

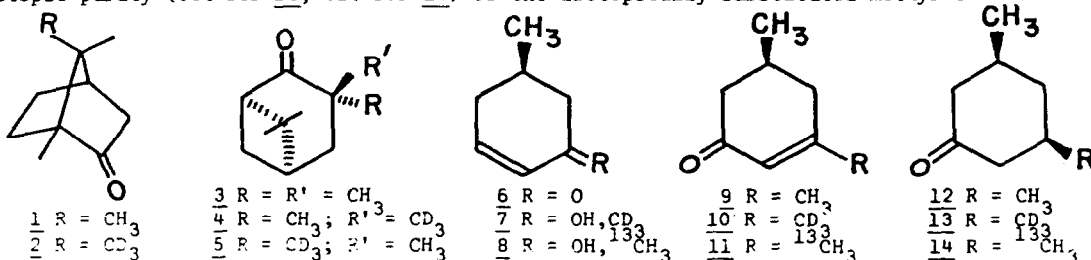
OPTICAL ROTATORY DISPERSION STUDIES CXXVI.<sup>1</sup> SYNTHESIS AND CHIROPTICAL  
 PROPERTIES OF CYCLOHEXANONES WITH CHIRALITY SOLELY DUE TO  
 ISOTOPIC SUBSTITUTION:  $^{12}\text{CH}_3$  vs.  $^{13}\text{CH}_3$  AND  $\text{CH}_3$  vs.  $\text{CD}_3$ .

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Several recent communications<sup>1-5</sup> have dealt with the synthesis, chiroptical properties and theoretical significance of cyclohexanones, whose chirality was solely due to the replacement of one ring hydrogen by deuterium. The only example in which the rotational contribution of  $\text{CD}_3$  is contrasted with that of  $\text{CH}_3$  has been Meyer and Lobo's<sup>6</sup> ORD comparison of (+)-camphor (1) with its trideuteriomethyl analog 2. Since the intrinsically large Cotton effects (due to the other chiral centers) of 1 and 2 differ by only 3%, such comparisons are fraught with uncertainty as we observed<sup>7</sup> by comparing (+)-2,2-dimethylnorpinone (3) with its two trideuteriomethyl analogs 4 and 5.<sup>7</sup> We should now like to report the synthesis and chiroptical properties of two cyclohexanones (13 and 14) in which for the first time the chirality is only due to the isotopically substituted methyl group ( $\text{CD}_3$  and  $^{13}\text{CH}_3$ ), thus eliminating the need for comparison with unlabelled material.

Standard 1,2-addition of the Grignard reagents prepared from  $\text{CD}_3\text{I}$  (99% isotopic purity) or  $^{13}\text{CH}_3\text{I}$  (82% isotopic purity) to (R)-(-)-5-methylcyclohex-2-en-1-one (6)<sup>8</sup> followed (without purification) by pyridinium chlorochromate oxidation<sup>9</sup> of the allylic alcohols 7 and 8 led to the oxygen-transposed  $\alpha,\beta$ -unsaturated ketones 10 and 11. Catalytic hydrogenation with 10% Pd/C in absolute ethanol gave the expected<sup>10</sup> cis/trans 98:2 mixture, from which the trace of undesired trans-2,6-dimethylcyclohexanone was removed by preparative gas chromatography (10' x 0.25" column packed with 15% carbowax, oven temp. 120°C, flow rate 60 ml/min; retention time 29.3 min. for cis and 32.6 min. for trans isomer).<sup>11</sup> The purity of the resulting (3*S*,5*R*)-3-methyl-5-trideuteriomethylcyclohexanone (13) [ $M^+$  = 129; nmr ( $\text{CDCl}_3$ )  $\delta$  1.03 (d, 3H), 1.2-2.5 ppm (m, 8H); ir ( $\text{CCl}_4$ ) 2060, 2120, 2210, 1707  $\text{cm}^{-1}$ ] and (3*S*,5*R*)-3-methyl-5- $^{13}\text{C}$ -methylcyclohexanone (14) [ $M^+$  = 127; nmr ( $\text{CCl}_4$ )  $\delta$  1.02 (d, 3.54H,  $J = 7$  Hz); ir ( $\text{CCl}_4$ ) 1715  $\text{cm}^{-1}$ ] is, therefore, identical with the isotopic purity (99% for 13; 82% for 14) of the isotopically substituted methyl iodides.



The CD spectra together with the calculated rotational strengths and octant diagrams of the energetically preferred diequatorial conformations of 13 and 14 are reproduced in Fig. 1, the  $^{13}\text{CH}_3$  group making approximately one-sixth the rotatory contribution compared to  $\text{CD}_3$ . Qualitatively, in all but one case ( $\beta$ -axial deuterium<sup>2b</sup>) of isotopic chirality (D vs. H;  $\text{CD}_3$  vs.  $\text{CH}_3$ ;  $^{13}\text{CH}_3$  vs.  $^{12}\text{CH}_3$ ) so far investigated, the heavier isotope has been the weaker perturber. Additional synthetic work with other chiral  $\text{CD}_3$  and  $^{13}\text{CH}_3$  substituted cyclohexanones is in progress in our laboratory.

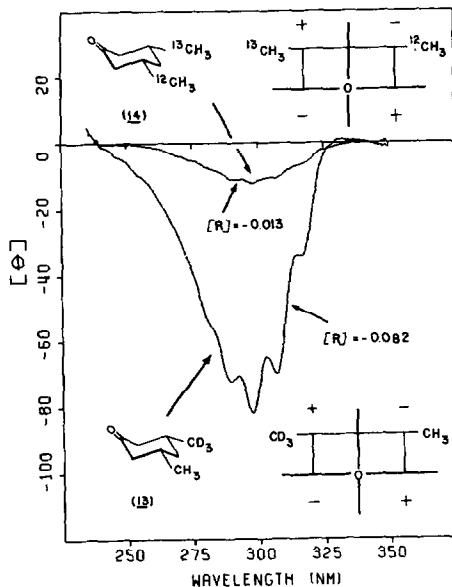


Fig. 1. Circular dichroism curves (20°C, 4:1 isopentane-methylcyclohexane solution of (3*S*,5*R*)-3-methyl-5-trideuteriomethylcyclohexanone (13) and (3*S*,5*R*)-3-methyl-5- $^{13}\text{C}$ -methylcyclohexanone (14) (corrected for 100% purity).

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11. To demonstrate the completeness of this gas chromatographic separation, the entire reaction sequence was repeated with methyl iodide (6-9+12). The resulting *cis*-3,5-dimethylcyclohexanone (12) exhibited no optical activity on the sensitivity scale employed to measure the CD (Fig. 1) of 13 and 14.

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