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Intramolecular Diels-Alder Reaction of Dinitro-olefin derivatives of Furan for the Preparation of a Versatile Tool: 3,7-Dinitro-11-oxatricycloundec-9-ene

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‡Dedicated to the memory of Professor R.V. Stevens

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Abstract: Recurrent additions of nitromethane on furfuraldehyde followed by an intramolecular Diels-Alder reaction allowed the obtention of the title compound **1** in good yield with excellent stereoselectivity. Aromatization, ether cleavage and stereocontrolled oxidation reactions give evidence of the synthetic versatility of this adduct in the preparation of ergot alkaloids and valienamine bicyclic analogues.

During the past decade the intramolecular Diels-Alder reaction has received considerable attention in the total synthesis of natural products.[1] The use of furan as the diene in this reaction has led to the development of IMDAF (intramolecular Diels-Alder reaction employing a furan diene) which has been extensively studied due to its excellent stereocontrol.[2]

The introduction of a nitro group on the side chain of the furan diene has not yet been thoroughly investigated[3] despite the synthetic interest of combining the reactivity induced by the nitro group and the potential amine functionality.

We therefore thought that 3,7-dinitro-11-oxatricycloundec-9-ene **1** should be an interesting and readily available target for the IMDAF methodology. Compound **1** provides a number of different reactive sites and consequently should act as a versatile synthetic tool. Indeed, taking advantage of its two nitro groups, the aromatization of the oxabicycloheptane moiety should give access to a series of biologically important dopaminergic and serotoninergic drugs including diaminotetralin derivatives, 1,3,4,5-tetrahydrobenz[c,d]indoles and ergot alkaloids. In this respect the two nitro groups are the direct precursors of amino functions and may facilitate construction of these target molecules according to the retrosynthetic Scheme 1. In this new approach towards ergot alkaloids introduction of the indole nucleus is intended at the very end of the synthesis by known methods.[4]

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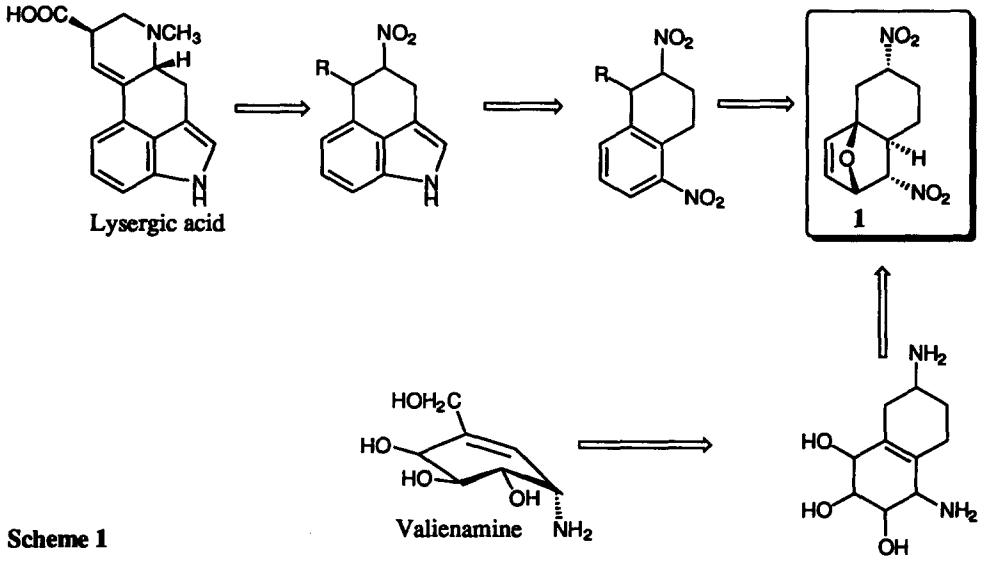
On the other hand, the excellent stereocontrol provided by the IMDAF reaction should allow stereoselective oxidation of the 9,10 double bond of **1** and give an interesting entry into new bicyclic amino-polyols related to valienamine: the acarbose aglycone (Scheme 1).[5] The search of structural analogues of acarbose, a potent glycosidase inhibitor currently used for the oral treatment of diabetes, has become the subject of intense research investigations.



Scheme 1

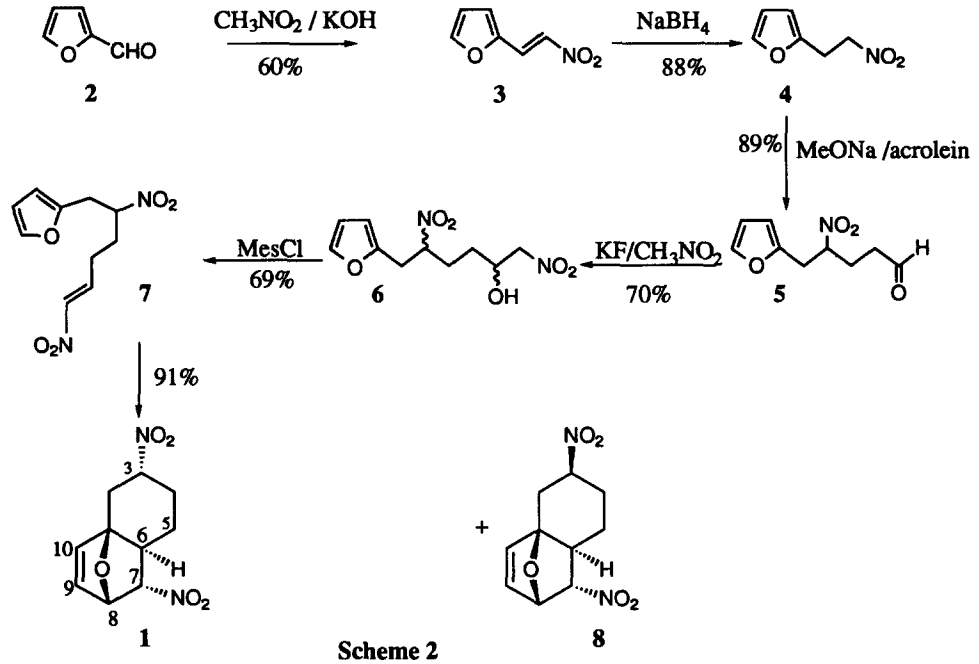
We wish to describe here a simple, stereocontrolled synthesis of compound **1** and the preliminary explorations of its synthetic potential.

Results and Discussion :

As outlined in Scheme 2, the first step of the synthesis was the preparation of 2-(2-nitroethyl)furan **4** starting from furfuraldehyde **2** and nitromethane. This was achieved by a Henry reaction to give the unsaturated compound **3** in 60% yield,[6] followed by selective reduction of the double bond in 88% yield using $NaBH_4$.[7] Compound **4** was a good precursor for a nucleophile in a Michael reaction[8] and its treatment with sodium methanolate followed by addition of acrolein provided the required 5-(2-furyl)-4-nitropentanal **5** (Scheme 2) in 89% yield.

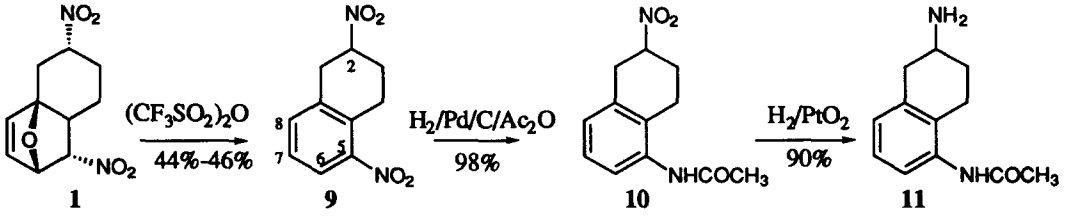
A second Henry reaction[9] with nitromethane yielded the condensation product **6** as a diastereomeric mixture (overall yield : 70%). Since conjugated nitroalkenes are versatile synthetic intermediates,[10] different approaches for their synthesis have been reported.[11] In our case, classical mesyl chloride dehydration applied to nitroalcohols[12] furnished the crude 2-(1,5-dinitro-1-hexenyl)furan **7**, the precursor for the intended cycloaddition. Indeed, during purification by flash chromatography over silica, *trans*-nitroolefin **7** was obtained in 69% yield together with a 14:1 mixture (determined by ^{1}H-NMR) of Diels-Alder adducts **1** and **8** (overall yield: 10% from **6**) (Scheme 2). Alternatively, when nitroolefin **7** was left at room temperature for 5 days, only the cycloadduct **1** was obtained in 91% yield. The *endo* structures of both **1** and **8** could be unambiguously assigned from the ^{1}H-NMR spectral data ($J_{H\text{-}8/H\text{-}7}$ = 5 Hz in both compounds) by comparison with those of various 7-oxabicyclo[2.2.1]hept-5-enes including simple nitro derivatives.[13]

In the IMDAF reaction employing a substituted side chain with four carbon atoms, only the adducts with a *trans* relationship between the angular hydrogen at C-6 and the oxygen bridge have previously been observed.[2] Indeed, the major cycloadduct **1** bears a nitro group at C-3 in a equatorial position in the newly formed six-membered ring while cycloadduct **8** possesses the nitro group at C-3 in an axial position and suffers a 1,3-diaxial interaction with the bridging oxygen atom.



Scheme 2

With the goal of preparing dopaminergic amino derivatives, ether cleavage and aromatization of **1** was attempted. The application of such reactions to this type of Diels-Alder adduct is a major challenge, due to several difficulties which have to be overcome. These reactions have been previously examined[14] but in our case basic media had to be excluded due to the sensitivity of the nitro group.[14d] The desired aromatic compound **9** could be obtained either by heating the crude mixture of **1** and **8** with BF_3. Et_2O / Ac_2O (yield: 44%) or by treating **1** with triflic anhydride (yield: 46%) (Scheme 3). In both cases, small amounts of 1-nitronaphthalene were also isolated from the reaction mixture.

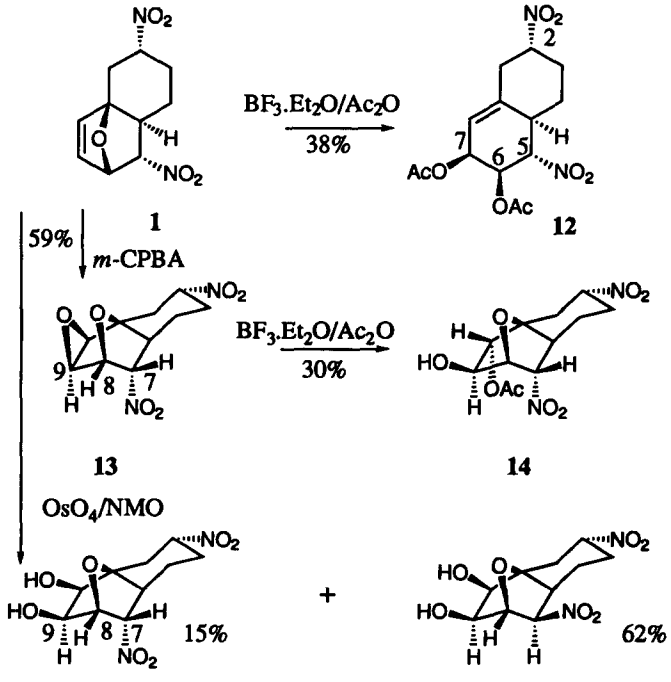


Scheme 3

Selective reduction of the aromatic nitro group[15] of **9** by H_2/Pd/C in the presence of Ac_2O led quantitatively to the crystalline 5-acetylamino-2-nitrotetralin **10** (Scheme 3). This new tetralin **10** should in principle give access to a series of dopaminergic and serotoninergic derivatives[16] either through conversion into

ergot type indole derivatives or by direct reduction to give diaminotetralins. Classical methods have already been described for the conversion of 5-aminotetralins into indole compounds.[17] In addition, the previously described[16a] dopaminergic drug 5-acetylamino-2-aminotetralin **11** was obtained by further reduction of **10** using H_2/ Adams catalyst.

7-Oxabicyclo[2.2.1]heptene derivatives constitute promising tools allowing regioselective and stereocontrolled reactions through ether cleavage and double bond oxidation. This methodology has been extensively applied by Vogel[18] in the synthesis of natural products and "naked" sugars. The major challenge of this type of chemistry lies in the cleavage conditions of the ether bridge which greatly depends on the nature of the substituents. The presence of a nitro group at C-7 in compound **1** offers new perspectives in this important field, leading to a novel entry into aminocyclohexitol derivatives. In addition, the *endo* nitro substituent present in compound **1** is not expected to participate in the opening of the ether bridge in contrast with other substituents.[19] The action of $BF_3.Et_2O/Ac_2O$ at room temperature gave smoothly 6,7-diacetoxy-2,5-dinitro-1,2,3,4,5,6,7,10-octahydronaphthalene **12** in 38% yield from the tricyclic compound **1** (Scheme 4). The relative *cis* configuration of the acetoxy substituents was easily deduced from the ^{1}H-NMR spectra ($J_{H\text{-}5/H\text{-}6}$ = 11.5 Hz, $J_{H\text{-}6/H\text{-}7}$ = 4 Hz).



Scheme 4

In order to further explore the potential of **1** as a tool for the synthesis of fused aminocyclitol derivatives, the oxidation of the double bond into *cis* and *trans* diols was undertaken. Because of the tricyclic structure of **1**, the C-9, C-10 double bond was expected to react preferentially on its *exo* face, thus ensuring good selectivity when submitted to epoxidation.[18a,b]

Treatment of **1** with *m*-CPBA led to epoxide **13** (Scheme 4). Its analysis by ^{1}H-NMR was in full agreement with the data previously published[18a] for this type of compound ($J_{H\text{-}8/H\text{-}7}$ = 5 Hz, *exo*; $J_{H\text{-}8/H\text{-}9}$ = 0

Hz, *endo*). Selective epoxide opening in such compounds is known to be difficult and leads frequently to rearranged products. In our case, once again, $BF_3.Et_2O/Ac_2O$ was an efficient epoxide opening reagent, leading to *trans* ester **14**.[18b] In contrast, the classical oxidation of **1** with OsO_4/N-methylmorpholine oxide[20] yielded the *cis* compounds **15** and **16** (Scheme 4). Epimerisation of the nitro group at C-7 was observed and can be explained by the presence of N-methylmorpholine in the reaction mixture.[13e] In structures of type **15** and **16**, coupling of the H-8 proton is only observed with vicinal protons which are *exo*.[13c] Thus the relative configurations were easily established, since for compound **15** H-8 appeared as a singlet while for compound **16** H-8 was a doublet ($J_{H\text{-}8/H\text{-}7}$ = 6 Hz)

In summary, we have described a new versatile synthetic tool, 3,7-dinitro-11-oxatricycloundec-9-ene **1** which can be easily prepared from furfuraldehyde. The presence of a nitro group in the 7-oxabicyclo[2.2.1]heptene subunit greatly influences the reactivity of this system and allows aromatization under mild conditions giving a new entry towards dopaminergic 2,5-diaminotetralins. Construction of the indole nucleus of ergot alkaloids and introduction of convenient substituents in the α position of the nitro group at C-2 are currently under study. In addition, **1** can be opened smoothly to give the dinitro compound **12**, a potential precursor of bicyclic aminocyclitols. Stereocontrolled oxidation reactions of **1** provide evidence of its versatility towards the synthesis of new bicyclic valienamine analogues.

Experimental

2-(2-Nitrovinyl)furan (3): 13.5 mL (0.25 mol) of nitromethane was slowly added to 125 mL of a 20% aqueous KOH solution and the reaction mixture cooled to 0 °C. 21 mL (0.25 mol) of freshly distilled furfuraldehyde was added at such a rate that the temperature was maintained at 0 °C. The reaction mixture was then vigorously stirred for 10 min at the same temperature, then poured into 300 mL of ice cold 50% aqueous HCl. The yellow precipitate was filtered and washed with water. Crystallization from MeOH afforded yellow needles of 2-(2-nitrovinyl)furan (20.7 g, 60%): mp: 74-75 °C; IR (film) 3125 (w), C=C 1636 (m), 1502 (m), 1330 (m), furan 740 (s) cm^{-1}; ^1H NMR δ 6.57 (dd, 1, J = 3.5, 1.5 Hz, H-4), 6.89 (d, 1, J = 3.5 Hz, H-3), 7.23 (d, 1, J = 13 Hz, H-1') 7.59 (d, 1, J = 1.5 Hz, H-5), 7.77 (d, 1, J = 13 Hz, H-2'); ^{13}C NMR δ 113.2 (C-4), 119.9 (C-3), 125.3 (C-2'), 134.7 (C-1'), 146.7 (C-5), 146.7 (C-2); MS (CI, NH_3), *m/z* : 157 $(M+18)^+$; Anal. Calcd for $C_6H_5NO_3$ (139.110): C, 51.80; H, 3.62; N, 10.07. Found: C, 51.42; H, 3.71; N, 10.01.

2-(2-Nitroethyl)furan (4): A solution of 20 g (0.144 mol) of 2-(2-nitrovinyl)furan in 200 mL of dioxan was slowly added to a suspension of 12 g (0.312 mol) of $NaBH_4$ in a mixture of 200 mL of dioxan and 70 mL of methanol. The temperature was maintained below 20 °C during the addition (50 min) and the reaction was then stirred for 1 h. The reaction was quenched by adding carefully 30 mL of a 30% aqueous acetic acid solution. The resulting mixture was filtered through Celite and the filtrate concentrated under vacuum. The acidic solution was made alcaline (pH 8) by addition of a saturated aqueous sodium bicarbonate solution and extracted with ethyl acetate. The organic layer was dried (Na_2SO_4), filtered and evaporated. Distillation of the dark residual oil under vacuum (75 °C/1 Torr) yielded 17.8 g (88%) of 2-(2-nitroethyl)furan as a pale yellow oil: IR (neat) 3125 (w), 1555 (s), 1372 (s), furan 738 (s) cm^{-1}; ^1H NMR δ 3.35 (t, 2, J = 7 Hz, H_2-1'), 4.63 (t, 2, J = 7 Hz, H_2-2'), 6.13 (dd, 1, J = 3, 1 Hz, H-3), 6.30 (dd, 1, J = 3, 2 Hz, H-4), 7.33 (dd, 1, J = 2, 1 Hz, H-5); ^{13}C NMR δ 25.9 (C-1'), 73.2 (C-2'), 107.2 (C-3 or C-4), 110.4 (C-4 or C-3), 142.1 (C-5), 149.3 (C-1); MS (CI, NH_3) *m/z* 159 $(M+18)^+$; Anal. Calcd for $C_6H_7NO_3$ (141.126): C, 51.06; H, 5.00; N, 9.92. Found: C, 51.04; H, 5.25; N, 9.75.

5-(Furan-2-yl)-4-nitropentanal (5): 17.8 g (0.126 mol) of 2-(2-nitroethyl)furan was dissolved with stirring under an argon atmosphere in 100 mL of a 0.4 *N* sodium methanolate solution. The reaction mixture was then cooled to - 60 °C and a solution of 10 mL (0.14 mol) of freshly distilled acrolein in 200 mL of methanol was added over 1 h. The temperature was allowed to rise to - 20 °C and the stirring under argon continued for 2 h. The solution was neutralized with 6 mL of glacial acetic acid. The resulting mixture was concentrated under vacuum and filtered through Celite. The filtrate was evaporated to yield a crude yellow syrup. Flash chromatography of the residue on silica gel (400 g) with 6:4 cyclohexane-ether furnished 22.2 g (89%) of the pure oily aldehyde **5**: IR (neat) 3125 (w), C=O 1719 (s), 1549 (s), 1362 (m), 1008 (m), furan 744 (s) cm^{-1}; ^1H NMR δ 2.19 (dt, 2, *J* = 14, 7 Hz, H-3), 2.57 (dt, 2, *J* = 7, 1 Hz, H-2), 3.12 (dd, 1, *J* = 15, 6 Hz, H-5), 3.34 (dd, 2, *J* = 15, 8 Hz, H-5), 4.81 (m, 1, H-4), 6.13 (dd, 1, *J* = 3, 0.5 Hz, H-3'), 6.28 (dd, 1, *J* = 3, 2 Hz, H-4'), 7.32 (dd, 1, *J* = 2, 0.5 Hz, H-5'), 9.74 (bs, 1, H-1); ^{13}C NMR δ 25.2 (C-3), 29.5 (C-5), 39.4 (C-2), 85.7 (C-4), 104.6 (C-3'), 110.4 (C-4'), 142.3 (C-5'), 148.7 (C-2'), 199.4 (C-1); MS (CI, NH_3), *m/z* 215 $(M+18)^+$; Anal. Calcd for $C_9H_{11}NO_4$ (197.190): C, 54.82; H, 5.62; N, 7.10. Found: C, 54.71; H, 5.49; N, 6.91.

6-(Furan-2-yl)-1,5-dinitrohexan-2-ol (6): 7 mL (129.5 mmol) of nitromethane was added to a suspension of 3 g of 40 % potassium fluoride on alumina in 30 mL of isopropanol. A solution of 4.2 g (21.3 mmol) of 5-(furan-2-yl)-4-nitropentanal in 40 ml of isopropanol was added dropwise with stirring at room temperature. The mixture was stirred for 60 h, then diluted with methylene chloride and filtered through Celite. The filtrate was concentrated under vacuum and purified by flash chromatography on silica gel (120 g), using methylene chloride as eluent to yield 3.85 g (70%) of a diastereoisomeric mixture of 6-(furan-2-yl)-1,5-dinitrohexan-2-ol **6** as a yellow oil: IR (film) 3500 (m), 1545 (s), 1375 (m), 1360 (m), furan 740 (s) cm^{-1}; ^1H NMR δ 1.5-2.2 (m, 4, H_2-3 and H_2-4), 2.90 (br. s,1, OH), 3.11 (dd, 1, *J* = 15, 6 Hz, H-6), 3.35 (m, 1, H-6), 4.51 (m, 3, H-2, H_2-1), 4.95 (m, 1, H-5), 6.13 (m, 1, H-3'), 6.29 (m, 1, H-4'), 7.45 (m, 1, H-5'); ^{13}C NMR δ 28.5, 29.0, 29.2, 29.4 (C-3, C-4), 32.1, 32.3 (C-6), 67.0, 67.7 (C-2), 80.1 (C-1), 86.0 (C-5), 108.1 (C-3'), 110.4 (C-4'), 142.3 (C-5'), 148.7 (C-1'); MS (CI, NH_3) *m/z* 276 $(M+18)^+$; HRMS (CI, CH_4), *m/z* $(M+H)^+$ calc. for $C_{10}H_{14}N_2O_6$+H: 258.8184 found 258.8190.

2-(2,6-Dinitrohex-5-enyl)furan (7) and 3,7-Dinitro-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-ene (1) and (8): To a stirred solution of 6-(furan-2-yl)-1,5-dinitrohexan-2-ol (4g, 15.6 mmol) in 100 mL of ethyl acetate at 0°C under argon atmosphere were added successively 11.2 mL (80 mmol) of triethylamine and 6.1 mL (80 mmol) of mesyl chloride at such a rate that the temperature was maintained at 0°C. The reaction mixture was stirred for 2 h at 0°C and was then treated with 100 mL of a saturated aqueous sodium bicarbonate solution. The organic layer was dried (Na_2SO_4) and evaporated to dryness under vacuum. The resulting brownish oil (5.45 g) was submitted to flash chromatography on silica gel (150 g), using cyclohexane/CH_2Cl_2 8:2 as eluent to furnish pure olefin **7** (2.57 g, 69%) as a pale yellow oil and 375 mg (10%) of a 14:1 diastereomeric mixture of the Diels-Alder adducts **1** and **8** (^1H NMR). Crystallization from CH_2Cl_2 afforded the pure adduct **1** (280 mg, 7.5 %). Careful flash chromatography of the mother liquors using CH_2Cl_2 as eluent yielded an analytical sample of pure **8**.

2-(2,6-dinitrohex-5-enyl)furan (7): IR (film) : 1720 (w), 1545 (s), 1365 (m), 1335 (m), 1145 (m), 1110 (m), furan 740 (s) cm^{-1}; ^1H NMR δ 1.3-1.5 (m, 1, H-3'), 1.8-2.0 (m, 1, H-4'), 2.1-2.2 (m, 1, H-3'), 2.3-2.4 (m, 1, H-4'), 3.10 (dd, 1, *J* = 17, 6 Hz, H-1'), 3.30 (dd, 1, *J* = 17, 9 Hz, H-1'), 4.75 (m, 1, H-2'), 6.12 (d, 1, *J* = 3 Hz, H-3), 6.30 (dd, 1, *J* = 3, 1.5 Hz, H-4), 6.97 (d, 1, *J* = 15 Hz, H-6'), 7.14 (dd, 1, *J* = 15, 7 Hz, H-5'), 7.33 (d, 1, *J* = 1.5 Hz, H-5); ^{13}C NMR δ 24.4, 30.6, 32.0 (CH_2), 85.6 (C-2'), 108.3 (C-3'), 110.4 (C-3' or C-4'), 138.1 (C-5' or C-6'), 140.5 (C-6' or C-5'), 142.4 (C-5), 148.4 (C-2); MS (CI,

NH_3) *m/z* 258 $(M+18)^+$; HRMS (CI, CH_4), *m/z* $(M+H)^+$ calc. for $C_{10}H_{12}N_2O_5$+H: 241.0824 found 241.0818.

3,7-Dinitro-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-ene (8): ^1H NMR δ 1.62 (qd, 1, *J* = 14, 3 Hz, H-5a), 1.84 (tt, 1, *J* = 14, 3 Hz, H-4a), 2.23 (m, 1, H-5e or H-4e), 2.40 (m, 1, H-4e or H-5e), 2.48 (dd, 1, *J* = 16, 6 Hz, H-2a), 2.73 (dt, 1, *J* = 16, 3 Hz, H-2e), 4.50-4.65 (m, 2, H-3, H-7), 5.30 (d, 1, *J* = 5 Hz, H-8), 6.35, 6.37 (m, 2, H-9, H-10); ^{13}C NMR δ 24.0 (C-5), 25.7 (C-4), 30.0 (C-2), 40.5 (C-6), 77.4 (C-3), 79.2 (C-8), 89.6 (C-7), 134.0 (C-9), 141.0 (C-10); MS (CI, NH_3) *m/z* 258 $(M+18)^+$; HRMS (CI, CH_4), *m/z* $(M+H)^+$ calc. for $C_{10}H_{12}N_2O_5$+H: 241.0824 found 241.0828.

3,7-Dinitro-11-oxa-ricyclo[6.2.1.0^{1,6}]undec-9-ene (1): Olefin **7** (1 g, 4.16 mmol) was dissolved in CH_2Cl_2 (50 mL) and the solution was left at room temperature for 5 days. Filtration of the reaction mixture afforded Diels-Alder cycloadduct **1** as pale yellow crystals (910 mg, 91%): mp 125-127 °C; IR (film): 1543 (s), 1378 (m), 908 (s) cm^{-1}; ^1H NMR δ 1.35-1.55 (m, 1, H-5a), 1.85-2.10 (m, 1, H-4a), 2.25-2.50 (m, 3, H-4, H-5, H-6), 2.57 (dd, 1, *J* = 14, 12 Hz, H-2a), 2.85 (ddd, 1, *J*= 14, 5, 2 Hz, H-2e), 4.50-4.70 (m, 2, H-3, H-7), 5.36 (dd, 1, *J* = 5, 1.5 Hz, H-8), 6.39 (dd, 1, *J* = 6, 1.5 Hz, H-9), 6.43 (d, 1, *J* = 6 Hz, H-10); ^{13}C NMR δ 27.7 (C-5), , 29.6 (C-4), 32.5 (C-2), 40.0 (C-6), 79.3 (C-8), 80.5 (C-3), 88.2 (C-1), 89.5 (C-7), 134.0 (C-9), 140.8 (C-10); MS (CI, NH_3) *m/z* 258 $(M+18)^+$; Anal. Calcd for $C_{10}H_{12}N_2O_5$ (240.215): C, 50.00; H, 5.03; N, 11.66. Found: C, 50.11; H, 5.27; N, 11.42.

2,5-Dinitro-1,2,3,4-tetrahydronaphthalene (9): Method A: 200 mg (0.83 mmol) of a diastereomeric mixture **1** and **8** was dissolved in 4 mL of acetic anhydride and the resulting solution was cooled to 0°C in an ice bath. 0.1 mL of freshly distilled $BF_3.Et_2O$ was added dropwise with stirring under an argon atmosphere. The mixture was allowed to warm to room temperature, then heated at 80°C for 15 h. The cooled reaction mixture was then filtered through Celite and concentrated under reduced pressure. Purification by flash chromatography on silicagel using cyclohexane/CH_2Cl_2 2:1 as eluent gave 19 mg (13%) of 1-nitronaphthalene. Further elution afforded 81 mg (44%) of 2,5-dinitro-1,2,3,4-tetrahydronaphthalene **9**: IR (film): 1548 (NO_2), 764 (Ar) ν cm^{-1}; ^1H NMR δ 2.20-2.70 (m, 2, H-3, H-4), 3.10-3.25 (m, 2, H-3, H-4), 3.41 (dd, 1, *J* = 17, 6 Hz, H-1), 3.53 (dd, 1, *J* = 17, 8 Hz, H-1), 4.80-4.90 (m, 1, H-2), 7.34 (t, 1, *J* = 8 Hz, H-7), 7.41 (d, 1, *J* = 8 Hz, H-8), 7.81 (d, 1, *J* = 8 Hz, H-6); ^{13}C NMR δ 23.8 (C-3), 26.6 (C-4), 32.9 (C-1), 79.8 (C-2), 123.1 (C-6), 127.0 (C-7), 134.3 (C-8), 129.4 (C-10), 134.9 (C-9), 149.3 (C-5); MS (CI, NH_3), *m/z* 240 $(M+18)^+$; HRMS (CI, CH_4), *m/z* $(M+H)^+$ calc. for $C_{10}H_{10}N_2O_4$+H: 223.0719 found 223.0732.

Method B: 1.7 mL (10 mmol) of triflic anhydride was added to a solution of 200 mg (0.83 mmol) of adducts **1** and **8** in 2 mL of CH_2Cl_2. The reaction mixture was stirred under an argon atmosphere at room temperature for 10 h. Work-up as before followed by purification on silica gel (eluent: cyclohexane/EtOAc 6:1) gave 85 mg (46%) of 2,5-dinitro-1,2,3,4-tetrahydronaphthalene **9**, accompanied by 1-nitronaphtalhene (19 mg, 13%).

5-Acetylamino-2-nitro-1,2,3,4-tetrahydronaphthalene (10): 45 mg(0.2 mmol) of 2,5-dinitro-1,2,3,4-tetrahydronaphthalene **9** and 95 mg (0.8 mol) of Ac_2O were dissolved in 3 mL of glacial acetic acid. Palladium/C (10%, 10 mg) was added to the solution and the stirred reaction mixture was flushed with hydrogen and allowed to react for 24 h. The catalyst was removed by filtration through Celite and the reaction mixture was evaporated to dryness under vacuum. The product was purified by filtration on a short silica gel column. Elution with CH_2Cl_2 yielded 46 mg (98%) of the pure crystallized acetylaminonitrotetralin **10**: mp: 176-180°C; IR (film): 3436 (NH), 1654 (amide), 1549 (NO_2), 760 (Ar) ν cm^{-1}; ^1H NMR δ 2.24 (s, 3, CH_3CO), 2.2-2.5 (m, 2, H-3, H-4), 2.7-2.9 (m, 2, H-3, H-4), 3.35 (dd, 1, *J*=16.5, 6 Hz, H-1), 3.45 (dd, 1, *J*=16.5, 9 Hz, H-1),

4.80 (m, 1, H-2), 6.89 (br. s, 1, NH), 7.01 (d, 1, *J*= 8 Hz, H-8), 7.21 (t, 1, *J*= 8 Hz, H-7), 7.51 (d, 1, *J*= 8 Hz, H-6); ^{13}C NMR 22.7 (C-3), 23.9 (CH_3), 26.8 (C-4), 33.2 (C-1), 80.6 (C-2), 123.0 (C-6), 126.7 (C-7), 126.9 (C-8), 127.4 (C-10), 132.8 (C-9), 134.9 (C-5), 168.4 (C=O, amide); MS (CI, NH_3), *m/z* 252 $(M+18)^+$, 235 $(M+1)^+$; HRMS (CI, CH_4) *m/z* $(M+H)^+$, calc. for $C_{12}H_{14}N_2O_3$+H: 235.1086 found 235.1087.

5-Acetylamino-2-amino-1,2,3,4-tetrahydronaphthalene (11): 23 mg (0.1 mmol) of **10** was dissolved in 3 mL of MeOH. PtO_2 (Adams catalyst, 10 mg) was added to the solution. The reduction was achieved with H_2 at room temperature under pressure (5 bars) over 24 h. Filtration through Celite and evaporation of the solvent gave 18 mg (90%) of the title compound.[16a] HRMS (CI, CH_4), *m/z* $(M+H)^+$ calc. for $C_{12}H_{16}N_2O$+H: 205.13408 found 205.1341.

6,7-Diacetoxy-2,5-dinitro-1,2,3,4,5,6,7,10-octahydronaphthalene (12): 3.3 g (13.7 mmol) of Diels-Alder adduct **1** was dissolved in 50 mL of acetic anhydride and the solution was cooled to 0°C in an ice bath. 1.7 mL of freshly distilled $BF_3.Et_2O$ was added dropwise with stirring and under an argon atmosphere. The mixture was stirred at room temperature for 6 h. The crude reaction mixture was poured slowly into 150 mL of EtOAc and extracted with 150 mL of a saturated aqueous sodium bicarbonate solution. The organic extract was dried over sodium sulfate and the solvent was removed under reduced pressure. The crude residue was purified by flash chromatography on silicagel using cyclohexane/CH_2Cl_2 4:1 as eluent to afford 1.78 g (38%) of pure diacetate **12**: ^{1}H NMR δ 1.40-1.60 (m, 1, H-4a), 1.9-2.1 (m, 1, H-3a), 1.99 (s, 3, CH_3C=O), 2.11 (s, 3, CH_3C=O), 2.18-2.28 (m, H, H-4e), 2.50 (m, 1, H-3e), 2.67 (dt, 1, *J* = 13, 1.5 Hz, H-1a), 2.79 (m, 1, H-10), 3.02 (ddd, 1, *J* = 13, 4, 2.5 Hz, H-1e), 4.44 (m, 1, H-2), 4.73 (dd, 1, *J* = 11.5, 9.5 Hz, H-5), 5.44 (dd, 1, *J* = 11.5, 4 Hz, H-6), 5.64 (dd, 1, *J* =4, 3.5 Hz, H-7), 5.74 (d, 1, *J* = 3.5 Hz, H-8); ^{13}C NMR δ 20.3 (CH_3), 20.7 (CH_3), 28.3 (C-4), 29.0 (C-3), 37.5 (C-1), 41.1 (C-10), 64.4 (C-7), 69.3 (C-6), 82.2 (C-2), 86.6 (C-5), 119.9 (C-8), 140.2 (C-9), 169.1 (C=O, ester), 169.8 (C=O, ester); MS (CI, NH_3), *m/z* 360 $(M+18)^+$; Anal. Calcd for $C_{14}H_{18}N_2O_8$ (342.304): C, 49.12; H, 5.30; N, 8.18. Found: C, 49.19; H, 5.43; N, 8.12

9,10-epoxy-3,7-dinitro-11-oxatricyclo[6.2.1.0^{1,6}]undecane (13): 408 mg (1.7 mmol) of **1** was dissolved in 10 mL of CH_2Cl_2 and added dropwise to a cold solution (0° C) of 700 mg of *m*-CPBA (57%-86%) in 10 mL of CH_2Cl_2. The resulting mixture was allowed to reach room temperature and was stirred for 24 h. Addition of a saturated aqueous $NaHCO_3$ solution and extraction with CH_2Cl_2 yielded a crude residue which was purified by flash chromatography (eluent: CH_2Cl_2). 200 mg of the starting material **1** and 130 mg (30% and 59% based on recovered starting material) of epoxide **13** were isolated: mp: 170-175°C; ^{1}H NMR ($(CD_3)_2CO$) δ 1.3-1.6 (m, H-5a), 1.8-2.0 (m, 1, H-4a), 2.2-2.4 (m, 2, H-4e, H-5e), 2.46 (dd, 1, *J* = 15, 12 Hz, H-2a), 2.62 (ddd, 1, *J* = 10, 7, 2.5 Hz, H-6), 2.85 (ddd, 1, *J* = 15, 4.5, 2.5 Hz, H-2e), 3.54 (d, 1, *J* = 3 Hz, H-9), 3.59 (d, *J* = 3Hz, H-10), 4.70 (tdd, 1, *J* = 12.5, 4.5, 3 Hz, H-3), 4.94 (d, 1, *J* = 5 Hz, H-8), 5.03 (dd, 1, *J* = 5, 2.5 Hz, H-7); ^{13}C NMR ($(CD_3)_2CO$) δ 26.9 (C-5), 28.8 (C-4), 31.0 (C-2), 40.8 (C-6), 47.3 (C-9), 51.3 (C-10), 74.7 (C-8), 80.8 (C-3), 83.8 (C-1), 92.3 (C-7); MS (CI, NH_3), *m/z* 274 $(M+18)^+$, 257 $(M+1)^+$; Anal. Calcd for $C_{10}H_{12}N_2O_6$ (256.214): C, 46.87 ; H, 4.72; N, 10.93. Found: C, 46.63 ; H, 4.64 ; N, 10.49.

10-Acetoxy-9-hydroxy-3,7-dinitro-11-oxatricyclo[6.2.1.0^{1,6}]undecane (14): 0.13 mL (0.95 mmol) of freshly distilled BF_3. Et_2O and 250 µl (2.4 mmol) of Ac_2O were added to a cold (0°C) solution of epoxide **13** (50 mg, 0.2 mmol) in 5 mL of CH_2Cl_2. The resulting mixture was allowed to reach the room temperature and was stirred for 24 h. Addition of a saturated aqueous $NaHCO_3$ solution and extraction with ether yielded 19 mg of acetate **14** (yield: 30%) which crystallized from CH_2Cl_2: mp: 177-180° C; ^{1}H NMR ($CDCl_3$) δ 1.3-1.4 (m, 1, H-5a), 1.8-2.0 (m, 1, H-4a), 2.17 (s, 3, Me), 2.18 (d, 1, *J* = 9.5 Hz, OH), 2.1-2.2 (m, 2 H, H-2a, H-5e), 2.39 (dt, 1, *J*=13, 3.5 Hz, H-4e), 2.62 (ddd, 1, *J* = 12, 7, 2.5 Hz, H-6), 2.83 (ddd, 1, *J* = 15, 4.5,

2 Hz, H-2e), 4.14 (dd, 1, J = 9.5, 6 Hz, H-9), 4.5-4.7 (m, 2, H-3, H-7), 4.81 (d, 1, J = 6 Hz, H-8), 4.97 (d, 1, J =6Hz, H-10); ^{1}H NMR ($CDCl_3/D_2O$) : 4.14 (d, 1, J = 6Hz, H-9), 4.62 (m, 1, H-3), 4.7-4.8 (m, 2, H-7 and H-8), 4.97 (d, 1, J=6Hz, H-10); ^{13}C NMR ($CDCl_3$) : 20.3 (Me), 27.4 (C-5), 28.9 (C-4), 29.9 (C-2), 41.2 (C-6), 70.4 (C-9), 76.8 (C-10), 80.4 (C-3), 82.4 (C-8), 86.8 (C-1), 88.8 (C-7), 169.6 (C=O, ester); MS (CI, NH_3), m/z 334 $(M+18)^+$; HRMS (CI, CH_4) m/z $(M+H)^+$, calc. for $C_{12}H_{16}N_2O_8$+H: 317.0985 found 317.0989.

9,10-Dihydroxy-3,7-dinitro-11-oxatricyclo[6.2.1.0^{1,6}]undecane (15) and (16): 200 mg (0.83 mmol) of compound **1** was dissolved in 10 mL of a 20/6/2 mixture of *t*-butanol, THF and water. 125 mg (0.9 mmol) of NMO and 0.5 mL (0.05 mmol) of a OsO_4 solution (2.5% in *t*-butanol) were added. The reaction mixture was stirred during 18 h at room temperature. Addition of 10 mL of a 25% sodium bisulfite aqueous solution, extraction with CH_2Cl_2 and evaporation to dryness furnished a crude mixture which was crystallized from CH_2Cl_2 to furnish 142 mg (62%) of diol **15**. The mother liquors yielded, after filtration over silica, 40 mg (15%) of diol **16** as an amorphous compound.

15 : mp 138-142°C; ^{1}H NMR ($(CD_3)_2CO$): 1.1-1.3 (m, 1, H-5a), 1.72 (m, 1, H-5e), 1.8-2.0 (m, 1, H-4a), 2.26 (dd, 1, J=14.5, 12.5 Hz, H-2a), 2.40 (ddd, 1, J = 13, 4.5, 2.5 Hz, H-4e), 2.59 (ddd, 1, J = 12.5, 8.5, 6 Hz, H-6), 2.84 (ddd, 1, J = 14.5, 4.5, 2 Hz, H-2e), 3.96 (d, J = 6Hz, H-9), 4.12 (d, 1, J = 6Hz, H-10), 4.69 (tt, 1, J = 12.5, 4.5 Hz, H-3), 4.86 (s, 1, H-8), 5.15 (d, 1, J = 8.5 Hz, H-7) ; ^{13}C NMR ($(CD_3)_2CO$) δ 23.0 (C-5), 30.1 (C-4), 31.7 (C-2), 43.3 (C-6), 72.0 (C-9), 76.6 (C-10), 85.6 (C-3), 86.0 (C-8), 88.8 (C-1), 89.1 (C-7); MS (CI, NH_3), m/z 292 $(M+18)^+$; Anal. Calcd for $C_{10}H_{14}N_2O_7$ (274.229): C, 43.79 ; H, 5.14 ; N, 10.21. Found: C, 43.63 ; H, 4.99 ; N, 10.01.

16: ^{1}H NMR ($(CD_3)_2CO$) δ 1.4-1.6 (m, 1, H-5a), 1.9-2.1 (m, 1, H-4a), 2.2-2.5 (m, 3, H-2, H-4e, and H-5e), 2.65 (ddd, 1, J = 9, 6.5,3 Hz, H-6), 2.80 (ddd, 1, J = 16, 2, 4 Hz, H-2), 3.95 (d, 1, J = 6 Hz, H-9), 4.12 (d, 1, J = 6 Hz, H-10), 4.6-4.7 (m, 1, H-3), 4.73 (d, 1, J = 6 Hz, H-8), 4.87 (dd, 1, J = 3, 6Hz, H-7); ^{13}C NMR ($(CD_3)_2CO$) : 28.8 (C-5), 30.5 (C-4), 32.0 (C-2), 41.8 (C-6), 70.7 (C-9), 76.5 (C-10), 83.1 (C-3), 83.7 (C-8), 89.9 (C-1), 90.9 (C-7); MS (CI, NH_3), m/z 292 $(M+18)^+$; Anal. Calcd for $C_{10}H_{14}N_2O_7$ (274.229): C, 43.79 ; H, 5.14 ; N, 10.21. Found: C, 43.32 ; H, 5.11 ; N, 9.78.

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