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Synthetic Transformation of Abietic Acid III[a]. Photoconversion of Diene Adducts

Dieter Hofner[1] and **Ernst Haslinger**[2,*]

[1] Institute of Pharmaceutical Chemistry, University of Graz, A-8010 Graz, Austria
[2] CU Chemie Uetikon GmbH, D-77933 Lahr, Germany

Summary. *Diels-Alder* addition of 2-chloroacrylonitrile to the abietic acid skeleton affords, *via* an α-chloronitrile adduct, the tetracyclic β,γ-unsaturated ketone **1**. Photochemical conversions of **1** to **2** and **3** are described. The cyclopropane ring of **3** is cleaved by a *Birch* reduction yielding **4**.

Keywords. Abietic acid diene adducts; Photochemistry; Oxa-di-π-methane rearrangement; *Birch* reduction.

Synthetische Umwandlung des Abietinsäuregerüstes, 3. Mitt. Photochemische Umwandlung von Dien-Addukten

Zusammenfassung. *Diels-Alder*-Addition von 2-Chloracrylnitril an das Abietinsäuregerüst führt über das entsprechende α-Chlornitril-Addukt zu einem tetracyclischen Keton (**1**). Dieses kann photochemisch in **2** bzw. **3** umgewandelt werden. *Birch*-Reduktion öffnet den Cyclopropanring von **3** und führt zum tetracyclischen Keton **4**.

Introduction

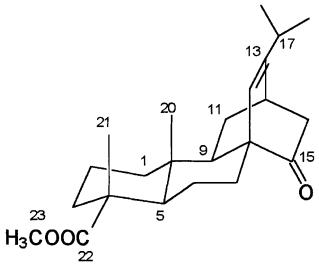
In previous publications we have described the synthesis of β,γ-enone **1** by *Diels-Alder* addition of 2-chloroacrylonitrile to abietic acid methyl ester and subsequent treatment of the adduct with NaOH [1, 2]. β,γ-Enones have two chromophores and are capable of undergoing a variety of photochemical reactions, *e.g.* 1,2- and 1,3-acyl migration and intramolecular oxetane formation [3].

Results and Discussion

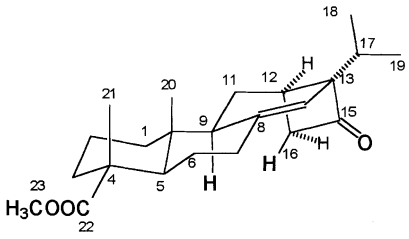
Irradiation without sensitizer

Irradiation of **1** in *THF* or diethyl ether with a mercury vapour lamp yielded, depending on the irradiation time, a mixture of resin acid esters and cyclobutanone **2** in different ratios. After three days, only resin acids could be detected.

[a] For part I see [1], for part II see [2].
* Corresponding author



1



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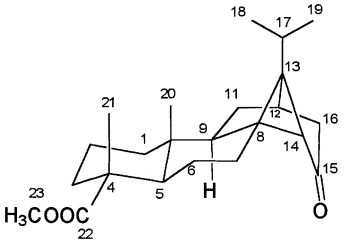

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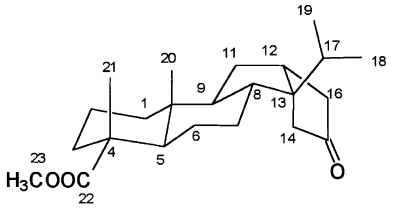

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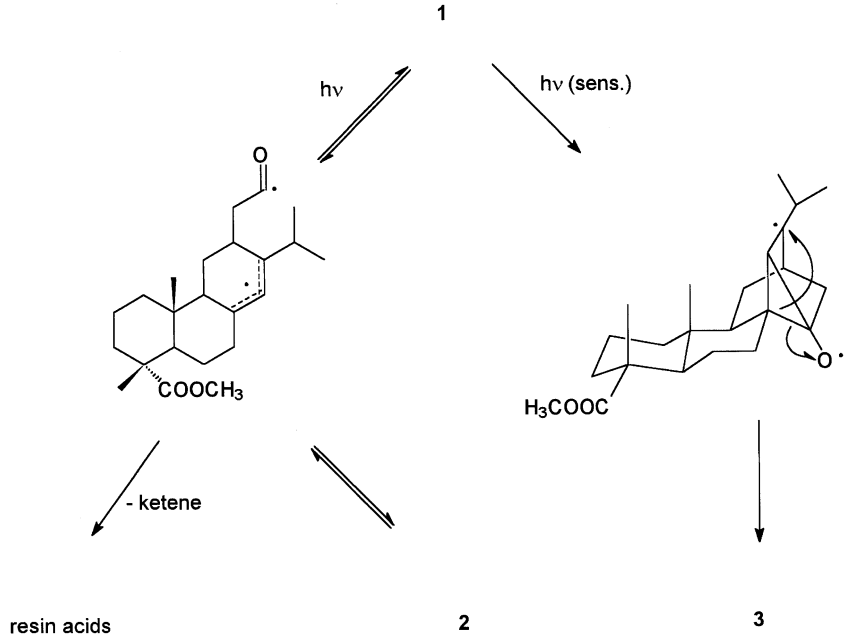
Scheme 1

From the FD mass spectrum of **2** a molecular mass of 358 was determined. The IR spectrum shows a carbonyl stretching vibration at 1770 cm^{-1} which is typical for cyclic four membered ketones [4]. The resonances of the cyclobutane protons (H-16) appear at $\delta = 2.71$ and 2.64 ppm. Both are coupled to H-12 ($J = 8.8$ Hz) and exhibit a geminal coupling constant of 17.0 Hz typical for the cyclobutanone structure [5]. The signal of H-12 has only small couplings to both protons at C-11. A diaxial arrangement between H-11_{ax} and H-12 can therefore be ruled out. COSY correlations from the olefinic proton H-14 to H-9 and to both protons on C-7 served to determine the position of the double bond. NOE correlations between H-16_{endo} and H-9, which shows a further NOE cross peak with H-5, and the correlation of H-12 with one of the isopropyl methyl groups have been used to derive the relative configuration of C-12 and C-13. In a COLOC spectrum (7 Hz), long range couplings between the CO resonance at $\delta = 209.6$ ppm and H-14, H-17, and both H-16 are observed.

Sensitized irradiation

When irradiation is performed in the presence of a sensitizer, the β,γ-enone **1** is converted to the cyclopropane derivative **3** *via* an 1,3-acylmigration. Mechanistic studies have revealed that the molecules most likely react from a low lying π-π triplet state [3, 6] in a stepwise process, the acylgroup migrating to yield an intermediate biradical [7, 8]. This reaction is of considerable synthetic utility for the construction of a variety of tricyclic compounds with high enantioselectivity or as a key step in the synthesis of natural products [9, 11].



Scheme 2

If a 1% solution of **1** in acetone (sensitizer) is irradiated for several days, cyclopropyl ketone **3** is obtained in high yield. No olefinic resonances are observed in the ^{13}C NMR spectrum. The COLOC spectrum (7 Hz) shows correlations from the bridgehead atom C-13 to H-9, H-11β, H-16α, and the methyl protons of the isopropyl group.

A possible reaction path is given in Scheme 2. Direct irradiation leads from a singulet state to a 1,3 acyl shift [12, 13]. Sometimes a biradical intermediate has been discussed, but also a concerted stereospecific mechanism has been proposed [14–17]. The reversible recombination of the diradical gives product **2**. The irreversible loss of ketene in a competitive reaction yields a mixture of abietic acid isomers. During irradiation in the presence of a sensitizer **1** will be excited to a triplet state which undergoes an 1,2-acyl migration in the form of an oxa-di-π-methane rearrangement [3, 18–20] to **3**.

Birch reduction of **3**

Treating cyclopropyl ketone **3** with Li and ^{t}butanol in liquid ammonia [19] affords the tetracyclic ketone **4** in 84% yield. The chemo-, regio-, and stereoselectivity was achieved by low temperature (−70°C) and short reaction time (2 min). The M^+ peak is observed at $m/z = 360$ in the mass spectrum and shows that two hydrogen atoms have been added to the molecule. From the COSY spectrum it could be shown that they are attached to carbons 8 and 14. A NOESY spectrum shows that H-11$_{ax}$ and CH_3-20 as well as H-7$_{ax}$ and H-14$_{endo}$ are close in space. From the latter correlation we have derived the configuration of C-8 as *R*. This result is confirmed by the resonance of H-8 which is heavily overlapped in the 1D ^1H NMR

spectrum but can be clearly observed in a shift correlation spectrum. This cross signal shows two large couplings (*ca.* 13 Hz) to H-9 and to H-7$_{ax}$ proving that H-8 is in axial position and C-8 has *R* configuration.

Experimental

Analytical methods

Preparative thin layer chromatography: Chromatotron 8924 Harrison Research, 1 mm Kieselgel 60 PF_{254} (Merck) with gypsum; column chromatography (CC): Kieselgel 60 (Merck, 70–230 mesh), pore-diameter 60 Å; thin-layer chromatography (TLC): TLC sheets, ALUGRAM®; SIL G/UV_{254} (Machery-Nagel) and TLC sheets POLYGRAM®, SIL G/UV_{254} (Machery-Nagel); solvents frequently used: cyclohexane (CH) and AcOEt; the substances were detected in UV light at 254 nm and by spraying with molybdatophosphoric acid or methanol/sulfuric acid (9:1) and subsequent heating. Melting points: melting point apparatus SM-LUX (Leitz), uncorrected; optical rotation: polarimeter 241 MC (Perkin Elmer); IR spectra: spectrometer 883 (Perkin Elmer); UV/Vis: Lambda 17 UV/Vis-spectrometer (Perkin Elmer); NMR spectra: Bruker AC 200 and AMX 500 (300 K), 5 mm tubes, solvent resonance as internal standard. Before NOE experiments were performed, dissolved oxygen was removed by bubbling Ar through the solutions. ^{1}H and ^{13}C resonances were assigned using ^{1}H, ^{1}H and ^{1}H, ^{13}C correlation spectra (sometimes optimized for small CH-couplings) and are numbered as given in the formulas. MS: Varian MAT 711 spectrometer (70 eV electron impact and field desorption); elementary analyses: Laboratory for Microanalysis, Institute of Physical Chemistry of the University of Vienna, and Sektion Analytik, University of Ulm; photochemical equipment: Mercury vapour medium pressure lamp Heraeus TQ 150 Original Hanau, 150 W.

Methyl (4R-(4α,4aα,7aβ,9aβ,10aα,10bβ))-4,10b-Dimethyl-7a-(1-methylethyl)-8-oxo-1,2,3,4,4a,5,6,7a,8,9,9a,10,10a,10b-tetradecahydro-cyclobuta[b]phenanthrene-4-carboxylate (**2**)

Through a solution of 160 mg (0.45 mmol) **1** in 10 ml dry *THF* Ar was bubbled for 15 min, and the oxygen free solution was irradiated with a medium pressure mercury vapour lamp in a quartz vessel for 18 h. After evaporation and CC (CH/AcOEt = 30:1), 10 mg of a mixture of resin acid esters and 70 mg **2** (44%) were obtained. Colourless oil; $R_f = 0.37$ (CH/AcOEt = 6:1); $[\alpha]_D^{20} = -318.0$ ($c = 0.1$, $CHCl_3$); IR (neat); $\nu = 2922$ (m), 1770 (vs), 1727 (vs), 1462 (m), 1245 (s), 1130 (s) cm^{-1}; UV (MeOH): λ_{max} (lgε) = 210 (3.049), 306, (3.049) nm; ^{1}H NMR ($CDCl_3$): $\delta = 0.80$ (s, 3H, 20-H), 0.84 (d, $J = 6.8$ Hz, 3H, 18-H/19-H), 0.91 (d, $J = 6.8$ Hz, 3H, 19-H/18-H), 1.15 (m, 1H, 6-H$_{eq}$), 1.18 (m, 1H, 1-H$_{ax}$), 1.19 (s, 3H, 21-H), 1.39 (ddd, $J = 13.8$ Hz, $J = 10.4$ Hz, $J = 4.5$ Hz, 1H, 11-H$_{ax}$), 1.45–1.6 (m, 2H, 2-H), 1.48 (m, 1H, 6-H$_{ax}$), 1.57 (m, 1H, 3-H$_{eq}$), 1.68 (m, 1H, 1-H$_{eq}$), 1.73 (m, 1H, 3-H$_{ax}$), 1.80 (ddd, $J = 13.8$ Hz, $J = 7.2$ Hz, $J = 2.6$ Hz, 1H, 11-H$_{eq}$), 1.87 (dd, $J = 10.4$ Hz, $J = 7.2$ Hz, 1H, 9-H), 1.95 (sept, $J = 6.8$ Hz, 1H, 17-H), 2.01 (dd, $J = 12.5$ Hz, $J = 2.6$ Hz, 1H, 5-H), 2.16 (m, 1H, 7-H$_{ax}$), 2.32 (ddd, $J = 15.0$ Hz, $J = 4.8$ Hz, $J = 1.8$ Hz, 1H, 7-H$_{eq}$), 2.45 (m, 1H, 12-H), 2.64 (dd, $J = 17.0$ Hz, $J = 8.8$ Hz, 1H, 16-Hβ), 2.71 (dd, $J = 17.0$ Hz, $J = 8.8$ Hz, 1H, 16-Hα), 3.63 (s, 3H, 23-H), 5.07 (s_{br}, 1H, 14-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 15.2$ (q, C-20), 17.1 (q, C-21), 17.8 (q, C-18/C-19), 18.0 (q, C-19/C-18), 18.1 (t, C-2), 21.4 (t, C-11), 24.2 (t, C-6), 25.8 (d, C-12), 31.0 (d, C-17), 35.5 (t, C-7), 36.9 (t, C-3), 37.1 (s, C-10), 38.7 (t, C-1), 45.5 (t, C-16), 46.1 (d, C-9), 47.5 (s, C-4), 48.9 (d, C-5), 51.9 (q, C-23), 70.9 (s, C-13), 118.0 (d, C-14), 142.2 (s, C-8), 179.1 (s, C-22), 209.6 (s, C-15) ppm; MS (FD): *m/z* (%) = 358 (100) [M^+]; MS (70 eV): *m/z* (%) = 358 (12) [M^+], 316 (90), 299 (38), 239 (50), 187 (49), 146 (83), 121 (100), 91 (75), 43 (73); $C_{23}H_{34}O_3$ (358.5); calc.: C 77.05, H 9.56; found: C 77.02, H 9.57.

Methyl (2aR,2bS,4aR,5R,8aR,8bR,9aR,9bR)-5,8a-Dimethyl-9b-(1-methylethyl)-2-oxo-perhydrocyclopropa[1,6]pentaleno[2,1-a]naphthalene carboxylate (**3**)

An oxygen free solution of 300 mg (0.84 mmol) **1** in 40 ml dry acetone under Ar was irradiated by a mercury vapour medium pressure lamp for 2 days. Evaporation and CC over silica (CH/AcOEt = 6:1) gave 250 mg (83%) **3** (colourless oil).

$R_f = 0.29$ (CH/AcOEt = 6:1), 0.43 (CH/AcOEt = 3:1); $[\alpha]_D^{20} = +24.6$ ($c = 0.1$, $CHCl_3$); IR (KBr): $\nu = 2952$ (s), 1728 (vs), 1461 (m), 1243 (s), 1136 (m) cm^{-1}; UV (MeOH): λ_{max} (lgε) = 216 (3.699), 281 (1.952) nm; ^{1}H NMR (C_6D_6): $\delta = 0.70$ (s, 3H, 20-H), 0.74 (m, 1H, 1-H$_{ax}$), 0.81 (d, $J = 6.8$ Hz, 3H, 18-H/19-H), 0.82 (d, $J = 6.8$ Hz, 3H, 19-H/18-H), 0.96 (m, 1H, 7-H$_{eq}$), 1.01 (dd, $J = 12.4$ Hz, $J = 6.4$ Hz, 1H, 11-Hβ), 1.19 (m, 1H, 1-H$_{eq}$), 1.20 (m, 1H, 17-H), 1.2–1.4 (m, 2H, 2-H), 1.28 (s, 3H, 21-H), 1.34 (s$_{br}$, 1H, 14-H), 1.37 (m, 1H, 6-H$_{eq}$), 1.55 (m, 1H, 3-H$_{eq}$), 1.55 (m, 1H, 6-H$_{ax}$), 1.56 (m, 1H, 11-Hα), 1.57 (m, 1H, 7-H$_{ax}$), 1.62 (d, $J = 17.2$ Hz, 1H, 16-Hα), 1.74 (dd, $J = 10.4$ Hz, $J = 6.4$ Hz, 1H, 9-H), 1.78 (td, $2\times J = 13.1$–13.3 Hz, $J = 3.5$ Hz, 1H, 3-H$_{ax}$), 2.01 (dd, $J = 10.9$ Hz, $J = 6.8$ Hz, 1H, 5-H), 2.22 (dd, $J = 17.2$ Hz, $J = 9.3$ Hz, 1H, 16-Hβ), 2.33 (m, 1H, 12-H), 3.35 (s, 3H, 23-H) ppm; ^{13}C NMR (C_6D_6): $\delta = 17.0$ (q, C-20), 17.2 (q, C-21), 17.9 (t, C-2), 19.5 (q, C-18/C-19), 20.8 (q, C-19/C-18), 21.1 (t, C-6), 25.9 (t, C-7), 27.6 (d, C-17), 36.0 (s, C-10), 36.7 (d, C-12), 37.0 (t, C-3), 38.2 (t, C-11), 41.1 (t, C-1), 46.2 (s, C-8), 46.4 (d, C-5), 46.8 (s, C-4), 49.0 (t, C-16), 51.5 (q, C-23), 52.2 (d, C-14), 56.7 (d, C-9), 58.9 (s, C-13), 177.9 (s, C-22), 212.2 (s, C-15) ppm; MS (70 eV): *m/z* (%) = 358 (17) [M^+], 316 (100), 299 (35), 239 (31), 187 (26), 146 (63), 121 (48), 91 (49), 43 (33); $C_{23}H_{24}O_3$ (358.5); calc.: C 77.05, H 9.56; found: C 77.06, H 9.55.

Methyl (3aR-(3aα,3bα,5aβ,6β,9aα,9bβ,10aα))-7,9a-Dimethyl-3b-(1-methylethyl)-2-oxo-perhydropentaleno[2,1-a]naphthalene-6-carboxylate (**4**)

A solution 120 mg (0.33 mmol) **3** in 2 ml dry *THF*, 0.2 ml dry ^{t}BuOH and 50 mg (7.2 mmol) Li were added sucessively to 30 ml liquid NH_3 at −70°C. After 2 min, the reaction was quenched by addition of 300 mg NH_4Cl. After evaporation of NH_3 the residue was dissolved in 50 ml H_2O and 30 ml $CHCl_3$. The aqueous layer was extracted three times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated. CC over silica (CH/AcOEt = 5:1) gave 100 mg white crystals of **4** (84%).

M.p. = 122–124°C; $R_f = 0.44$ (CH/AcOEt = 5:1), $[\alpha]_D^{20} = +13.0$ ($c = 0.1$, $CHCl_3$); IR (KBr): $\nu = 2946$ (s), 1738 (vs), 1723 (vs), 1434 (m), 1254 (s), 1173 (m) cm^{-1}; UV (MeOH): λ_{max} (lgε) = 201 (2.910), 282 (1.519) nm; ^{1}H NMR ($CDCl_3$): $\delta = 0.82$ (d, $J = 6.8$ Hz, 3H, 18-H/19-H), 0.83 (d, $J = 6.8$ Hz, 3H, 19-H/18-H), 0.85 (s, 3H, 20-H), 1.06 (m, 1H, 7-H$_{ax}$), 1.08 (m, 1H, 1-H$_{ax}$), 1.11 (m, 1H, 6-H$_{eq}$), 1.14 (s, 3H, 21-H), 1.21 (m, 1H, 11-Hα), 1.27 (m, 1H, 9-H), 1.37 (qd, $3\times J = 12.8$–13.0 Hz, $J = 3.8$ Hz, 1H, 6-H$_{ax}$), 1.4–1.6 (m, 2H, 2-H), 1.46 (m, 1H, 1-H$_{eq}$), 1.53 (m, 1H, 3-H$_{eq}$), 1.54 (m, 1H, 11-Hβ), 1.55 (m, 1H, 8-H), 1.64 (m, 1H, 5-H), 1.66 (sept, $J = 6.8$ Hz, 1H, 17-H), 1.69 (m, 1H, 7-H$_{eq}$), 1.72 (m, 1H, 3-H$_{ax}$), 1.92 (ddd, $J = 18.5$ Hz, $J = 4.3$ Hz, $J_{14\alpha,16\alpha} = 1.8$ Hz, 1H, 16-Hα), 2.00 (dd, $J = 18.5$ Hz, $J_{14\beta,16\beta} = 2.2$ Hz, 1H, 14-Hβ), 2.25 (dd, $J = 18.5$ Hz, $J_{14\alpha,16\alpha} = 1.8$ Hz, 1H, 14 Hα), 2.44 (m, 1H, 12-H), 2.52 (ddd, $J = 18.5$ Hz, $J = 10.6$ Hz, $J_{14\beta,16\beta} = 2.2$ Hz, 1H, 16-Hβ), 3.61 (s, 3H, 23-H) ppm; ^{13}C NMR (C_6D_6): $\delta = 13.8$ (q, C-20), 16.5 (q, C-21), 17.8 (t, C-2), 18.6 (q, C-18, C-19), 24.4 (t, C-6), 29.5 (t, C-7), 32.5 (t, C-11), 36.1 (s, C-10), 37.1 (t, C-3), 37.4 (d, C-17), 39.1 (t, C-1), 40.1 (d, C-12), 43.5 (t, C-14), 45.1 (d, C-8), 47.06 (s, C-4), 47.10 (t, C-16), 49.9 (d, C-5), 51.8 (q, C-23), 54.8 (s, C-13), 55.9 (d, C-9), 179.1 (s, C-22), 213.1 (s, C-15) ppm; MS (70 eV): *m/z* (%) = 360 (13) [M^+], 300 (100), 257 (41), 123 (28), 81 (25), 41 (26); $C_{23}H_{36}O_3$ (360.5); calc.: C 76.62, H 10.06; found: C 76.68, H 10.06.

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