was precipitated as the crystalline perchlorate (mp 116–117 °C; IR 1680 cm^{-1}) in 93% yield. Alternatively, the reaction mixture could be treated with hydrogen after the addition of 10% Pd-on-carbon to produce *N*-β-phenylethylpyrrolidine (bp 131 °C (21 mm); lit.[8] bp 139° (21 mm)) in 91% yield. Similarly, *N*-methylpipecolic acid (**4**)[9] was converted to *N*-methyl-Δ^1-tetrahydropyridinium (**5**) perchlorate (mp 85–86 °C; IR 1700 cm^{-1}) or tetraphenylborate (mp 184 °C), both in 94% yield.

As examples of the synthetic convenience and utility of this method, we have applied it to the synthesis of a 1-azabicyclo[5.4.0]undecane and a tetrahydroberberine. The 1-azabicyclo compound was prepared starting with hexahydroazepine-2-carboxylic acid (**6**)[10] which as the benzyl ester **7** was alkylated with diethyl 3-bromopropylmalonate[11] in benzene/DMF in the presence of K_2CO_3 to the α-tertiary amino ester **8** (bp 205–210 °C (0.1 mm), bulb to bulb). Hydrogenolysis gave acid **9** which was heated at 100 °C in $POCL_3$ for 3 min to form iminium salt **10** (IR 1690 cm^{-1}). Diluting with water, adjusting the pH to 6.5, and standing over night gave diethyl 1-azabicyclo[5.4.0]undecane-8,8-dicarboxylate (**11**, bp 100–105 °C (0.1 mm)) in 77% overall yield.

The tetrahydroberberine example was synthesized from 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid hydrochloride (**12**),[12] which as the isopropyl ester **13** (bp 125 °C (0.1 mm)) was alkylated with β-(3,4-dimethoxyphenyl)ethyl bromide[13] to the α-tertiary amino ester **14** ($R' = CH(CH_3)_2$, bp 180 °C (0.6 mm). Hydrolysis to acid **14** (R' = H, mp 157 °C) and heating at 100 °C for 2.5 min in $POCl_3$ gave iminium salt **15** which was warmed in hydrochloric acid to give 2,3-dimethoxy-5,8,13,13a-tetrahydro-6*H*-dibenzo[*a*,*g*]quinolizine hydrochloride (**16**, mp 238–241 °C; lit.[14] mp 236–238 °C) in 79% overall yield from acid **14.**

A significant feature of this scheme for preparing iminium salts is the wide availability of α-amino acids. This broad scope in starting materials provides a potent handle for directing the stereochemical course of a synthesis, including the cyclization step. Further details of these syntheses and that of other 1-azabicyclanes and berberines, as well as applications to other systems and for the preparation of enamines, will be forthcoming.

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Octamethyl-1,4-cyclohexanedione. Chair Conformation in the Crystal State

Sir:

The parent 1,4-cyclohexanedione has been studied by a wide variety of physical and theoretical techniques and, as a consequence, has become the example par excellence of a six-membered ring which adopts a twist-boat conformation in the solid,[1a-c] in solution,[1d-f] and possibly in the gas phase.[1g,h] Similarly, at least four derivatives of 1,4-cyclohexanedione, namely the *cis*- and *trans*-2,5-dimethyl compounds,[2a] as well as *cis*- and *trans*-2,5-di-*tert*-butylcyclohexanedione[2b] have been considered to prefer boat conformations in solution. We have now determined the x-ray crystal structure of octamethyl-1,4-cyclohexanedione[3] (**1**) and report that the molecule exists as a centrosymmetric chair in the solid.[4]

Crystals of **1** were obtained as very thin plates by slow sublimation in a long vertical tube at atmospheric pressure. A fragment of approximate dimensions 0.01 × 0.2 × 0.2 mm was used for x-ray study. Preliminary photography indicated the orthorhombic system with space group *Cmca* or *C2ca*, the former being confirmed during structure analysis. Cell dimensions were determined by least-squares refinement of setting angles for 15 reflections with $30 < \theta < 40°$, centered automatically on a Nonius CAD4 diffractometer, as a = 15.441 (5), b = 10.832 (4), c = 7.525 (2) Å. Using Cu Kα radiation, four octants ($\pm h$, $\pm k$, $+l$) of intensity data (1809 reflections) were recorded, yielding 392 independent, observed ($I > 3\sigma(I)$) reflections after merging (R = 0.018).

The structure was solved using the automatic centrosymmetric direct methods routine in the SHELX program[5] and refined by full-matrix least squares (C, O anisotropic, H isotropic, 64 parameters) to a final R_w of 0.037 (unweighted R = 0.048) in space group *Cmca*. The alternative space group *C2ca*, which would require the molecule to have only C_2 symmetry, was investigated, but because of correlation effects, no acceptable refinement could be obtained. We decided against any artificial damped refinement since the low R value, the reasonable anisotropic thermal parameters, and the accurate definition of hydrogen atoms (U_{iso} = 0.047 – 0.073 (8)) for the space group *Cmca* seemed to us to confirm adequately the centrosymmetric model. The molecule occupies a position of symmetry $2/m$ in the unit cell. Figure 1 shows the atomic numbering used and some of the more important bond lengths and angles; Figure 2 is a Newman projection of the molecule.

It is instructive to compare the molecular geometries of octamethyl-1,4-cyclohexanedione (**1**) and 1,4-cyclohexanedione (**2**).[1a,b] The C1–C2 bond in **1** (1.532 Å) is longer than the corresponding bond in **2** (1.511 Å) and the crowded diquaternary C2–C3 bond in **1** (1.571 Å) is also longer than the C2–C3 bond in **2** (1.545 Å), which in turn is longer than a cyclohexane C–C bond (1.520 Å from electron diffraction[6]).

The internal carbonyl angle C2–C1–C6 in **1** is 4° larger than

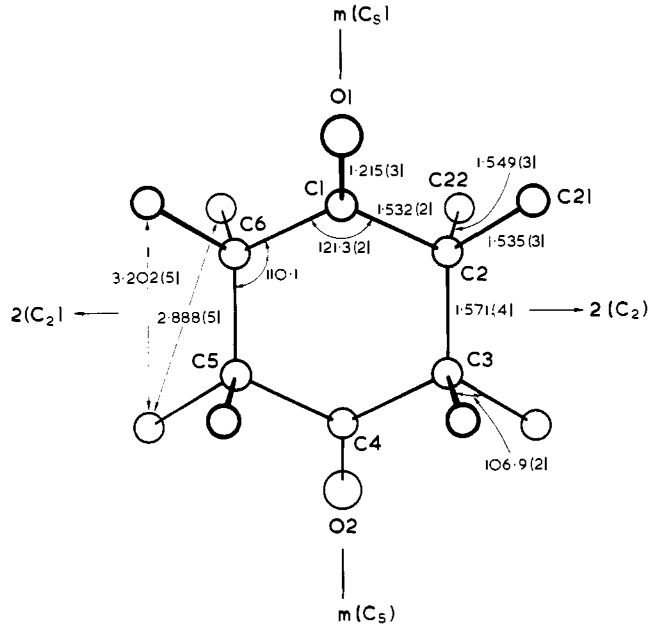

Figure 1. Structural data for octamethyl-1,4-cyclohexanedione. Note that atoms C1 and C4, O1 and O2, and C2, C3, C5, C6, and their substituents are crystallographically equivalent.

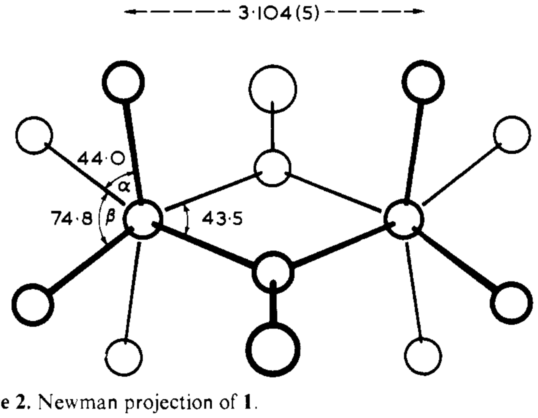

Figure 2. Newman projection of **1**.

in the parent **2**, as expected on general grounds and consistent with the relatively low IR$_{CO}$ frequency (1689 cm^{-1}) of **1**.[3] The presence of two internal carbonyl angles of 121.3° in **1** necessitates a marked flattening of the ring, as can be seen perhaps most clearly from the three consecutive torsion angles C1-C2-C3-C4 = 43.5°, C2-C3-C4-C5 = 49.2°, and C3-C4-C5-C6 = 43.5° and their sum of 136.2°. By comparison, the three torsion angles in cyclohexane, which is slightly flattened, sum to about 56 × 3 = 168°[6,7] compared with a value of 180° in "ideal" cyclohexane. The marked contraction of the axial-equatorial methyl-methyl torsion angle α by 16° from the ideal value of 60° and the corresponding expansion of the equatorial-equatorial angle β by 15° can be regarded as a further consequence of the adoption of a strongly flattened six-membered chair. Apart from generating unusual torsion angles the flattened chair conformation of **1** introduces an extremely short contact of 2.88 Å within each of the four equivalent pairs of vicinal axial-equatorial methyl groups. The resulting repulsion combined with the syndiaxial clash of 3.10 Å involving the two pairs of methyl groups may be a contributory cause of the compression of the four geminal dimethyl interbond angles to 106.9°.[8]

Supplementary Material Available: Atomic coordinates and temperature factor parameters for octamethyl-1,4-cyclohexanedione (1 page). Ordering information is given on any current masthead page.

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Asymmetric Syntheses Using *tert*-Leucine. 1. An Asymmetric Synthesis of β-Substituted Aldehydes via 1,4-Addition of Grignard Reagents to Chiral α,β-Unsaturated Aldimines

Sir:

The exciting development of a variety of methods for asymmetric induction continues to present a major challenge to the syntheses of optically active natural products, pharmaceuticals, etc.[1,2]

Meyers and Whitten have recently reported an asymmetric 1,4-addition of organolithium reagents to chiral oxazoline derivatives giving, after hydrolysis, β-substituted carboxylic acids in high enantiomeric purity.[3] We now wish to report that the 1,4-addition of Grignard reagents to the chiral α,β-unsaturated aldimines **3**, prepared from α,β-unsaturated aldehydes **1** and optically active α-amino acid *tert*-butyl esters **2**, gave, after hydrolysis, optically active β-substituted aldehydes **6**, which are useful intermediates for the synthesis of various optically active compounds.