (CH₃); 33,43 (CH₂); 42,58 (CH₂); 71,91 (CH); 116,21 (CH₂); 128,07; 128,16; 130,03; 130,87; 131,15; 131,50; 132,20; 132,50; 136,36; 138,16; 144,73; 169,05.

2'-Allylcarbamoil-biphenyl-2-carboxylic acid (**5**): 4,578 g (81 %) C₁₇H₁₅NO₃ MW 281,31 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3,401 min.; m/z = 304 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 3,57-3,76 (m, 2H, H₂C=CHCH₂NH); 4,75-4,89 (m, 2H, H₂C=CHCH₂NH); 5,32-5,42 (m, 1H, H₂C=CHCH₂NH); 6,95 (t, 1H, NH); 7,07-7,75 (m, 8H, Ar-CH); 10,61 (br, 1H, COOH). **¹³C-NMR (CDCl₃, 100 MHz)**: δ 42,15 (CH₂); 116,41 (CH₂); 127,23; 127,81; 129,05; 129,63; 129,87; 130,10; 131,04; 131,78; 132,85; 134,66; 139,06; 140,04; 170,71(CONH); 171,44 (COOH).

Cyclohexane-1,2-dicarboxylic acid monopent-4-enyl ester (**6**): 840mg (87%) C₁₃H₂₀O₄ MW 240,30 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3,597min.; m/z = 239 [M-H]⁻; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 1,42 (m, 4H, 2xCH₂); 1,73 (m, 4H, 2xCH₂); 2,07 (m, 4H, 2xCH, CH₂); 2,83 (br, 2H, CH₂); 4,04 (m, 2H, CH₂); 4,95-5,03 (m, 2H, CH₂); 5,73-5,83 (m, 1H, CH); 10,94 (br, 1H, COOH). **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 23,22; 23,46; 25,54; 25,99; 27,33; 29,66; 42,03 (CH₂); 63,55 (CH₂); 114,88 (CH₂); 137,11 (CH); 173,17 (CO); 179,99 (CO).

Representative Procedure for the preparation of isocyano-acetic acid 2,4-dimethyl-hepta-2,6-dienylester (**7**), **method A**: To a solution of 10 mmol (1,230 g) potassium isocyanopropionate and 12 mmol (1,555 mg) 2-chloro-1-methylpyridinium iodide in 30 ml THF (dry), 15,5 mmol (2,173 g) 2,4-dimethyl-2,6-heptadien-1-ol and 50 mmol (6,96 ml) triethylamine were added. The mixture is stirred at 45 °C for 3 hours while its color becomes red. The insoluble residue was filtered off and the reaction mixture concentrated in vacuum. The product was purified by preparative chromatography on silica gel with ethylacetat to give 1,917 g (92%) as pale yellow oil. According to this procedure also compound (**10**) was prepared from the corresponding alcohol.

Representative Procedure for the preparation of isocyano-acetic acid allyl ester (**8**), **method B**: To a suspension of 20 mmol (2,46 g) potassium isocyanacetat in 15 ml DMF, 20 mmol (2,42 g) allyl bromide were added and stirred at 55-60 °C for 3 hours. DMF is evaporated and the residue is diluted in 40 ml ethylacetat and washed with water (3 x 15 ml). The organic layer was separated and dried over MgSO₄ and concentrated. The product was purified by distillation (p:1,2 mbar, T(oilbath) 91 °C, T 58-60°C) to give 1,392 g (55 %) as a colorless oil. According to this procedure also compound (**9**), (**11**) and (**12**) were prepared from the corresponding bromide.

Isocyano-acetic acid 2,4-dimethyl-hepta-2,6-dienylester (**7**): 497 mg (60%) C₁₂H₁₇NO₂ MW: 207,27 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3,819 min; m/z = 208 [M+H]⁺; 230 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 0,88-0,90 (d, 3H, CH₃); 1,59 (s, 3H, CH₃); 1,97 (m, 2H, CH₂); 2,40 (m, 1H, CH); 3,91 (s, 2H, OCH₂); 4,18 (s, 1H, CH₂); 4,52 (s, 1H, CH₂); 4,90-4,95 (m, 2H, CH=CH₂); 5,13-5,26 (m, 1H, =CH); 5,67 (m, 1H, =CH); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 13,78; 14,06 (CH₃); 20,04; 20,36 (CH₃); 31,97; 32,19 (CH); 41,24; 41,57 (CH₂); 68,74 (CH₂); 72,45 (CH₂); 115,52; 115,90 (CH₂); 127,57 (C); 131,71 (CH); 137,11 (CH); 162,2 (NC); 136,71 (CO) (some signals are doubled as a consequence of rotational isomers).

Isocyano-acetic acid allyl ester (**8**): 1,392 g (55%) C₆H₇NO₂ MW 125,12 g/mol; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 4,25 (s, 2H, COCH₂NC); 4,69 (d, 2H, OCH₂); 5,28-5,38 (m, 2H, H₂C=CH); 5,86-5,95 (m, 1H, H₂C=CH); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 43,39 (CH₂); 67,00 (CH₂); 119,75 (H₂C=CH); 130,59 (H₂C=CH); 161,28 (NC); 163,56 (CO).

Isocyano-acetic acid but-3-enyl ester (**9**): 1,881 g (45%) C₇H₉NO₂ MW 139,16 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 2,972 min ; m/z = 162 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 2,42 (d, 2H, CH₂); 4,22-4,28 (m, 4H, 2xCH₂); 5,08-5,14 (m, 2H, H₂C=CH); 5,70-5,80 (m, 1H, H₂C=CH); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 32,70 (CH₂); 43,37 (CH₂); 65,49 (OCH₂); 117,87 (H₂C=CH); 132,99 (H₂C=CH); 161,24 (NC); 163,81 (CO).

Isocyano-acetic acid pent-2-enyl ester (**10**): 14,396 g (52%) C₈H₁₁NO₂ MW 153,18 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3,898 min ; m/z = 190 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 0,93-0,99 (3H, t, CH₃); 1,27-1,31 (0,3 H, t, CH₂); 1,88-1,90 (1H, d, CH); 2,01-2,14 (2H, m, CH₂); 4,14-4,21 (2H, t, CH₂); 5,43-5,56 (2H, m, CH₂); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 14,18 (CH₃); 20,81 (CH₂); 58,27 (CH₂); 62,16 (CH₂); 127,76 (CH); 134,40 (CH); 161,00 (NC); 163,78 (COO) (some signals are doubled as a consequence of different isomers).

Isocyano-acetic acid 3-methyl-but-2-enyl ester (**11**): 1,459 g (32%) C₈H₁₁NO₂ MW 153,18 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3,307 min; m/z = 154 [M+H]⁺; 176 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 1,71 (s, 3H, CH₃); 1,75 (s, 1H, CH₃); 4,20 (s, 2H, CH₂); 4,68 (d, 2H, OCH₂); 5,30-5,35 (m, 1H, =CH); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 17,93 (CH₃); 25,65 (CH₃); 43,43 (CH₂); 63,31 (OCH₂); 117,12 (=CH); 140,92 (=C(CH₃)₂); 161,06 (NC); 163,82 (CO).

Isocyano-acetic acid 4-methyl-pent-3-enyl ester (**12**): 6,822 g (20%) C₉H₁₃NO₂ MW 167,20 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3,898 min.; m/z = 190 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 1,61 (s, 3H, CH₃); 1,69 (s, 3H, CH₃); 2,36 (q, 2H, CH₂); 4,15-4,21 (m, 4H, 2 x CH₂); 5,06 (m, 1H, CH); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 17,70 (CH₃); 25,60 (CH₃); 27,25 (CH₂); 43,40 (CH₂); 66,21 (OCH₂); 118,19 (CH₂); 135,35 (C); 161,11 (NC); 163,86 (CO).

3-Dimethylamino-2-isocyano-acrylic acid 2,4-dimethyl-hepta-2,6-dienyl ester (**13**): 279 mg (21%) C₁₅H₂₂N₂O₂ MW 262,35 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 4,100 min; m/z = 263 [M+H]⁺; 285 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 0,94 (d, 3H, CH₃); 1,66 (s, 3H, CH₃); 2,02 (t, 2H, CH₂); 2,43-2,50 (m, 1H, CH); 3,22 (br, 6H, N(CH₃)₂); 4,52 (s, 2H, CH₂); 4,94-5,01 (m, 2H, CH₂); 5,27 (d, 1H, CH); 5,68-5,78 (m, 1H, CH); 7,17 (s, 1H, CH); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 14,03 (CH₃); 20,16 (CH₃); 32,12 (CH); 41,44 (CH₂); 70,35 (CH₂); 115,67 (CH₂); 128,98 (C); 134,64 (CH); 136,91 (CH); 145,96 (CH); 164,68 (NC); 169,34 (CO).

Representative Procedure for the preparation of *N*-Ethyl-2-isocyano-*N*-(2-methyl-allyl)-acetamide (**18**): To 30 mmol (2,975 g) *N*-Ethyl-2-methylamine 30 mmol (2,973 g) Isocyanoacetic acid methylester were added and stirred for 12 h at room temperature. The formed methanol is evaporated and the residue was purified by column chromatography (SiO₂/Ethylacetat) to give 2.079g (42 %) product as orange oil.

N-Allyl-2-isocyano-3-phenyl-propionamide (**14**): 429 mg (40%) C₁₃H₁₄N₂O MW 214,27 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3,192 min; m/z = 215 [M+H]⁺; 237 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 3,11-3,27 (m, 2H, CH₂Ph); 3,83 (m, 2H, H₂C=CHCH₂N); 4,42 (m, 1H, CHCH₂Ph); 5,04-5,11 (m, 2H, H₂C=CHCH₂N); 5,67-5,76 (m, 1H, H₂C=CHCH₂N); 6,62 (br, 1H, NH); 7,23-7,31 (m, 5H, Ph); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 38,46 (CH₂); 41,35 (CH₂); 59,53 (CH); 116,83 (CH₂); 127,46; 128,43; 129,35; 132,71; 134,37; 161,79 (NC); 164,56 (CO).

N-Allyl-2-isocyano-acetamide (**15**): 1,781 g (95 %) C₆H₈N₂O MW 124,14 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 0,423-0,892; m/z = 125 [M+H]⁺; 147 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 3,87-3,90 (d, 2H, CH₂NH); 4,17 (s, 2H, COCH₂NC); 5,14-5,21 (m, 2H, H₂C=CH); 5,75-5,85 (m, 1H, H₂C=CH); 6,86 (br, 1H, NH). **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 42,01 (CH₂); 45,07 (CH₂); 117,02 (H₂C=CH); 132,80 (H₂C=CH); 161,42 (NC); 162,32 (CO).

N-Allyl-2-isocyano-*N*-methyl-acetamide (**16**): 3.452 g (83 %) C₇H₁₀N₂O MW 138,17 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 1.059 min; m/z = 139 [M+H]⁺; 161 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 2,91-2,98 (m, 3H, CH₃); 3,81 (s, 1H, CHCH₂N); 3,99 (s, 1H, CHCH₂N); 4,30 (d, 2H, COCH₂NC); 5,15-5,29 (m, 2H, H₂C=CHCH₂N); 5,73 (m, 1H, H₂C=CHCH₂N); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 34,12; 34,42 (CH₃); 44,03; 44,47 (CHCH₂N); 50,64; 51,61 (COCH₂NC); 117,46; 118,35 (H₂C=CHCH₂N); 131,12; 131,62 (H₂C=CHCH₂N); 160,45 (NC); 162,08; 162,46 (CO) (signals are doubled as a consequence of rotational isomers around the tertiary amide).

2-Isocyano-4-methyl-pentanoic acid allylamide (**17**): 37 mg (10%) C₁₀H₁₆N₂O MW 180,25 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3,134 min; m/z = 181 [M+H]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 0,94-0,99 (m, 6H, 2xCH₃); 1,75-1,93 (m, 3H, CHCH₂CH(CH₃)₂); 3,90-3,93 (m, 2H, H₂C=CHCH₂N); 4,19-4,23 (m, 1H, COCHNC); 5,17-5,24 (m, 2H, H₂C=CHCH₂N); 5,78-5,88 (m, 1H, H₂C=CHCH₂N); 6,57 (br, 1H, NH); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 20,67 (CH₃); 22,75 (CH₃); 24,85 (CH); 41,48 (CH₂); 42,17 (CH₂); 57,09 (COCHNC); 117,21 (H₂C=CH); 132,95 (H₂C=CH); 161,55 (NC); 165,79 (CO).

N-Ethyl-2-isocyano-*N*-(2-methyl-allyl)-acetamide (**18**): 2.079g (42 %) C₉H₁₄N₂O MW 166.22 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3.446 min; m/z = 167 [M+H]⁺; 189 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 1,12-1,80 (t, 3H, CH₃CH₂); 1,67-1,71 (s, 3H, CH₃C); 3,20-3,42 (q, 2H, NCH₂CH₃); 3,66 (s, 2H, CCH₂N); 4,24; 4,34 (s, 2H, COCH₂NC); 4,78; 4,95 (s, 2H, H₂C=C); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 12,45; 13,40 (CH₃CH₂); 19,84; 19,92 (CH₃C); 40,99; 42,36 (NCH₂CH₃); 43,26; 44,11 (CCH₂N); 50,47; 52,38; 53,30 (COCH₂NC); 111,76; 112,97 (H₂C=C); 139,19; 139,85 (H₂C=C); 161,21; 161,93; 162,32 (NC); 164,33 (CO) (signals are doubled as a consequence of rotational isomers around the tertiary amide).

Procedure of the Passerini-3-component reaction for the preparation of Biphenyl-2,2'-dicarboxylic acid 2-({[(allyl-methyl-carbamoyl)-methyl]-carbamoyl}-methyl) ester 2'-(2,4-dimethyl-hepta-2,6-dienyl) ester (**19**): 1 mmol (364 mg) Biphenyl-2,2'-dicarboxylic acid 2-(2,4-dimethyl-hepta-2,6-dienyl) ester (**2**) were diluted in 2 ml diethylether, 1 mmol (30 mg) paraformaldehyde and 1 mmol (138 mg) *N*-Allyl-2-isocyano-*N*-methyl-acetamide (**16**) were added and stirred for 3 d at room temperature. The solution is evaporated and the residue was purified by column chromatography (SiO₂/Ethylacetat) to give 355 mg (67 %) product as a colorless oil.

Biphenyl-2,2'-dicarboxylic acid 2-({[(allyl-methyl-carbamoyl)-methyl]-carbamoyl}-methyl) ester 2'-(2,4-dimethyl-hepta-2,6-dienyl) ester (**19**): 355 mg (67 %) C₃₁H₃₆N₂O₆ MW 532.64 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 4,193 min; m/z = 555 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 0,9 (d, 3H, CH₃); 1,2 (s, 3H, CH₃); 1,9 (CH₂); 2,3 (CH₂); 2,9 (CH₃); 3,7-4,0 (CH₂); 4,3 (CH₂); 4,4 (CH₂); 4,9 (CH₂); 5,0-5,2 (CH₂); 5,5-5,8 (CH); 6,9 (NH); 7,2 (Ar-CH); 7,3-7,5 (Ar-CH); 7,9-8,1 (Ar-CH); **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 14,27 (CH₃CH); 20,38 (CH₃C=); 32,39 (CH); 33,69 (NCH₃); 34,08 (NCH₃); 40,75 (H₂C=CHCH₂); 41,06 (H₂C=CHCH₂); 41,62 (H₂C=CHCH₂); 50,52 (CH); 51,27 (COCH₂N); 63,31 (COCH₂O); 71,13 (OCH₂); 115, 97 (H₂C=CHCH₂); 117,45 (H₂C=CHCH₂); 118,14 (H₂C=CHCH₂); 127,45; 127,77; 128,58; 128,82; 129,99; 130,28; 130,41; 130,50; 130,70; 131,74; 132,31; 132,40; 135,59; 137,15; 142,98 (C); 143,76 (C); 165,66 (CO); 167,16 (CO); 167,21 (CO); 167,33 (CO).

Procedure of the ring closing metathesis reaction for the preparation of the macrocycle (**20**): 0.66 mmol (355 mg) Biphenyl-2,2'-dicarboxylic acid 2-({[(allyl-methyl-carbamoyl)-methyl]-carbamoyl}-methyl) ester 2'-(2,4-dimethyl-hepta-2,6-dienyl) ester (**19**) were diluted under nitrogen in 200 µL dry DCM. 0.23 mmol (69 µL) Titanisopropoxide were added using a syringe via a septum. The solution is refluxed for one hour and 0.07 mmol (58 mg) Grubbs catalyst diluted in 6.25 ml dry DCM were added under nitrogen. The reaction was refluxed for another 6 h and controlled via TLC. The mixture was stirred over night at room temperature and followed again with TLC for completion. Another 0.07 mmol Grubbs catalyst were added and refluxed for another 6 h.

The reaction mixture is quenched with 80 ml water, and forms a suspension. The aqueous layer is separated and the organic layer is extracted for three times with 50 ml water each. The mixture is filtered through cellite and washed with DCM. The filtrate is evaporated to give 504 mg crude product as an oil. The macrocycle was purified via preparative HPLC on reversed phase Grom Sil 120 ODS-4 HE column (10 µM, 100 x 30 mm) using 30 min. methanol/water gradient (40-100% MeOH) with single wavelength detection at 254 nm, flow 50 ml to give 91 mg (26 %) of compound **20**. For X-ray analysis the macrocycle was crystallized from CHCl₃.

macrocycle (**20**): 91 mg (26 %) C₂₉H₃₂N₂O₆ MW 504.59 g/mol; **HPLC-MS (ESI-TOF)**: t_R = 3,925 min; m/z = 505 [M+H]⁺; 527 [M+Na]⁺; **¹H-NMR (CDCl₃, 400 MHz)**: δ = 0,82-0,92 (m, 4H); 1,19 (s, 1H); 1,45 (s, 1H); 1,53-1,85 (m, 1H); 2,04-2,22 (m, 1H); 2,23-2,50 (m, 1H); 2,89 (s, 3H, NCH₃); 3,48-4,16 (m, 4H); 4,22-4,46 (m, 1H); 4,55-5,16 (m, 3H); 7,11-7,26 (m, 2H, Ar-CH); 7,37-7,52 (m, 4H, Ar-CH); 7,76-8,05 (m, 2H, Ar-CH). **¹³C-NMR (CDCl₃, 100 MHz)**: δ = 13,30; 13,58; 13,89 (CH₃CH); 20,90; 21,29 (CH₃C=); 32,60 (CH); 34,75; 34,98 (NCH₃); 39,78; 40,26 (H₂C=CHCH₂); 40,82; 41,10 (H₂C=CHCH₂); 50,51; 50,92; 53,69 (COCH₂N); 62,49; 63,30 (COCH₂O); 68,00; 70,01; 70,69; 71,72 (OCH₂); 124,26; 127,80; 130,64; 132,38; 134,40; 143,16; 167,98 (CO). Signals are doubled cause of diastereomers and conformers, nmr measurement at different temperatures shows not simplification of the spectra.

X-ray single crystal Structure determination of **20**: *Crystal data*: $C_{29}H_{32}N_2O_6$, $M_r = 504.57$, colorless crystal, $0.10 \times 0.14 \times 0.24 \text{ mm}^3$, monoclinic, space group $P2_1/c$ (No. 14), $a = 10.9075(5)$, $b = 28.2502(12)$, $c = 9.5064(3) \text{ \AA}$, $\beta = 114.099(2)^\circ$, $V = 2674.0(2) \text{ \AA}^3$, $Z = 4$, $\rho_{\text{calcd}} = 1.253 \text{ g cm}^{-3}$, $F(000) = 1072$, $\mu(\text{Mo K}\alpha) = 0.088 \text{ mm}^{-1}$, $T = 293 \text{ K}$. *Data collection*: Nonius MACH3 κ -axis CCD-diffractometer, $\lambda = 0.71073 \text{ \AA}$, unit cell parameters by least-squares for 3973 reflections. A total of 12128 reflections were integrated. After merging ($R_{\text{int}} = 0.056$) 2762 reflections remained and were used for all further calculations. *Structure solution and refinement*: Direct methods (*SIR92*^b), full-matrix least-squares refinements on F^2 (*SHELXL-97*^c) converged with $R1 = 0.0630 [I_o > 2\sigma(I_o)]$, $wR2 = 0.1742$ [all data], $GOF = 1.048$ and shift/error < 0.001 . 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-200226 (**26**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk]. (b) Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. "*SIR92*" *J. Appl. Cryst.* **1994**, *27*, 435. (c) Sheldrick G. M. "*SHELXL-97*" University of Göttingen: Germany, **1998**.

Procedure of the Passerini-3-component reaction and oxazole formation for the preparation of compound (**22**): 4 mmol (608 mg) phenylglyoxale hydrate were suspended in 8 ml diethylether, 4 mmol (960 mg) freshly distilled carboxylic acid (**21**) prepared according to procedure of compounds (**1**) to (**6**) with 2,4-dimethyl-2,6-heptadien-1-ol and succinic anhydride, and 4 mmol (268 mg) allylisocyanide were added and stirred for 12 h at room temperature. The solvent is completely removed to get 1,558 g (88%) passerini product. For the oxazole formation 10 eq (4,585 g) trifluoroammonia acetate were added and were heated to 150° for 4 h under frequently stirring to make sure that these two layers are completely mixed. The melt is cooled to 70°C and diluted in 10 ml ethyl acetate. The resulting solid is filtered off and washed with ethyl acetate. All ethyl acetate is combined and extracted for three times with water, dried over Na_2SO_4 and evaporated. The crude product is purified with flash chromatography on silica gel with petrol ether and ethyl acetate in a 3:2 mixture to give 473 mg (32%) of (**22**).

Procedure of the ring closing metathesis reaction for the preparation of the macrocycle (**23**): 0.56 mmol (237 mg) compound (**22**) were diluted under nitrogen in 180 μL dry DCM. 0.19 mmol (57 μL) Titanisopropoxide were added using a syringe via a septum. The solution is refluxed for one hour and 0.06 mmol (46 mg) Grubbs catalyst diluted in 5 ml dry DCM were added under nitrogen. The reaction was refluxed for another 6 h and controlled via TLC. The mixture was stirred over night at room temperature and followed again with TLC for completion. Another 0.06 mmol Grubbs catalyst were added and refluxed for another 6 h.

The reaction mixture is quenched with 50 ml water, and forms a suspension. The aqueous layer is separated and the organic layer is extracted for three times with 30 ml water each. The mixture is filtered through cellite and washed with DCM. The filtrate is evaporated to give 307 mg crude product as an oil. The macrocycle was purified via preparative HPLC on reversed phase Grom Sil 120 ODS-4 HE column (10 μM , $100 \times 30 \text{ mm}$) using 30 min. methanol/water gradient (40-100% MeOH) with single wavelength detection at 254 nm, flow 50 ml to give 56 mg (25 %) of compound **23**.

macrocycle (**23**): 56 mg (25 %) $C_{23}H_{26}N_2O_4$ MW 394,47 g/mol; **HPLC-MS (ESI-TOF)**: $t_R = 3,831 \text{ min}$; $m/z = 395 [M+H]^+$; 417 $[M+Na]^+$; **$^1\text{H-NMR}$ (CDCl_3 , 400 MHz)**: $\delta = 0,96$ (d, 3H, CH₃); 1,58 (s, 3H, CH₃); 1,87 (m, 1H, CH); 2,22 (d, 1H, CH); 2,40-2,48 (m, 1H, CH); 2,89 (m, 2H, CH₂); 3,15-3,5 (m, 2H, CH₂); 3,84-3,89 (m, 1H); 4,05-4,11 (m, 1H); 4,39-4,43 (d, 1H); 4,63-4,66 (d, 1H); 5,21 (d, 1H); 5,53 (m, 2H); 6,16 (t, 1H, NH); 7,35-7,43 (m, 3H, ArCH); 8,23-8,25 (m, 2H, ArCH); **$^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz)**: $\delta = 14,07$ (CH₃); 21,20 (CH₃); 23,41 (CH₂); 30,59 (CH); 32,58 (CH); 39,69; 39,98; 71,48 (CH); 125,96; 128,04; 129,18; 129,30; 130,02; 131,12; 136,14; 138,42; 143,82; 157,27; 162,00; 171,42.

Biphenyl-2,2'-dicarboxylic acid 2-(2,4-dimethyl-hepta-2,6-dienyl) ester

Biphenyl-2,2'-dicarboxylic acid 2-(2,4-dimethyl-hepta-2,6-dienyl) ester

10.610

2'-Allylcarbamoyl-biphenyl-2-carboxylic acid 2.0

5

7.749
7.536
7.349
7.390
6.946
7.065
7.413
7.515
7.771

5.321
5.418

4.754
4.797
4.861
4.887

3.761
3.566
3.632
3.831

4.3

1.1

1.0

1.0

1.0

1.0

1.0

1.0

0.2

1.0

0.9

170.708
171.439
140.039
139.058
134.661
132.848
127.230
127.811
131.776
116.407
131.044
130.098
129.628

2'-Allylcarbamoyl-biphenyl-2-carboxylic acid

5

42.151

11.021

Cyclohexane-1,2-dicarboxylic acid monopent-4-enyl ester

5.784

5.032

4.949

4.078

2.836

2.102

2.007

1.696

1.417

4.3 4.4 4.5

0.7

1.8

2.1

2.0

6

Cyclohexane-1,2-dicarboxylic acid monopent-4-enyl ester

Isocyano-acetic acid 2,4-dimethyl-hepta-2,6-dienyleste

Isocyano-acetic acid 2,4-dimethyl-hepta-2,6-dienylester

7

Isocyano-acetic acid allyl ester

8

5.855
5.952
5.896
5.282
5.308
5.340
5.383
4.686
4.698
4.249

2.0

2.0

1.8

0.8

Isocyano-acetic acid allyl ester

8

SI - page 15

Isocyano-acetic acid but-3-enyl ester

9

0.8

1.8

4.0

2.0

5.801
5.700

5.142
5.103
5.081

4.281
4.265
4.248
4.216

2.431
2.415

Isocyano-acetic acid but-3-enyl ester

9

SI - page 17

Isocyano-acetic acid pent-2-enyl ester

Isocyano-acetic acid pent-2-enyl ester

10

Isocyano-acetic acid 3-methyl-but-2-enyl ester

11

5.352
5.300
5.325
4.697
4.679
4.201
1.751
1.708

0.8

2.0

2.3

3.2

3.0

Isocyano-acetic acid 3-methyl-but-2-enyl ester

11

Isocyano-acetic acid 4-methyl-pent-3-enyl ester

12

0.8

4.1

2.0

3.2

2.9

Isocyano-acetic acid 4-methyl-pent-3-enyl ester

12

SI - page 23

3-Dimethylamino-2-isocyano-acrylic acid 2,4-dimethyl-hepta-2,6-dienyl ester

13

51.0
tZ eged - page 24

3-Dimethylamino-2-isocyano-acrylic acid 2,4-dimethyl-hepta-2,6-dienyl ester

13

SI - page 25

N-Allyl-2-isocyano-3-phenyl-propionamide

N-Allyl-2-isocyano-acetamide

15

16

N-Allyl-2-isocyano-N-methyl-acetamide

N-Allyl-2-isocyano-N-methyl-acetamide

16

2-Isocyano-4-methyl-pentanoic acid allylamide

17

N-Ethyl-2-isocyano-N-(2-methyl-allyl)-acetamide

18

18

N-Ethyl-2-isocyano-N-(2-methyl-allyl)-acetamide

gl_16_
STANDARD 1H OBSERVE

Automation directory: /export/home/vnmr1/auto/auto_05.06.01
File : gl_16_02

Pulse Sequence: s2pu1

Solvent: cdcl3
Ambient temperature

Sample #24

File: gl_16_01

Mercury-400BB "mercury400"

Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.995 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 400.4503117 MHz
DATA PROCESSING
FT size 32768
Total time 2 min, 12 sec

Biphenyl-2,2'-dicarboxylic acid 2-({[(allyl-methyl-carbamoyl)-methyl]-carbamoyl}-methyl) ester
2'-(2,4-dimethyl-hepta-2,6-dienyl) ester

19

19

Biphenyl-2,2'-dicarboxylic acid 2-({[(allyl-methyl-carbamoyl)-methyl]-carbamoyl}-methyl) ester 2'-(2,4-dimethyl-hepta-2,6-dienyl) ester

19

g1_39_2_in
STANDARD 1H OBSERVE

Automation directory: /export/home/vnmr1/auto/auto_24.07.01
File : g1_39_2_in_02

Pulse Sequence: s2pul

Solvent: cdc13
Ambient temperature
Sample #22

File: g1_39_2_in_01
Mercury-400BB "mercury400"

Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.995 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 400.4503015 MHz
DATA PROCESSING
FT size 32768
Total time 2 min, 12 sec

macrocycle 20

SI - page 39

gl_39_2_in_
STANDARD 1H OBSERVE

Automation directory: /export/home/vnmr1/auto/auto_24.07.01
File : gl_39_2_in_03

Pulse Sequence: s2pu1

Solvent: cdc13
Ambient temperature
Sample #22
File: gl_39_2_in_02
Mercury-400BB "mercury400"

macrocycle 20

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.199 sec
Width 25188.9 Hz
256 repetitions
OBSERVE C13, 100.6932799 MHz
DECOUPLE H1, 400.4522673 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 9 min, 46 sec

macrocycle 20

CH3 carbons

CH2 carbons

CH carbons

all protonated carbons

220

200

180

160

140

120

100

80

60

40

20

0

ppm

23

171.420
162.001
157.270
143.821
138.432
136.140
129.181
125.960
128.036
130.020
131.118

71.475

39.688
39.980
30.592
32.576
21.200
23.416
14.074

=====

S U P P L E M E N T A R Y M A T E R I A L

=====

BECG 4159-293

Compound 20 ($C_{29}H_{32}N_2O_6$)

B E L O N G I N G T O T H E P A P E R

A Short And Diverse Route Towards Complex Natural Product-Like
Macrocycles

by

Barbara Beck, Gregor Larbig, Beatrice Mejat, Marina Magnin-

Lachaux, Anne Picard, Eberhardt Herdtweck, Alexander Dömling

C o n t e n t s

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Table S1 - Crystal Data and Details of the Structure Determination
for: BECG 4159-293

Table S2 - Final Coordinates and Equivalent Isotropic Thermal
Parameters of the non-Hydrogen atoms
for: BECG 4159-293

Table S3 - Hydrogen Atom Positions and Isotropic Thermal
Parameters
for: BECG 4159-293

Table S4 - (An)isotropic Thermal Parameters
for: BECG 4159-293

Table S5 - Bond Distances (Å)
for: BECG 4159-293

Table S6 - Bond Angles (Degrees)
for: BECG 4159-293

Table S1 - Crystal Data and Details of the Structure
Determination for BECG 4159-293

Crystal Data

Empirical Formula	C29 H32 N2 O6
Formula Weight	504.57
Crystal System	Monoclinic
Space group	P21/c (No. 14)
a, b, c [Å]	10.9075(5) 28.2502(12) 9.5064(3)
alpha, beta, gamma [deg]	90 114.099(2) 90
V [Å**3]	2673.98(19)
Z	4
Mosaicity	0.729(3)
D(obs), D(calc) [g/cm**3]	0.000, 1.253
F(000) [Electrons]	1072
Mu(MoKa) [/mm]	0.088
Crystal Size [mm]	0.10 x 0.14 x 0.24

Data Collection

Temperature (K)	293
Radiation [Å]	Drehanode 50 / 60 MoKa 0.71073
Theta Min-Max [Deg]	1.44, 20.81
Kollimator [Nr.;mm]	0540.353; 0.61
Device	Nonius Kappa CCD
Scan Characteristics set 1 [mm; Deg; Deg]:	
	Dx = 50; Phi movement mode; Delta-Phi = 1
Exposure time [s] x repetition	5 x 2
Data set	-10: 10 ; -28: 28 ; -9: 9
Resolution [min; max]	20.40; 1.00
Completeness of the data set	98.9%
Tot., Uniq. Data, R(int)	12127, 2762, 0.056
Observed data [I > 2.0 sigma(I)]	1868

Refinement

Nref, Npar	2762, 341
R1 [I > 2.0 sigma(I)]	0.0630
R1, wR, S [all data]	0.1042, 0.1742, 1.048
Weighting Scheme : w = 1 / [sigma ² (Fo ²)+(a*P) ² +b*P]	
with a: 0.0677; b: 3.3111; P: [Maximum(0 or Fo ²)+2*Fc ²]/3	
Max. and Av. Shift/Error	0.00, 0.00
Min. and Max. resd. dens. [e/Ång ³]	-0.33, 0.26

Table S2 - Final Coordinates and Equivalent Isotropic Thermal
Parameters of the non-Hydrogen atoms for BECG 4159-293

Atom	x	y	z	U(eq) [$\text{\AA}^2$]
----	----	----	----	-----
O2	0.0965(4)	0.12029(12)	0.4331(5)	0.0880(16)
O3	0.2760(3)	0.16659(11)	0.4969(4)	0.0534(12)
O6	0.2870(3)	0.26915(12)	0.7136(4)	0.0674(16)
O10	0.6102(4)	0.24335(15)	0.4971(5)	0.0909(17)
O23	0.4828(3)	0.08404(11)	0.7241(4)	0.0587(12)
O25	0.3473(4)	0.10946(14)	0.8328(4)	0.0812(17)
N7	0.3993(5)	0.24875(15)	0.5691(6)	0.0572(17)
N11	0.7373(5)	0.29482(15)	0.6780(5)	0.0666(17)
C1	0.2059(6)	0.12710(17)	0.4369(6)	0.0533(19)
C4	0.2161(5)	0.20014(16)	0.5636(6)	0.0626(19)
C5	0.3050(5)	0.24277(17)	0.6215(6)	0.0511(19)
C8	0.4989(5)	0.28612(17)	0.6243(6)	0.061(2)
C9	0.6198(6)	0.2727(2)	0.5957(7)	0.060(2)
C12	0.7538(6)	0.3289(2)	0.8003(7)	0.092(3)
C13	0.8562(7)	0.2826(3)	0.6541(8)	0.107(3)
C14	0.9337(8)	0.2416(4)	0.7472(14)	0.161(5)
C15	0.9304(14)	0.2091(5)	0.7964(13)	0.218(7)
C16	1.0114(7)	0.1687(3)	0.8851(9)	0.117(4)
C17	0.9418(6)	0.1207(3)	0.8433(7)	0.096(3)
C18	1.0317(7)	0.0809(3)	0.9393(10)	0.159(4)
C19	0.8099(6)	0.11917(19)	0.8600(7)	0.076(2)
C20	0.6879(6)	0.12116(17)	0.7562(6)	0.058(2)
C21	0.6504(6)	0.1245(2)	0.5842(6)	0.080(3)
C22	0.5722(5)	0.12370(18)	0.7972(6)	0.068(2)
C24	0.3725(5)	0.08145(19)	0.7516(6)	0.057(2)
C26	0.2872(5)	0.03973(16)	0.6766(6)	0.0523(19)
C27	0.2392(6)	0.0153(2)	0.7697(7)	0.075(3)
C28	0.1618(7)	-0.0251(2)	0.7186(10)	0.086(3)
C29	0.1319(6)	-0.0407(2)	0.5722(10)	0.085(3)
C30	0.1772(5)	-0.01597(18)	0.4772(7)	0.067(2)
C31	0.2564(4)	0.02451(16)	0.5274(6)	0.0485(19)
C32	0.3001(5)	0.04727(16)	0.4139(5)	0.0478(17)
C33	0.3651(5)	0.01989(18)	0.3424(6)	0.0588(19)
C34	0.4096(5)	0.0392(2)	0.2387(6)	0.065(2)
C35	0.3901(6)	0.0864(2)	0.2019(6)	0.067(2)
C36	0.3272(5)	0.11467(18)	0.2716(6)	0.0564(19)
C37	0.2816(4)	0.09541(17)	0.3753(5)	0.0473(17)

=====
U(eq) = 1/3 of the trace of the orthogonalized U

Table S3 - Hydrogen Atom Positions and Isotropic Thermal
Parameters for BECG 4159-293

Atom	x	y	z	U(iso) [Å ²]
----	---	---	---	-----
H	0.404(6)	0.2334(19)	0.496(6)	0.08(2)
H41	0.2023	0.1854	0.6482	0.075
H42	0.1292	0.2099	0.4868	0.075
H81	0.5248	0.2910	0.7337	0.074
H82	0.4613	0.3155	0.5711	0.074
H121	0.8442	0.3407	0.8428	0.138
H122	0.7354	0.3137	0.8799	0.138
H123	0.6925	0.3548	0.7585	0.138
H131	0.9149	0.3099	0.6784	0.128
H132	0.8296	0.2754	0.5458	0.128
H141	1.0238	0.2479	0.7716	0.194
H151	0.8412	0.2029	0.7770	0.262
H161	1.0359	0.1745	0.9938	0.141
H162	1.0938	0.1674	0.8694	0.141
H171	0.9229	0.1145	0.7350	0.115
H181	1.1128	0.0800	0.9229	0.239
H182	0.9855	0.0513	0.9091	0.239
H183	1.0534	0.0865	1.0465	0.239
H191	0.8176	0.1163	0.9607	0.091
H211	0.5884	0.0996	0.5321	0.120
H212	0.7298	0.1213	0.5649	0.120
H213	0.6094	0.1546	0.5468	0.120
H221	0.6022	0.1220	0.9082	0.081
H222	0.5251	0.1534	0.7618	0.081
H271	0.2594	0.0262	0.8689	0.090
H281	0.1307	-0.0412	0.7827	0.102
H291	0.0810	-0.0680	0.5364	0.102
H301	0.1541	-0.0266	0.3771	0.081
H331	0.3785	-0.0122	0.3656	0.070
H341	0.4530	0.0202	0.1934	0.078
H351	0.4189	0.0993	0.1307	0.080
H361	0.3155	0.1468	0.2486	0.068

=====
The Temperature Factor has the Form of $\text{Exp}(-T)$ Where
 $T = 8 * (\text{Pi}^{**2}) * U * (\text{Sin}(\text{Theta}) / \text{Lambda})^{**2}$ for Isotropic
Atoms

Table S4 - (An)isotropic Thermal Parameters for BECG 4159-293

Atom	U(1,1)	U(2,2)	U(3,3)	U(2,3)	U(1,3)	U(1,2)
O2	0.054(2)	0.057(2)	0.156(4)	-0.013(2)	0.046(3)	-0.011(2)
O3	0.056(2)	0.043(2)	0.065(2)	-0.0125(18)	0.0286(18)	-0.0071(18)
O6	0.081(3)	0.061(2)	0.071(3)	-0.012(2)	0.042(2)	-0.0013(19)
O10	0.081(3)	0.108(3)	0.093(3)	-0.055(3)	0.045(2)	-0.015(2)
O23	0.054(2)	0.056(2)	0.065(2)	-0.0144(18)	0.0231(19)	-0.0097(18)
O25	0.098(3)	0.085(3)	0.079(3)	-0.018(2)	0.055(3)	-0.011(2)
N7	0.071(3)	0.050(3)	0.059(3)	-0.017(2)	0.035(3)	-0.014(2)
N11	0.074(3)	0.073(3)	0.061(3)	-0.014(3)	0.036(3)	-0.020(3)
C1	0.049(3)	0.037(3)	0.064(4)	0.011(3)	0.013(3)	-0.004(3)
C4	0.058(3)	0.048(3)	0.083(4)	-0.001(3)	0.030(3)	0.005(3)
C5	0.057(4)	0.045(3)	0.052(3)	0.002(3)	0.023(3)	0.001(3)
C8	0.073(4)	0.046(3)	0.069(4)	-0.013(3)	0.033(3)	-0.009(3)
C9	0.072(4)	0.058(4)	0.064(4)	-0.006(3)	0.041(3)	-0.007(3)
C12	0.101(5)	0.097(5)	0.089(5)	-0.044(4)	0.051(4)	-0.042(4)
C13	0.075(5)	0.159(7)	0.105(6)	-0.058(5)	0.056(4)	-0.035(5)
C14	0.060(5)	0.175(10)	0.185(12)	-0.115(9)	-0.015(6)	0.030(6)
C15	0.157(11)	0.286(17)	0.136(9)	0.113(11)	-0.017(7)	-0.130(11)
C16	0.069(5)	0.184(8)	0.097(6)	-0.029(6)	0.032(4)	-0.042(5)
C17	0.052(4)	0.149(7)	0.079(5)	-0.030(4)	0.019(3)	-0.009(4)
C18	0.069(5)	0.182(9)	0.173(8)	-0.070(7)	-0.005(5)	0.038(5)
C19	0.066(4)	0.089(4)	0.064(4)	-0.023(3)	0.018(4)	-0.007(3)
C20	0.057(4)	0.055(3)	0.058(4)	-0.009(3)	0.020(3)	-0.009(3)
C21	0.074(4)	0.099(5)	0.059(4)	0.005(3)	0.018(3)	-0.012(3)
C22	0.055(3)	0.063(4)	0.081(4)	-0.018(3)	0.023(3)	-0.014(3)
C24	0.062(4)	0.064(4)	0.050(3)	0.009(3)	0.029(3)	0.005(3)
C26	0.055(3)	0.041(3)	0.066(4)	0.008(3)	0.030(3)	-0.003(3)
C27	0.076(4)	0.068(4)	0.093(5)	0.011(4)	0.048(4)	0.002(3)
C28	0.090(5)	0.068(5)	0.126(6)	0.028(4)	0.072(5)	0.005(4)
C29	0.069(4)	0.047(4)	0.146(7)	0.009(4)	0.050(5)	-0.008(3)
C30	0.063(4)	0.045(3)	0.093(4)	0.006(3)	0.031(3)	-0.003(3)
C31	0.042(3)	0.034(3)	0.064(4)	0.003(3)	0.016(3)	0.001(2)
C32	0.051(3)	0.037(3)	0.045(3)	-0.002(3)	0.009(3)	-0.006(2)
C33	0.067(4)	0.044(3)	0.054(3)	-0.004(3)	0.013(3)	0.005(3)
C34	0.084(4)	0.062(4)	0.048(3)	0.000(3)	0.026(3)	0.003(3)
C35	0.084(4)	0.070(4)	0.043(3)	0.006(3)	0.022(3)	-0.007(3)
C36	0.069(4)	0.047(3)	0.046(3)	0.003(3)	0.016(3)	-0.003(3)
C37	0.047(3)	0.045(3)	0.042(3)	-0.007(3)	0.010(3)	-0.008(3)

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The Temperature Factor has the Form of $\text{Exp}(-T)$ Where
 $T = 8 \cdot (\pi^2) \cdot U \cdot (\sin(\text{Theta}) / \text{Lambda})^2$ for Isotropic Atoms
 $T = 2 \cdot (\pi^2) \cdot \sum_{ij} (h(i) \cdot h(j) \cdot U(i,j) \cdot \text{Astar}(i) \cdot \text{Astar}(j))$, for
Anisotropic Atoms. Astar(i) are Reciprocal Axial Lengths and
h(i) are the Reflection Indices.

Table S5 - Bond Distances (Å) for BECG 4159-293

O2	-C1	1.195(8)	N7	-H	0.84(6)
O3	-C1	1.341(6)			
O3	-C4	1.437(6)	C4	-H41	0.97
O6	-C5	1.225(6)	C4	-H42	0.97
O10	-C9	1.223(7)	C8	-H81	0.97
O23	-C22	1.461(6)	C8	-H82	0.97
O23	-C24	1.333(7)	C12	-H121	0.96
O25	-C24	1.213(7)	C12	-H122	0.96
N7	-C5	1.324(8)	C12	-H123	0.96
N7	-C8	1.451(7)	C13	-H131	0.97
N11	-C9	1.351(8)	C13	-H132	0.97
N11	-C12	1.463(7)	C14	-H141	0.93
N11	-C13	1.447(10)	C15	-H151	0.93
C1	-C37	1.490(8)	C16	-H161	0.97
C4	-C5	1.503(7)	C16	-H162	0.97
C8	-C9	1.500(9)	C17	-H171	0.98
C13	-C14	1.493(14)	C18	-H181	0.96
C14	-C15	1.038(18)	C18	-H182	0.96
C15	-C16	1.478(16)	C18	-H183	0.96
C16	-C17	1.525(12)	C19	-H191	0.93
C17	-C18	1.526(11)	C21	-H211	0.96
C17	-C19	1.511(10)	C21	-H212	0.96
C19	-C20	1.294(9)	C21	-H213	0.96
C20	-C21	1.518(7)	C22	-H221	0.97
C20	-C22	1.467(9)	C22	-H222	0.97
C24	-C26	1.490(7)	C27	-H271	0.93
C26	-C31	1.386(7)	C28	-H281	0.93
C26	-C27	1.383(8)	C29	-H291	0.93
C27	-C28	1.384(9)	C30	-H301	0.93
C28	-C29	1.366(12)	C33	-H331	0.93
C29	-C30	1.383(10)	C34	-H341	0.93
C30	-C31	1.395(7)	C35	-H351	0.93
C31	-C32	1.492(7)	C36	-H361	0.93
C32	-C37	1.402(7)			
C32	-C33	1.399(8)			
C33	-C34	1.377(8)			
C34	-C35	1.373(8)			
C35	-C36	1.385(8)			
C36	-C37	1.384(7)			

Table S6 - Bond Angles (Degrees) for BECG 4159-293

C1	-O3	-C4	117.0(4)	C5	-N7	-H	124(4)
C22	-O23	-C24	115.4(4)	C8	-N7	-H	113(4)
C5	-N7	-C8	122.6(5)				
C9	-N11	-C12	123.0(6)	O3	-C4	-H41	109.57
C9	-N11	-C13	119.9(5)	O3	-C4	-H42	109.61
C12	-N11	-C13	117.0(5)	C5	-C4	-H41	109.61
O3	-C1	-C37	110.8(5)	C5	-C4	-H42	109.50
O2	-C1	-C37	126.7(5)	H41	-C4	-H42	108.12
O2	-C1	-O3	122.4(5)	N7	-C8	-H81	109.79
O3	-C4	-C5	110.4(5)	N7	-C8	-H82	109.81
O6	-C5	-N7	124.5(5)	C9	-C8	-H81	109.73
O6	-C5	-C4	118.8(5)	C9	-C8	-H82	109.71
N7	-C5	-C4	116.7(5)	H81	-C8	-H82	108.24
N7	-C8	-C9	109.5(4)	N11	-C12	-H121	109.57
N11	-C9	-C8	118.3(5)	N11	-C12	-H122	109.55
O10	-C9	-N11	121.4(6)	N11	-C12	-H123	109.48
O10	-C9	-C8	120.2(6)	H121	-C12	-H122	109.46
N11	-C13	-C14	114.8(7)	H121	-C12	-H123	109.35
C13	-C14	-C15	147.0(13)	H122	-C12	-H123	109.42
C14	-C15	-C16	144.8(16)	N11	-C13	-H131	108.68
C15	-C16	-C17	114.8(8)	N11	-C13	-H132	108.53
C18	-C17	-C19	108.8(6)	C14	-C13	-H131	108.50
C16	-C17	-C19	113.1(6)	C14	-C13	-H132	108.54
C16	-C17	-C18	111.7(6)	H131	-C13	-H132	107.59
C17	-C19	-C20	130.2(6)	C13	-C14	-H141	106.51
C19	-C20	-C22	121.9(5)	C15	-C14	-H141	106.53
C19	-C20	-C21	124.4(6)	C14	-C15	-H151	107.66
C21	-C20	-C22	113.6(5)	C16	-C15	-H151	107.51
O23	-C22	-C20	108.4(4)	C15	-C16	-H161	108.53
O23	-C24	-O25	123.1(5)	C15	-C16	-H162	108.48
O25	-C24	-C26	124.1(5)	C17	-C16	-H161	108.61
O23	-C24	-C26	112.7(5)	C17	-C16	-H162	108.67
C24	-C26	-C31	125.3(5)	H161	-C16	-H162	107.51
C24	-C26	-C27	114.5(5)	C16	-C17	-H171	107.55
C27	-C26	-C31	120.2(5)	C18	-C17	-H171	107.75
C26	-C27	-C28	121.5(6)	C19	-C17	-H171	107.73
C27	-C28	-C29	118.8(7)	C17	-C18	-H181	109.42
C28	-C29	-C30	120.1(6)	C17	-C18	-H182	109.46
C29	-C30	-C31	121.8(6)	C17	-C18	-H183	109.45
C26	-C31	-C32	126.2(4)	H181	-C18	-H182	109.60
C30	-C31	-C32	116.2(5)	H181	-C18	-H183	109.43
C26	-C31	-C30	117.5(5)	H182	-C18	-H183	109.47
C33	-C32	-C37	117.2(5)	C17	-C19	-H191	114.90
C31	-C32	-C33	119.2(4)	C20	-C19	-H191	114.92
C31	-C32	-C37	123.6(4)	C20	-C21	-H211	109.45
C32	-C33	-C34	121.7(5)	C20	-C21	-H212	109.43
C33	-C34	-C35	120.3(5)	C20	-C21	-H213	109.53
C34	-C35	-C36	119.6(5)	H211	-C21	-H212	109.41
C35	-C36	-C37	120.4(5)	H211	-C21	-H213	109.54
C32	-C37	-C36	120.8(5)	H212	-C21	-H213	109.46
C1	-C37	-C32	121.6(4)	O23	-C22	-H221	110.03
C1	-C37	-C36	117.5(4)	O23	-C22	-H222	110.02

Table S6 (cont.) - Bond Angles (Degrees) for BECG 4159-293

C20	-C22	-H221	110.00
C20	-C22	-H222	109.97
H221	-C22	-H222	108.42
C26	-C27	-H271	119.30
C28	-C27	-H271	119.17
C27	-C28	-H281	120.49
C29	-C28	-H281	120.75
C28	-C29	-H291	119.93
C30	-C29	-H291	119.95
C29	-C30	-H301	119.06
C31	-C30	-H301	119.11
C32	-C33	-H331	119.04
C34	-C33	-H331	119.25
C33	-C34	-H341	119.87
C35	-C34	-H341	119.87
C34	-C35	-H351	120.22
C36	-C35	-H351	120.21
C35	-C36	-H361	119.83
C37	-C36	-H361	119.76