An Unusual Uncatalyzed Baeyer−Villiger Oxidation of Cyclobutanones to γ-Lactones by Air and Its Mechanistic Implications

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The cyclobutanone moieties in 5-aryl-7,11,11-trimethyltricyclo[5.4.0.0^{3,6}]undec-1-en-4-ones **4a**–**e** undergo an unusual, uncatalyzed Baeyer–Villiger (BV) oxidation when their methanolic solutions are exposed to air at room temperature for 45 d, quantitatively producing mixtures of γ-lactones (**5a**–**e**, **6a**–**e**); the ratio **5/6** varies with the nature of the substituent on the aryl ring (9:1 to ca. 1:1). BV oxidations of **4a**–**c** and **4e** with H_2O_2 and of **4c**–**d** with performic acid have also been carried out, and the results are compared with those of air oxidation; in the latter case an unusual enhancement of the migratory aptitude of a benzylic carbon atom, in a BV oxidation, by the presence of halogen substituents on the aryl ring is observed. A mechanistic interpretation of the obtained results is proposed.

Introduction

Baeyer−Villiger (BV) oxidation of aldehydes and ketones to afford esters/lactones is one of the most frequently used reactions in organic synthetic methodology, and is also exploited commercially.[1] A wide range of peroxy acids/peroxides have been employed under varied reaction conditions to accomplish this reaction.[1,2] The use of dioxygen as an alternative to the use of peroxyacids/peroxides has been limited to some commercial processes in which the molecular oxygen is used in the presence of excess of aldehydes under acidic conditions;[2f,2g,3] reagents such as organoseleninic acid/diselenides and Ru complexes are sometimes also employed.[2q] Use has also been made of molecular oxygen and an aldehyde combination in the presence of catalysts such as bis(dipivaloylmethanato)nickel(II),[3d] $RuCl_3$ [3e] and Fe_2O_3.[4] In the last case, the reaction is postulated[4] to proceed by a free radical initiation rather than the generally accepted ionic addition mechanism.[1] More recently, use of *N*-hydroxyphthalimides and molecular oxygen has been reported for BV oxidation of KA-oil (a mixture of cyclohexanone and cyclohexanol).[5] Although the role of stereoelectronic effects in determining the regiochemical outcomes of BV oxidations is well known,[6] the mechanistic bases of such influences are far from clear and continue to receive attention.[6d] We report here a serendipitously discovered uncatalyzed BV oxidation of cyclobutanones to γ-lactones by air. Comparison of the obtained regiochemical outcome with the results of corresponding BV oxidations of these cyclobutanones by H_2O_2/performic acid has revealed, in the latter case, some hitherto unknown influences of aryl ring halo substituents on the migratory aptitude of a benzylic carbon atom in a BV oxidation. Mechanistic implications of the obtained results are discussed.

Results and Discussion

We have recently reported that photochemical transformation of (*E*,*E*)-arylidene-β-ionones **1a**−**e** in anhydrous solvents affords 1,7,7-trimethyl-3-[(*E*)-2′-arylethenyl]-2-oxabicyclo[4.4.0]deca-3,5-dienes **2a**−**e** (ca. 90%), which, on irradiation in aqueous methanol, are converted into 11-*exo*-aryl-1,7,7-trimethyltricyclo[4.4.0.1^{2,4}]undec-5-en-3-ones **3a**−**e** (Scheme 1). These rearrange, quantitatively, on silica gel to give 5-aryl-7,11,11-trimethyltricyclo[5.4.0.0^{3,6}]undec-1-en-4-ones **4a**−**e**.[7] During an attempted slow crystallization of compound **4c** in order to obtain a crystal for X-ray crystallography, it was serendipitously discovered that if pure **4c** is dissolved in warm methanol and the solution is left exposed to air for 45 d at room temperature, it is quantitatively transformed into a 9:1 mixture of two products, which resisted various attempts to separate them completely by column chromatographic techniques. However, one of them was isolated in pure form by column chromatography on silica gel, and was characterized as lactone **5c**

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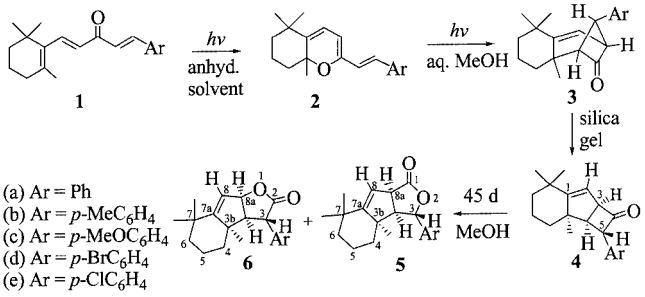
by rigorous spectroscopic analysis and eventually by X-ray crystallography (Figure 1); the structure of **6c** has been established only in mixture with **5c**. This highly unusual uncatalyzed air oxidation of a cyclobutanone to a lactone was subsequently extended to other derivatives (**4a**, **4b**, **4d** and **4e**; Scheme 1 and Table 1).



Scheme 1

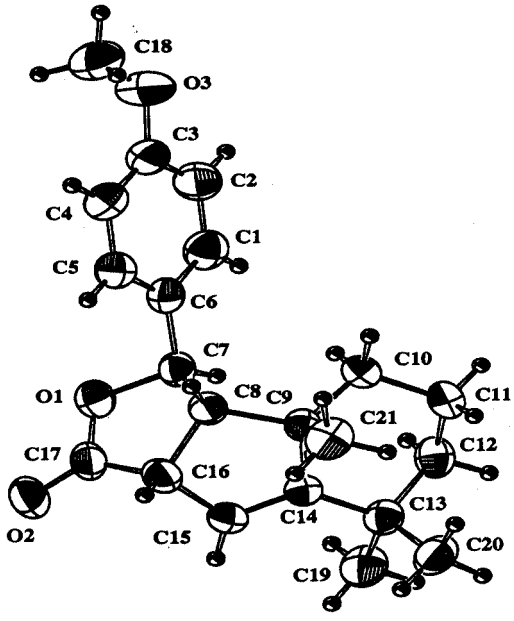


Figure 1. ORTEP diagram of **5c**

Initial observations indicated that the obtained transformation is a typical BV oxidation. For instance, the migration of the benzylic carbon atom C-5 in cyclobutanone **4a** shows a slight preference over the allylic carbon atom C-3, resulting in increased formation of **5a**. This preference for migration of the benzylic carbon atom increases with the presence of electron-donating substituents on the phenyl ring in the cases of **4b** and **4c**, which is in consonance with reported development of electron deficiency at the migrating center in a BV reaction.[8] In the cases of **4d** and **4e**, the presence of electron-withdrawing substituents (Cl, Br) on the phenyl ring gives rise to reversal of migratory aptitudes, resulting in increased formation of **6** relative to **5**. Apparently, the observed effects of aryl ring substituents on the migratory aptitude of a benzylic carbon atom also appeared to be in consonance with earlier findings of substituent effects on BV oxidation of substituted acetophenones[8] and, as would be anticipated for a BV reaction, the stereochemistry at the migrating center is also retained.[1]

In general, BV oxidation of cyclobutanones is reported to be relatively facile, the high reactivity having definite contributions from the strained cyclobutanone structure. For instance, hypochlorous acid is reported to bring about BV oxidation of cyclobutanone, but fails in the cases of cyclopentanones or cyclohexanones.[9] However, BV oxidations of cyclobutanones with H_2O_2 (30% H_2O_2, 2.4−3.0 equiv., 16 h for completion of reaction) are generally carried out under highly acidic conditions.[10] Testing of the methanol after periods of air exposure similar to those required for the completion of reaction indicated it to be only slightly acidic (pH ≈ 6.6), and the concentration of peracid (performic acid), if any, was extremely low (5×10^{-3} M).[11] This was in contrast to the very high concentrations of aldehydes used for BV oxidation by molecular oxygen along with an acid or a catalyst.[2l,2m,3−5] Therefore, for purposes of comparison (to establish mechanistic similarities), ketones **4a** and **4c**−**e** were treated with 30% H_2O_2 (1.5−2.0 mol-equiv., without any acid) in methanol as solvent. These ketones were observed to display very high reactivity, and the reactions were completed in 5−6 h in all cases. There was not much change in the product distributions in the cases of **4a** and **4c**. However, a dramatic change in the ratios of products (**5**:**6**) derived from **4d** and **4e** was observed (Table 1), indicating greatly enhanced migration of the benzylic carbon moiety (C-5) in the latter case, with a migratory aptitude similar to that of **4c**. Compounds **4c** and **4d** were subsequently also treated with performic acid,[12] and the relative proportions of products were analysed by ^{1}H NMR spectroscopy on the crude samples. The ^{1}H NMR spectrum of the crude product derived from **4c** revealed the presence of only one product (**5c**), whereas the ratio of

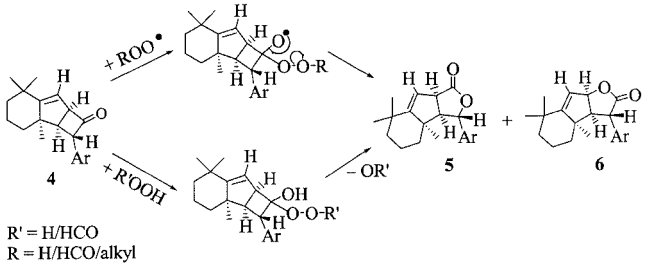
Table 1. Reaction times and product compositions for the Baeyer−Villiger oxidation of cyclobutanones **4** with air and with H_2O_2

Starting **4**	By air Reaction time [d]	Product ratio (**5**/**6**)[a]	By H_2O_2 Reaction time [h]	Product ratio (**5**/**6**)[a]
a	40−45	52:48	5	56:44
b	40−45	70:30	−	−
c	45	90:10	6	90:10
d	45	40:60	5	90:10
e	45	40:60	5	90:10

[a] Based on ^{1}H NMR data of the mixture.

products obtained from **4d** was almost identical with the ratio of **5/6** obtained from treatment of **4d** with H_2O_2. Reducing the amount of performic acid resulted only in prolongation of reaction time without any change in the product ratio. It should be mentioned here that a lower ratio (1:2) of H_2O_2 and 80% formic acid was employed in this case, contrary to the higher ratios generally used to generate performic acid,[12] because use of higher relative amounts of formic acid resulted in the formation of multiple products.

The above results indicate that the air oxidation and H_2O_2/performic acid reactions follow two distinct pathways. A plausible explanation for this unusual reversal of the migratory aptitude of a benzylic carbon atom in the case of a halo-substituted aryl ring in an H_2O_2/performic acid catalyzed BV oxidation, as compared to air oxidation, is that the air oxidation is an entirely free radical process (Scheme 2) initiated by a peroxyl radical generated in situ, and thus no mesomeric electron release from the halo substituents is involved, whereas a *p*-methoxy substituent assists the rearrangement, as its free radical stabilizing capabilities are well known.[13] On the other hand, the migrating center develops a positively charged character under the conditions of catalysis by H_2O_2/performic acid, as is well established for BV oxidation,[1,8] forcing the halo substituents to act as electron donors. The above conclusions are also supported by the fact that the product ratio from **4a**, in case of the unsubstituted aryl ring, remains essentially the same under both air oxidation and H_2O_2/performic acid catalysis conditions.



Scheme 2

Therefore, the two reactions, oxidation by air and oxidation by H_2O_2/performic acid, follow two distinct mechanistic pathways, with a free radical mechanism intervening in the air oxidation and contrasting with the normally accepted ionic mechanism for peroxide/peracid-assisted BV oxidation. It might be mentioned here that very high reactivity of these cyclobutanones towards BV oxidation may have a definite contribution from the allylic/benzylic nature of the migrating centers, in addition to the strained cyclobutanone structure.

The butyrolactone moiety is an essential component of a large number of natural products and biologically active molecules, and also represents an important class of compounds used as key intermediates and a methodology for stereocontrolled synthesis of a wide range of organic molecules, including natural products.[14] Butyrolactones may be synthesized by a variety of approaches,[14,15] and a number of reagents are employed for their preparation from cyclobutanones,[10,14,16] including microbial transformations.[17] In general, the use of acidic conditions is avoided in the presence of acid-labile moieties in the molecules, for example unsaturated groups in the molecules, and alternatively the use of alkaline conditions and buffered media are employed.[2,14–16] Air oxidation of cyclobutanones to butyrolactones, however, has not been reported so far.

Experimental Section

General Information: Starting materials and reagents were purchased from commercial suppliers and used after further purification (crystallization/distillation). A Bruker AC 200FT (200 MHz) spectrometer was used to record ^1H and ^{13}C NMR spectra. Chemical shifts are reported in ppm as downfield displacements from tetramethylsilane used as internal standard, and *J* values in Hz. IR spectra were recorded with a Shimadzu DR 2001 FT-IR spectrophotometer either as thin layers with a few drops of $CHCl_3$ or as KBr pellets. Mass spectra (EI) were recorded with a Shimadzu GCMS-QP-2000A spectrometer. Elemental analyses were performed at RSIC-USIC, Punjab University, Chandhigarh, and are reported in percent atomic abundance. All melting points are uncorrected and were measured in open glass capillaries.

General Procedure for Air Oxidation of 4a–e in Methanol: Compounds **4a–e** (100 mg)[7] were dissolved in warm methanol (10 mL) and the reaction mixtures were kept for 45 d at room temperature. After completion of the reaction (TLC), the solvent was removed under reduced pressure in an Eyela rotary evaporator. Products were subjected to column chromatography on silica gel (Acme Synthetic Chemicals Mumbai, India, 60–120 mesh, 20 g, column packed in hexane), with hexane/chloroform (gradient) as eluent, to obtain pure **5a–e** and/or mixtures of **5a–e** with **6a–e**, respectively.

Mixture of 5a and 6a: Colorless semi-solid. IR (thin film with $CHCl_3$): $\tilde{\nu}$ = 756 (m-s), 982 (w), 1015 (w-m), 1076 (w), 1150 (m), 1219 (w), 1275 (w), 1364 (w), 1385 (w-m), 1456 (m-s), 1499 (w-m), 1585 (w-m), 1633 (w), 1773.4 (br, C=O) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.13 (s, CH_3), 1.15 (s, CH_3), 1.17 (s, CH_3), 1.19 (s, CH_3), 1.23 (s, CH_3), 1.29 (s, CH_3), 1.75–1.48 (m, 12 H, 6 × CH_2), 2.86 [dd tending to t, $J \approx 7.68$ Hz, 1 H, C(3a)-H in **5a**], 3.06 [dd, J = 9.92 and 6.88 Hz, C(3a)-H in **6a**], 3.72 [d, J = 9.82 Hz, C(3)-H in **6a**], 3.78 [dd, J = 7.13 and 1.78 Hz, 1 H, C(8a)-H in **5a**], 5.32 [d, J = 8.23 Hz, C(3)-H in **5a**], 5.38 [d, J = 1.78 Hz, 1 H, C(8)-H in **5a**], 5.52 [br. s, C(8)-H in **6a**], 5.60 [dd, J = 6.89 and 1.38 Hz, 1 H, C(8a)-H in **6a**], 7.40–7.26 (m, 10 H, arom. H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.8 [C(5) in **5a**], 19.0 [C(5) in **6a**], 28.3 (CH_3), 28.6 (CH_3), 28.9 (CH_3), 29.3 (CH_3), 31.3 (CH_3), 31.5 (CH_3), 34.3 [C(3b) in **6a**], 34.4 [C(3b) in **5a**], 35.2 [C(4) in **6a**], 40.6 [C(6) in **5a**], 40.7 [C(6) in **6a**], 48.6 [C(3a) in **5a**], 49.1 [C(7) in **5a**], 50.0 [C(7) in **6a**], 51.1 [C(3a) in **6a**], 59.8 [C(8a) in **5a**], 60.0 [C(3) in **6a**], 82.6 [C(3) in **5a**], 85.5 [C(8a) in **6a**], 115.6 [C(8) in **5a**], 119.4 [C(8) in **6a**], 127.5 (CH), 127.7 (CH), 128.87 (CH), 128.92 (CH), 128.97 (CH), 129.1 (CH), 137.6 (q. arom. in **5a**), 139.5 (q. arom. in **6a**), 160.5 [C(7a) in **5a**], 162.4 [C(7a) in **6a**], 175.1 (C=O in **6a**), 176.9 (C=O in **5a**) ppm. MS: *m*/*z* (%) = 69 (28), 70 (19), 71 (26), 77 (35), 79 (17), 81 (18), 91 (100), 104 (53), 114 (18), 116 (12), 122 (27), 165 (24), 169 (22), 179 (16), 237 (65), 252 (30) [M^+ − 44 (CO_2)], 253 (7) [M^+ + 1 − 44 (CO_2)].

3b,7,7-Trimethyl-3-tolyl-3,3a,3b,4,5,6,7,8a-octahydro-1*H*-indeno-[1,2-*c*]furan-1-one (5b): Colorless crystals, m.p. 133–134 °C (hex-

ane). IR (KBr): $\tilde{\nu}$ = 756 (m), 818 (s), 833 (m), 982 (m), 1007 (m), 1018 (m), 1134 (m), 1180 (m), 1200 (s), 1225 (m), 1273 (m), 1354 (m), 1385 (m), 1460 (m), 1589 (m), 1638 (m), 1772.5 (C=O) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.15 (s, 3 H, CH_3), 1.19 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3), 1.81−1.40 (m, 6 H, 3 × CH_2), 2.37 (s, 3 H, PhCH_3), 2.82 [dd, tending to t, $J \approx$ 7.69 Hz, 1 H, C(3a)-H], 3.74 [dd, J = 7.08 and 1.76 Hz, 1 H, C(8a)-H], 5.25 [d, J = 8.30 Hz, 1 H, C(3)-H], 5.3 [d, J = 1.76 Hz, 1 H, C(8)-H], 7.26−7.15 (m, 4 H, arom. H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.69 [C(5)], 21.13 (arom. CH_3), 28.02 (CH_3), 28.62 (CH_3), 31.19 (CH_3), 34.02 [C(4)], 34.30 [C(3b)], 40.29 [C(6)], 49.61 [C(7)], 50.76 [C(8a)], 59.36 [C(3a)], 81.95 [C(3)], 115.47 [C(8)], 127.16 (CH), 129.25 (CH), 136.15 (q. arom.), 138.19 (q. arom.), 159.90 [C(7a)], 175.94 (C=O) ppm. MS: *m*/*z* (%) = 69 (27), 70 (36), 71 (42), 83 (22), 91 (34), 104 (100), 111 (20), 118 (25), 169 (38), 251 (53), 266 (27) [M^+ − 44 (CO_2)], 267 (8) [M^+ + 1−44 (CO_2)]. $C_{21}H_{26}O_2$: calcd. C 81.25, H 8.44; found C 81.01, H 8.99.

Mixture of 5b and 6b: Colorless semi-solid. IR (thin film in $CHCl_3$): $\tilde{\nu}$ = 760 (m), 816 (m), 842 (w), 987 (w), 1004 (s), 1021 (s), 1154 (s), 1188 (s), 1222 (w), 1278 (w), 1342 (w), 1384 (m), 1367 (m), 1393 (w), 1461 (s), 1521 (s), 1547 (w), 1581 (w-m), 1636 (m), 1777.7 (br, C=O) cm^{-1}. ^1H NMR (200 MHz $CDCl_3$): δ = 1.14 (s, CH_3), 1.15 (s, CH_3), 1.18 (s, CH_3), 1.19 (s, CH_3), 1.23 (s, CH_3), 1.30 (s, CH_3), 1.81−1.40 (m, 12 H, 6 × CH_2), 2.35 (s, 3 H, PhCH_3), 2.37 (s, 3 H, PhCH_3), 2.82 [dd tending to t, $J \approx$ 7.69 Hz, 1 H, C(3a)-H in **5b**], 3.04 [dd, J = 9.9, 6.9 Hz, C(3a)-H in **6b**], 3.66 [d, J = 9.9 Hz, 1 H, C(3)-H in **6b**], 3.74 [dd, J = 7.08 and 1.76 Hz, 1 H, C(8a)-H in **5b**], 5.25 [d, J = 8.30 Hz, C(3)-H in **5b**], 5.37 [d, J = 1.76 Hz, 1 H, C(8)-H in **5b**], 5.52 [br. s, 1 H, C(8)-H in **6b**], 5.59 [dd, J = 6.9 and 1.18 Hz, 1 H, C(8a)-H in **6b**], 7.27−7.15 (m, 8 H, arom. H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.6 [C(5) in **5b**], 18.8 [C(5) in **6b**], 21.1 (arom. CH_3 in **5b**), 21.2 (arom. CH_3 in **6b**), 28.1 (CH_3), 28.4 (CH_3), 28.6 (CH_3), 29.1 (CH_3), 31.1 (CH_3), 31.2 (CH_3), 32.9 [C(3b) in **6b**], 34.1 [C(4) in **5b**], 34.3 [C(3b) in **5b**], 34.9 [C(4) in **6b**], 40.3 [C(6) in **5b**], 40.5 [C(6) in **6b**], 47.9 [C(3a) in **6b**], 48.8 [C(7) in **6b**], 49.6 [C(7) in **5b**], 50.8 [C(3a) in **5b**], 59.4 [C(8a) in **5b**], 59.8 [C(3) in **6b**], 82.0 [C(3) in **5b**], 84.9 [C(8a) in **6b**], 115.5 [C(8) in **5b**], 119.4 [C(8) in **6b**], 127.2 (CH), 128.5 (CH), 129.3 (CH), 129.6 (CH), 134.3 (q. arom. in **6b**), 136.2 (q. arom. in **5b**), 137.0 (q. arom. in **6b**), 138.2 (q. arom. in **5b**), 159.9 [C(7a) in **5b**], 162.4 [C(7a) in **6b**], 175.3 (C=O in **6b**), 176.9 (C=O in **5b**) ppm. MS: *m*/*z* (%) = 267 (7) [M^+ + 1 − 44 (CO_2)], 266 (28) [M^+ − 44 (CO_2)], 253 (14), 251 (71), 181 (15), 171 (28), 119 (22), 105 (100), 91 (42), 83 (22), 77 (18), 71 (43), 70 (34), 69 (30), 58 (85), 57 (26), 56 (77).

3-Anisyl-3b,7,7-trimethyl-3,3a,3b,4,5,6,7,8a-octahydro-1*H*-indeno-[1,2-*c*]furan-1-one (5c): Colorless crystals, m.p. 104−105 °C (hexane). IR (KBr): $\tilde{\nu}$ = 754 (w), 835 (s), 980 (m), 989 (m), 1009 (w-m), 1018 (w-m), 1038 (m), 1109 (w), 1134 (w), 1177 (m-s), 1200 (m), 1225 (m), 1254 (s), 1277 (m-s), 1354 (w), 1385 (m), 1460 (m), 1518 (s), 1587 (m), 1611 (s), 1764.7 (C=O) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.14 (s, CH_3); 1.18 (s, CH_3), 1.22 (s, CH_3), 1.79−1.37 (m, 6 H, 3 × CH_2), 2.82 [dd, tending to a t, $J \approx$ 7.73 Hz, 1 H, C(3a)-H], 3.74 [dd, J = 7.04 and 1.8 Hz, 1 H, C(8a)-H], 3.81 (s, 3 H, OCH_3), 5.23 [d, J = 8.48 Hz, 1 H, C(3)-H], 5.36 [d, J = 1.8 Hz, 1 H, C(8)-H], 6.88 (d, J = 6.68 Hz, 2 H, arom. H), 7.28 (d, J = 6.68 Hz, 2 H, arom. H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.95 (C=O), 160.03 [C(7a)], 159.73 (q. arom.), 131.10 (q. arom.), 128.76 (CH), 115.63 [C(8)], 114.14 (CH), 82.03 [C(3)], 59.39 [C(8a)], 55.21 (OCH_3), 50.99 [C(3a)], 49.70 [C(7)], 40.46 [C(6)], 34.46 [C(3b)], 34.09 [C(4)], 31.34 (CH_3), 28.78 (CH_3), 28.15 (CH_3), 18.69 [C(5)] ppm. MS: *m*/*z* (%) = 121 (100), 152 (16), 153 (15), 159 (20), 161 (40), 162 (17), 165 (24), 198 (19), 197 (46), 211 (29), 213 (16), 267 (90), 268 (41), 282 (90), 283 (42), 326 (30) [M^+], 327 (8) [M^+ + 1], (8). $C_{21}H_{26}O_3$: calcd. C 77.27, H 8.03; found C 77.20, H 8.24.

Crystallographic Data for Compound 5c: Crystal system monoclinic; space group $P2_1/n$; unit cell dimensions a = 9.6065(2), b = 7.6983(2), c = 24.7363(7) Å, β = 98.436(1)°; V = 1809.55(3) $Å^3$; Z = 4, D_X = 1.198 Mg m^{-3}; final R indices [$I > 2\sigma(I)$] $R1$ = 0.0532, $wR2$=0.1520; R indices (all data) $R1$ = 0.0720, $wR2$ = 0.1658; goodness-of-fit on F^2 = 1.044. CCDC-169322 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Mixture of 5c and 6c: Colorless semi-solid. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.14 (s, CH_3), 1.15 (s, CH_3), 1.18 (s, CH_3), 1.19 (s, CH_3), 1.22 (s, CH_3), 1.29 (s, CH_3), 1.79−1.37 (m, 12 H, 6 × CH_2), 2.82 [dd, tending to a t, $J \approx$ 7.73 Hz, 1 H, C(3a)-H in **5c**], 3.02 [dd, J = 9.93 and 6.9 Hz, 1 H, C(3a)-H in **6c**], 3.90−3.73 [m, 8 H, 2 × OCH_3, and C(8a)-H in **5c** and C(3)-H in **6c**], 5.23 [d, J = 8.48 Hz, 1 H, C(3)-H in **5c**], 5.36 [br. d, J = 1.80 Hz, 1 H, C(8)-H in **5c**], 5.55 [br. s, C(8)-H in **6c**], 5.60 [dd, J = 6.9 and 1.13 Hz, 1 H, C(8a)-H in **6c**], 6.88 (d, J = 6.68 Hz, 4 H, arom. H), 7.28 (d, J = 6.68 Hz, 4 H, arom. H) ppm.

3-(4-Bromophenyl)-3b,7,7-trimethyl-3,3a,3b,4,5,6,7,8a-octahydro-1*H*-indeno[1,2-*c*]furan-1-one (5d): Colorless crystals, m.p. 124−125 °C (hexane). IR (KBr): $\tilde{\nu}$ = 768 (w), 794 (w), 839 (w), 984 (w), 1013 (w-m), 1074 (w), 1223 (w), 1354 (w-m), 1385 (w), 1460 (w), 1493 (w), 1593 (s), 1759 (C=O) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.19 (s, CH_3), 1.24 (s, CH_3), 1.27 (s, CH_3), 1.80−1.44 (m, 6 H, 3 × CH_2), 2.77 [dd, tending to t, $J \approx$ 7.64 Hz, 1 H, C(3a)-H], 3.76 [dd, J = 7.08 and 1.76 Hz, 1 H, C(8a)-H], 5.26 [d, J = 8.14 Hz, 1 H, C(3)-H], 5.41 [d, J = 1.76 Hz, 1 H, C(8)-H], 7.27 (d, J = 8.4 Hz, 2 H, arom. H), 7.54 (d, J = 8.4 Hz, 2 H, arom. H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.71 [C(5)], 28.05 (CH_3), 28.65 (CH_3), 31.22 (CH_3), 34.24 [C(4)], 34.34 [C(3b)], 40.26 [C(6)], 49.66 [C(7)], 50.53 [C(3a)], 59.64 [C(8a)], 80.91 [C(3)], 115.55 [C(8)], 128.71 (CH), 130.21 (q. arom.), 131.80 (CH), 138.39 (q. arom.), 159.78 [C(7a)], 175.19 (C=O) ppm. MS: *m*/*z* (%) = 69 (38), 70 (66), 71 (82), 83 (40), 84 (26), 94 (25), 97 (16), 111 (38), 112 (26), 169 (100), 341 (15), 355 (24) [M^+ − 44 (CO_2)], 356 (18) [M^+ + 1 − 44 (CO_2)]. $C_{20}H_{23}BrO_2$: calcd. C 64.01, H 6.18; found C 63.87, H 6.37.

Mixture of 5d and 6d: Colorless semi-solid. ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.17 (s, CH_3), 1.19 (s, CH_3), 1.22 (s, CH_3), 1.24 (s, CH_3), 1.27 (s, CH_3), 1.30 (s, CH_3), 1.80−1.44 (m, 12 H, 6 × CH_2), 2.77 [dd, tending to a t, $J \approx$ 7.64 Hz, 1 H, C(3a)-H in **5d**], 3.01 [dd, J = 9.98 and 6.97 Hz, 1 H, C(3a)-H in **6d**], 3.67 [d, J = 10.04 Hz, 1 H, C(3)-H in **6d**], 3.76 [dd, J = 7.08 and 1.76 Hz, 1 H, C(8a)-H in **5d**], 5.26 [d, J = 8.14 Hz, 1 H, C(3)-H in **5d**], 5.41 [d, J = 1.76 Hz, 1 H, C(8)-H in **5d**], 5.51 [br. s, 1 H, C(8)-H in **6d**], 5.61 [d, J = 6.97 Hz, 1 H, C(8a)-H in **6d**], 7.27 (d, J = 8.4 Hz, 4 H, arom. H), 7.54 (d, J = 8.4 Hz, 4 H, arom. H) ppm.

3-(4-Chlorophenyl)-3b,7,7-trimethyl-3,3a,3b,4,5,6,7,8a-octahydro-1*H*-indeno[1,2-*c*]furan-1-one (5e): Colorless solid, m.p. 110−111 °C (hexane). IR (KBr): $\tilde{\nu}$ = 735 (w-m), 764 (w), 822 (w-m), 835 (w-m), 986 (w), 1017 (s), 1092 (m-s), 1145 (w), 1181 (w), 1225 (w), 1270 (w), 1356 (m), 1385 (m), 1458 (m), 1493 (m), 1593 (s), 1772.8 (br, C=O) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.15 (s, CH_3), 1.18 (s, CH_3), 1.23 (s, CH_3), 1.80−1.44 (m, 6 H, 3 × CH_2), 2.79 [dd, tending to a t, $J \approx$ 7.67 Hz, 1 H, C(3a)-H], 3.77 [dd, J = 7.07

and 1.72 Hz, 1 H, C(8a)-H], 5.28 [d, J = 8.29 Hz, 1 H, C(3)-H], 5.37 [d, 1 H, J = 1.72 Hz, C(8)-H], 7.39−7.27 (m, 4 H, arom. H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.95 [C(5)], 28.30 (CH_3), 28.90 (CH_3), 31.46 (CH_3), 34.48 [C(4)], 34.65 [C(3b)], 40.62 [C(6)], 50.03 [C(7)], 51.04 [C(3a)], 59.93 [C(8a)], 81.75 [C(3)], 115.52 [C(8)], 128.91 (CH), 129.20 (CH), 134.79 (q. arom.), 138.01 (q. arom.), 160.54 [C(7a)], 176.62 (C=O) ppm. MS: *m/z* (%) = 67 (22), 69 (72), 70 (84), 71 (100), 77 (25), 79 (19), 81 (21), 82 (16), 83 (49), 84 (33), 91 (32), 94 (33), 95 (16), 97 (22), 104 (30), 110 (17), 111 (44), 112 (28), 114 (18), 124 (59), 126 (23), 128 (19), 138 (18), 147 (15), 150 (22), 163 (15), 170 (92), 200 (12), 271 (56), 272 (12), 273 (20), 283 (10), 286 (25), 287 (8) [$M^+ - 44$ (CO_2)], 288 (5) [$M^+ + 1 - 44$ (CO_2)]. $C_{20}H_{23}ClO_2$: calcd. C 72.61, H 7.01; found C 71.93, H 7.31.

Mixture of 5e and 6e: Colorless semi-solid. IR (thin film): $\tilde{\nu}$ = 737 (w), 837 (w-m), 984 (w), 1015 (s), 1092 (m-s), 1149 (m), 1181 (m), 1219 (w), 1263 (w), 1362 (w), 1376 (w), 1493 (m-s), 1460 (w-m), 1598 (w-m), 1773.25 (br, C=O) cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.14 (s, CH_3), 1.15 (s, CH_3), 1.18 (s, CH_3), 1.20 (s, CH_3), 1.23 (s, CH_3), 1.31 (s, CH_3), 1.80−1.44 (m, 12 H, 6 × CH_2), 2.79 [dd, tending to a t, $J \approx$ 7.67 Hz, C(3a)-H in **5e**], 3.00 [dd, J = 6.91 and 10.01 Hz, 1 H, C(3a)-H in **6e**], 3.65 [d, J = 10.06 Hz, C(3)-H in **6e**], 3.77 [dd, J = 7.07 and 1.72 Hz, C(8a)-H in **5e**], 5.28 [d, J = 8.29 Hz, C(3)-H in **5e**], 5.37 [d, J = 1.72 Hz, C(8)-H in **5e**], 5.52 [br. s, 1 H, C(8)-H in **6e**], 5.57 [d, J = 6.95 Hz, C(8a)-H in **6e**], 7.39−7.17 (m, 8 H, arom. H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.4 [C(5) in **6e**], 18.9 [C(5) in **5e**], 28.0 (CH_3 in **6e**), 28.3 (CH_3 in **5e**), 28.6 (CH_3 in **6e**), 28.9 (CH_3 in **5e**), 30.9 (CH_3 in **6e**), 31.4 (CH_3 in **5e**), 34.0 [C(4) in **6e**], 34.4 [C(4) in **5e**], 34.6 [C(3b) in **5e**], 34.9 [C(3b) in **6e**], 40.6 [C(6) in **5e** and **6e**], 47.5 [C(3a) in **6e**], 48.7 [C(7) in **6e**], 50.0 [C(7) in **5e**], 51.0 [C(3a) in **5e**], 59.9 [C(8a) in **5e** and C(3) in **6e**], 81.7 [C(3) in **5e**], 84.7 [C(8a) in **6e**], 115.5 [C(8) in **5e**], 119.3 [C(8) in **6e**], 128.4 (CH in **6e**), 128.8 (CH in **6e**), 128.9 (CH in **5e**), 129.2 (CH in **5e**), 134.7 (q. arom. in **5e**), 135.5 (q. arom. in **6e**), 137.8 (q. arom. in **5e** and **6e**), 159.7 [C(7a) in **5e**], 162.33 [C(7a) in **6e**], 175.0 (C=O in **6e**), 176.62 (C=O in **5e**) ppm. MS: *m/z* (%) = 67 (22), 69 (72), 70 (84), 71 (100), 77 (25), 97 (19), 81 (21), 83 (49), 84 (34), 85 (15), 91 (33), 94 (34), 97 (22), 104 (30), 111 (45), 112 (28), 114 (18), 124 (59), 126 (24), 128 (19), 138 (18), 150 (22), 169 (93), 271 (57), 273 (20), 286 (25), 287 (8) [$M^+ - 44$ (CO_2)], 288 (6) [$M^+ + 1 - 44$ (CO_2)].

General Procedure for Conversion of 4a and 4c−e into Mixtures of 5a/c−e and 6a/c−e, Respectively, by Treatment with H_2O_2 and Recording of the ^{1}H NMR Spectra of the Product Mixtures: Compounds **4a** or **4c−e** (100 mg) were dissolved in warm methanol (10 mL), and H_2O_2 (30%, 1.5−2.0 mol-equiv.) was added to the solution. The progress of the reaction was monitored by TLC. At the end of the reaction (5 h), the solvent was distilled off under reduced pressure in an Eyela rotary evaporator and the ^{1}H NMR spectra of the crude product mixtures were recorded.

General Procedure for Treatment of 4c and 4d with Performic Acid and Recording of the ^{1}H NMR Spectra of the Product Mixtures: Solutions of compounds **4c** or **4d** (50 mg, ca. 0.16 mmol) in 8 mL of methanol were added to solutions of H_2O_2 (30%, 304 mg, 2.68 mmol) and formic acid (80%, 316 mg, ca. 5.50 mmol). The reaction mixtures were stirred vigorously and the progress of the reactions was monitored by TLC. At the end of each reaction (1 h), the solvent was distilled off under reduced pressure and the reaction mixture was extracted with CH_2Cl_2. The extracts were washed with water and dried with anhydrous sodium sulfate and the solvent was completely removed under vacuum and the ^{1}H NMR spectra of the crude products were recorded. When the amount of performic acid was reduced to half (H_2O_2, 152 mg and formic acid, 158 mg), the reaction took 13 h for completion without any change in the product ratio (**5/6**).

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