A Preliminary Approach to Nonenolizable *β,β*-Tricarbonyls: Assembly of a Hyperevolutin Prototype[1]

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Abstract: A synthetic approach to the hyperevolutin A acylated phloroglucinol ring system is described. Thus, intramolecular allene−nitrile oxide cycloaddition of **10** was used to construct the bicyclic framework and vicinal quaternary centers in cycloadduct **20** in the key bond-forming step. Treatment of **20** with Raney nickel and hydrogen gas produced primary enamine **21** which contains a nonenolizable *β,β*-tricarbonyl group in latent form.

The "hyperforins" are a family of natural products isolated from various sources of *guttiferae* (*clusia*) that have recently attracted attention from medicinal and synthetic chemists.[2] As shown in Figure 1, hyperevolutin A (**1**), garsubellin A (**2**), and sampsonione J (**3**) as well as other members of the hyperforin family are structurally related by virtue of an acylated phloroglucinol A-ring and a prenylated bicyclo[3.3.1]nonanone core.[3−5]

From a synthetic standpoint **1**−**3** and other family members contain asymmetric vicinal quaternary centers (C1−C2 in **1**, for example) and a densely functionalized tetracarbonyl array. No total synthesis has been described for any of the more than 50 members of the class; however, a single report on an approach to **2** was recently described.[6,7] Nonetheless, antitumor, antibiotic, antidepressant, antiHIV, and potential anti-neurodegenerative properties have been associated with the hyperforins for a number of years.[8−12]

Scheme 1 outlines a hypothetical approach to the *β,β*-tricarbonyl cluster following a cycloaddition−reductive cleavage strategy. Examination of the potential cycloadducts (**4** → **5** + **6**) suggested that **6** should be favored thermodynamically due to the bridgehead double bond present in **5**. Intramolecular nitrile oxide−allene cycloadditions had not been reported prior to the studies described here, however, and it was not clear whether **6** or an analogous structure could be acquired using the chemistry.[13,14] Reduction of the N−O bond in **6** was expected to produce *β,β*-tricarbonyl **7**, or a surrogate.[15]

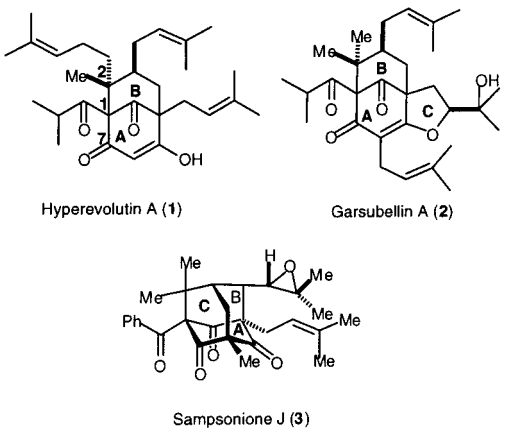

Figure 1. Biologically active structures from *guttiferae.*

Prenyl groups were removed for the pilot study, which led to the selection of **8** as a synthetic target (Scheme 2). Application of the proposed allene−nitrile oxide disconnection to **8** led to isoxazoline tricycle **9**, which was disconnected to *gem*-dimethylcyclohexanone **10**, a structural relative of **4** in which it was not possible for the exocyclic allene *π*-bond to migrate.

Efforts toward **10** were initiated from benzylidene ketone **11** as shown in Scheme 3.[16] Thus, **11** was treated with the cerate derived from propynylmagnesium bromide, which afforded a quantitative yield of the propargyl alcohol (not pictured).[17] Alkene-selective ozonolysis of the

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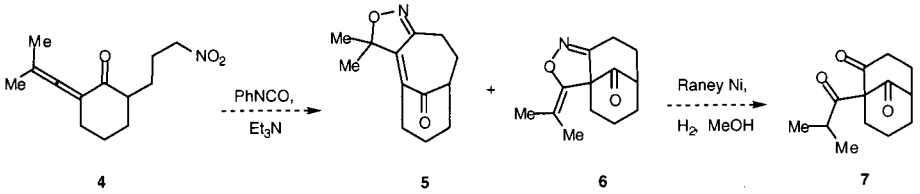
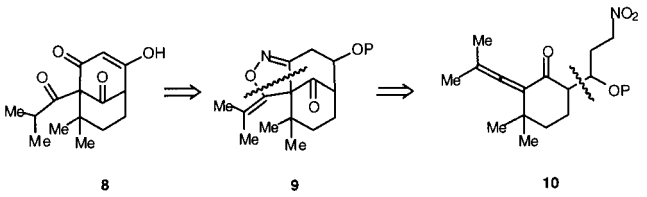
Scheme 1. Nitrile Oxide−Allene Cycloaddition



Scheme 2. Retrosynthetic Analysis of 8



product afforded α-hydroxyketone **13** that was subjected to lithium aluminum hydride reduction to yield the expected diols **14** as a mixture of diastereomers.[18] After initial attempts to convert **13** or **14** to the propargyl acetate led to decomposition, carbonate **15** was prepared and subjected to displacement by Gilman's reagent to yield alcohol **16**.[19] This material was oxidized under Swern's conditions to yield allenyl ketone **17**.[20] Aldol condensation between **17** and 3-nitropropanal was the initial plan for introducing the nitro side chain. This approach was abandoned, however, when material tentatively identified as a pyrone was isolated, presumably formed via Michael addition of the aldol hydroxyl group to the central carbon of the allene. Accordingly, the dimethylacetal derived from 3-nitropropanal (**19**) was employed in a Lewis acid-catalyzed Mukaiyama aldol condensation with silylenol ether **18**.[21] The reaction of **18** and **19** in the presence of titanium tetrachloride produced methoxy diastereomers **10a**,**b** in 44% yield (Scheme 4).[22] In the key event, **10** was exposed to phenyl isocyanate in refluxing benzene to produce **20** as a single diastereomer in 40% yield.[23]

Although structural assignments were not possible via ^{1}H NMR data, X-ray diffraction showed that the methoxy and carbonyl groups in **20** reside on opposite faces of the cycloadduct. The "syn" diastereomeric cycloadduct was not produced, indicating that although two diastereomers entered the cycloaddition, only one emerged. Moreover, if one assumes that epimerization did not occur under the reaction conditions, it is evident that one isomer cyclized in 80% yield while the other disintegrated. Treatment of **10a**,**b** with triethylamine in benzene at reflux did not lead to decomposition, however, which suggests β-elimination of the methoxy group did not occur during the cycloaddition.

Reductive cleavage was briefly investigated through the exposure of **20** to methanolic Raney nickel which gave **21** in quantitative yield via N−O bond reduction and tautomerization of the resulting imine (Scheme 5).[24] Bicyclo[3.3.1]nonanone **21** embodies requisite vicinal quaternary centers of the natural product family and is functionalized at all appropriate locations for hyperevolutin A.

In conclusion, a synthetic approach to the hyperevolutin A framework has been achieved, starting from a known readily available ketone. The current route requires ten steps and proceeds in 9% overall yield. The key bond-forming step occurs in modest yield (40%), but is the first example of an intramolecular allene−nitrile oxide [3 + 2] cycloaddition. Studies toward the synthesis of analogues and the preparation of hyperevolutin A are underway.

Experimental Section

6-Benzylidene-2,2-dimethylprop-1-ynylcyclohexanol (12). Cerous chloride heptahydrate (3.90 g, 10.5 mmol) was dried using the slow dry method, and then cooled to room temperature. To the resulting white powder was added a solution of 2.14 g (10 mmol) of **11** in 180 mL of THF all at once. The resulting slurry was stirred at room temperature for 4 h and then cooled to 0 °C, and 23 mL of a 0.5 M solution (11.5 mmol) of 1-propynylmagnesium bromide in THF was added. The resulting mixture was gradually warmed to room temperature and stirred overnight. The reaction was quenched with 50 mL of saturated aqueous NH_4Cl. The aqueous layer was extracted with three 25-mL portions of ether. The combined organic layers were washed with 100 mL of brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was flash chromatographed over 50 g of silica gel (eluted with hexanes−ethyl acetate, 10:1) to afford 2.40 g of **12** as a pale viscous oil (95%): IR (neat) 3472, 3056,3023,2969, 2929, 2864, 2235, 1599, 1457 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.18−7.35 (m, 5H), 6.93 (s, 1H), 2.50−2.60 (m, 2H), 2.20 (s, 1H), 1.91 (s, 3H), 1.51−1.68 (m, 4H), 1.12 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 144.99 (s), 137.99 (s), 128.80 (d), 127.86 (d), 126.04 (d), 123.22 (d), 82.83 (s), 80.31 (s), 77.85 (s), 40.58 (s), 35.98 (t), 25.26 (t), 24.59 (q), 22.56 (q), 22.24 (t), 3.48 (q); exact mass calcd for $C_{18}H_{22}O$ *m*/*z* 254.1671; found *m*/*z* 254.1670.

2-Hydroxy-3,3-dimethyl-2-prop-1-ynylcyclohexanone (13). A solution of 2.18 g (8.59 mmol) of alcohol **12** in 150 mL of dichloromethane was cooled to −78 °C. Ozone was passed through the solution until a light blue color persisted. The solution was then purged with nitrogen until the blue color disappeared. Dimethyl sulfide (4 mL) was added, and the resulting solution was warmed to room temperature and stirred overnight. The solvent was removed in vacuo, and the residue was chromatographed over 80 g of silica gel (eluted with hexanes−ethyl acetate, 40:1) to afford 1.17 g (76%) of **13** as a yellow oil which solidified at room temperature: mp 38−39 °C (from diethyl ether); IR (neat) 3464, 2964, 2923, 2876, 2227, 1720 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.05 (s, 1H), 2.95−3.09 (m, 1H), 2.36−2.44 (m, 1H), 2.06−2.14 (m, 1H), 1.94 (s, 3H), 1.70−1.92 (m, 2H), 1.40−1.47 (m, 1H), 1.19 (s, 3H), 0.70 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 209.02 (s), 84.01 (s), 79.36 (s), 77.78 (s), 44.00 (s), 35.96 (t), 35.69 (t), 24.85 (q), 21.76 (t), 19.27 (q), 3.61 (q); exact mass calcd for $C_{11}H_{16}O_2$ *m*/*z* 180.1150; found *m*/*z*

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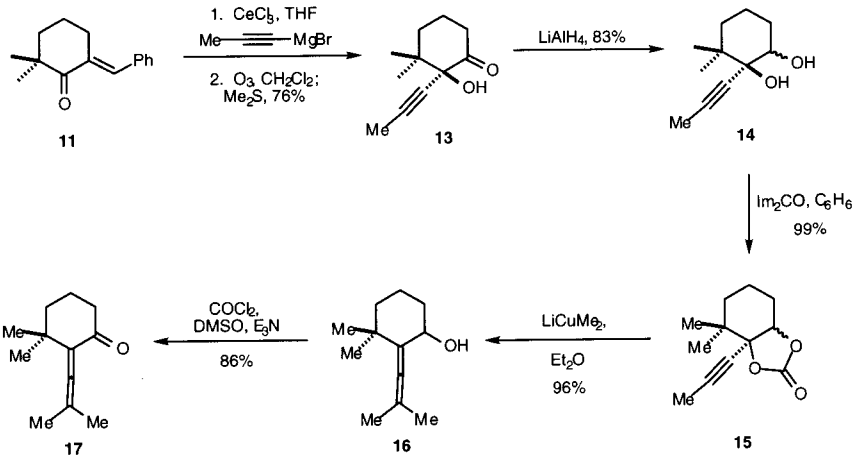
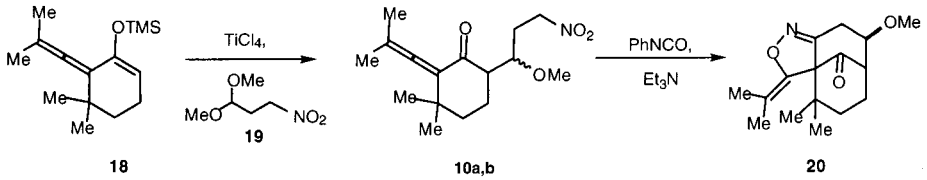
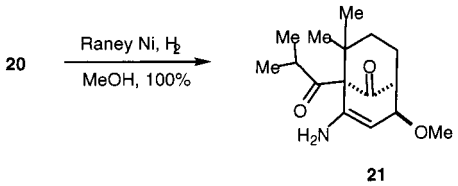
Scheme 3. Preparation of Allenyl Ketone 16



Scheme 4. Assembly of Tricycle 20



Scheme 5. Reduction of the Isoxazoline N−O Bond in 20



180.1155. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.33; H, 8.89. Found: C, 73.30; H, 8.99.

6,6-Dimethyl-1-prop-1-ynylcyclohexane-1,2-diol (14). Ketone **13** (450 mg, 2.5 mmol) was added at room temperature to a slurry of 474 mg (12.5 mmol) of $LiAlH_4$ in 7 mL of THF. The mixture was stirred at room temperature for 16 h, quenched with 50 mL of 1 N HCl, and extracted with 100 mL of ether. The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo, and the residue was chromatographed over 80 g of silica gel (eluted with hexanes−ethyl acetate, 5:1) to afford 245 mg of **14a** as a colorless oil which crystallized on standing: mp 64−65 °C (diethyl ether); ^{1}H NMR (250 MHz, $CDCl_3$) (3.80 (t, J = 5.7, 1H), 2.65 (s, 1H), 2.37 (s, 1H), 1.88 (s, 3H), 1.73 (m, 1H), 1.45−1.57 (m, 4H), 1.12−1.17 (m, 1H), 1.09 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) (81.43 (s), 80.12 (s), 76.35 (s), 72.39 (d), 38.48 (s), 32.94 (t), 27.65 (t), 25.78 (q), 23.47 (q), 19.31 (t), 3.50 (q); exact mass calcd for $C_{11}H_{18}O_2$ m/z 182.1307; found m/z 182.1305. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.53; H, 9.89. Found: C, 72.62; H, 10.06.

Continued elution using the same solvent produced 132 mg of **14b** as a white solid: mp 91−92 °C (diethyl ether); ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.66 (m, 1H), 2.80 (s, 1H), 1.95 (s, 1H), 1.90−1.99 (m, 1H), 1.90 (s, 3H), 148−1.58 (m, 4H), 1.23−1.27 (m, 1H), 1.12 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 84.18 (s), 79.49 (s), 78.24 (s), 73.05 (d), 39.16 (s), 37.02 (t), 32.39 (t), 26.68 (q), 19.93 (q), 19.76 (t), 3.59 (q); exact mass calcd for $C_{11}H_{18}O_2$ m/z 182.1307; found m/z 182.1307. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.53; H, 9.89. Found: C, 72.74; H, 10.08.

4,4-Dimethyl-3a-prop-1-ynylhexahydrobenzo[1,3]dioxol-2-one (15a). A solution of 0.558 g (3.07 mmol) of diol **14a** and 1.99 g (12.3 mmol) of carbonyldiimidazole in 45 mL of benzene was heated under reflux for 18 h. The mixture was cooled to room temperature, and 30 mL of water was added. The aqueous layer was extracted with four 15-mL portions of ether and four 15-mL portions of ethyl acetate. The combined organic layers were washed with 40 mL of water, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over 8 g of silica gel (eluted with hexanes−ethyl acetate, 5:1) to afford 633 mg of **15a** as a white solid (99%): mp 91−92 °C (Et_2O); ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.59 (t, J = 6.6 Hz, 1H), 2.11−2.19 (m, 1H), 1.87 (s, 3H), 1.36−1.56 (m, 5H), 1.14 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 154.46 (s), 84.86 (s, 2C), 80.71 (d), 75.35 (s), 36.39 (s), 33.18 (t), 27.51 (t), 25.50 (q), 25.26 (q), 16.49 (t), 3.47 (q); exact mass calcd for $C_{12}H_{16}O_3$ m/z 208.1099; found m/z 208.1095. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.23; H, 7.69. Found: C, 69.35; H, 7.80. Single-crystal structure showed a cis relationship.

4,4-Dimethyl-3a-prop-1-ynylhexahydrobenzo[1,3]dioxol-2-one (15b). A solution of 36.4 mg (0.20 mmol) of diol **14b** and 130 mg (0.80 mmol) of carbonyldiimidazole were heated in 2.5 mL of refluxing benzene for 18 h. The mixture was cooled to room temperature, and 3 mL of water was added. The aqueous layer was extracted with four 4-mL portions of ether and four 4-mL portions of ethyl acetate. The combined organic layers were washed with 4 mL of water, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over 4 g silica gel (eluted with hexanes−ethyl acetate, 5:1) to afford 40.0 mg of **15b** as a colorless oil which crystallized on standing (96%): mp 74−75 °C (diethyl ether); ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.40 (dd, J = 9.0, 7.05 Hz, 1H), 2.09−2.13 (m, 2H), 2.08 (s, 3H), 1.41ñ1.91 (m, 4H), 1.19 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 154.83 (s), 89.41 (s), 88.34 (s), 80.29 (d), 72.97 (s), 38.14 (s), 36.45 (t), 26.59 (q), 25.98 (t), 19.71 (t), 19.59 (q), 3.59 (q); exact mass calcd for $C_{12}H_{16}O_3$ m/z 208.1099; found m/z 208.1098. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.23; H, 7.69. Found: C, 69.15; H, 7.73.

3,3-Dimethyl-2-(2-methylpropenylidene)cyclohexanol (16). To a suspension of 237 mg (1.24 mmol) of cuprous iodide in 5 mL of ether at ice−salt temperature was added methyllithium (1.4 M in ether) such that a yellow precipitate formed and redissolved. To the resulting colorless solution was added a solution of 215 mg (1.04 mmol) of carbonates **15** in 9 mL of ether, and the resulting mixture was stirred at 0 °C for 5 h followed by quenching with 15 mL of saturated aqueous NH_4Cl. The aqueous layer was extracted with four 20-mL portions of ether, and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed over 10 g of silica gel (eluted with hexanes−ethyl acetate, 10:1) to afford 151.4 mg of **16** as a colorless oil (81%): IR (neat) 3456, 2957, 2930, 2864, 1813, 1448, 1391, 1361, 1081, 1021 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.10 (dd, J = 10.8, 4.5 Hz, 1H), 2.15 (m, 1H), 1.92 (s, 1H), 1.75 (s, 3H), 1.74 (s, 3H), 1.43−1.68 (m,

3H), 1.09−1.31 (m, 2H), 1.05 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 192.15 (s), 115.58 (s), 103.18 (s), 66.10 (d), 40.31 (t), 36.76 (t), 35.64 (s), 30.51 (q), 26.55 (q), 21.56 (q), 21.14 (q), 20.17 (t); exact mass calcd for $C_{12}H_{20}O$ *m*/*z* 180.1514; found *m*/*z* 180.1515.

3,3-Dimethyl-2-(2-methylpropenylidene)cyclohexanone (17). To a solution of 132 mg (1.04 mmol) of oxalyl chloride in 2.5 mL of methylene chloride at −78 °C was added 172 mg (2.20 mmol) of dimethyl sulfoxide. The resulting mixture was stirred for 30 min, and a solution of 149 mg (0.83 mmol) of alcohol **16** in 1.5 mL of methylene chloride was added. The resulting slurry was stirred at −78 °C for an additional 1.5 h, and 0.6 mL of triethylamine was then added. The mixture was stirred at −78 °C for 30 min, warmed to room temperature, and stirred for 1.5 h, and then 5 mL of water was added. The aqueous layer was extracted with four 10-mL portions of methylene chloride. The combined organic layers were washed with 30 mL of brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was flash chromatographed over 8 g of silica gel (eluted with pentane−methylene chloride, 1:1) to afford 131 mg of **17** as a pale yellow oil (89%): IR (neat) 2958, 2868, 1949, 1679, 1451, 1383, 1180 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.41 (t, J = 6.6 Hz, 2H), 1.85−1.89 (m, 2H), 1.76 (s, 6H), 1.62−1.67 (m, 2H), 1.07 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 204.86 (s), 201.95 (s), 113.85 (s), 100.89 (s), 40.33 (t), 37.99 (t), 35.94 (s), 30.18 (q, 2C), 19.58 (q, 2C), 19.30 (t); exact mass calcd for $C_{12}H_{18}O$ *m*/*z* 178.1358; found *m*/*z* 178.1355.

[5,5-Dimethyl-6-(2-methylpropenylidene)cyclohex-1-enyloxy]trimethylsilane (18). A solution of 0.165 mL (0.119 g, 1.18 mmol) of diisopropylamine in 3 mL of THF at −78 °C was treated with 0.71 mL of a 1.6 M solution of n-BuLi in hexane (1.13 mmol). The resulting solution was stirred at −78 °C for 10 min warmed to 0 °C, stirred 30 min, and recooled to −78 °C. To the resulting solution of LDA was added a solution of 0.175 g (0.98 mmol) of ketoallene **17** in 2 mL of THF. The mixture was stirred at −78 °C for 1 h, and 0.150 mL (0.128 g, 1.18 mmol) of chlorotrimethylsilane was added. The reaction was allowed to warm to room temperature over 3 h and then stirred for an additional 18 h. The solvent was removed in vacuo. The residue was dissolved in hexane and filtered through 1.5 g of Florisil to afford 232 mg (95%) of **18** as an unstable colorless oil: IR (neat) 2959, 2871, 1951, 1699, 1452, 1386, 1364, 1251, 844 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.00 (t, J = 4.2 Hz, 1H), 2.14 (pt, J = 6.1 Hz, 2H), 1.73 (s, 6H), 1.44 (t, J = 6.2 Hz, 2H), 1.03 (s, 6H), 0.14 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 198.59 (s), 145.19 (s), 109.96 (s), 107.26 (d), 99.37 (s), 36.23 (t), 34.15 (s), 28.23 (q, 2C), 21.40 (t), 20.69 (q, 2C), −0.03 (q, 3C).

6-(1-Methoxy-3-nitropropyl)-3,3-dimethyl-2-(2-methylpropenylidene)cyclohexanone (10a,b). To a solution of 87.1 mg of nitropropanal dimethylacetal **19** (0.59 mmol) in 5 mL of methylene chloride at −78 °C was added 63.7 μL (110 mg, 0.59 mmol) of titanium(IV) chloride. The resulting yellow solution was stirred for 10 min before a solution of 0.121 g (0.48 mmol) of enol ether **18** in 1 mL of methylene chloride was added. The mixture was stirred at −78 °C for 2 h and then quenched with 10 mL of aqueous K_2CO_3. The aqueous layer was extracted with three 15-mL portions of ethyl acetate. The combined organic layers were washed with 20 mL of brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over 2 g of silica gel (eluted with hexanes−ethyl acetate, 10:1) to afford 62.5 mg of **10a**,**b** as a 1:1 mixture of diastereomers (44%): IR (neat) 2959, 1948, 1667, 1553, 1448, 1383, 1156, 1093 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.47 (t, J = 6.8 Hz, 2H), 4.01−4.04 (m, 1H), 3.83−3.90 (m, 1H), 3.28 (s, 3H), 2.71−2.75 (m, 1H), 2.08−2.24 (m, 2H), 1.90−1.92 (m, 1H), 1.78 (s, 3H), 1.76 (s, 3H), 1.48−1.53 (m, 1H), 1.25−1.37 (m, 2H), 1.11 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 205.31 (204.98) (s), 201.90 (201.27) (s), 113.98 (s), 101.29 (101.05) (s), 77.51 (76.49) (d), 73.27 (72.75) (t), 59.28 (57.08) (s), 52.89 (49.98) (d), 37.27 (36.82) (t), 36.00 (35.79) (s), 31.03 (28.94) (t), 30.57 (q), 29.70 (q), 19.63 (19.35) (q, 2C), 18.78 (18.62) (t); exact mass calcd for $C_{16}H_{25}NO_4$ *m*/*z* 295.1784; found *m*/*z* 295.1776.

2-Isopropylidene-7-methoxy-11,11-dimethyl-3-oxa-4-aza-tricyclo[6.3.1.0.1.5]dodec-4-en-12-one (20). To a solution of 29.0 mg (0.098 mmol) of nitro-allene **10a**,**b** and 32.2 mg (0.147 mmol) di-*tert*-butyl carbonate in 2 mL of benzene and 1 mL of acetonitrile at room temperature was added 1 mg of 4-(dimethylamino)pyridine. The mixture was stirred for 10 min, heated to 80 °C, and stirred for 18 h. Saturated aqueous NH_4Cl (2 mL) was added, and the aqeuous layer was extracted with three 10-mL portions of ethyl acetate. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was chromatographed over 2 g of silica gel (eluted with hexanes−ethyl acetate, 10:1) to afford 11 mg of **20** as a white solid (40%): mp 148−150 °C (MeOH); ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.59 (m, 1H), 3.36 (s, 3H), 3.22 (dd, J = 16.5, 7.4 Hz, 1H), 2.95−2.98 (m, 1H), 2.79 (dd, J = 16.5, 10.5 Hz, 1H), 2.30−2.34 (m, 1H), 1.99−2.03 (m, 2H), 1.82 (s, 3H), 1.80 (m, 3H), 1.46−1.50 (m, 1H), 1.07 (s, 3H), 0.96 (m, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 203.57 (s), 156.88 (s), 144.54 (s), 110.90 (s), 77.87 (d), 73.82 (s), 56.71 (q), 50.25 (d), 48.39 (t), 36.49 (t), 31.75 (q), 26.44 (q), 25.89 (t), 22.29 (q), 22.13 (q), 19.13 (q); exact mass calcd for $C_{16}H_{23}NO_3$ *m*/*z* 277.1678; found *m*/*z* 277.1673. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.31; H, 8.30; N, 5.05. Found: C, 69.40; H, 8.38; N, 4.98.

2-Amino-1-isobutyryl-4-methoxy-8,8-dimethylbicyclo-[3.3.1]non-2-en-9-one (21). A solution of 25.2 mg (0.09 mmol) of **20** and 5 mg of Raney nickel in 3 mL of methanol was stirred under hydrogen for 24 h. The mixture was filtered and concentrated in vacuo to afford 25 mg of **21** as a white solid (100%): mp 135−137 °C (MeOH); ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.17 (d, J = 2.2 Hz, 1H), 4.15 (dd, J = 6.5, 2.4 Hz, 1H), 3.34 (s, 3H), 31.2 (s, 2H), 2.93 (t, J = 5.6 Hz, 1H), 2.59 (m J = 6.5 Hz, 1H), 1.92−2.08 (m, 2H), 1.73−1.81 (m, 1H), 1.60 (m, 1H), 1.33 (s, 3H), 1.17 (d, J = 6.5 Hz, 3H), 1.13 (d, J = 6.5 Hz, 1H), 1.09 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 214.78 (s), 209.87 (s), 139.04 (d), 101.84 (s), 76.48 (d), 72.84 (s), 56.01 (q), 48.95 (d), 43.79 (s), 39.99 (d), 37.11 (t), 27.62 (q), 23.41(t), 22.19 (q, 2C), 20.84 (q); exact mass calcd for $C_{16}H_{25}NO_3$ *m*/*z* 279.1834; found *m*/*z* 279.1827. Anal. Calcd for $C_{16}H_{25}NO_3$ C, 68.82; H, 8.96; N, 5.02. Found: C, 68.95; H, 9.08; N, 5.03.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for all new compounds and X-ray structural data for **20** and **15** is available free of charge via the Internet at http://pubs.acs.org.

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