Vicinal Diamination of Terminal Olefins

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Dedicated to Professor *Rolf Huisgen* on the occasion of his 85th birthday

The present publication describes an efficient and mild three-step conversion of a terminal olefin **1** into the corresponding 1,2-diamine **5**. The sequence includes: azidoiodination, substitution with NaN_3, and catalytic hydrogenolysis. The terminal 1,2-diamine **5** was converted into its *cis*-dichloroplatinum(II) complex **6**.

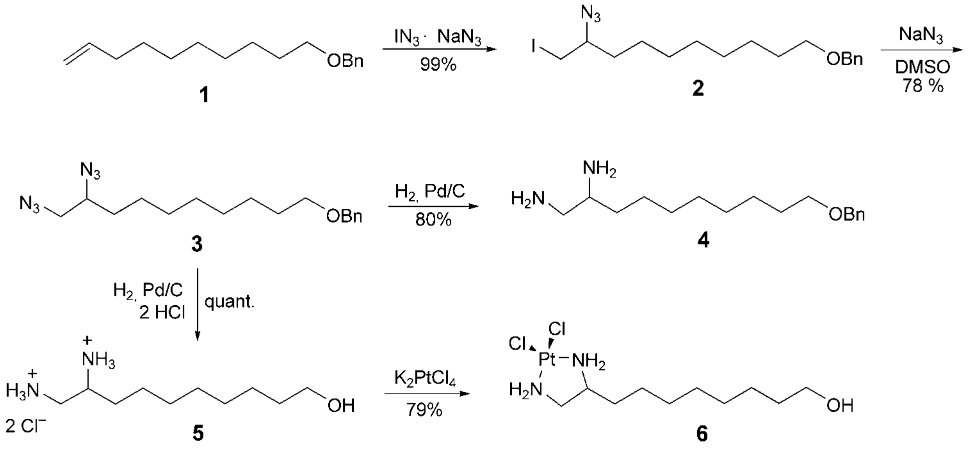
Introduction. – Reagents that oxidize olefins to vicinal diols belong to the standard tools in synthetic organic chemistry. On the other hand, the transformation of alkenes leading to the corresponding vicinal diamines is far more difficult to achieve and has been the subject of several investigations. An early stereospecific multistep conversion was realized *via* oxiranes or aziridines as intermediates [1]. Other methods were limited to conjugated dienes as starting materials [2] or led to *N*,*N*-disubstituted or *N*,*N*,*N*-trisubstituted 1,2-diamines as products [3]. A stereospecific 1,2-diamination of simple aliphatic olefins used a prepared nitrosyl-Co complex, gaseous NO, and $LiAlH_4$ [4].

During our investigations of new ether lipid-linked Pt complexes as potential antineoplastic agents [5], we evaluated several synthetic preparations leading to aliphatic 1,2-diamines.

Results and Discussion. – We wish to report here a convenient and efficient three-step process with conventional and commercially available reagents. It is exemplified by the following preparation: 10-(benzyloxy)dec-1-ene (**1**) reacted at 0° with the $IN_3 \cdot NaN_3$ complex [6] to give 2-azido-10-(benzyloxy)-1-iododecane (**2**; *Scheme*). – The $IN_3 \cdot NaN_3$ complex was prepared from iodine monochloride and NaN_3 according to the method of *Hassner* and co-workers [7]. A full conversion, **1** → **2**, was achieved when 1.3 equiv. of the $IN_3 \cdot NaN_3$ reagent was prepared *in situ* (without removal of NaCl and excess NaN_3) at $-15°$, followed by subsequent addition of olefin **1**. After workup, chromatographic purification of the crude product led to pure **2** in 72% yield. However, for further synthesis it was more convenient to proceed with the crude material **2** obtained in 99% yield.

Subsequently, the azido-iodo intermediate **2** was converted to 1,2-diazido-10-(benzyloxy)decane (**3**) with NaN_3. Initially, when the conversion **2** → **3** was carried out in DMF with Bu_4NBr as phase-transfer catalyst, the reaction required 48 h at 100° for completion. *Alvarez* and *Alvarez* [8] suggested to prepare alkyl azides in DMSO, which dissolves NaN_3 much better than most other dipolar aprotic solvents. Indeed, in DMSO

Scheme



the above reaction proceeded smoothly at room temperature within 20 h. After workup, chromatographic purification on silica gel gave pure **3** in 78% yield.

Aliphatic amines can poison hydrogenation catalysts [9]. This might be the reason why the hydrogenolysis of **3** in EtOH Pd/C led to 10-(benzyloxy)decane-1,2-diamine (**4**), without removing the Bn protection group. However, we found that complete hydrogenolysis could be easily achieved upon addition of 2 equiv. of HCl. This procedure quantitatively yielded pure 9,10-diaminodecan-1-ol dihydrochloride (**5**, m.p. 125–128°).

Finally, the diamino-alcohol **5** reacted with K_2PtCl_4 at 65° to give the yellow platinum complex **6** in 79% yield.

Different from earlier methods, our three-step sequence avoids intermediates, delicate to handle, such as aziridines. An other advantage lies in the mild reduction process of the vicinal diazide intermediate **3** with H_2, facilitating workup of the diamines **4** or **5**. In our hands, the above sequence was the method of choice for the conversion of terminal aliphatic olefins into vicinal diamines.

Experimental Part

General. Reactions were carried out in dry glassware and under dry N_2. Reagents were purchased from *Fluka* and *Aldrich*. Dry MeCN and DMSO (stored over molecular sieves) were purchased from *Fluka* (Product Nos. 00695 and 41647) and not purified further. THF was freshly distilled over $LiAlH_4$ before use. TLC was performed on 0.2-mm *Merck silica gel-60-F*$_{254}$ plates. TLC plates were investigated for UV absorption, after staining in the I_2 chamber and/or after spraying with a 10% soln. of molybdophosphoric acid (MPA) in EtOH, followed by development with a heat gun. From concentrated solns. a sample was diluted with an appropriate solvent before spotting. From DMSO solns. small samples were diluted with hexane/AcOEt 9 : 1 and washed with a few drops of H_2O prior to spotting on TLC. IR Spectra were recorded on a *Perkin-Elmer 1420-Ratio-Recording* and on a *Nicolet 520* FT-IR-spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a *Bruker ARX-300* and a *Varian VXR-400-S* spectrometer. Reaction monitoring was performed on a *Varian Mercury-200* spectrometer. Mass spectra were recorded on a *Finigan MAT-90* and a *Finigan MAT-90-Q* spectrometer. The method of ionization is indicated with the reported spectral data. Electron ionization (EI), chemical ionization

(CI), and fast atom bombardment (FAB) were the applied methods. 2-Nitrobenzyl alcohol was used as sample matrix and the reacting gas was isobutane. The molecular peak and characterized fragment peaks are given as well as all signals, having a relative intensity of 10% or more. Elemental analysis was performed in a *Heraeus (Universal Standard)* apparatus.

10-(Benzyloxy)dec-1-ene (**1**). In a 100-ml three-necked flask, fitted with a magnetic stirrer, thermometer, rubber septum, and a bubbler, to a dispersion of NaH in mineral oil (60% NaH, 2.00 g, 50 mmol) in dry THF (40 ml) were added BnBr (7.66 g, 44.8 mmol) and dec-9-en-1-ol within 5 min at r.t. The reaction mixture was allowed to stir at r.t. overnight until gas evolution came to an end. The colorless mixture was poured on ice water and extracted twice with portions (400 ml) of AcOEt. The combined AcOEt layers were washed twice with portions (400 ml) of sat. aq. NaCl, dried ($MgSO_4$), filtered, and the solvent was removed *in vacuo* to leave a yellow oil (12.00 g). Chromatographic purification on silica gel (450 g; 0.063 – 0.200 mm) with toluene (10 *Fractions*, 400 ml each) gave **1** as a colorless oil (10.03 g, 91 %) from *Fr. 6* and *7*, after drying in high vacuum. R_f (hexane/AcOEt 9 : 1) 0.5. IR (CH_2Cl_2): 3030*w*, 2930vs, 2850*s*, 1725*w*, 1635*w*, 1490*w*, 1450*m*, 1360*w*, 1200*w*, 1095*m*, 1025*w*, 995*w*, 910*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.15 – 1.45 (*m*, $CH_2(4)$, $CH_2(5)$, $CH_2(6)$, $CH_2(7)$, $CH_2(8)$); 1.53 – 1.68 (*m*, H–C(9)); 1.95 – 2.10 (*m*, $CH_2(3)$); 3.45 (*t*, $^3J = 6.6$, $CH_2(10)$); 4.48 (*s*, $PhCH_2$); 4.89 – 4.95 (*m*, $^3J = 10.2$, $^2J = 2.2$, 1 H–(1)); 4.95 – 5.03 (*m*, $^3J = 17.1$, $^2J = 2.2$, 1 H–C(1)); 5.80 (*ddt*, $J = 17.1$, 10.2, 6.6, H–C(2)); 7.18 – 7.40 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 26.2 (C(8)); 28.9, 29.1, 29.4, 29.8 (C(2, 4, 5, 6, 7, 9)); 33.8 (C(3)); 70.5 (C(10)), 72.8 ($PhCH_2$), 114.1 (C(1)); 127.4, 127.6, 128.3, 138.7, 139.1 (arom. C). FAB-MS: 246 (2, M^+), 245, (24, $[M - H]^+$), 147 (12), 123 (23), 111 (20), 109 (30), 107 (62), 105 (28), 103 (51), 101 (64), 93 (15), 91 (98, $C_7H_7^+$), 85 (28), 83 (70), 81 (50), 79 (20), 77 (11), 74 (24), 71 (44), 69 (86), 67 (35), 57 (78), 55 (100), 43 (56), 41 (42). Anal. calc. for $C_{17}H_{26}O$ (246.39): C 82.87, H 10.64; found: C 82.29, H 10.92.

2-Azido-10-(benzyloxy)-1-iododecane (**2**). In a 25-ml *Schlenk* flask, fitted with a magnetic stirrer and a rubber septum, to a suspension of NaN_3 (211 mg, 3.25 mmol) in MeCN (1.0 ml) was added a soln. of ICl (211 mg, 1.30 mmol) in MeCN (1.0 ml) at – 15°. After 10 min, neat **1** (246 mg, 270 μl, 1.00 mmol) was added at – 15° by means of a precision syringe within 15 min, and the mixture allowed to warm to r.t. Stirring was continued at r.t. After 2 h, TLC indicated a full conversion. Hexane (15 ml) and H_2O (15 ml) were added, and the violet color (I_2) of the org. layer was removed by addition of a few drops of a 10% aq. soln. of sodium thiosulfate. The org. layer was washed again with H_2O (15 ml), and the aq. layers were re-extracted with hexane (10 ml). The combined org. solns. were dried ($MgSO_4$), filtered, and the solvent was removed *in vacuo*, and the residue was dried in high vacuum to afford a colorless oil (412 mg, 99%). Chromatographic purification on silica gel (10.0 g; 40 – 60 μm) with hexane/AcOEt 95 : 5 (15 *Fractions*, 4.5 ml each) gave pure **2** (299 mg, 72%) as a colorless oil from *Fr. 4 – 9*. R_f (hexane/AcOEt 9 : 1) 0.4. IR(CH_2Cl_2): 3030*w*, 2940*s*, 2860*s*, 2100*s*, 1455*m*, 1365*m*, 1260*s*, 1205*w*, 1190*w*, 1105*s*, 1030*w*, 910*w*, 890*w*, 820*w*, 670*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.18 – 1.63 (*m*, $CH_2(3)$, $CH_2(4)$, $CH_2(5)$, $CH_2(6)$, $CH_2(7)$, $CH_2(8)$ $CH_2(9)$); 3.15 – 3.28 (*m*, $CH_2(1)$), 3.28 – 3.41 (*m*, H–C(2)); 3.45 (*t*, $^3J = 6.6$, $CH_2(10)$), 4.49 (*s*, $PhCH_2$); 7.20 – 7.35 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 8.5 (C(1)); 25.7 (C(4)); 26.1 (C(8)); 29.1, 29.1, 29.3, 29.7 (C(5, 6, 7, 9)), 34.4 (C(3)); 62.6 (C(2)); 72.8 ($PhCH_2$); 127.4, 127.5, 128.3, 138.7 (arom. C). CI-MS: 416 (0.4, $[M + H]^+$), 389 (16), 388 (100, $[416 - N_2]$), 282 (15), 262 (10), 260 (11, $[M - N_2 - I]^+$), 246 (15, $[260 - CH_2]$), 232 (13, $[246 - N]$), 131 (13), 91 (34, $C_7H_7^+$). Anal. calc. for $C_{17}H_{26}N_3OI$: C 49.16, H 6.31, N 10.12; found: 48.90, H 6.14, N 10.01.

1,2-Diazido-10-(benzyloxy)decane (**3**). In a 25-ml *Schlenk*-flask, fitted with a magnetic stirrer and a balloon filled with N_2, a suspension containing **2** (crude reaction product; 412 mg, 0.99 mmol) and NaN_3 (97 mg, 1.5 mmol) in DMSO (1.0 ml) was stirred at r.t. for 20 h. TLC indicated a complete conversion. The colorless suspension was transferred into a separatory funnel with hexane (20 ml) and H_2O (20 ml). The org. layer was washed with two additional portions of H_2O (20 ml each), and the aq. layers were re-extracted with hexane (10 ml). From the combined hexane solns. the solvent was removed *in vacuo*, and the remaining colorless oil (315 mg, 95%, after drying in high vacuum) was purified by column chromatography (CC) on silica gel (9.0 g; 40 – 60 μm) with hexane/AcOEt 95 : 5 (15 *Fractions*, 9 ml each). Pure **3** was obtained from *Fr. 5 – 10* as a colorless oil (257 mg, 78%, after drying in high vacuum). It solidified at – 20°. M.p. 10 – 15°. R_f (hexane/AcOEt 9 : 1) 0.3. IR (CH_2Cl_2): 3030*w*, 2930*s*, 2860*s*, 2100vs, 1715*w*, 1490*w*, 1445*w*, 1350*m*, 1260*s*, 1100*s*, 1030*w*, 915*w*, 660*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.18 – 1.70 (*m*, $CH_2(3)$, $CH_2(4)$, $CH_2(5)$, $CH_2(6)$, $CH_2(7)$, $CH_2(8)$, $CH_2(9)$); 3.20 – 3.44 (*m*, $CH_2(1)$, H–C(2)); 3.46 (*t*, $J = 6$, $CH_2(10)$); 4.50 (*s*, $PhCH_2$); 7.20 – 7.40 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 25.9 (C(4)); 26.1 (C(8)); 29.2, 29.3, 29.3, 29.7 (C(5, 6, 7, 9)); 31.8 (C(3)); 54.8 (C(1)); 62.1 (C(2)); 70.5 (C(10)); 72.9 ($PhCH_2$); 127.5, 127.6, 128.3, 138.7 (arom. C). CI-MS: 331 (1, $[M + H]^+$), 330 (0.2, M^+), 303 (27, $[331 - N_2]$), 282 (21), 275 (47, $[303 - N_2]$), 248 (15), 247 (16), 246 (100, $[275 - NCH_3]$), 170 (21), 154 (10), 138 (10), 107 (12, $[C_7H_7O]^+$), 91 (47, $C_7H_7^+$). Anal. calc. for $C_{17}H_{26}N_6O$: C 61.79, H 7.93, N 25.43; found C 62.19, H 8.11, N 24.93.

10-(Benzyloxy)decane-1,2-diamine (**4**). In a hydrogenation apparatus, a soln. of **3** (247 mg, 0.75 mmol) in MeOH (10 ml) was hydrogenolyzed with Pd/C (10 % Pd, 120 mg) at r.t. for 30 min. The catalyst was removed from the mixture by filtration through a *G-4* glass filter. The residue was washed with MeOH (5 ml), and the combined MeOH solns. were evaporated *in vacuo*, and the residue was dried in high vacuum for 6 h: **4** (435 mg, 80%). Colorless oil. R_f (AcOEt/MeOH/NH_3 (25%) 7:3:0.5; UV and MPA staining) 0.2. IR (CH_2Cl_2): 3480*w*, 3420*w*, 3030*w*, 2930v*s*, 2860*s*, 1715*w*, 1580*w*, 1570*w*, 1490*w*, 1450*w*, 1365*w*, 1265*m*, 1205*w*, 1100*s*, 1030*w*, 820*w*, 610*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.13–1.73 (*m*, CH_2(3), CH_2(4), CH_2(5), CH_2(6), CH_2(7), CH_2(8), CH_2(9)); 2.42 (*dd*, $J = 12.0$, 8.0, 1 H–C(1)); 2.55–2.67 (*m*, $J = 8.0$, $J = 3.0$, 1 H–C(2)); 2.72 (*dd*, $J = 12.0$, 3.0, 1 H–C(1)); 3.46 (*t*, $J = 6.6$, CH_2(10)); 4.49 (*s*, PhCH_2); 7.20–7.40 (*m*, 5 arom. H). ^{13}C-NMR (CH_2Cl_2, 75 MHz): 26.2 (C(4)); 26.2 (C(8)); 29.4, 29.7, 29.8 (C(5, 6, 7, 9)); 35.7 (C(3)); 48.6 (C(1)); 53.6 (C(2)); 70.5 (C(10)); 72.8 (PhCH_2); 127.4, 127.6, 128.3, 138.7 (arom. C). EI-MS: 279 (1, $[M + H]^+$), 278 (0.1, M^+), 249 (15, [279 − CH_4N]), 248 (93, $[M - CH_4N])^+$, 149 (13), 91 (100, $C_7H_7^+$), 56 (12).

9,10-Diaminodecan-1-ol Dihydrochloride (**5**). In a hydrogenation apparatus, a soln. of **3** (247 mg, 0.75 mmol in MeOH (10 ml) was hydrogenolyzed with Pd/C (120 mg) at r.t. for 30 min. Aq. HCl (1.00N soln.; 1.5 ml, 1.5 mmol) and fresh catalyst (70 mg) were added, and hydrogenolysis was continued for 24 h at r.t. Then, TLC indicated that starting material **3** and intermediate **4** had disappeared. The catalyst was removed from the mixture by filtration through a *G-4* glass filter. The residue was washed with MeOH (5 ml), and the combined MeOH solns. were evaporated *in vacuo*, and the residue was dried in high vacuum over P_2O_5 for 2 days: **5** (196 mg, 100 %). Colorless solid. M.p. 125–128°. R_f ((AcOEt/MeOH/NH_3 (25%) 7:3:0.5; only MPA staining) 0.1. IR (KBr): 3340*m*, 3160*s*, 3020*s*, 2930v*s*, 2850*s*, 1625*m*, 1610*m*, 1569*m*, 1532*m*, 1490*m*, 1465*m*, 1454*m*, 1405*w*, 1381*w*, 1332*w*, 1305*w*, 1193*w*, 1150*w*, 1094*w*, 1060*s*, 1040*m*, 1020*m*, 994*w*, 940*w*, 886*w*, 850*w*, 812*w*, 725*w*, 688*w*, 489*w*, 463*w*. ^{1}H-NMR (D_2O, 300 MHz): 1.14–1.83 (*m*, CH_2(2), CH_2(3), CH_2(4), CH_2(5), CH_2(6), CH_2(7), CH_2(8)); 3.31 (*d*, $J = 6.3$, CH_2(10)); 3.47–3.67 (*m*, 1 H–C(9), CH_2(1)). ^{13}C-NMR (D_2O, 75 MHz): 24.4 (C(7)); 25.4 (C(3)); 28.5, 28.6, 28.7, 30.4, 31.6 (C(2, 4, 5, 6, 8)); 41.2 (C(10)); 49.9 (C(9)); 62.3 (C(1)).

(9,10-Diamino-1-decanol)dichloroplatinum(II) (**6**). In a 25-ml round-bottom flask, fitted with a magnetic stirrer, a soln. of **5** (165 mg, 0.63 mmol) in H_2O (5 ml) was heated to 65°, and K_2PtCl_4 (262 mg, 0.63 mmol), dissolved in H_2O (2 ml) was added. Over a 15-min period, aq. NaOH soln. (1.00N; 1.10 ml, 1.10 mmol) was added from a syringe at 65°. The initially red reaction soln. (pH 2) was decolorized during this process with simultaneous precipitation of a pale yellow solid. The mixture was not allowed to get alkaline in order to avoid precipitation of grey-black $PtO \cdot H_2O$. At the end of the reaction, the pH was 6. The suspension was kept in an ice bath for 10 min, and then the precipitate was separated by centrifugation. The solvent was removed by decantation, and the yellow solid was washed twice with portions (4 ml each) of cold H_2O. After drying in high vacuum, pure **6** (228 mg, 79%) was obtained. Pale yellow solid, M.p. >220°. IR (KBr): 3450*s*, 3202*s*, 3121*m*, 2931*s*, 2857*s*, 1630*m*, 1561*m*, 1465*m*, 1460*m*, 1400*w*, 1383*w*, 1306*w*, 1266*w*, 1189*m*, 1131*w*, 1107*w*, 1055*m*, 1021*m*, 929*w*, 882*w*, 764*m*, 723*w*, *628w*, 574*m*, 538*m*, 513*m*, 449*m*, 310*m*. ^{1}H-NMR ((D_6)DMSO, 400 MHz): 1.12–1.32 (br. *s*, CH_2(3), CH_2(4), CH_2(5), CH_2(6), CH_2(7)); 1.32–1.45 (*m*, CH_2(2)); 1.45–1.60 (*m*, CH_2(8), OH); 2.12–2.45 (*m*, 1 H–C(10)); 2.52–2.72 (*m*, 1 H–C(10)); 2.72–2.95 (*m*, 1 H–C(9)); 3.31–3.39 (*m*, CH_2(1)); 4.98–5.60 (*m*, 2 NH_2). ^{13}C-NMR ((D_6)DMSO, 100 MHz): 25.6 (C(3)); 26.1 (C(7)); 28.8, 28.9, 28.9 (C(4, 5, 6)); 30.8 (C(8)); 32.5 (C(2)); 50.8 (C(10)); 59.8 (C(9); 60.8 (C(1)). Anal. calc. for $C_{10}H_{24}Cl_2N_2OPt$: C 26.44, H 5.33, N 6.17; found: C 26.55, H 5.20, N 5.86.

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