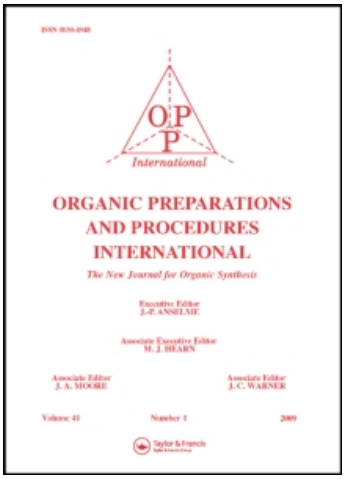

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A CONVENIENT PREPARATION OF *trans*-3,4-DIPHENYL- AND *trans, trans*-2,3,4-TRIPHENYLVALEROLACTONES

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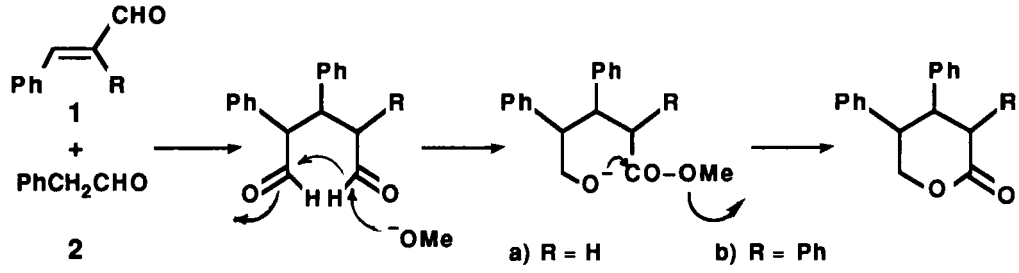
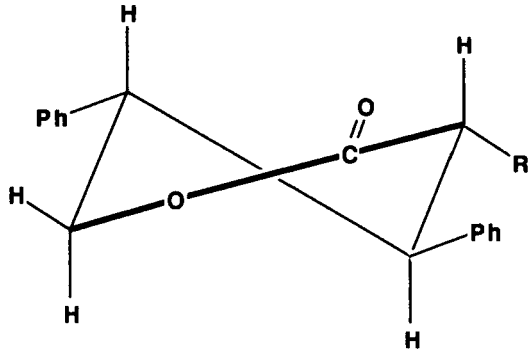
Although the preparation of aryl-substituted valerolactones has been of interest to organic chemists since the days of Meerwein, adequate methods for the synthesis of these materials from readily available precursors have been lacking.[1] We now report a convenient procedure for the preparation of the otherwise difficultly accessible *trans*-3,4-diphenyl- and the all *trans*-2,3,4-triphenylvalerolactone (3a and 3b respectively) and present unambiguous spectroscopic data in support of their stereochemistry. The formation of both δ-lactones may be viewed as proceeding by initial Michael addition of 2-phenylethanal to α,β-unsaturated aldehydes (α-phenylcinnamaldehyde generated *in situ* in the case of 3b), presumably producing 1,5-dialdehydes. These dialdehydes then underwent an internal Cannizzaro reaction, followed by cyclization to the lactones. In the case of 3a, steric interactions seemed to play a role, directing the base to the less hindered aldehyde.



The conformations of δ-lactones have been of interest to chemists since X-ray data showed that the atoms comprising the lactone moiety are coplanar.[2] The half-chair and boat are preferred conformations as shown by the X-ray data and supported by molecular mechanics calculations.[3] Although the carbonyl frequency of the δ-lactone has been used as a determinant for lactone conformation,[4] many discrepancies have been documented. NMR spectroscopy has proven to be a more reliable and readily accessible method. It has been shown that the magnitude of the geminal coupling constant at C-2 can be used as a determinant of the conformations.[5] Geminal coupling constants of 17 Hz or greater have been assigned to the half-chair form while those of less than 17 Hz are attributed to the boat form.[5,6]

In 3a, geminal coupling constants of -17.8 Hz were observed, indicative of the half-chair form. The large coupling constant (greater than 9 Hz) observed between protons H-2a and H-3, H-3

and H-4, H-4 and H-5 specify the *trans* orientation of these protons, thus placing the phenyls on C-3 and C-4 in a *trans* relationship. This δ-lactone also provided further NMR information that will be useful in the assessment of other δ-lactone conformations. The geminal coupling constant for the protons on C-5 can be used as a standard for systems that lack methylene protons on C-2. Thus the coupling constant of -11.3 Hz for H5a-H5b is indicative of the half-chair form. In 3b, the large coupling



a) R = H

b) R = Ph

observed for protons H-2:H-3 and H-3:H-4 is indicative of the all *trans* relationship of the phenyl substituents. The observed geminal coupling constant of 10.8 Hz for the methylene protons at C-5 shows the half-chair conformation.[7] The ^{13}C chemical shifts of C-5 and C-4 in 3a and 3b further demonstrate the half-chair conformation.

EXPERIMENTAL SECTION

Mps were taken in open capillary tubes using a Mel-Temp apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1310 spectrophotometer as thin films on NaCl plates. Samples for IR were typically made by dissolving the compound in a volatile solvent, such as acetone, then placing a small amount on a sodium chloride plate and allowing the solvent to evaporate thus forming a thin film. All NMR spectra were recorded on a Bruker NR/200 FT NMR spectrometer in $CDCl_3$ solutions using TMS as internal standard unless otherwise stated. Methanol, anhydrous ether and KOH pellets were purchased from Fisher Scientific Company; all other chemicals were purchased from Aldrich Chemical Company and were used without further purification.

Synthesis of *trans* 3,4-Diphenylvalerolactone (3a).- Cinnamaldehyde (0.2 mol, 25.7 mL) and 2-phenylethanal (0.4 mol, 45.9 mL) and methanol (60 mL) were placed in a 600 mL beaker, and potassium methoxide (3 g potassium in 40 mL ice-cold methanol) was added. The mixture turned dark red and was allowed to stand at room temperature overnight. Then a smaller amount of potassium methoxide (1 g potassium in 12 mL cold methanol) was added to the red solution and the contents warmed at 35° for 6 hrs. To the viscous dark brown material was added a solution of 5.5 g potassium hydroxide in 100 mL 95% ethanol. The mixture was then heated at 45° for 12 hrs and at reflux for 2 hrs. The cooled viscous brown substance was then dissolved in 800 mL water with heating. The aqueous mixture was extracted six times with 100 mL portions of ether. The aqueous layer was acidified (pH 3) with 6M HCl and allowed to stand at room temperature overnight. The

precipitated white crystals of 3a were collected and recrystallized from ethanol to give 7.4 g, mp. 120.5-121.5°. A second crop was obtained by partitioning the remainder of the material between ether (500 ml) and 6M NaOH (200 ml) to give a cloudy yellow ethereal layer, an aqueous layer and a red oil. The aqueous layer was allowed to stand overnight then acidified (pH 3) with 6M HCl to give a yellow solid, which was recrystallized from ethanol to give a further portion (5.1 g) of less pure 3a (overall crude yield 12.5 g, 25%), mp. 120.5-121.5°, lit.[1] mp. 123-123.5°. IR: 1732 cm^{-1} (C=O). ^1H NMR (200 MHz, $CDCl_3$): δ 7.15 (10H, aromatic), 4.5 (m, 2H, H-5a and H-5b $J_{5a,5b}$ = -11.3 Hz, $J_{5a,4}$ = 9.6 Hz, $J_{5b,4}$ = 5.5 Hz), 3.4 (m, 2H, H-3 and H-4 $J_{3,4}$ = 10.3 Hz), 3.1 (dd, 1H, H-2b, $J_{2b,3}$ = 6.3 Hz, $J_{2a,2b}$ = -17.6 Hz), 2.8 (dd, 1H, H-2a, $J_{2a,3}$ = 9.5 Hz, $J_{2a,2b}$ = -17.6 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 171 (C-1), 124-142 (aromatic), 73 (C-5), 47 (C-4), 44 (C- 3), 37 (C-2).

trans, trans-2,3,4-Triphenylvalerolactone (3b).- 2-Phenylethanal (0.30 mol, 35.0 mL) was added to benzaldehyde (0.10 mol, 10.0 mL) in a 250 mL round bottom flask. Concentrated sodium methoxide (made by adding 4.0 g Na in small pieces to 50 mL ice-cold methanol) was added to the flask. The solution immediately turned deep red; then, 70 mL methanol was added and the solution was heated at reflux for 10 hrs. The contents of the flask were then placed in a 400 mL beaker and half the methanol evaporated. The waxy crystals that resulted were dissolved in water and the solution acidified (pH 3) with 6M HCl. The acidified solution was allowed to stand at room temperature for about 2 hrs, and solid which appeared was recrystallized from ethanol to yield 7.5 g (25%) of colorless needles, mp. 163-165° (uncorr.), lit.[1] mp. 161-162°. IR: 1733 cm^{-1} (C=O). ^1H NMR (200 MHz, $CDCl_3$): δ 7.0 (15H, aromatic), 4.7 (t, 1H, H-5a, $J_{5a,5b}$ = -10.8 Hz, $J_{5a,4}$ = 10.6 Hz) 4.5 (dd, 1H, H-5b, $J_{5b,5a}$ = -10.8 Hz, $J_{5b,4}$ = 6.0 Hz), 4.0 (d, 1H, H-2, $J_{2,3}$ = 10.3 Hz), 3.6 (m, 1H, H-4), 3.5 (t, 1H, H-3, $J_{3,4}$ = 11.0 Hz, $J_{3,2}$ = 10.6 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 172 (C-1), 126-140 (aromatic), 74 (C-5), 56 (C-2), 54 (C-3), 47 (C-4).

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