Functionalized Oxatriquinanes and Their Structural Equilibrium in Protic Solvent

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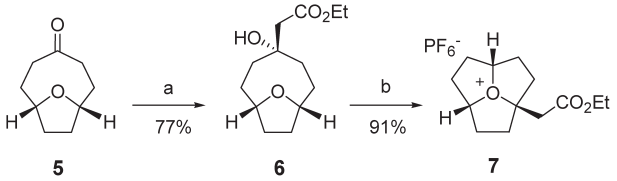
We synthesized oxatriquinane hexafluorophosphate bearing an ethoxycarbonylmethyl group 7 or a 2-oxopropyl group 11. Both of these organic oxonium cation compounds were obtained as stable solids. However, ^{1}H-NMR analysis showed that oxatriquinane 7 was present as the oxonium cation in aprotic solvent CD_3CN, but was in rapid equilibrium with ring-opened bicyclic compound 8 in protic solvent CD_3OD. The oxatriquinane 11 also showed similar behavior in protic solvent. Phenyl-substituted oxatriquinanes 12 and 14 were also obtained as stable solids, and showed similar properties to 7 and 11.

Key words oxatriquinane; organic oxonium cation; equilibrium; protic solvent

There have been few reports on stable organic oxonium salts,[1)] though alkyl oxonium salts such as triethyl oxonium tetrafluoroborate **1** (known as Meerwein's reagent) have been utilized in organic synthesis as powerful alkylation reagents for alcohol or amine[2,3)] (Fig. 1). However, they are chemically unstable and sensitive to moisture, so they are difficult to handle. Recently, Mascal *et al.* reported the synthesis of oxatriquinane **2** and oxatriquinacene **3**, which have a tricyclic condensed ring structure with an oxygen cationic center.[4)] Compound **2** was isolated as a crystalline solid suitable for X-ray crystal structure analysis. Interestingly, **2** could be purified by column chromatography and was stable under reflux in alcohol or water. Subsequently, they synthesized several oxatriquinanes with simple alkyl groups and carried out X-ray crystal structure analysis.[5,6)] A unique S_N2 reaction at tertiary carbon in the α-position to the oxygen center was also reported.[7)] Most recently, oxatriquinane having a hydroxy group at the α-position to oxygen (**4**) was found to have the longest C–O bond length so far reported among organic compounds.[8)] We became interested in these stable oxonium cation species, and set out to synthesize further examples for examination of their potential utility in materials science or medicinal chemistry.

First, we focused on oxatriquinane having a simple ester group, to see whether such a group is compatible with the oxonium cation. As shown in Chart 1, the starting ketone **5**,[7)] which was synthesized from 1,5-cyclooctadiene, was subjected to Reformatsky reaction to afford β-hydroxyester **6** in good yield. Compound **6** was obtained as nearly a single stereoisomer, and its stereochemistry was determined by examination of the nuclear Overhauser effect (NOE) between methine proton at C1 and methylene protons at the α-position to the carbonyl group. Next, **6** was treated with trifluoromethanesulfonic acid (TfOH) in acetonitrile to give oxatriquinane trifluoromethanesulfonate, but we could not obtain this in crystalline form, so the salt was purified by simple anion exchange using sat. aqueous KPF_6 to afford oxatriquinane hexafluorophosphate **7** in an excellent yield as a stable off-white solid after usual work-up. Recrystallization from CH_2Cl_2/Et_2O afforded colorless fine needles. Compound **7** showed good solubility in acetonitrile, dichloromethane, acetone, and lower alkyl alcohols such as methanol or ethanol, but was hardly soluble in chloroform, ethyl acetate, and diethylether.

Though the ^{1}H-NMR spectrum of **7** in CD_3CN showed symmetric proton signals consistent with oxatriquinane structure, the spectrum in CD_3OD solution showed another set of signals in addition to the original oxatriquinane signals. The new signals indicated that **7** was predominantly cleaved to bicyclic compound **8** in CD_3OD. The ^{1}H-NMR spectra in CD_3OD at two concentrations (0.02 M and 0.2 M) are shown in Fig. 2. At 0.02 M almost all the oxatriquinane signals were lost, except for weak signals at δ 5.5, 4.15–4.22, and 3.14. On the other hand, at 0.2 M, peaks due to **7** were more marked. These results suggest that oxatriquinane **7** and bicyclic compound **8** exist in equilibrium in CD_3OD solution (Fig. 3). The structure of **8** was confirmed by isolation and by ^{1}H-NMR measure-



Reagents and conditions: (a) Zn, $BrCH_2CO_2Et$, PhH, reflux (1 h); (b) TfOH, CH_3CN, rt (15 min), then sat. KPF_6 aq.

Chart 1. Synthesis of Oxatriquinane with Ester Functionality **7**

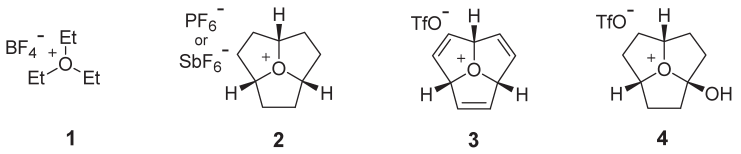


Fig. 1. Organic Oxonium Cation Species

The authors declare no conflict of interest.

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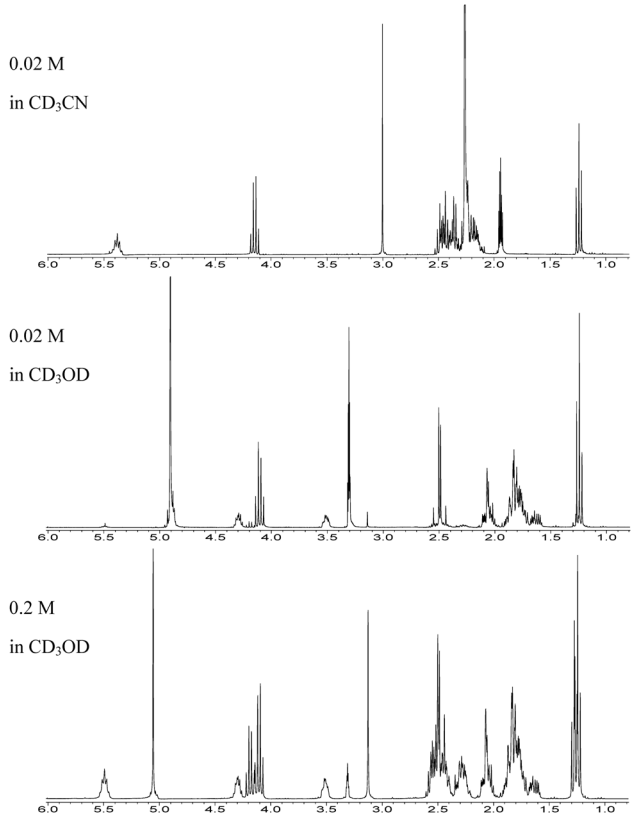
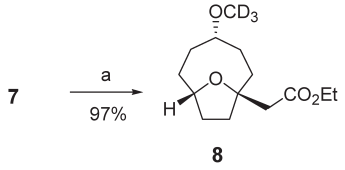


Fig. 2. ^{1}H-NMR Spectra of Oxatriquinane **7** in CD_3CN[a] or CD_3OD[b]

a) The quintet peak of deuterated solvent (1.94 ppm) was used as an internal standard. *b*) The singlet peak of tetramethylsilane (0.00 ppm) was used as an internal standard.



Reagents and conditions: (a) K_2CO_3, CD_3OD, rt (30 min).

Chart 2. K_2CO_3 Treatment of Oxatriquinane **7**

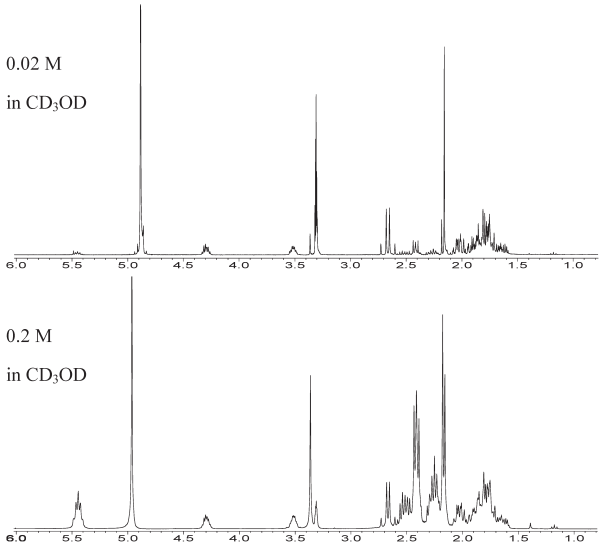


Fig. 4. ^{1}H-NMR Spectra of Oxatriquinane **11** in CD_3OD[a]

a) The singlet peak of tetramethylsilane (0.00 ppm) was used as an internal standard.

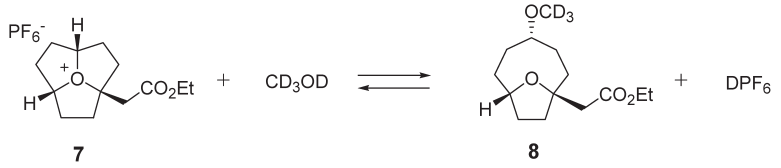


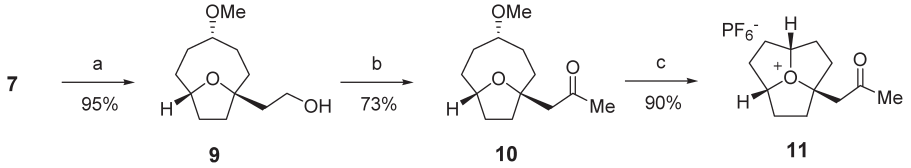
Fig. 3. Equilibrium State between Oxatriquinane Hexafluorophosphate **7** and Ring-Opened Bicyclic Compound **8** in CD_3OD

ments after potassium carbonate treatment of **7** in CD_3OD (Chart 2).

The stereochemistry at C4 was determined on the basis of NOE between a methine proton at C4 and methylene protons at the α-position to the carbonyl group in the ester functionality. Cleavage on the side of the ethoxycarbonylmethyl substituent was not detected. The ^{1}H-NMR spectrum of oxatriquinane **7** in D_2O showed a simular signal pattern to that in CD_3OD. In addition, the ^{1}H-NMR signals of the ring-opened bicyclic compound were also recognized in DMSO-d_6 or acetone-d_6 containing a small amount of water. However, the ^{1}H-NMR spectrum in aprotic CD_3CN afforded only the signals of **7**, even though a little water was present (Fig. 2). This suggests that the acidity of protic solvent present in the organic solvent greatly affects the equilibrium. Mascal *et al.* reported that oxatriquinane is stable in alcohol or water, but is present as an equilibrium mixture in a protic solvent, and is almost entirely present as the bicyclic compound in highly dilute solution. We found that the original oxatriquinane could be recovered from the equilibrium mixture by concentrating the solution to dryness. We also confirmed that Mascal's oxatriquinane **2** was in an equilibrium state in a protic solvent such as CD_3OD or D_2O. Thus, it is reasonable that oxatriquinane **7** could be purified by column chromatography without any problem using an aprotic solvent system of CH_3CN/CH_2Cl_2 as the eluent.

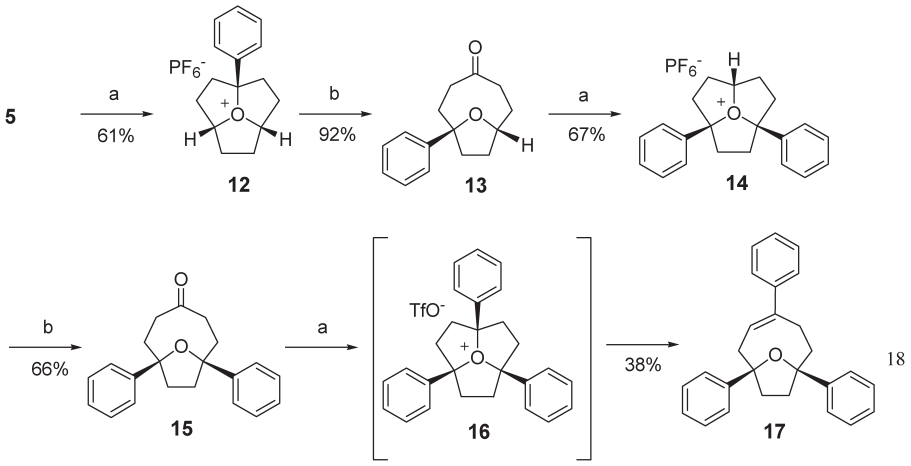
We next aimed to synthesize oxatriquinane bearing a ketone functionality. Namely, compound **7** was ring-opened with methanol and base followed by hydride reduction to give bicyclic ether **9** (Chart 3). The side chain unit in **9** was converted to an acetomethyl group in three steps (oxidation, Grignard reaction, and oxidation) to afford bicyclic ketone **10**. Finally, compound **10** was treated with TfOH in CH_3CN and anion exchange afforded oxatriquinane **11** in an excellent yield as a stable white powder. Thus, a carbonyl group is compatible with oxonium cation structure. The ^{1}H-NMR spectra of **11** in CD_3OD at two concentrations (0.02 M and 0.2 M) are also shown in Fig. 4. The behavior of **11** was similar to that of oxatriquinane **7**.

Next, we focused on oxatriquinane bearing a phenyl group, since aromatically substituted derivatives might have potential for materials chemistry. As shown in Chart 4, the starting ketone **5** was treated with phenylmagnesium bromide to give



Reagents and conditions: (a) (i) K_2CO_3, MeOH, rt (30 min); (ii) $LiAlH_4$, Et_2O, rt (15 min); (b) (i) CrO_3, pyridine, CH_2Cl_2, rt (1 h); (ii) MeMgBr, THF, rt (30 min); (iii) CrO_3, pyridine, CH_2Cl_2, rt (1 h); (c) TfOH, CH_3CN, rt (15 min), then sat. KPF_6 aq.

Chart 3. Synthesis of Oxatriquinane Bearing an Acetomethyl Group **11**



Reagents and conditions: (a) (i) phenylmagnesium bromide, THF, rt (30 min); (ii) TfOH, CH_3CN, rt (15 min), then sat. KPF_6 aq.; (b) (i) K_2CO_3, H_2O, acetone, rt (1 h); (ii) CrO_3, pyridine, CH_2Cl_2, rt (1 h).

Chart 4. Synthesis of Oxatriquinanes Bearing Phenyl Groups **12** and **14**

a crude adduct, which was treated with TfOH in CH_3CN and subjected to anion exchange to afford the desired oxatriquinane **12** in modest yield. Phenylation at the α-position to the oxygen center in **12** was also performed. Compound **12** was hydrolyzed with aqueous potassium carbonate solution to afford bicyclic alcohol, which was oxidized to ketone **13** using Collins reagent. The same procedures used in the synthesis of oxatriquinane **12** then afforded oxatriquinane **14**, which has two phenyl groups. Oxatriquinanes **12** and **14** showed similar properties to **7**, and purification by column chromatography or recrystallization afforded a stable white powder. Finally, further phenylation of oxatriquinane **14** was examined. The same reaction sequence as above provided ketone **15** and its Grignard adduct. Treatment of the crude Grignard adduct with excess TfOH afforded a product that showed the ^{1}H-NMR and ^{13}C-NMR signals of oxatriquinane **16** in CD_3CN, although usual isolation failed, probably because the instability of **16** except under strongly acidic conditions. The usual work-up resulted in yielding an olefin **17**. The geometry of the C=C double bond in **17** was determined to be (*E*) based on NOE between the C=C double bond and phenyl group protons. The ^{1}H-NMR spectrum of **16** derived from **17** in the presence of excess TfOH in CD_3CN is shown in Fig. 5. Clear symmetrical peaks of aliphatic and aromatic protons were observed.

In summary, we synthesized several organic oxonium cation species, *i.e.*, oxatriquinane hexafluorophosphate derivatives, bearing carbonyl or phenyl groups. These compounds were obtained as stable solids. ^{1}H-NMR analysis suggested that ethoxycarbonylmethyl-substituted oxatriquinane **7** is stable in aprotic solvent, but is in rapid equilibrium with the ring-opened bicyclic compound in protic solvent. Oxatriquinanes

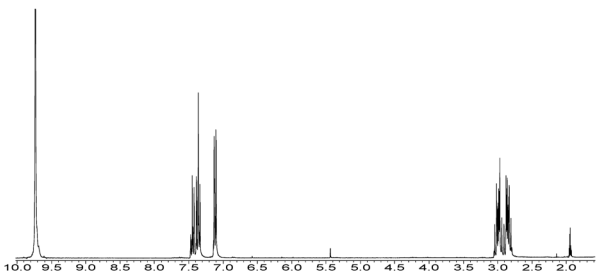


Fig. 5. ^{1}H-NMR Spectrum of **16** in the Presence of Excess TfOH in CD_3CN[a)]

a) This spectrum was measured in the presence of 5 eq of TfOH in 0.60 mL of CD_3CN. The quintet peak of deuterated solvent (1.94 ppm) was used as an internal standard.

12 and **14** bearing a phenyl group at the α-position to the oxygen center were also synthesized and isolated as stable solids. Oxatriquinane **16** bearing three phenyl groups could not be isolated, though its formation was confirmed by ^{1}H-NMR studies in excess TfOH/CD_3CN. Our findings demonstrate that a carbonyl or phenyl group is compatible with oxonium cation structure, and further synthetic studies aimed at novel functional or bioactive oxatriquinane molecules are in progress.

Experimental

General Melting points (mp) were determined on a Yanagimoto micro melting point apparatus (hot plate) and are uncorrected. Low-resolution electron-ionization mass spectra (LR-EI-MS) and high-resolution (HR)-EI-MS were recorded on a JEOL JMS-AX505HA. Proton nuclear magnetic resonance (^{1}H-NMR) spectra and carbon nuclear magnetic reso-

nance (^{13}C-NMR) spectra were measured with a Varian Mercury instrument at 300 MHz and at 75 MHz, respectively. The chemical shifts are recorded in ppm, and coupling constants (J) in Hz. ^{1}H- and ^{13}C-NMR chemical shifts are given relative to that of either tetramethylsilane (0.00 ppm for ^{1}H-NMR in $CDCl_3$ and CD_3OD) or residual solvent (1.94 ppm for ^{1}H-NMR in CD_3CN, 1.32 ppm for ^{13}C-NMR in CD_3CN, 49.00 ppm for ^{13}C-NMR in CD_3OD, and 77.00 ppm for ^{13}C-NMR in $CDCl_3$). Fluorine NMR (^{19}F-NMR) spectra and phosphorus NMR (^{31}P-NMR) spectra were measured with a Varian Mercury instrument at 282 MHz and at 121 MHz, respectively. ^{19}F- and ^{31}P-NMR chemical shifts are given relative to that of fluorobenzene (−115.30 ppm for ^{19}F-NMR) or phosphoric acid (0.00 ppm for ^{31}P-NMR). Splitting patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br; broad peak. Column chromatography was carried out with silica gel [Fuji Davison BW200] as the absorbent. Thin layer chromatography (TLC) was carried out on Merck Silica gel 60 PF_{254}. Solutions were dried over anhydrous sodium sulfate or anhydrous magnesium sulfate and the solvent was removed by rotary evaporation under reduced pressure.

(4-Hydroxy-10-oxa-bicyclo[5.2.1]dec-4-yl)acetic Acid Ethyl Ester (6) To a solution of **5** (336.4 mg, 2.181 mmol) in benzene (7 mL) were added zinc powder (430.1 mg, 6.578 mmol) and ethyl bromoacetate (0.36 mL, 3.255 mmol). The mixture was heated to reflux for 1 h, then allowed to cool to ambient temperature. Sat. NH_4Cl aq. (10 mL) was added, and the whole was extracted with AcOEt×3. The combined organic layer was dried. The solvent was evaporated and the residue was chromatographed on silica gel (15% to 30% AcOEt/*n*-hexane as the eluent) to give **6** (407.1 mg, 1.680 mmol, 77%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.27 (3H, t, J=7.0 Hz), 1.40 (1H, dt, J=4.9, 4.3 Hz), 1.45 (1H, dt, J=4.9, 4.3 Hz), 1.70–2.21 (10H, m), 2.52 (2H, s), 4.09 (1H, br s), 4.15 (2H, q, J=7.0 Hz), 4.25–4.35 (2H, m); ^{13}C-NMR ($CDCl_3$) δ: 14.16, 29.63 (2C), 30.11 (2C), 34.99 (2C), 50.09, 60.11, 70.42, 76.98 (2C), 171.53; LR-EI-MS m/z: 224 (M^+-H_2O); HR-EI-MS m/z: 224.1410 (Calcd for $C_{13}H_{20}O_3$: 224.1412).

2-(Ethoxycarbonyl)oxatriquinanium Hexafluorophosphate (7) To a stirred solution of **6** (350.7 mg, 1.447 mmol) in CH_3CN (4 mL) was added dropwise TfOH (192 μL, 2.170 mmol). Stirring was continued for 10 min, then additional TfOH (192 μL, 2.170 mmol) was added dropwise and stirring was continued for 1 h. Sat. KPF_6 aq. (10 mL) was added, and stirring was continued for 10 min. The reaction mixture was extracted with CH_2Cl_2×6, and the combined organic layer was dried. The solvent was evaporated and the residue was dissolved in a small amount of CH_2Cl_2 and then precipitated with Et_2O. The resulting precipitate was collected on a filter and washed with Et_2O to give **7** (488.7 mg, 1.320 mmol, 91%) as an off-white solid. Colorless needles (CH_2Cl_2/Et_2O); mp= 101.5–103.5°C; ^{1}H-NMR (CD_3CN) δ: 1.24 (3H, t, J=7.0 Hz), 2.10–2.26 (4H, m), 2.30–2.54 (8H, m), 3.00 (2H, s), 4.15 (2H, q, J=7.0 Hz), 5.39 (2H, apparant quint, J=5.8 Hz); ^{13}C-NMR (CD_3CN) δ: 14.43, 29.99 (2C), 30.21 (2C), 34.95 (2C), 41.23, 62.17, 102.88 (2C), 113.30, 169.17; ^{19}F-NMR (CD_3CN) δ: −73.17 (d, $J_{F\text{-}P}$=708 Hz); ^{31}P-NMR (CD_3CN) δ: −143.18 (sept, $J_{P\text{-}F}$=708 Hz); LR-EI-MS m/z: 225 (M^+); HR-EI-MS m/z: 225.1486 (Calcd for $C_{13}H_{21}O_3^+$: 224.1485).

(4-[$^2H_3$]Methoxy-10-oxa-bicyclo[5.2.1]dec-1-yl)acetic Acid Ethyl Ester (8) To a solution of **7** (100.5 mg, 0.271 mmol) in CD_3OD (2 mL) was added K_2CO_3 (39.4 mg, 0.285 mmol). The mixture was stirred for 30 min, and then diluted with Et_2O. The resulting suspension was filtered on Celite pad, which was well washed with Et_2O. The filtrate was evaporated and the residue was chromatographed on silica gel (10% to 15% AcOEt/*n*-hexane as the eluent) to give **8** (68.3 mg, 0.263 mmol, 97%) as a colorless oil. ^{1}H-NMR (CD_3OD) δ: 1.24 (3H, t, J=7.0 Hz), 1.57–1.92 (9H, m), 1.99–2.12 (3H, m), 2.47 (1H, d, J=14.1 Hz), 2.51 (1H, d, J=14.1 Hz), 3.46–3.55 (1H, m), 4.10 (2H, q, J=7.0 Hz), 4.25–4.34 (1H, m); ^{13}C-NMR (CD_3OD) δ: 14.52, 30.46, 30.57, 31.24, 33.71, 35.11, 38.02, 47.12, 61.38, 79.46, 83.70, 84.27, 172.57; LR-EI-MS m/z: 259 (M^+); HR-EI-MS m/z: 259.1858 (Calcd for $C_{14}H_{21}D_3O_4$: 259.1860).

2-(4-Methoxy-10-oxa-bicyclo[5.2.1]dec-1-yl)ethanol (9) To a solution of **7** (522.3 mg, 1.450 mmol) in MeOH (10 mL) was added K_2CO_3 (210.5 mg, 1.523 mmol). The resulting suspension was stirred for 30 min, then concentrated *in vacuo* and the residue was diluted with Et_2O. The suspension was filtered on a Celite pad, and the pad was well washed with Et_2O. The filtrate was evaporated to afford a crude product (358.6 mg). This product was dissolved in tetrahydrofuran (THF) (5 mL), and $LiAlH_4$ (55.1 mg, 1.452 mmol) was carefully added. The suspension was stirred for 15 min and then quenched with H_2O (0.1 mL) and 3 M NaOH (0.1 mL). The suspension was filtered on a Celite pad, and the pad was well washed with Et_2O. The filtrate was concentrated *in vacuo* and the residue was chromatographed on silica gel (40% to 80% AcOEt/*n*-hexane as the eluent) to give **9** (296.5 mg, 1.384 mmol, 95%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.58–2.00 (13H, m), 2.00–2.12 (1H, m), 3.28 (3H, s), 3.46–3.62 (2H, m), 3.69–3.82 (2H, m), 4.30–4.39 (1H, m); ^{13}C-NMR ($CDCl_3$) δ: 28.89, 29.59 (2C), 32.06, 34.52, 36.64, 42.09, 55.44, 59.31, 77.77, 81.53, 85.01; LR-EI-MS m/z: 214 (M^+); HR-EI-MS m/z: 214.1570 (Calcd for $C_{12}H_{22}O_3$: 214.1569).

1-(4-Methoxy-10-oxa-bicyclo[5.2.1]dec-1-yl)propan-2-one (10) Compound **9** (247.3 mg, 1.154 mmol) was taken up in CH_2Cl_2 (5 mL) and added to a stirred solution of Collins reagent, which had been prepared from CrO_3 (579.2 mg, 5.793 mmol) and pyridine (0.93 mL, 11.56 mmol) in CH_2Cl_2 (15 mL). After 1 h, 3 M NaOH (20 mL) was added, and the mixture was extracted with CH_2Cl_2×3. The combined organic phase was washed with 2 M HCl (20 mL) and brine (20 mL), and dried. The solvent was evaporated and the residue (210.9 mg) was dissolved in THF (3 mL). To this stirred solution was added dropwise methylmagnesium bromide (3.0 M solution in Et_2O; 0.58 mL, 1.740 mmol) and stirring was continued for 15 min. Sat. NH_4Cl aq. (5 mL) was added, and the mixture was extracted with AcOEt×3. The combined organic layer was dried. The solvent was evaporated and the residue (218.8 mg) was taken up in CH_2Cl_2 (5 mL). This solution was added to a stirred solution of Collins reagent, which had been prepared from CrO_3 (589.3 mg, 5.894 mmol) and pyridine (0.93 mL, 11.56 mmol) in CH_2Cl_2 (15 mL). After 1 h, 3 M NaOH (20 mL) was added, and the mixture was extracted with CH_2Cl_2×3. The combined organic phase was washed with 2 M HCl (20 mL) and brine (20 mL), and dried. The solvent was evaporated and the residue was chromatographed on silica gel (15% to 25% AcOEt/*n*-hexane as the eluent) to give **10** (190.4 mg, 0.841 mmol, 73%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.56–2.09 (12H, m), 2.18 (3H, s), 2.59 (1H, d, J=14.4 Hz), 2.67 (1H, d, J=14.4 Hz), 3.27 (3H, s), 3.46–3.54

(1H, m), 4.26–4.38 (1H, m); ^{13}C-NMR ($CDCl_3$) δ: 29.41, 29.52, 30.14, 31.94, 32.61, 34.03, 37.19, 54.49, 55.56, 77.67, 82.05, 83.08, 207.92; LR-EI-MS *m/z*: 226 (M^+); HR-EI-MS *m/z*: 226.1559 (Calcd for $C_{13}H_{22}O_3$: 226.1569).

2-(2-Oxopropyl)oxatriquinanium Hexafluorophosphate (11) To a stirred solution of **10** (173.7 mg, 0.768 mmol) in CH_3CN (3 mL) was added dropwise TfOH (204 μL, 2.305 mmol). Stirring was continued for 15 min, then the reaction mixture was concentrated *in vacuo*, and the resulting residue was treated with sat. KPF_6 aq. (10 mL). The mixture was extracted with CH_2Cl_2×6, and the combined organic layer was dried. The solvent was evaporated and the residue was dissolved in a small amount of CH_2Cl_2 and then precipitated with Et_2O. The resulting precipitate was collected on a filter and washed with Et_2O to give **11** (236.1 mg, 0.694 mmol, 90%) as an off-white solid. Colorless needles (CH_2Cl_2/Et_2O); mp=101.5–103.5°C; ^{1}H-NMR (CD_3CN) δ: 2.07–2.23 (4H, m), 2.12 (3H, s), 2.25–2.50 (8H, m), 3.22 (2H, s), 5.34 (2H, apparent quint, J=5.8 Hz); ^{13}C-NMR (CD_3CN) δ: 30.15 (2C), 30.50 (2C), 31.09, 35.14 (2C), 49.12, 102.24 (2C), 114.77, 205.02; ^{19}F-NMR (CD_3CN) δ: −73.12 (d, $J_{F\text{-}P}$=708 Hz); ^{31}P-NMR (CD_3CN) δ: −143.21 (sept, $J_{P\text{-}F}$=708 Hz); LR-EI-MS *m/z*: 195 (M^+); HR-EI-MS *m/z*: 195.1387 (Calcd for $C_{12}H_{19}O_2^+$: 195.1380).

2-Phenyloxatriquinanium Hexafluorophosphate (12) To a solution of **5** (195.4 mg, 1.267 mmol) in THF (2 mL) was added dropwise phenylmagnesium bromide (1.08 M solution in THF; 1.76 mL, 1.901 mmol). The solution was stirred for 30 min, then sat. NH_4Cl aq. (5 mL) was added, and the mixture was extracted with AcOEt×3. The combined organic layer was dried. The solvent was evaporated and the residue was dissolved in CH_3CN (3 mL). To this solution was added dropwise TfOH (112 μL, 1.266 mmol). Stirring was continued for 15 min, then the reaction mixture was concentrated *in vacuo*, and the resulting residue was treated with sat. KPF_6 aq. (10 mL). The mixture was extracted with CH_2Cl_2×6, and the combined organic layer was dried. The solvent was evaporated and the residue was dissolved in a small amount of CH_2Cl_2 and then precipitated with Et_2O. The resulting precipitate was collected on a filter and washed with Et_2O to give **12** (278.8 mg, 0.774 mmol, 61%) as an off-white solid. Colorless needles (CH_2Cl_2/Et_2O); mp=121.5–123.5°C; ^{1}H-NMR (CD_3CN) δ: 2.21–2.58 (10H, m), 2.65–2.77 (2H, m), 5.57 (2H, apparent quint, J=5.8 Hz), 7.37–7.51 (5H, m); ^{13}C-NMR (CD_3CN) δ: 30.04 (2C), 30.47 (2C), 37.56 (2C), 103.40 (2C), 116.08, 118.34, 125.23 (2C), 130.08 (2C), 139.95; ^{19}F-NMR (CD_3CN) δ: −73.20 (d, $J_{F\text{-}P}$=708 Hz); ^{31}P-NMR (CD_3CN) δ: −143.17 (sept, $J_{P\text{-}F}$=708 Hz); LR-EI-MS *m/z*: 215 (M^+); HR-EI-MS *m/z*: 215.1425 (Calcd for $C_{12}H_{22}O_3$: 215.1430).

1-Phenyl-10-oxa-bicyclo[5.2.1]decan-4-one (13) To a solution of **12** (368.8 mg, 1.024 mmol) in acetone (10 mL) was added 20% K_2CO_3 aq. (5 mL). The biphasic mixture was stirred vigorously for 1 h, and then concentrated *in vacuo*. The residue was extracted with $CHCl_3$×5, and the combined organic extracts were dried. The solvent was evaporated and the residue was taken up in CH_2Cl_2 (10 mL). This solution was added to a stirred solution of Collins reagent, which had been prepared from CrO_3 (611.3 mg, 6.114 mmol) and pyridine (0.98 mL, 12.18 mmol) in CH_2Cl_2 (20 mL). After 1 h, 3 M NaOH (40 mL) was added, and the mixture was extracted with CH_2Cl_2×3. The combined organic phase was washed with 2 M HCl (40 mL) and brine (30 mL), and dried. The solvent was evaporated and the residue was chromatographed on silica gel (20% to 40% AcOEt/*n*-hexane as the eluent) to give **13** (215.8 mg, 0.937 mmol, 92%) as an off-white solid. Colorless needles (Et_2O/*n*-hexane); mp=66.5–67.5°C; ^{1}H-NMR ($CDCl_3$) δ: 1.88–2.27 (7H, m), 2.32–2.49 (4H, m), 2.67 (1H, ddd, J=3.6, 10.6, 13.8 Hz), 4.41–4.51 (1H, m), 7.15–7.38 (5H, m); ^{13}C-NMR ($CDCl_3$) δ: 29.14, 34.25, 35.02, 37.37, 37.59, 40.32, 77.25, 85.65, 124.73 (2C), 126.40, 127.88 (2C), 146.60, 210.49; LR-EI-MS *m/z*: 230 (M^+); HR-EI-MS *m/z*: 230.1305 (Calcd for $C_{15}H_{18}O_2$: 230.1307).

2,4-Diphenyloxatriquinanium Hexafluorophosphate (14) To a solution of **13** (215.8 mg, 0.937 mmol) in THF (3 mL) was added dropwise phenylmagnesium bromide (1.08 M solution in THF; 1.73 mL, 1.868 mmol) and the solution was stirred for 30 min. Additional phenylmagnesium bromide (1.08 M solution in THF; 0.50 mL, 0.540 mmol) was added dropwise. Stirring was continued for 1 h, then sat. NH_4Cl aq. (5 mL) was added, and the mixture was extracted with AcOEt×3. The combined organic layer was dried. The solvent was evaporated and the residue was dissolved in CH_3CN (3 mL). To this solution was added dropwise TfOH (150 μL, 1.695 mmol), and stirring was continued for 15 min. The reaction mixture was concentrated *in vacuo*, and the resulting residue was treated with sat. KPF_6 aq. (10 mL). The mixture was extracted with CH_2Cl_2×5, and the combined organic layer was dried. The solvent was evaporated and the residue was dissolved in a small amount of CH_2Cl_2 and then precipitated with Et_2O. The resulting precipitate was collected on a filter and washed with Et_2O to give **14** (275.9 mg, 0.632 mmol, 67%) as an off-white solid. White powder (CH_2Cl_2/Et_2O); mp=153–155°C; ^{1}H-NMR (CD_3CN) δ: 2.36–2.62 (6H, m), 2.63–2.97 (6H, m), 5.98 (1H, apparent quint, J=5.8 Hz), 7.27–7.55 (10H, m); ^{13}C-NMR (CD_3CN) δ: 30.78 (2C), 36.86 (2C), 38.76 (2C), 104.46, 118.58 (2C), 126.07 (4C), 130.21 (4C), 130.57 (2C), 139.27 (2C); ^{19}F-NMR (CD_3CN) δ: −73.21 (d, $J_{F\text{-}P}$=708 Hz); ^{31}P-NMR (CD_3CN) δ: −143.15 (sept, $J_{P\text{-}F}$=708 Hz); LR-EI-MS *m/z*: 291 (M^+); HR-EI-MS *m/z*: 291.1742 (Calcd for $C_{21}H_{23}O^+$: 291.1743).

1,7-Diphenyl-10-oxa-bicyclo[5.2.1]decan-4-one (15) To a solution of **14** (275.9 mg, 0.632 mmol) in acetone (6 mL) was added 20% K_2CO_3 aq. (3 mL). The biphasic mixture was stirred for 15 h, and then concentrated *in vacuo*. The residue was extracted with $CHCl_3$×4, and the combined organic extracts were dried. The solvent was evaporated and the residue was taken up in CH_2Cl_2 (6 mL). This solution was added to a stirred solution of Collins reagent, which had been prepared from CrO_3 (385.5 mg, 3.855 mmol) and pyridine (0.62 mL, 7.705 mmol) in CH_2Cl_2 (12 mL). After 1 h, 3 M NaOH (30 mL) was added, and the solution was extracted with CH_2Cl_2×3. The combined organic phase was washed with 2 M HCl (30 mL) and brine (30 mL), and dried. The solvent was evaporated and the residue was chromatographed on silica gel (15% to 30% AcOEt/*n*-hexane as the eluent) to give **15** (127.1 mg, 0.415 mmol, 66%) as an off-white solid. Colorless needles (CH_2Cl_2/Et_2O); mp=183.5–185°C; ^{1}H-NMR ($CDCl_3$) δ: 1.56–2.09 (12H, m), 2.18 (3H, s), 2.59 (1H, d, J=14.4 Hz), 2.67 (1H, d, J=14.4 Hz), 3.27 (3H, s), 3.46–3.54 (1H, m), 4.26–4.38 (1H, m); ^{13}C-NMR ($CDCl_3$) δ: 36.39 (2C), 36.46 (2C), 41.16 (2C), 86.70 (2C), 124.91 (4C), 126.51 (2C), 128.04 (4C), 146.98 (2C), 210.54; LR-EI-MS *m/z*: 306 (M^+); HR-EI-MS *m/z*: 306.1611 (Calcd for $C_{21}H_{22}O_2$: 306.1620).

1,4,7-Triphenyl-10-oxa-bicyclo[5.2.1]dec-3-ene (17) To

a solution of **15** (96.0 mg, 0.313 mmol) in THF (1 mL) was added dropwise phenylmagnesium bromide (1.08 M solution in THF; 0.58 mL, 0.626 mmol) and the solution was stirred for 30 min. Additional phenylmagnesium bromide (1.08 M solution in THF; 0.29 mL, 0.313 mmol) was added dropwise. Stirring was continued for 2 h, then sat. NH_4Cl aq. (5 mL) was added, and the mixture was extracted with AcOEt×3. The combined organic layer was dried. The solvent was evaporated and the residue was dissolved in CH_3CN (1 mL). To this solution was added dropwise TfOH (42 μL, 0.475 mmol), and stirring was continued for 15 min. The reaction mixture was concentrated *in vacuo* to dryness. The ^{1}H-NMR spectrum of the crude product in CD_3CN indicated the presence of a bicyclic compound bearing three phenyl groups **17** as the main component. The crude product was taken up in sat. $NaHCO_3$ aq. (10 mL), and the mixture was extracted with CH_2Cl_2×3. The combined organic layer was dried and then evaporated, and the residue was chromatographed on silica gel (10% to 30% benzene/*n*-hexane as the eluent) to give **17** (44.0 mg, 0.120 mmol, 38%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 2.03–2.22 (3H, m), 2.31–2.47 (2H, m), 2.61–2.84 (4H, m), 3.14 (1H, br t, J=11 Hz), 6.15 (1H, dd, J=7.3, 8.5 Hz), 7.13 (1H, tt, J=1.4, 7.3 Hz), 7.19–7.29 (4H, m), 7.30–7.42 (6H, m), 7.51 (2H, br d, J=7 Hz), 7.58 (2H, br d, J=7 Hz); ^{13}C-NMR ($CDCl_3$) δ: 26.78, 37.34, 39.29, 41.38, 43.68, 86.67, 89.73, 124.31, 124.42 (2C), 125.05 (2C), 125.95 (2C), 126.28, 126.88, 127.89 (2C), 128.04 (2C), 128.32, 128.36 (2C), 142.79, 143.66, 148.84, 151.59; LR-EI-MS *m*/*z*: 366 (M^+); HR-EI-MS *m*/*z*: 366.1996 (Calcd for $C_{27}H_{26}O$: 366.1984).

2,4,6-Triphenyloxatriquinanium Trifluoromethanesulfonate (16) To a stirred solution of **17** (33.1 mg, 0.090 mmol) in CD_3CN (0.6 mL) was added dropwise TfOH (40 μL, 0.452 mmol). Stirring was continued for 15 min, then the reaction mixture was transferred into an NMR tube, and ^{1}H- and ^{13}C-NMR spectra were recorded. Both spectra indicated that compound **17** had been completely converted to oxatriquinane **16**. ^{1}H-NMR (CD_3CN) δ: 2.78–2.91 (6H, m), 2.92–3.05 (6H, m), 7.11 (6H, dt, J=7.1, 1.8 Hz), 7.36 (6H, tt, J=1.8, 7.1 Hz), 7.44 (3H, tt, J=1.8, 7.1 Hz); ^{13}C-NMR (CD_3CN) δ: 37.89 (6C), 120.45 (3C), 127.30 (6C), 130.36 (6C), 131.14 (3C), 137.74 (3C).

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