

Cyclobutanone-3,3- d_2 and Trimethylene-2,2- d_2

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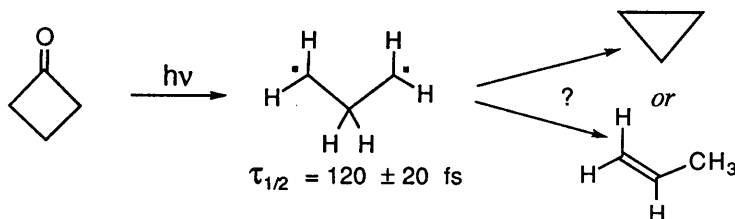
Summary

An efficient five-step synthesis of cyclobutanone-3,3- d_2 is reported. This ketone gives direct access through laser flash photolysis to the trimethylene-2,2- d_2 diradical. The life-time of trimethylene-2,2- d_2 provides an experimental showing that trimethylene and deuterium-labeled trimethylene diradicals decay to form cyclopropanes, rather than propenes.

Key Words: Trimethylene diradical, laser flash photolysis, kinetic isotope effects, femtosecond reaction dynamics

Introduction

Gas phase laser flash photolysis of cyclobutanone gives CO and the trimethylene diradical, and ketene and ethylene.¹ Femtosecond reaction dynamics experiments on this photolysis reported in 1994 followed the formation and decay of the trimethylene diradical; a lifetime of 120 ± 20 fs for the diradical was deduced.² Whether the diradical isomerized to form cyclopropane or to give propene could not be inferred from the experiment.²

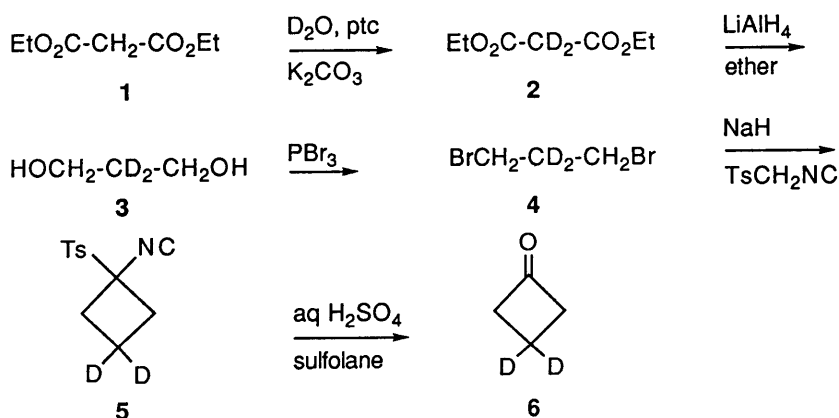


A preparation of cyclobutanone-3,3- d_2 (**6**) was undertaken to address this question. Laser flash photolysis of **6** would generate the trimethylene-2,2- d_2 diradical (**7**), and the lifetime of this reactive intermediate could be determined. Isomerization of **7** to form cyclopropane-1,1- d_2 would involve no primary deuterium kinetic isotope effects, and the lifetime of **7** would be little changed; were **7** to give propene- d_2 isomers the lifetime of the intermediate would be notably increased, for primary deuterium kinetic isotope effects would be involved.

Results

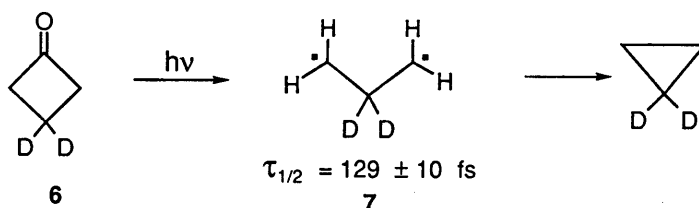
Of the some 30 to 40 preparations of cyclobutanone recorded in the literature,³⁻⁷ one reported by van Leusen and van Leusen⁸ using toluenesulfonylmethyl isocyanide as a formaldehyde dianion equivalent proved to be particularly attractive for making the desired labeled analog. A synthetic plan based on their work (Scheme 1) was implemented and found to be quite practicable.⁹

Scheme 1



The sequence of three steps shown in Scheme 1 leading from diethyl malonate (**1**) to 1,3-dibromopropane-2,2- d_2 (**4**) is well established.¹⁰⁻¹² Analyses of the labeled diester (**2**), diol (**3**, as the bis(phenylurethan) derivative¹³), and dibromide (**4**) through ^1H

NMR spectroscopy indicated essentially complete incorporation of deuterium at C2, for no residual C2 proton absorptions were detected. The ^1H NMR absorption spectrum of 1-isocyano-1-tosyl-cyclobutane-3,3- d_2 (5) showed the methyl singlet and a simple AB pattern for the geminal protons ($J = 13.5$ Hz). Hydrolysis of 5 on a 5-g scale gave pure cyclobutane-3,3- d_2 (6) in 65% yield. A second run on the same scale provided additional material; both samples were sealed in glass, mailed, and used to determine the lifetime of trimethylene-2,2- d_2 (7), 129 ± 10 fs.^{14,15}



This lifetime, a more precisely determined lifetime for trimethylene, 122 ± 8 fs,^{14,15} and one for trimethylene-1,1,3,3- d_4 (183 ± 12 fs)^{14,15} made clear that the trimethylene diradicals decay through isomerizations to cyclopropanes, a finding subsequently supported by theory based on diverse calculational approaches.¹⁵⁻²²

The rapidly developing methods associated with femtosecond reaction dynamics experiments combine molecular beam, laser flash photolytic, and fs-resolved mass spectrometric techniques.²³ They make possible experimental determinations of gas-phase lifetimes of transient reactive intermediates, but they allow neither routine identifications of molecular structures associated with species having measured m/z ratios and lifetimes nor determinations of structure for reaction products. The structures of intermediates and the unimolecular reaction paths through which they decay can only be postulated. Fortunately, additional experimental data may be gained when isotopically labeled

precursors are used in such kinetic experiments: lifetimes as functions of isotopic substitutions may strengthen or fail to support a particular interpretation of the femtosecond dynamics data secured for the unlabeled species.

In other femtosecond organic reaction dynamics studies, such isotopic labeling experiments have not yet been undertaken, and the m/z and lifetime data secured remain only tentatively associated with specific chemical structures and reaction paths. An important instance of such an ambiguity relates to the m/z 66 transient C_5H_6 intermediate observed when norbornene is subjected to laser flash photolysis (two photons, 184 kcal/mol); the measured lifetime is 220 ± 20 fs,²⁴ but whether it should be considered a cyclopent-2-ene-1,4-diyl²⁴ or some other structure, such as 2Z,4-pentadienylidene²⁵ or bicyclo[2.1.0]pentane-2,5-diyl, remains uncertain.²⁶ A combination of deuterium isotope effect experiments and theory may solve this structural problem and similar puzzles.

Experimental Section

The general procedures used and the instrumentation employed have been described elsewhere.²⁷ Authentic unlabeled samples of all compounds described below were available or were prepared for GC, MS, and 1H NMR comparisons.

Diethyl malonate- d_2 (2) was prepared in 93% yield from diethyl malonate through three equilibrations with D_2O , using K_2CO_3 as base and cetyltrimethylammonium bromide as catalyst; 1H NMR (300 MHz, $CDCl_3$) OCH_2CH_3 absorptions; no signal for C2 protons at δ 3.37.

Propane-1,3-diol-2,2- d_2 (3). The reduction of 2 with $LiAlH_4$ in ether, followed by a standard workup, gave an ethereal solution of crude diol. The salts collected were extracted with THF at reflux. The ethereal and THF solutions were combined, concentrated, and distilled at 0.2 torr. The center cut (41% yield) was 98% pure by

GC. For the bis(phenylurethan) derivative,¹³ ¹H NMR δ 4.29 (s); no signal for C2 protons at δ 2.06.

1,3-Dibromopropane-2,2-d₂ (4). Phosphorus tribromide (37 g) was added dropwise over 100 min to diol **3** (9.0 g) with stirring under nitrogen while the temperature of the reaction mixture was kept below 50 °C. The reaction mixture was stirred for 1 h at rt, heated to reflux for 19 h, cooled, and diluted cautiously with water. An orange precipitate was removed by filtration. The aqueous phase was extracted with ether, and the combined organic material was washed with aqueous NaHCO₃ and dried (Na₂SO₄). Filtration, concentration, and vacuum distillation gave **4** (16 g, 68% yield, 97% pure by GC); ¹H NMR δ 3.54 (s); no signal for C2 protons at δ 2.36.

1-Isocyano-1-tosylcyclobutane-3,3-d₂ (5) was obtained from dibromide **4**, tosylmethyl isocyanide, and NaH in DMSO-ether as described;⁸ ¹H NMR δ 3.02 (d, J = 13.5 Hz, 2 H), 2.48 (d, J = 13.5 Hz, 2 H), 2.48 (s, 3 H); no absorption for C3 protons at δ 2.20.

Cyclobutanone-3,3-d₂ (6). The labeled intermediate **5** (5 g) was hydrolyzed with aqueous H₂SO₄ in sulfolane, following van Leusen and van Leusen,⁸ except the reaction flask and the vacuum system were separated by two traps, one at rt and the second cooled to -78 °C, rather than by u-tubes containing K₂CO₃ and P₂O₅. Ketone **6** was isolated from the cold trap and dried over K₂CO₃ (1.0 g, 65% yield, 99% pure by GC analyses on two capillary columns); ¹H NMR δ 3.05 (s); no signal for C3 protons at δ 1.98.

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