Pauson−Khand Reaction on the 1,2-Isopropylidenedioxyfuranoside Scaffold: Expedient Access to a Chiral Cyclopenta[*c*]pyran Ring System

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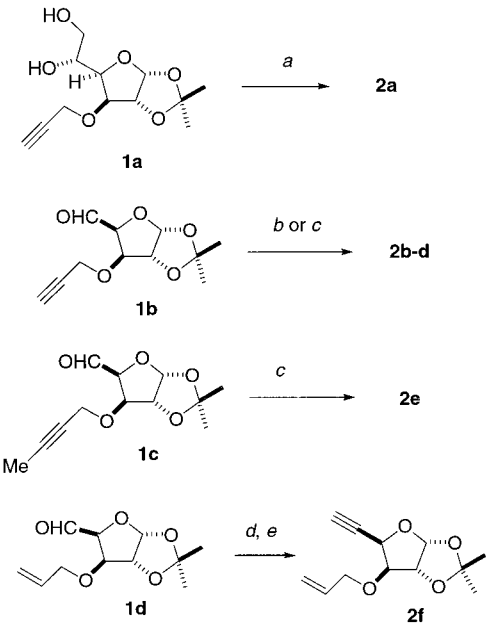
Introduction

The Pauson−Khand reaction (PKR) has been established as a powerful method for the synthesis of cyclopentenone derivatives by way of union of an alkene and alkyne moieties in the presence of dicobaltoctacarbonyl and other related metal species.[1] The intramolecular variety of the reaction has gained much popularity because it can furnish cyclopentenone-fused ring systems, which are otherwise difficultly accessible. Although the utility of this useful reaction in the construction of chiral ring skeletons has been well documented, its application to the carbohydrate template for the purpose is relatively recent.[1,2] The majority of such reactions using carbohydrate derivatives have been reported for pyranoside rings with on-template ene systems.[2] Recent reports from our laboratory have demonstrated the utility of the 1,2-isopropylidenedioxyfuranside ring system as a potentially useful scaffold for carrying out cycloaddition reactions.[3a−f] The important features of this scaffold are the ready availability of the starting material, easy characterizability of the products, and the scope of further transformations of the products giving rise to diverse types of molecules. Herein, we describe a brief study on the PKR of enyne systems built on the 1,2-isopropylidenedioxyfuranoside scaffold leading to the chiral cyclopenta[*c*]pyran skeleton, which constitutes the frameworks of irridoids such as loganin, iridomyrmecin and boschnialactone.[4]

Results and Discussion

The olefinic precursors **2a** and **2f** were prepared by established procedures[5,6] from the known carbohydrate derivatives **1a**[3c] and **1d**[7], whereas **2b**−**e** were prepared from **1b**[3c] and **1c**[3c] (Scheme 1). The trans geometry of the olefins formed in these reactions was indicated by the vicinal *J* (9−12 Hz) observed for the olefinic protons.

Scheme 1



Reagents: *a* I_2, imidazole, Ph_3P, toluene, reflux *b* Ph_3PEt Br, n-BuLi,THF, - 48 °C - 25 °C (for **2b**) *c* Ph_3PCH_2Ar Br, 10% aq. NaOH, CH_2Cl_2-H_2O (5:1), 0 - 25 °C (for **2c-e**) *d* CBr_4, Zn, Ph_3P, CH_2Cl_2, 0 - 25 °C *e* *n*-BuLi, THF, - 78 - 0 °C

The PKR of **2a**−**f** was effected by $Co_2(CO)_8$ in CH_2Cl_2 at 25 °C using NMO as the promoter, and yields of the resulting pyranocyclopentenone derivatives **3a**−**f** are shown in Table 1. The IR, mass, and ^1H and ^{13}C NMR spectra of the products were consistent with the structures. As a representative case, the structure of **3c** was also secured by H,H-COSY and C,H-COSY analysis, and its stereochemistry was established by NOESY analysis. The trans relationship between the newly formed chiral centers 1-H and 9b-H was apparent from the appearance of strong cross-peaks between 9b-H and one of the ortho protons of the phenyl indicating the cis orientation of the phenyl ring and 9b-H. Cross-peaks between 9b-H and 5a-H established the α orientation of 9b-H. The coupling constant values viz $J_{9a,9b} = \sim 3.4$ Hz and $J_{1,9b} = \sim 3.6$ Hz are consistent with the assigned orientation of 9b-H. The alternative orientation of 9b-H would have resulted in a higher $J_{9a,9b}$ due to their pseudoaxial geometry leading to a discernible multiplet instead of a broad singlet. The stereochemistry of the other PKR products was assigned on the basis of the expected analogous stereochemistry of the cycloaddition of the alkyne−cobalt complex with the olefinic bond.

It is worth mentioning that the yields of the products arising out of the olefins substituted by aromatic substituents were much higher than the others, although reasons for this difference in yields are not known at present.

The PKR products **3a**−**f** incorporate a cyclopenta[*c*]pyran ring system fused to a furanoside ring.

The presence of this ring system in irridoids led us to demonstrate the feasibility of degradation of these PKR

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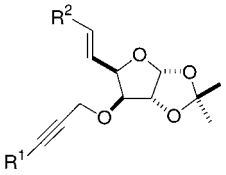
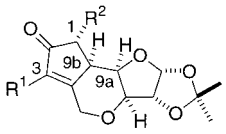
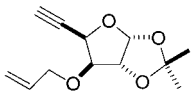
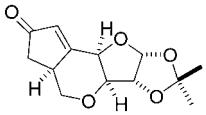
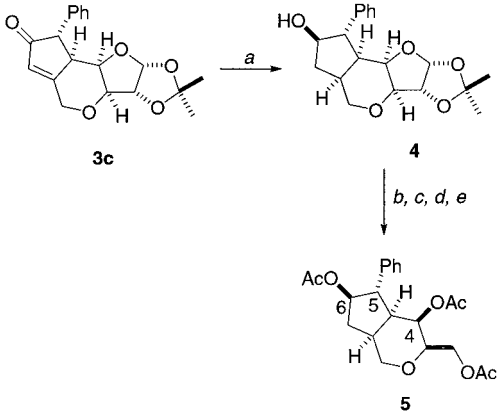
Table 1. Pauson–Khand Reaction of 2a–f

Ene-yne derivatives	Products (yield, %)[a]
	
2a: R^1 = H, R^2 = H	**3a** (44)
2b: R^1 = H, R^2 = Me	**3b** (35)
2c: R^1 = H, R^2 = Ph	**3c** (87)
2d: R^1 = H, R^2 = (4-OBn-3-OMe)Ph	**3d** (93)
2e: R^1 = Me, R^2 = (4-OBn-3-OMe)Ph	**3e** (30)
 **2f**	 **3f** (23)

[a] chromatographic yields

Scheme 2



Reagents *a* $NaBH_4$, Bu_4NBr, THF, reflux, 14 h *b* IN aq. HCl-dioxane (1:2), 50 °C, 1.5 h *c* $NaIO_4$, MeOH, 0 - 25 °C, 1h e $NaBH_4$, EtOH, 0 - 25 °C, 15 h *f* Ac_2O, pyridine. DMAP, 0 - 25 °C, 48 h, 9% (from **3c**)

products in order to unveil the core cyclopentanopyran ring system. With this end in view **3c** was subjected to reduction[8] of the enone moiety by $NaBH_4$ in the presence of tetrabutylammonium bromide in THF giving the alcohol **4** followed by a well established[3a,c,d,7] shown in Scheme 2. The intermediates in all these reactions were not purified, and the final product was characterized to be the triacetate **5**, obtained in 9% overall yield from **3c**. The gross structure of **5** was established by mass, NMR, and H,H-homodecoupling NMR spectral analysis. The stereochemistry at 6-C was established on the basis of the NOESY spectrum, which exhibited strong cross-peaks between 6-H and the protons of the phenyl ring, thus indicating the cis relationship between 6-H and 5-phenyl group. The 6-OAc was therefore assigned β orientation, because α orientation of the 5-Ph in **3c** was already established.

Conclusion

In conclusion, the work described above established that PKR on the 1,2-isopropylidenefuranoside scaffold is an expedient method for generating cylopenta[*c*]pyran derivatives because of the facile assemblage of the enyne systems in this scaffold as well as the readiness with which the furanoside ring can give rise to other ring systems through degradation and further reactions.[3c,d]

Experimental Section

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz in $CDCl_3$ using TMS as the internal standard. Elemental analyses were performed at the Indian Association for the Cultivation of Science, Kolkata. IR spectra were obtained as neat or in KBr pellets. Reactions were monitored by thin-layer chromatography using Merck 60 F_{254} precoated silica gel plate (No.1.05554). Organic extracts were dried over anhydrous sodium sulfate. For column chromatography 60–120 mesh silica gel (SRL, India) was used. Solvents were distilled and dried immediately prior to use. Room temperature refers to 25 °C.

(3a*R*,5*R*,6*S*,6a*R*)-2,2-Dimethyl-6-prop-2-ynyloxy-5-styryltetrahydrofuro[2,3-*d*][1,3]dioxole (2a). A solution of **1a**[3c] (2 g, 0.008 mol), imidazole (2.24 g, 0.03 mol), and Ph_3P (8.64 g, 0.03 mol) in toluene (150 mL) was heated under reflux. At the initiation of reflux, iodine (3.2 g, 0.012 mol) was added in portions over a period of 1 h. After completion of addition, reflux was continued for 5 h. The mixture was cooled, and the solution was transferred to a separatory funnel. The residue remaining in the reaction flask was washed repeatedly with toluene, and the combined washings were mixed with the solution in the separatory funnel. The combined organic extracts were then washed successively with saturated sodium thiosulfate solution (100 mL), 1 M NaOH solution (100 mL), and water (3 × 100 mL) and dried. Removal of solvent afforded a dark yellow syrup, which on chromatography over silica gel (EtOAc–petroleum ether, 1:9) afforded **2a** (1.2 g, 69%) as a pale yellow oil: $[\alpha]_D^{25}$ −50.7 (*c* 0.16, $CHCl_3$); MS (EI) *m/z* 224 (M^+); IR (neat) 2117 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 3H), 1.52 (s, 3H), 2.46 (t, J = 2.3 Hz, 2H), 4.05 d, J = 3.0 Hz, 1H), 4.22 (d, J = 2.3 Hz, 2H), 4.65 (d, J = 3.8 Hz, 2H), 5.31 (d, J = 10.5 Hz, 1H), 5.42 (d, J = 17.3 Hz, 1H), 5.93 (d, J = 3.7 Hz, 1H), 5.95 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.19 (CH_3), 26.73 (CH_3), 57.67 (CH_2), 75.00 (q), 79.03 (CH), 81.26 (CH), 82.80 (CH), 83.04 (CH), 104.75 (CH), 111.6 (q), 119.4 (CH_2), 132.3 (CH).

(3a*R*,5*R*,6*S*,6a*R*)-2,2-Dimethyl-5-propenyl-6-prop-2-ynyloxytetrahydrofuro[2,3-*d*][1,3]dioxole (2b). To a suspension of ethyltriphenylphosphonium bromide (600 mg, 1.62 mmol) in THF (10 mL) cooled to −48 °C was added *n*-BuLi (0.8 mL). The resulting yellowish orange mixture was stirred at −48 °C for 2 h. A solution of **1b**[3c] (400 mg, 1.77 mmol) in THF (10 mL) was then added to it dropwise, and the yellowish orange color of the mixture disappeared. It was then allowed to come to room temperature, and stirring was continued for further 5 h. The mixture was quenched with a saturated aqueous NH_4Cl solution and concentrated. Extraction with CH_2Cl_2 followed by washing of the combined organic extracts with water, drying, and removal of solvent yielded a dark yellow syrup, which on chromatography over silica gel (EtOAc–petroleum ether, 1:4) afforded **2b** as a pale yellow syrup (173 mg, 41%): $[\alpha]_D$25–55.9 (*c* 1.8, $CHCl_3$); MS (EI) *m/z* 223 (M^+ − 15); ^1H NMR δ 1.33 (s, 3H), 1.54 (s, 3H), 1.74 (dd, J = 6.9, 11.7 Hz, 3H), 2.45 (t, J = 2.3 Hz, 1H), 4.00 (d, J = 3.0 Hz, 1H),4.22 (d, J = 2.4 Hz, 2H), 4.65 (d, J = 3.8 Hz, 1H), 4.99 (dd, J = 2.8, 8.2 Hz, 1H), 5.60 (t, J = 8.4 Hz, 1H), 5.80 (m, 1H), 5.93 (d, J = 3.9 Hz, 1H); ^{13}C NMR δ 13.8 (CH_3), 26.8 (CH_3), 57.4 (CH_2), 74.9 (q), 75.5 (CH), 77.2 (CH), 82.9 (CH), 83.0 (CH), 104.6 (CH), 111.5 (q), 124.0 (CH), 130.0 (CH).

(3a*R*,5*R*,6*S*,6a*R*)-2,2-Dimethyl-6-prop-2-ynyloxy-5-styryltetrahydrofuro[2,3-*d*][1,3]dioxole (2c), (3a*R*,5*R*,6*S*,6a*R*)-5-[2-(4-Benzyloxy-3-methoxyphenyl)vinyl]-2,2-dimethyl-

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6-prop-2-ynyloxytetrahydrofuro[2,3-*d*][1,3]dioxole (2d), and (3a*R*,5*R*,6*S*,6a*R*)-5-[2-(4-Benzyloxy-3-methoxyphenyl)vinyl]-6-but-2-ynyloxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]-dioxole (2e). The general method of the Wittig reaction for the preparation of the above compounds is illustrated by that of **2d**.

A 10% aq. NaOH solution (4 mL) was added dropwise with stirring to a solution of **1b**[3c] (1 g, 0.004 mol), (4-benzyloxy-3-methoxy)phenylmethyltriphenylphosphonium bromide (4.5 g, 0.008 mol), CH_2Cl_2 (30 mL), and water (6 mL) at 0 °C. After addition was over, the mixture was brought to 25 °C and diluted with water (10 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with water and dried, and removal of solvent yielded a yellow oil, which on chromatography over silica gel (EtOAc−petroleum ether) afforded **2d** (1.25 g, 65%) as a pale yellow syrup:

$[\alpha]^{25}_D$ −34.5 (*c* 2.6, $CHCl_3$); IR (neat) 1646 cm^{-1}; MS (EI) *m*/*z* 436 (M^+), 421 ($M^+ - 15$); ^1H NMR δ 1.30 (s, 3H), 1.42 (s, 3H), 2.40 (brs,1H), 3.92 (s, 3H), 4.02 (d, J = 2.7 Hz, 1H), 4.27 (brs, 2H), 4.68 (d, J = 3.8 Hz, 1H), 5.00 (dd, J = 2.4, 9.0 Hz, 1H), 5.16 (s, 2H), 5.86 (dd, J = 9.2, 11.2 Hz, 1H), 5.97 (d, J = 3.8 Hz, 1H), 6.73−6.84 (m, 3H), 7.07 (s, 1H), 7.26−7.44 (m, 5H); ^{13}C NMR δ 26.2 (CH_3), 26.6 (CH_3), 55.9 (CH_3), 57.6 (CH_2), 70.9 (CH_2), 75.1 (q), 75.8 (CH), 79.0 (CH), 82.8 (CH), 82.9 (CH), 104.6 (CH), 111.4 (q), 112.3 (CH), 113.7 (CH), 121.5 (CH), 122.1 (CH), 127.2 (CH), 127.8 (CH), 128.5 (CH), 129.8 (q), 135.5 (CH), 137.0 (q), 147.7 (q), 149.4 (q).

Compounds **2c** and **2e** were prepared similarly from **1b** (1.3 g, 5.8 mmol) and **1c**[3c] (2 g, 8.8 mmol), respectively.

2c: yield (2.12 g, 80%); oil; $[\alpha]^{25}_D$ −65.9 (*c* 2.60, $CHCl_3$); IR (neat) 2117 cm^{-1}; MS (EI) *m*/*z* 300 (M^+), 285 ($M^+ - 15$); ^1H NMR δ 1.32 (s, 3H), 1.41 (s, 3H), 2.45 (t, J = 2.1 Hz, 1H), 4.05 (d, J = 3.0 Hz, 1H), 4.26 (d, J = 2.1 Hz, 1H), 4.67 (d, J = 3.8 Hz, 1H), 5.03 (dd, J = 2.8, 8.9 Hz, 1H), 5.91 (dd, J = 9.2, 11.6 Hz, 1H), 6.81 (d, J = 11.6 Hz, 1H), 7.34 (m, 5H); ^{13}C NMR δ 26.4 (CH_3), 26.6 (CH_3), 57.7 (CH_2), 75.1 (q), 75.8 (CH), 79.0 (CH), 82.9 (CH), 83.2 (CH), 104.7 (CH), 111.6 (q), 124.2 (CH), 127.6 (CH), 128.2 (CH),128.7 (CH), 135.0 (CH), 136.3 (q).

2e: yield (380 mg, 15%); oil; $[\alpha]^{25}_D$ −33.3 (*c* 0.99, $CHCl_3$); IR (neat) 2223, 1646 cm^{-1}; ^1H NMR δ 1.31 (s, 3H), 1.81 (t, J = 2.0 Hz, 3H), 3.93 (s, 3H), 4.01 (d, J = 2.9 Hz, 1H), 4.24 (m, 2H), 4.67 (m, 1H), 5.02 (dd, J = 8.8, 12.6 Hz, 1H), 5.17 (s, 2H), 5.88 (dd, J = 8.9, 11.6 Hz, 1H), 5.90 (d, J = 3.8 Hz, 1H), 6.74 (d, J = 11.6 Hz, 1H), 6.84 (m, 2H), 7.07 (d, J = 1.2 Hz, 1H), 7.28−7.44 (m, 5H); ^{13}C NMR δ 3.6 (CH_3), 26.2 (CH_3), 26.7 (CH_3), 56.0 (CH), 58.3 (CH_2), 71.0 (CH_2), 74.5 (q), 75.1 (q), 83.0 (CH), 83.1 (CH), 104.7 (CH), 111.4 (q), 111.5 (CH), 112.5 (CH), 121.6 (CH), 122.6 (CH), 127.2 (CH), 127.8 (CH), 128.5 (CH), 130.0 (q), 135.2 (CH), 137.1 (q), 147.7 (q), 149.5 (q).

(3a*R*,5*R*,6*S*,6a*R*)-6-Allyloxy-5-ethynyl-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole (2f). To a suspension of Ph_3P (3.5 g, 13 mmol) and Zn dust (850 mg) in CH_2Cl_2 (13 mL) cooled to 0 °C and under a nitrogen atmosphere was added slowly a solution of CBr_4 (4.47 g, 13.5 mmol) in CH_2Cl_2 (10 mL) from a syringe. The mixture was stirred at 0 °C for 5 min until the greenish yellow color of the phosphorus ylide appeared. A solution of **1c** (1.52 g, 6.6 mmol) in CH_2Cl_2 (10 mL) was then added to it from a syringe, and the mixture was stirred at 25 °C for 24 h. Isolation of the dibromide was accomplished by addition of pentane (40 mL) to the mixture, which was then filtered to remove insoluble materials. Removal of solvent yielded a dark yellow syrup, which on chromatography over silica gel (EtOAc−petroleum ether, 1:9) furnished the corresponding α,α-dibromomethylene Wittig product of **1c** (1.61 g, 62%) as a light yellow oil: $[\alpha]^{25}_D$ −47.4 (*c* 1.13, $CHCl_3$); ^1H NMR δ 1.32 (s, 3H), 1.51 (s, 3H), 3.98 (d, J = 2.8 Hz,1H), 3.96 (d, J = 3.0 Hz, 1H), 4.23 (m, 2H), 4.57 (d, J = 3.7 Hz, 1H), 4.82 (t, J = 2.5 Hz, 1H), 5.23 (dd, J = 1.3, 10.4 Hz, 1H), 5.34 (dd, J = 1.5, 17.2 Hz, 1H), 5.92 (m, 1H), 5.94 (d, J = 3.8 Hz,1H); ^{13}C NMR δ 26.3 (CH_3), 26.8 (CH_3), 71.3 (CH_2), 80.5 (CH), 82.0 (CH), 82.7 (CH), 92.5 (q), 104.7 (CH), 111.9 (q), 117.7 (CH_2), 133.6 (CH), 133.7 (CH).

A solution of *n*-BuLi (5.1 mL,1.5 M in hexane) in THF(15 mL) was added dropwise with stirring to a solution of the above material in THF (15 mL) at −78 °C dropwise with stirring. After completion of addition, the reaction mixture was allowed to come to 25 °C, after which time it was quenched with a saturated aqueous NH_4Cl solution. The mixture was concentrated and the residue was extracted with CH_2Cl_2. The combined organic extracts were washed with water and dried, and removal of solvent gave **2f** as a yellow oil (500 mg, 55%), which was used immediately without purification for the PKR reaction: IR (neat) 2127, 1646 cm^{-1}; $[\alpha]^{25}_D$ −6.4 (*c* 1.1, $CHCl_3$); MS (EI) *m*/*z* 209 ($M^+ - 15$), 169; ^1H NMR δ 1.31 (s, 3H), 1.48 (s, 3H), 2.59 (d, J = 2.2 Hz, 1H), 3.96 (d, J = 3.0 Hz, 1H), 4.23 (m, 2H), 4.56 (d, J = 3.8 Hz, 1H), 4.82 (t, J = 2.5 Hz,1H), 5.23 (dd, J = 1.3, 10.4 Hz, 1H), 5.34 (dd, J = 1.5, 17.2 Hz, 1H), 5.90 (m, 1H), 5.94 (d, J = 3.8 Hz, 1H); ^{13}C NMR δ 26.0 (CH_3), 26.7 (CH_3), 70.5 (CH), 71.7 (CH_2), 76.3 (q), 82.3 (CH), 83.9 (CH), 104.6 (CH), 111.9 (q), 117.2 (CH_2), 133.8 (CH).

Typical Procedure for Pauson−Khand Reaction of 2a−f. The general procedure is illustrated by the preparation of **(5a*S*,5b*R*,8a*R*,9a*R*,9b*R*)-7,7-Dimethyl-1-phenyl-1,5a,5b,8a,-9a,9b-hexahydro-4*H*-5,6,8,9-tetraoxacyclopenta[*b*]-*as*-indacen-2-one (3a).**

A solution of **2a** (50 mg, 0.22 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise to a suspension of $Co_2(CO)_8$ (81 mg, 0.24 mmol) in dry CH_2Cl_2 (50 mL) at 25 °C under nitrogen atmosphere. Stirring was continued at the same temperature for 24 h, after which time *N*-methylmorpholine oxide (150 mg, 1.3 mmol) was added. The mixture was stirred for 30 min and kept overnight. It was then filtered through a Celite bed, and the residue was washed repeatedly with CH_2Cl_2. The combined filtrate and the washings were evaporated, and the residue was chromatographed over silica gel (EtOAc−petroleum ether, 1:4) giving **3a** (23 mg, 44%) as a pale yellow oil that solidified on standing: mp 125−126 °C (EtOAc−petroleum ether, white needles); $[\alpha]^{25}_D$ +84.6 (*c* 0.13, $CHCl_3$); MS (EI) *m*/*z* 252 (M^+), 209 ($M^+ - 15$); IR (KBr) 1698, 1634 cm^{-1}; ^1H NMR δ 1.32 (s, 3H), 1.51 (s, 3H), 2.50 (dd, J = 6.9, 18.3 Hz, 1H), 2.72 (dd, J = 3.6, 18.3 Hz, 1H), 3.17 (brs, 1H), 4.13 (s, 1H), 4.22 (d, J = 13.5 Hz, 1H), 4.44 (d, J = 3.9 Hz, 1H), 4.52 (d, J = 3.6 Hz, 1H), 4.60 (d, J = 13.5 Hz, 1H), 5.83 (d, J = 3.6 Hz, 1H), 6.03 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.0 (CH_3), 26.5 (CH_3), 37.2 (CH_2), 39.4 (CH), 64.8 (CH_2), 76.2 (CH), 78.7 (CH), 83.6 (CH), 105.0 (CH), 111.8 (q), 129.3 (CH), 170.1 (q), 207.1 (q). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.87; H, 6.39. Found: C, 61.92; H, 6.46.

Compounds **2b−f** were subjected to the above reaction maintaining the same conditions to yield **3b−f,** respectively.

(1*R*,5a*S*,5b*R*,8a*R*,9a*R*,9b*R*)-1,7,7-Trimethyl-1,5a,5b,8a,-9a,9b-hexahydro-4*H*-5,6,8,9-tetraoxacyclopenta[*b*]-*as*-indacen-2-one (3b): 35%; mp 131−132 °C (EtOAc−petroleum ether, white needles); $[\alpha]^{25}_D$ +94.9 (*c* 0.44, $CHCl_3$); IR (KBr) 1706, 1638 cm^{-1}; ^1H NMR δ 1.23 (d, J = 7.2 Hz, 3H), 1.32 (s, 3H), 1.53 (s, 3H), 2.70 (brs, 1H), 2.73 (m, 1H), 4.12 (s, 1H), 4.22 (d, J = 13.8 Hz, 1H), 4.48 (d, J = 2.1 Hz, 1H), 4.52 (d, J = 3.6 Hz, 1H), 4.60 (d, J = 13.8 Hz, 1H), 5.84 (d, J = 3.6 Hz, 1H), 6.00 (s, 1H); ^{13}C NMR δ 13.8 (CH_3), 26.1 (CH_3), 42.5 (CH), 47.7 (CH), 64.8 (CH_2), 75.2 (CH), 78.9 (CH), 83.6 (CH), 105.1 (CH), 111.9 (q), 127.9 (CH), 168.1 (q), 209.4 (q); HRMS calcd for $C_{14}H_{18}O_5 - CH_3$ 251.091949, found 251.092631.

(1*R*,5a*S*,5b*R*,8a*R*,9a*R*,9b*R*)-7,7-Dimethyl-1-phenyl-1,5a,5b,8a,9a,9b-hexahydro-4*H*-5,6,8,9-tetraoxacyclopenta-[*b*]-*as*-indacen-2-one (3c): yield 87%; mp 132−133 °C (EtOAc−petroleum ether, white needles); $[\alpha]^{25}_D$ +248.8 (*c* 0.10, $CHCl_3$); IR (KBr) 1701, 1638 cm^{-1}; MS (EI) *m*/z 328 (M^+), 313 ($M^+ - 15$); ^1H NMR: δ 1.32 (s, 3H), 1.48 (s, 3H), 3.21 (brs, 1H), 3.90 (d, J = 3.6 Hz, 1H), 4.12 (s, 1H), 4.29 (d, J = 13.8 Hz, 1H), 4.47 (brs, 1H), 5.89 (d, J = 3.6 Hz, 1H), 6.10 (s, 1H), 7.17−7.34 (m, 5H); ^{13}C NMR δ 26.1 (CH_3), 26.6 (CH_3), 48.7 (CH), 53.8 (CH), 64.6 (CH_2), 75.2 (CH), 78.9 (CH), 83.6 (CH), 105.1 (CH), 112.0 (q), 127.2 (CH), 127.8 (CH), 128.3 (CH), 128.9 (CH), 137.9 (q), 168.9 (q), 206.6 (q). Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.49; H, 6.14. Found: C, 69.92; H, 6.12.

(1*R*,5a*S*,5b*R*,8a*R*,9a*R*,9b*R*)-1-(4-Benzyloxy-3-methoxyphenyl)-7,7-dimethyl-1,5a,5b,8a,9a,9b-hexahydro-4*H*-5,6,8,9-tetraoxacyclopenta[*b*]-*as*-indacen-2-one (3d): yield 93%; mp 140−141 °C (EtOAc−petroleum ether, white microcrystalline solid); $[\alpha]^{25}_D$ +248.6 (*c* 0.10, $CHCl_3$); MS (EI) *m*/*z* 464 (M^+), 449 ($M^+ - 15$), 373 ($M^+ - 91$), 91; IR (KBr) 1710, 1639 cm^{-1}; ^1H NMR δ 1.32 (s, 3H), 1.48 (s, 3H), 3.16 (brs, 1H), 3.83 (d, J = 3.9 Hz, 1H), 3.88 (s, 3H), 4.12 (s, 1H), 4.29 (d, J = 13.8 Hz, 1H), 4.47 (d, J = 3.6 Hz, 1H), 4.54 (d, J = 3.6 Hz, 1H), 4.65 (d, J = 13.8 Hz, 1H), 5.13 (s, 2H), 5.88 (d, J = 3.6 Hz, 1H), 6.08 (s, 1H), 6.64 (dd, J = 1.5, 9.6 Hz, 1H), 6.71 (d, J = 1.5 Hz, 1H), 6.84 (d,

J = 8.1 Hz, 1H), 7.29−7.44 (m, 5H); ^{13}C NMR δ 26.1 (CH_3), 26.6 (CH_3), 48.8 (CH), 53.5 (CH) 56.1 (CH_3), 64.7 (CH_2), 71.2 (CH_2), 75.2 (CH), 78.9 (CH), 83.6 (CH), 105.1 (CH), 112.0 (q), 112.4 (CH), 114.6 (CH), 120.2 (CH), 127.2 (CH), 127.8 (CH), 128.5 (CH), 131.0 (q), 137.2 (q), 147.6 (q), 150.0 (q), 168.8 (q), 206.7 (q). Anal. Calcd for $C_{27}H_{28}O_6$: C, 69.81; H, 6.07. Found: C, 69.30; H, 6.23.

(1*R*,5a*S*,5b*R*,8a*R*,9a*R*,9b*R*)-1-(4-Benzyloxy-3-methoxyphenyl)-3,7,7-trimethyl-1,5a,5b,8a,9a,9b-hexahydro-4*H*-5,6,8,9-tetraoxacyclopenta[*b*]-*as*-indacen-2-one (3e). yield 30%; mp 165−166 °C (EtOAc−petroleum ether, white needles); $[\alpha]^{25}_D$ +129.9 (*c* 0.10, $CHCl_3$); IR (KBr) 1704, 1659 cm^{-1}; ^{1}H NMR δ 1.32 (s, 3H), 1.48 (s, 3H), 1.78 (s, 3H), 3.06 (brs, 1H), 3.76 (d, J = 3.9 Hz, 1H), 3.88 (s, 3H), 4.11 (s, 1H), 4.22 (d, J = 13.7 Hz, 1H), 4.46 (dd, J = 1.81, 4.17 Hz, 1H), 4.52 (d, J = 3.7 Hz, 1H), 4.70 (d, J = 13.8 Hz, 1H), 5.13 (s, 2H), 5.87 (d, J = 3.7 Hz, 1H), 6.62 (dd, J = 2.1, 8.2 Hz, 1H), 6.71 (d, J = 2.0 Hz, 1H), 6.84 (d, J = 8.2 Hz, 1H), 7.31−7.44 (m, 5H); ^{13}C NMR δ 8.2 (CH_3), 26.1 (CH_3), 26.6 (CH_3), 47.4 (CH), 52.5 (CH), 56.1 (CH_3), 63.2 (CH_2), 71.2 (CH_2), 75.1 (CH), 79.1 (CH), 83.7 (CH), 105.1 (CH), 111.9 (q), 112.6 (CH), 114.6 (CH), 120.1 (CH), 127.2 (CH), 127.8 (CH), 128.5 (CH), 131.5 (q), 134.9 (q), 137.3 (q), 147.5 (q), 150.0 (q), 159.9 (q), 206.9 (q); HRMS calcd for $C_{28}H_{30}O_7$ 478.183898, found 478.181593.

(3a*S*,5a*S*,5b*R*,8a*R*,9a*R*)-7,7-Dimethyl-3a,4,5a,5b,8a,9a-hexahydro-3*H*-5,6,8,9-tetraoxacyclopenta[*b*]-*as*-indacen-2-one (3f): yield 23%; mp 138−139 °C (EtOAc−petroleum ether, white needles); $[\alpha]^{25}_D$ +295.3 (*c* 0.10, $CHCl_3$); IR (KBr) 1704, 1659 cm^{-1}; ^{1}H NMR δ 1.35 (s, 3H), 1.56 (s, 3H), 1.90 (dd, J = 2.4, 19.2 Hz, 1H), 2.53 (dd, J = 6.9, 19.2 Hz, 1H), 3.07 (t, J = 10.5 Hz, 1H), 3.27 (m, 1H), 4.02 (d, J = 1.5 Hz, 1H), 4.20 (dd, J = 6.0, 10.5 Hz, 1H), 4.60 (d, J = 3.6 Hz, 1H), 4.96 (d, J = 1.5 Hz, 1H), 6.03 (d, J = 3.6 Hz, 1H), 6.23 (d, J = 1.2 Hz,1H); ^{13}C NMR δ 26.1 (CH_3), 26.7 (CH_3), 36.8 (CH_2), 37.2 (CH), 72.3 (CH_2), 73.5 (CH), 82.4 (CH), 83.8 (CH), 106.4 (CH), 112.4 (q), 131.4 (CH), 172.3 (q), 206.8 (q); HRMS calcd for $C_{13}H_{16}O_5$ − CH_3 237.076299, found 237.076344.

(3*R*,4*R*,4a*S*,5*S*,6*R*,7a*S*)-Acetic Acid 4-Acetoxy-3-acetoxymethyl-5-phenyloctahydrocyclopenta[*c*]pyran-6-yl Ester (5). To a suspension of $NaBH_4$ (45 mg, 1.2 mmol) in THF (20 mL) was added Bu_4NBr (450 mg, 1.4 mmol), and the mixture was heated at reflux for 4 h. To this refluxing solution was added **3c** (100 mg, 0.3 mmol) in THF (10 mL), and the reflux was continued for further 14 h. Solvent was removed, the residue was diluted with water, and glacial acetic acid was added dropwise until the mixture was acidic. It was then extracted with CH_2Cl_2, the organic layer was washed with water, and removal of solvent afforded a syrupy liquid, which was chromatographed over silica gel (EtOAc−petroleum ether, 1:4) giving **4** (40 mg) as a pale yellow sticky material, which was used for the next step without further purification: ^{1}H NMR ($CDCl_3$; peaks assignable to **4**) δ 1.33 (s, 3H), 1.49 (s, 3H), 1.81 (m, 1H), 2.27 (m, 3H), 2.76 (br m, exchangeable with D_2O, 1H), 3.40 (br m, 1H), 3.66 (dd, J = 11.8, 3.2 Hz, 1H), 3.77 (dd, J = 11.8, 2.8 Hz, 1H), 3.87 (d, J = 2.2 Hz, 1H), 4.32 (m, 2H), 4.57 (d, J = 3.6 Hz, 1H), 5.96 (d, J = 3.6 Hz, 1H), 7.19−7.42 (m, 5H). A solution of the above material in dioxane (1 mL) containing1N HCl (0.5 mL) was heated at 50 °C for 1.5 h. Solvent was removed and the product was obtained by leaching the residue repeatedly with EtOAc. The combined organic extracts were washed with water, dried, and removal of solvent afforded a thick oil, which was dissolved in MeOH, cooled to 0 °C and $NaIO_4$ (40 mg, 0.2 mmol) was added with stirring. Stirring was continued at 25 °C for 1 h after which it was filtered and MeOH was removed. The residue was extracted with CH_2Cl_2 and the organic layer was dried. Removal of solvent afforded a syrupy material that was dissolved in EtOH and cooled to 0 °C, and $NaBH_4$ (10 mg, 0.25 mmol) was added in portions with stirring. Stirring was continued at 25 °C for 15 h, EtOH was removed, and a few drops of water were added to the mixture. Extraction of the mixture with CH_2Cl_2 followed by removal of solvent afforded a syrup that was dissolved in pyridine (0.5 mL), and acetic anhydride (0.03 mL, 0.3 mmol) and DMAP (10 mg) were added at 0 °C. The mixture was allowed to stand for 48 h, and two drops of water were added to the mixture at 0 °C in order to destroy the excess acetic anhydride. The mixture was extracted with CH_2Cl_2. The organic layer was washed with water and dried, and removal of solvent afforded a pale yellow syrup, which was chromatographed over silica gel (EtOAc−petroleum ether, 1:1) yielding **5** (10 mg, 9% from **3c**) as a colorless syrup: $[\alpha]^{20}_D$ −7.5 (*c* 0.21, $CHCl_3$); ^{1}H NMR δ 1.99 (s, 3H), 2.02 (m, 1H), 2.21 (s, 3H), 2.25−2.38 (m, 3H), 2.99 (dd, J = 3.8, 5.9 Hz, 1H), 3.67 (dt, J = 1.4, 5.7 Hz, 1H), 3.81 (dd, J = 3.0, 11.9 Hz, 1H), 4.01 (dd, J = 2.7, 12.0 Hz, 1H), 4.05 (dd, J = 5.7, 11.4 Hz, 1H), 4.11 (dd, J = 5.8, 11.4 Hz, 1H), 5.23−5.30 (m, 2H), 7.17−7.33 (m, 5H); ^{13}C NMR 20.8 (CH_3), 21.1 (CH_3), 21.2 (CH_3), 35.50 (CH), 35.54 (CH_2), 46.4 (CH), 51.9 (CH), 63.3 (CH_2), 67.2 (CH_2), 67.4 (CH), 75.1 (CH), 81.1 (CH), 126.9 (CH), 127.1 (CH), 128.9 (CH), 143.3 (q), 170.5 (q), 170.7 (2 × q); HRMS calcd for $C_{21}H_{26}O_7$ − CH_3CO_2H, 330.146724, found 330.145547.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of **2a**−**f**, 1,1-dibromoethylene furanoside precursor of **2f**, **3b**,**c**,**e**,**f**, and **5**. ^{1}H NMR spectrum of **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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