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The *in*-Bicyclo[4.4.4]-1-tetradecyl Cation: A Stable Substance with a Three-Center, Two-Electron C–H–C Bond

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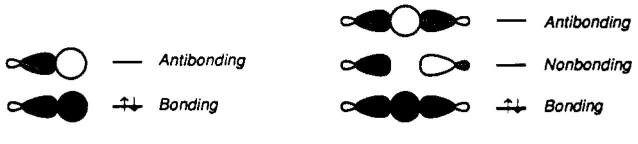
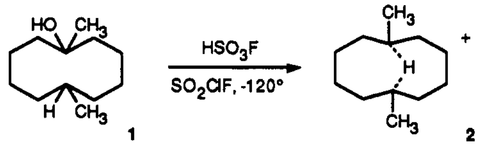
Abstract: The synthesis of the title cation **3** is presented, and evidence is amassed to show that the substance contains a three-center, two-electron C–H–C bond. Among the evidence obtained is the ^{1}H NMR spectrum of **3**, which shows a one-proton resonance for the C–H–C hydrogen at δ −3.46 with a coupling constant J_{C-H} = 47 Hz. Upon substitution of the inside hydrogen by deuterium, the corresponding C–D–C bridged cation shows an upfield shift to δ −3.36, characteristic of a single-minimum potential energy surface. Other confirming evidence includes the observation of a C–H–C stretching absorption at 2113 cm^{-1} in the IR spectrum and semiempirical (AM1) calculations.

The two-center, two-electron C–H bond is fundamental to organic chemistry. Every organic molecule contains one or more C–H bonds that can be described electronically in terms of a doubly occupied, two-center molecular orbital resulting from the combination of a singly occupied carbon hybrid orbital with a singly occupied hydrogen 1s orbital. The same is not true in organometallic and inorganic chemistry, however. In many inorganic substances, particularly the boron hydrides, *three*-center, two-electron bonds such as B–H–B are of equal or greater importance than their two-center counterparts. Such bonds can be described electronically in terms of a doubly occupied, three-center molecular orbital resulting from the combination of two boron (or metal) hybrid orbitals with a single hydrogen 1s orbital.[1]

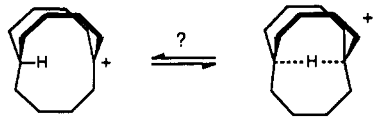


A 2-center, 2-electron bond **A 3-center, 2-electron bond**

Why does three-center C–H–C bonding not occur in organic chemistry? In fact, it *does* occur, but it's quite rare. Sorensen has shown[2] in elegant studies that the 1,6-dimethyl-1-cyclodecyl cation (**2**) and related ions contain transannular three-center C–H–C bonds when generated from the corresponding alcohols at −120 °C. The ions are not stable, however, rearranging and ultimately decomposing when warmed above −70 °C.

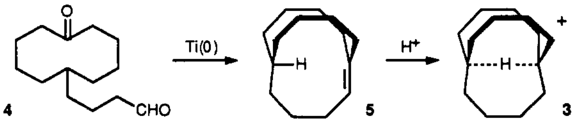


Is it possible to design, synthesize, and study ordinary *stable* organic substances that have three-center C–H–C bonding? Sorensen's cation **2**, which has a transannular interaction of a C–H hydrogen with a vacant orbital across a 10-membered ring, has the appropriate geometry and orbital alignment for three-center bonding, but further steric constraints are clearly necessary in order to prevent rearrangements and loss of the bridging proton. In principle, what's needed is a rigid, caged, bicyclic cation with an inside hydrogen. Molecular models suggest that the *in*-bicyclo[4.4.4]-1-tetradecyl cation (**3**) should be ideal.[3] All rings are 10-membered, the inside hydrogen is rigidly held within bonding distance of the inner orbital lobe on the positively charged bridgehead carbon, and the inside hydrogen is unable to escape through the sides of the cage. We now report the synthesis and study of cation **3** and show that it is indeed a stable, long-lived substance with a symmetrical three-center, two-electron C–H–C bond.[4]

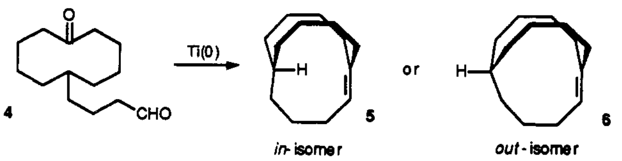


in-Bicyclo[4.4.4]-1-tetradecyl cation (**3**)

Synthesis of *in*-Bicyclo[4.4.4]-1-tetradecene (5). Our plan for the synthesis of cation **3** was to prepare it from the corresponding bridgehead alkene, *in*-bicyclo[4.4.4]-1-tetradecene (**5**). We hoped in turn, to prepare this alkene by titanium-induced carbonyl coupling[5] of the appropriate keto aldehyde, 6-(4-oxobutyl)-cyclodecanone (**4**).



Although the titanium-induced carbonyl-coupling reaction has been shown in numerous instances to be a remarkably powerful method for the synthesis of large rings and strained systems, the proposed cyclization of **4** to yield **5** represents a particularly difficult test. Not only is alkene **5** highly strained, there is also the possibility that the alternative out isomer **6** might result from the cyclization rather the desired in isomer **5**. Fortunately, though, molecular-mechanics calculations[6] predict that in isomer **5** should be less strained than out isomer **6** (36 kcal/mol strain energy for **5**; 43.4 kcal/mol for **6**), implying that the desired in isomer might well result if any cyclization occurs.



The synthesis and titanium-induced cyclization of keto aldehyde **4** are shown in Scheme I. The starting material **7**, available from

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[1] For a review of three-center, two-electron bonds, see: (a) Olah, G. A.; Surya Prakash, G. K.; Williams, R. E.; Field, L. D.; Wade, K. *Hypercarbon Chemistry*; Wiley-Interscience: New York, 1987. (b) DeKock, R. L.; Bosma, W. B. *J. Chem. Educ.* **1988**, *65*, 194–197.

[2] Kirchen, R. P.; Ranganayakulu, K.; Rauk, A.; Singh, B. P.; Sorensen, T. S. *J. Am. Chem. Soc.* **1981**, *103*, 588–596 and references therein.

[3] For a short review on medium-ring bicycloalkanes, see: Alder, R. W. *Acc. Chem. Res.* **1983**, *16*, 321–327.

[4] A preliminary account of this work has appeared: McMurry, J. E.; Hodge, C. N. *J. Am. Chem. Soc.* **1984**, *106*, 6450.

[5] For reviews of the titanium-induced carbonyl coupling reaction, see: (a) McMurry, J. E. *Acc. Chem. Res.* **1983**, *16*, 405–411. (b) McMurry, J. E. *Chem. Rev.*, in press.

[6] We thank Professor Schleyer (Universität Erlangen) for carrying out the calculations. The results have been published: McEwen, A. B.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1986**, *108*, 3951–3960.

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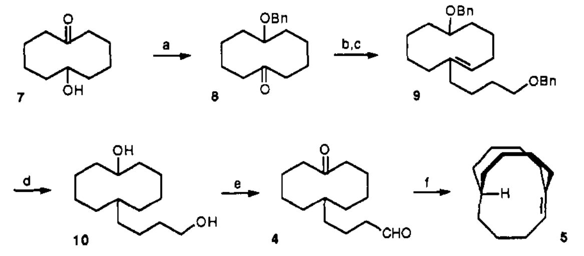
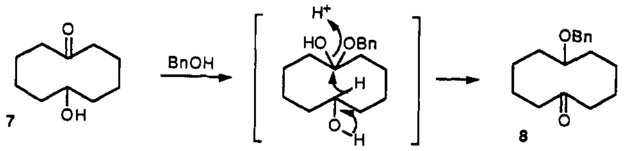
Scheme I



(a) BnOH, HCl, 66%; (b) $BnOCH_2CH_2CH_2CH_2MgCl$, benzene, Bu_4NBr, 75%; (c) TsOH, benzene, Δ, 77%; (d) H_2, Pd/C, CH_3OH, EtOAc, HOAc, 87%; (e) PCC, CH_2Cl_2, NaOAc, 95%; (f) $TiCl_3 \cdot (DME)_{1.5}$, Zn-Cu, DME, Δ, 30%.

decalin by photosensitized air oxidation,[7] was converted to benzyl ether **8** by reaction with an excess of benzyl alcohol and dry HCl gas. Since these are rather mild and unusual conditions for conversion of an alcohol into an ether, we suspect that the reaction probably involves initial addition of benzyl alcohol to the ketone carbonyl group, followed by loss of water and concurrent transannular hydride migration.[8]

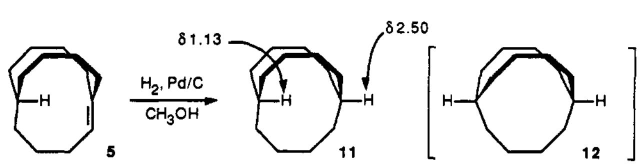


Grignard reaction of ketone **8** with 4-(benzyloxy)butylmagnesium chloride in benzene containing 0.3 equiv of Bu_4NBr then gave a tertiary alcohol, which was dehydrated by reaction with a catalytic amount of *p*-toluenesulfonic acid in refluxing benzene with azeotropic removal of water. Reduction and deprotection of bis(benzyloxy)alkene **9** was accomplished by catalytic hydrogenation over 10% Pd/C at 50 psi for 50 h, and oxidation of the resultant diol **10** with pyridinium chlorochromate in the presence of sodium acetate gave keto aldehyde **4**.

The titanium-induced cyclization of keto aldehyde **4** required careful optimization (see Experimental Section), but ultimately we were able to obtain a bicyclotetradecene product in a reproducible isolated yield of 30%. The product was obtained as waxy white crystals stable to both light and air at room temperature.

Structure and Properties of *in*-Bicyclo[4.4.4]-1-tetradecene (5). Proof that the bicyclo[4.4.4]-1-tetradecene obtained by cyclization of keto aldehyde **4** was indeed the in isomer **5** rather than the out isomer **6** was obtained by catalytic hydrogenation to yield the corresponding alkane. Hydrogenation of **5** over a 10% Pd/C catalyst in methanol solvent at 50 psi for 24 h yielded a saturated product that was readily identified as *in,out*-bicyclo[4.4.4]tetradecane (**11**). Had out alkene **6** been the cyclization product, reduction would have led to out,out alkane isomer **12**. It should be noted that alkene **5** is "hyperstable" in Schleyer's terminology[9] and that its reduction might be expected to be sluggish. We did indeed find the hydrogenation to require unusually vigorous conditions, but otherwise we encountered no problems.

Characterization of alkane **11** was accomplished by both ^1H and ^{13}C NMR spectroscopies. Thus, ^1H NMR spectroscopy of in,out alkane **11** showed two distinct one-proton resonances at δ 2.5 and 1.13, corresponding to the two different kinds of bridgehead protons. Assignment of the resonance at δ 2.5 to the outside hydrogen and the resonance at δ 1.13 to the inside hydrogen was easily made by repeating the hydrogenation step using D_2 rather than H_2. The deuterated product retained the higher field absorption but no longer had the peak at δ 2.5. ^{13}C NMR spectroscopy of **11** showed six peaks at δ 36.45 (t), 32.88 (d, J = 122.42 Hz), 31.48 (d, J = 111.2 Hz), 31.32 (t), 28.94 (t), and 25.31, indicating a 3-fold axis as the only symmetry element (C_3). By contrast, out,out alkane isomer **12** would be expected to show a single two-proton resonance in its ^1H NMR spectrum for the two equivalent bridgehead protons and to show only three peaks in its ^{13}C NMR spectrum, indicative of D_3 symmetry. Interestingly, the C–H coupling constant for the out bridgehead carbon, J = 111.2 Hz, indicates a slight distortion away from tetrahedral sp^3 geometry toward planar sp^2. Assuming that the relationship between C–H coupling constant and % s character of the carbon orbital is given by the equation[10]



$$J_{C\text{-}H} = 5.7(\%\ s) - 18.4\ Hz$$

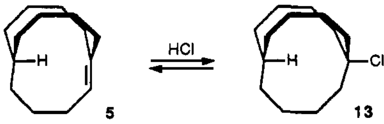
we calculate that the C–H bond to the out bridgehead carbon has only 22.7% s character and that the three C–C bonds must each have 25.8% s character.

Further structural characterization of **5** was accomplished by NMR and UV spectroscopies. The in bridgehead hydrogen occurs as a multiplet at δ 3.35 in the ^1H NMR spectrum of **5**, a result explained by molecular-mechanics calculations that indicate a minimum-energy conformation in which the hydrogen is anisotropically deshielded by the double bond at the opposite bridgehead. The ^{13}C NMR spectrum of **5** shows the expected 14 peaks, with 2 vinylic carbon resonances at δ 143.0 and 131.7. A gated decoupling experiment showed that the resonance at δ 131.7 belonged to the secondary vinylic carbon and that the C–H coupling constant was $J_{C\text{-}H}$ = 143.5 Hz. Again assuming the usual relationship[10] between C–H coupling constant and % s character of the carbon orbital, we calculate that the secondary vinylic carbon has 28.4% s character, that its hybridization is midway between sp^2 and sp^3, and that the double bond is strongly pyramidalized.

If the double bond in **5** is deformed as indicated by NMR, there should be a consequent increase in energy of the HOMO and lowering in energy of the LUMO, thus reducing the HOMO–LUMO gap and possibly moving the alkene $\pi \rightarrow \pi^*$ absorption into the normal UV range. In fact, the UV spectrum of **5** in dichloromethane shows a band at λ_{max} = 229 nm (ϵ = 2850).

Preparation and Study of the *in*-Bicyclo[4.4.4]-1-tetradecyl Cation (3). We initially thought it might be necessary to generate the *in*-bicyclo[4.4.4]-1-tetradecyl cation (3) by solvolysis of the corresponding tertiary bridgehead alkyl chloride **13**, and we therefore sought to prepare **13** by reaction of alkene **5** with HCl. Surprisingly, however, there was no evident reaction when **5** was treated with dry HCl in any of numerous solvents, including methanol, ether, dichloromethane, and cyclohexane. Only recovered starting material was obtained on workup.

An indication that something unusual might be going on, though, was found when we carried out the reactions of **5** with HCl in NMR tubes and looked at the ^1H NMR spectra of the resultant mixtures. When polar solvents such as methanol, ether, or dichloromethane were used, the NMR spectra showed neither starting alkene **5** nor addition product **13** but instead indicated formation of a substance with a one-proton resonance at δ −3.46 (see below). When cyclohexane was used as solvent, NMR indicated that tertiary chloroalkane **13** was in fact formed rapidly,



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[7] Our procedure is a modification of that reported by Mijs (see Experimental Section): Mijs, W. J.; DeVries, K. S.; Westra, J. S.; Angad-Gaur, H. A.; Smidt, J.; Vriend, J. *Recl. Trav. Chim. Pays-Bas.* **1968**, *87*, 580–584.

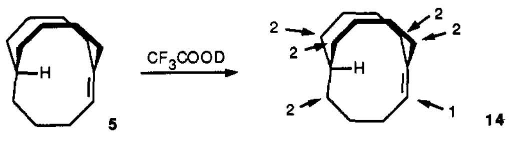
[8] For a review of transannular reactivity in medium rings, see: Prelog, V.; Traynham, J. G. *Molecular Rearrangements*; de Mayo, P., Ed.; Wiley-Interscience: New York, 1963; Vol. I, p 593.

[9] Maier, W. F.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 1891–1900.

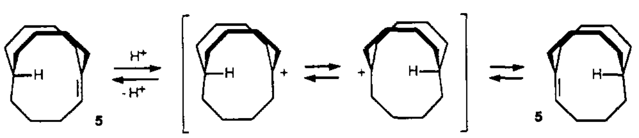
[10] Newton, M. D.; Schulman, J. M.; Manus, M. M. *J. Am. Chem. Soc.* **1981**, *103*, 17–23.

yet **13** underwent spontaneous loss of HCl by E1 reaction when solvent was removed. Such extraordinary solvolytic reactivity—the spontaneous elimination of HCl from an alkyl chloride simply on concentration of its cyclohexane solution—is unprecedented for any other tertiary chloroalkane[11] and clearly indicates extraordinary stability for the intermediate cation.

Further evidence for the unusual nature of the cation formed by protonation of alkene **5** was obtained when **5** was treated with deuteriotrifluoroacetic acid, CF_3COOD. Reaction with CF_3COOD at room temperature followed by bicarbonate quench and workup led to the nearly instantaneous exchange of 11 deuterium atoms into the molecule (mass spectroscopy) at every position next to *both* bridgehead carbons.



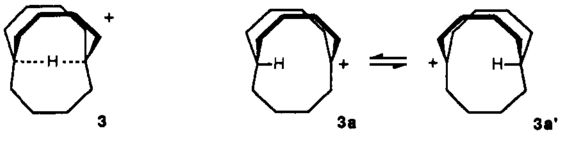
This deuterium-incorporation result can be explained only by assuming that a protonation/deprotonation equilibrium takes place and that the inside hydrogen rapidly and reversibly migrates from one bridgehead to the other, making all six carbons next to both bridgeheads equivalent.



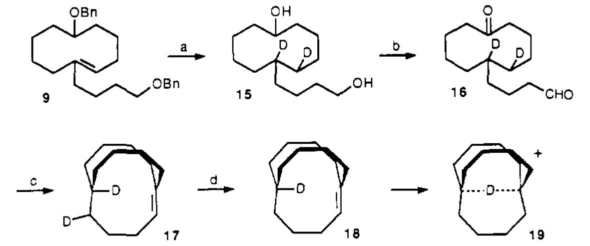
NMR Evidence for Three-Center C-H-C Bonding. As noted above, reaction of alkene **5** with acid at room temperature leads to the formation of a stable cation. Solutions of this cation are stable indefinitely at room temperature and show a one-proton absorption at δ −3.46 in their ^{1}H NMR spectra. Since ^{1}H NMR spectra of Sorensen's cation **2** and related ions also contain similar high-field peaks attributable to the bridging hydrogen,[2] we believe that our *in*-bicyclo[4.4.4]-1-tetradecyl cation contains a symmetrical three-center, two-electron C–H–C bond and can best be represented as structure **3**. Further evidence for the presence of three-center C–H–C bonding in cation **3** has been obtained in several ways.

The ^{13}C NMR spectrum of **3** shows three peaks at δ 19.3 (t), 41.6 (t), 139.3 (d) with a coupling constant $J_{\mathrm{C-H}} = 47$ Hz for the bridgehead peak at δ 139.3. Both the chemical shift and the coupling constant for this bridgehead peak are at abnormally low values for a classical carbocation—a normal chemical shift for a positively charged carbon is in the range δ 280–350, and a normal coupling constant is about 170 Hz[12]—but the data can be explained easily by the bridging structure **3**. The low chemical shift value is due to charge delocalization over both bridgehead carbons, and the low coupling constant is due to diminished spin density of the C–H–C bonding electrons at the carbon nuclei. Similar low values of chemical shift and coupling constant have been found for cation **2** and related substances.[2]

Although we felt confident at this point that the NMR results were best accounted for by the nonclassical bridging structure **3**, it is nevertheless possible that the results might also be explained by a pair of rapidly equilibrating classical structures **3a** and **3a′**.

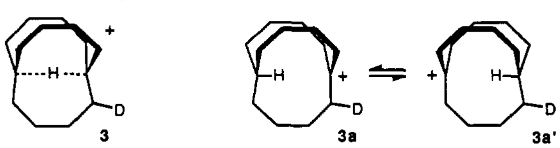


Scheme II



(a) D_2, Pd/C, CH_3OH, EtOAc, HOAc; (b) PCC, CH_2Cl_2, NaOAc; (c) $TiCl_3 \cdot (DME)_{1.5}$, Zn-Cu, DME, Δ; (d) HCl, H_2O.

In order to rule out the possibility of rapid equilibration and to obtain still further evidence for the nonclassical bridged structure **3**, we applied the deuterium isotope perturbation test of Saunders.[13] Without going into the theoretical background of the test, the idea is to break the symmetry of **3** (or the degeneracy of **3a** $\rightleftharpoons$ **3a′**) by introducing a deuterium atom next to one of the bridgehead carbons. If the ion has the nonclassical structure **3**, introduction of this deuterium will make the two bridgehead carbons nonequivalent, causing them to appear at slightly different positions in the ^{13}C NMR spectrum. According to the data of Saunders,



Expected ^{13}C NMR:
δ 138.8, 139.8 ($\Delta\delta = 1$ ppm)

Expected ^{13}C NMR:
δ 129, 149 ($\Delta\delta = 20$ ppm)

one would expect the difference in chemical shifts between the two absorptions to be on the order of 1 ppm. If, on the other hand, the ion has the classical equilibrating structure 3a $\rightleftharpoons$ 3a′, introduction of a deuterium atom will perturb the equilibrium, favoring one ion over the other and causing a chemical-shift difference between the two nonequivalent bridgehead absorptions on the order of 20 ppm.

The required deuterium atom was introduced by reaction of alkene **5** with deuteriofluorosulfonic acid in CD_2Cl_2 at −92 °C, and the ^{13}C NMR spectrum was run at −92, −45, −20, 0, and 25 °C. At −92 °C, the bridgehead carbon resonance was split into two peaks at δ 137.1 and 136.3 ($\Delta\delta = 0.8$ ppm) exactly as expected for bridged nonclassical structure **3**. The splitting showed a negative temperature dependence, decreasing to 0.2 ppm at 0 °C.

Still further NMR evidence for three-center C–H–C bonding in cation **3** was obtained by employing the $\Delta\delta(^{1}\mathrm{H}, ^{2}\mathrm{H})$ test of Altman and Forsén.[14] These authors have shown that the shape of the potential energy surface for an X–H–X bond can be probed by determining the effect of isotopic substitution on the chemical shift of the central hydrogen. If a downfield shift is observed in going from the protio substrate to the deuterio substrate (that is, a *negative value for* $\delta^{1}\mathrm{H}-\delta^{2}\mathrm{H}$), then a single-well potential surface indicative of a nonclassical structure is present. If no shift or an upfield shift is observed (that is, a positive value for $\delta^{1}\mathrm{H}-\delta^{2}\mathrm{H}$), then a double-well potential surface indicative of equilibrating nonclassical structures is present.

In order to carry out the test, it was first necessary to synthesize the *in*-deuteriobicyclo[4.4.4]-1-tetradecyl cation **19**, a synthesis accomplished by the route shown in Scheme II. Reduction of bis(benzyloxy)alkene **9** with D_2, rather than H_2, gave the doubly deuterated alcohol **15**, which was oxidized by pyridinium chlorochromate to yield keto aldehyde **16**. Titanium-induced cyclization by the standard method then gave doubly deuterated alkene **18**, whose unwanted deuterium on the carbon atom next to the

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(11) High reactivity for a bridgehead alkyl chloride has also been noted for 1-chlorobicyclo[3.3.3]undecane (1-chloromanxane): Parker, W.; Tranter, R. L.; Watt, C. I. F.; Chang, L. W. K.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1974**, *96*, 7121–7122.

(12) For a discussion of carbocation NMR spectra, see: Olah, G. A.; Surya Prakash, G. K.; Sommer, J. *Superacids*; Wiley-Interscience: New York, 1985; pp 75–85.

(13) Saunders, M.; Telkowski, L.; Kates, M. R. *J. Am. Chem. Soc.* **1977**, *99*, 8070–8071.

(14) Altman, L. J.; Laungani, D.; Gunnarsson, G.; Wennerström, H.; Forsén, S. *J. Am. Chem. Soc.* **1978**, *100*, 8264–8266.

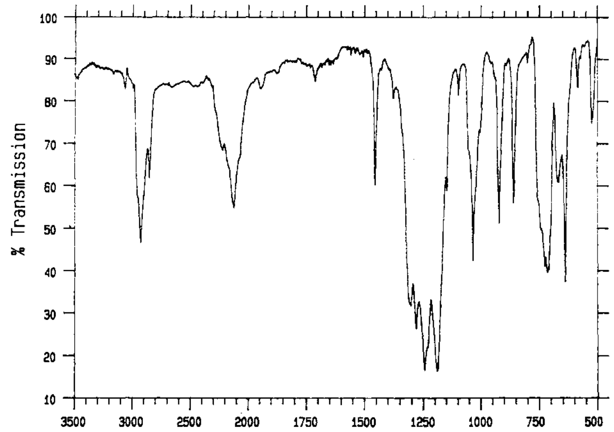


Figure 1. FTIR spectrum in CH_2Cl_2 of the trifluoromethanesulfonate salt of the *in*-bicyclo[4.4.4]tetradecyl cation **3**.

in bridgehead was exchanged by treatment with aqueous acid. The ^2D NMR spectrum of deuterated cation **19** showed a peak at δ −3.36, corresponding to a $\delta^1H-\delta^2H$ of −0.10 and clearly indicating a three-center bonded structure for the cation.

IR Evidence for Three-Center C-H-C Bonding. Reaction of alkene **5** with trifluoromethanesulfonic acid in CH_2Cl_2 gave a solution of cation **3** that was analyzed by FTIR spectroscopy to gain further information about the three-center C-H-C bond. The IR spectrum (Figure 1) showed the presence of a strong band at 2113 cm^{-1}, along with normal C-H and C-C bands. Similar analysis of the deuterated cation **19** showed a complete lack of any band at 2113 cm^{-1} but the presence of an absorption at 1558 cm^{-1}. All other bands in the spectrum remained essentially unaffected by the isotopic substitution.

The intensity of the C-H-C band at 2113 cm^{-1} and the large isotopic shift of 565 cm^{-1} on deuterium substitution allow us to assign it to an asymmetric stretching motion (A_2 in D_3 symmetry). Any bending motion, by contrast, should be fairly weak and should show a relative indifference to isotopic substitution. Most importantly, these IR data are consistent with a symmetric single-minimum potential surface for the three-center bond.[15] An alternative double-minimum potential surface should reveal a splitting of the fundamental asymmetric stretching frequency with a magnitude proportional to the height of the barrier between potential minima. Further, isotopic substitution might be expected to shift more than one band if a double-minimum potential were present.

A simple vibrational analysis of the C-H-C asymmetric stretch was carried out by approximating the three-center bond as a classical linear three-body oscillator with negligible coupling to other molecular vibrations.[16] Using the formula

$$A_2 \text{ frequency} = \frac{k(2m_C + m_H)}{m_C m_H}$$

where m_C is the mass of the carbon and m_H is the mass of the hydrogen, we calculate a force constant k of 1.26×10^5 dyn/cm for the three-center bond. A similar calculation on the C-D-C vibration gave a force constant of 1.32×10^5 dyn/cm, in excellent agreement with the C-H-C value. For comparison, we might note that an average force constant for a normal C-H *two*-electron bond is in the range $(4.8-5.9) \times 10^5$ dyn/cm. To our knowledge, this is the first time that such fundamental information has been obtained for a three-center bond in an organic molecule.

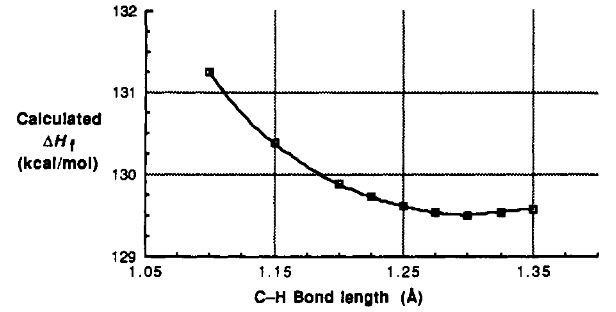


Figure 2. Plot of C-H bond length versus calculated (AM1) heat of formation for the C-H-C three-center bond in *in*-bicyclo[4.4.4]tetradecyl cation **3**.

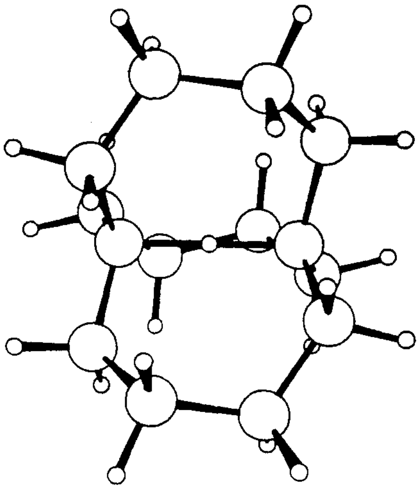
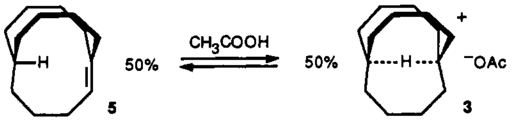


Figure 3. Computer-generated structure of the *in*-bicyclo[4.4.4]-1-tetradecyl cation using coordinates derived from semiempirical calculations.

A Quantitative Measure of Cation Stability. A dramatic measure of the extraordinary stability of cation **3** comes from simple tests to determine how strong an acid is required to cause 50% protonation of alkene **5**. By dissolving the pure alkene in acids of varying strength and analyzing the extent of protonation by NMR spectroscopy, we determined that H_2SO_4, HCl, and even CF_3COOH give quantitative protonation. Only in pure acetic acid solvent is the extent of protonation approximately 50%. In other words, the simple monounsaturated alkene **5** approaches acetate ion in basicity, and the cation **3** is nearly as weak an acid as acetic acid!



Theoretical Calculations on Cation 3. Although full details will be presented in a separate paper,[17] we summarize here the main conclusions of both semiempirical and ab initio calculations that have been carried out on cation **3**. Semiempirical (AM1) calculations were carried out on cation **3** by initially constraining the ion to C_3 symmetry while allowing the inside hydrogen to move along the C_3 axis. The ion converged to D_3 symmetry during optimization, with a bridging hydrogen symmetrically centered between the two bridgehead carbons at equal C-H bond distances of 1.312 Å. Symmetry constraints were then removed, and the calculations were repeated, but the geometry did not change.

The shape of the C-H-C potential well was probed by a series of single-point calculations obtained by constraining the length of one of the inside C-H distances. As shown by the plot in Figure 2, AM1 calculations predict a broad, shallow, and symmetrical potential well for the C-H-C three-center bond, in full agreement with our experimental data.

Further theoretical confirmation of three-center, two-electron bonding in cation **3** was obtained by ab initio MO calculations at the 6-31G level.[18] Although the ion was initially constrained

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to C_3 symmetry to conserve computer time, it converged to D_3 symmetry during optimization, with a symmetrical C–H–C three-center bond and a C–H bond length of 1.251 Å. A computer-generated display of the optimized structure is shown in Figure 3.

Summary and Conclusions. We have synthesized a stable organic ion, the *in*-bicyclo[4.4.4]-1-tetradecyl cation (**3**), and have presented firm evidence that it contains a three-center, two-electron C–H–C bond. The logic behind its synthesis and the techniques used in its preparation should be applicable to a range of other substances, and we are currently extending our work to the formation of other organic ions with other types of three-center bonds.

Experimental Section

General. Melting points were recorded on a Thomas-Hoover apparatus. The following were used to record spectra: UV, Perkin-Elmer Model 552A (samples run as solutions in matching cells, values given in nanometers); **IR**, Perkin-Elmer Model 298 (samples run as neat films or Nujol mulls), Polaris FTIR (samples run as dilute solutions in CH_2Cl_2 in matching cells); **NMR**, Varian VXR-200 (200 MHz), Varian VXR-400 (400 MHz, 100 MHz ^{13}C); **GC**, Hewlett Packard 5830A; **prep-GC**, Varian 3300; **MS**, Finnigan MS-902. All reactions were carried out under an atmosphere of argon unless otherwise noted.

6-Hydroxycyclodecanone (7). An adaptation of the procedure by Mijs[7] was used. Decahydronaphthalene (500 mL, Aldrich) was filtered through Florisil (75 g) and heated to 107 °C with rapid stirring in a 1000-mL three-neck flask equipped with a condenser and a gas dispersion tube connected directly to an oxygen tank. Rose Bengal photosensitizer (0.5 g) and 18-crown-6 (1.0 g) were added to the flask, and the red solution was purged with oxygen (300 mL/min) while being irradiated by a sunlamp. Heating, irradiation, and oxygen bubbling were continued until the solution was bright yellow and foaming (30–60 h). The solution was then cooled in an ice bath, washed with cold, aqueous NaOH (7%) in 100-mL portions until the aqueous layer was clear, and washed with brine (100 mL). Acetone (200 mL) was added to the pink organic layer, and the mixture was added dropwise over 10 min to 50% aqueous H_2SO_4 (500 mL) in a 2000-mL three-neck flask cooled in an ice bath and equipped with a mechanical stirrer. The mixture was stirred vigorously for 2 h and then allowed to separate into layers. The aqueous layer was diluted with 200 mL of ice water and extracted with $CHCl_3$ (8 × 100 mL). The extract was dried (MgSO4) and concentrated, and the solvent was removed at high vacuum to yield hydroxy ketone **7** as a pale yellow solid (40 g). Although recrystallization from hexane gave white crystals (mp 68.5–70 °C (lit.[7] mp 69–70 °C)), the material was a mixture of hydroxy ketone and hemiacetal isomers in solution. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.1 (m, 1 H), 3.9 (m, 1 H), 2.8–2.2 (m, 4 H), 2.1–1.2 (m, 12 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 214.3, 103.3, 75.9, 69.5, 42.5, 41.3, 34.6, 34.4, 25.6, 25.0, 23.6. IR (Nujol) 1700 cm^{-1}.

6-(Benzyloxy)cyclodecanone (8). 6-Hydroxycyclodecanone (**7**, 60 g, 0.41 mol) was dissolved in benzyl alcohol (200 mL). The resulting solution was stirred at 75 °C and saturated with dry HCl gas over 30 min. $NaHCO_3$ (0.5 g) was added to the solution, and excess benzyl alcohol was distilled off (80 °C, 1 mmHg). The pot residue was purified by chromatography on silica (1:4 ether–hexane) to yield keto ether **8** as a light yellow oil (71 g, 66%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.4–7.2 (m, 5 H), 4.5 (s, 2 H), 3.5 (m, 1 H), 2.6–2.2 (m, 4 H), 2.0–1.2 (m, 12 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 214.7, 139.0, 128.3, 127.8, 127.5, 76.0, 70.3, 41.9, 30.2, 23.4, 22.7. IR (Nujol) 1700 cm^{-1}.

4-(Benzyloxy)-1-chlorobutane. A mixture of 4-(benzyloxy)-1-butanol[19] (50 g, 277 mmol), PPh_3 (75 g, 286 mmol), and CCl_4 (200 mL) was heated to reflux (*caution*! reaction initially very exothermic) for 10 h, precipitating $Ph_3P{=}O$. The reaction mixture was cooled to room temperature, diluted with pentane (250 mL), and filtered through Florisil. Concentration and distillation under high vacuum yielded pure 4-(benzyloxy)-1-chlorobutane (51 g, 257 mmol, 93%). bp 110–125 °C (0.1 mmHg). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.4–7.3 (m, 5 H), 4.5 (s, 2 H), 3.7–3.5 (m, 4 H), 2.0–1.7 (m, 4 H).

6-(Benzyloxy)-1-(4-(benzyloxy)butyl)cyclodecene (9). A Grignard reagent was prepared from 4-(benzyloxy)-1-chlorobutane (35 g, 176 mmol), magnesium turnings (4.3 g, 177 mmol), and 200 mL of dry ether and was concentrated by removal of solvent at high vacuum to yield a thick paste. Benzene (200 mL) and Bu_4NBr (5.0 g) were added to the paste with stirring, and the resulting solution was cooled in an ice–salt bath. 6-(Benzyloxy)cyclodecanone (**8**, 43.2 g, 166 mmol) in 100 mL of benzene was added dropwise over 10 min, and the solution was allowed to stir an additional 4 h. The solution was then diluted with ether (200 mL) and washed with saturated aqueous NH_4Cl (1 × 100 mL) and water (1 × 100 mL). Drying ($MgSO_4$) and concentration, followed by chromatography on silica (1:3 ether–hexane), yielded 52.6 g (125 mmol, 75%) of the tertiary alcohol 6-(benzyloxy)-1-(4-(benzyloxy)butyl)-1-cyclodecanol as a colorless oil (mixture of diastereomers). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.4–7.2 (m, 10 H), 4.5–4.4 (m, 4 H), 3.7–3.4 (m, 4 H), 2.0–1.0 (m, 22 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.16, 139.12, 138.58, 128.48, 128.37, 128.33, 127.70, 127.60, 127.53, 127.49, 127.39, 126.93, 109.55, 78.31, 75.84, 72.91, 70.33, 70.18, 70.07, 65.09, 40.97, 40.91, 33.63, 33.43, 30.23, 28.81, 28.19, 22.55, 22.30, 21.26, 21.05, 19.55. IR (neat) 3450 cm^{-1}.

6-(Benzyloxy)-1-(4-(benzyloxy)butyl)-1-cyclodecanol (53 g, 125 mmol), prepared in the above manner, *p*-toluenesulfonic acid (0.5 g), and benzene (500 mL) were refluxed for 6 h with azeotropic removal of water. The solution was then diluted with ether (300 mL), washed with saturated aqueous $NaHCO_3$ (2 × 100 mL) and water (1 × 100 mL), dried ($MgSO_4$), and concentrated. The resulting oil was purified by chromatography on silica (5% ether–hexane) to afford olefin **9** as a light yellow liquid (34 g, 77%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.4–7.2 (m, 10 H), 5.15 (t, 1 H), 4.5 (s, 4 H), 3.5 (m, 3 H), 2.3–1.2 (m, 20 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.29, 138.69, 138.41, 128.35, 128.30, 127.65, 127.57, 127.48, 127.35, 125.39, 77.85, 72.89, 70.39, 70.03, 35.35, 31.62, 29.89, 29.63, 25.81, 24.52, 24.39, 22.69, 14.17.

6-(4-Hydroxybutyl)-1-cyclodecanol (10). A solution of olefin **9** (20 g, 50 mmol) in 50 mL of 20:2:1 MeOH–EtOAc–HOAc containing 4 g of 10% Pd–C was hydrogenated at 50 psi for 48 h in a Parr apparatus. The mixture was then filtered free of catalyst, diluted with ether, washed with saturated aqueous $NaHCO_3$ (1 × 50 mL), dried ($MgSO_4$), and concentrated. The resulting solid was recrystallized from diisopropyl ether to yield white crystals of diol **10** as a cis/trans mixture of diastereomers (10 g, 87%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.1 (m, 1 H), 3.9 (m, 1 H), 3.7 (m, 3 H), 1.9–1.1 (m, 23 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 72.2, 70.9, 63.0, 36.9, 36.3, 36.0, 35.0, 33.5, 33.3, 33.0, 32.5, 30.3, 23.8, 23.7, 23.6, 22.5, 22.0. IR (neat) 3440 cm^{-1}.

6-(4-Oxobutyl)cyclodecanone (4). Diol **10** (1.0 g, 4.4 mmol) in 80 mL of dry CH_2Cl_2 was added dropwise with stirring at 0 °C to a mixture containing CH_2Cl_2 (100 mL), pyridinium chlorochromate (3.5 g), NaOAc (1.0 g), and powdered molecular sieves. The brown suspension was stirred for 2 h at room temperature and diluted with ether (100 mL). Filtration through Florisil and concentration yielded a clear oil (950 mg, 95%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 9.75 (s, 1 H), 2.7–2.2 (m, 6 H), 0.8–2.0 (m, 17 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 215.00, 202.83, 44.20, 41.98, 35.31, 34.82, 30.13, 23.57, 23.34, 19.71. IR (neat) 1710, 1690 cm^{-1}.

***in*-Bicyclo[4.4.4]-1-tetradecene (5).** $TiCl_3$ (25.0 g, 0.162 mol) was suspended in 350 mL of dry dimethoxyethane (DME), and the mixture was refluxed for 2 days under argon. After cooling to room temperature, filtration under argon, washing with pentane, and drying under vacuum gave the fluffy, blue crystalline $TiCl_3(DME)_{1.5}$ complex (32.0 g, 80%) that was used in the coupling reaction.[20] $TiCl_3(DME)_{1.5}$ (7.0 g, 20.9 mmol) and the Zn–Cu couple (4.0 g, 61.9 mmol) were added to 250 mL of doubly distilled DME in a 500-mL two-neck flask via a Schlenk tube under argon. The mixture was stirred vigorously at reflux for 3 h to yield a black, homogeneous slurry. Keto aldehyde **4** (50 mg, 0.223 mmol) in 50 mL of DME was added to the stirred mixture via a syringe pump over 35 h. The mixture was then cooled to room temperature and diluted with distilled, degassed pentane (300 mL) and filtered through Florisil under argon. The solvent was distilled off at atmospheric pressure, and the residue was purified by preparative gas chromatography (OV-101 on Supelcoport at 170 °C) to yield 13 mg of **5** (30%) as a white solid: mp (sealed tube); phase change at 48–50 °C to a translucent solid that liquifies at 118–120 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.42 (br dd, $J = 11.5, 1$ Hz, 1 H), 3.45–3.25 (m, 1 H), 2.60–0.80 (m, 22 H). ^{13}C NMR ($CDCl_3$, 80 MHz) δ 143.2, 131.8, 36.5, 36.2, 35.3, 33.9, 33.7, 32.5, 29.8, 29.17, 27.7, 26.6, 26.0, 23.3. MS *m/e* 192 (M^+, 1%), 135 (30%), 67 (100%). High-resolution MS calcd for $C_{14}H_{24}$, 192.1878; found, 192.1880. UV (CH_2Cl_2) $\lambda_{max} = 229$ nm ($\epsilon = 2850$), (CH_3OH) $\lambda_{max} =$ 200 nm.

***in*-Deuteriobicyclo[4.4.4]-1-tetradecene (18).** Deuterated alkene **18** was prepared similarly to **5** except that D_2 gas was substituted for H_2 in the reduction/debenzylation of olefin **9**. The extra deuterium from a position adjacent to the bridgehead in **17** was removed by washing a

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(18) The ab initio calculations were performed by Dr. Erich R. Vorpagel of E. I. du Pont de Nemours & Company, using a modified version of HONDOG (Program QG01 from the National Resource for Computation in Chemistry). We thank Dr. Vorpagel for these results.

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8872 *J. Am. Chem. Soc.* **1989**, *111*, 8872–8878

pentane solution of **17** with dilute HCl, followed by neutralization of the aqueous layer and reextraction into pentane.

***in,out*-Bicyclo[4.4.4]tetradecane (11).** *in*-Bicyclo[4.4.4]-1-tetradecene (**5**, 10 mg, 0.1 mmol), platinum(IV) oxide (10 mg, 0.044 mmol), and 1 mL of MeOH were shaken in a Parr apparatus under 50 psi of H_2 pressure for 24 h. The mixture was diluted with 1:1 ether–pentane (5 mL) and filtered through a small amount of silica gel. The bulk of the solvent was removed by rotary evaporation (caution: product is highly volatile), followed by high vacuum for 15 s. The crude product was purified by preparative GC (10% SP 1000 on 80/100 Supelcoport at 170 °C) to yield 6 mg (60%) of a white solid: mp 159–161 °C (sealed tube). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.50 (m, 1 H), 1.73 (m, 6 H), 1.53 (m, 1 H), 1.13 (m, 1 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 36.45 (t), 32.88 (d, J = 122.4 Hz), 31.48 (d, J = 111.2 Hz), 31.32 (t), 28.94 (t), 25.31 (t). GC–MS (Cl) *m/e* 194 (M^+). High-resolution MS, calcd for $C_{14}H_{26}$, 194.2034; found, 194.2038.

***in*-Bicyclo[4.4.4]-1-tetradecenylium Triflate (3-Triflate).** Alkene **5** (2.0 mg, 0.01 mmol) was dissolved in dry CD_2Cl_2 (0.5 mL) in a dry NMR tube under an argon atmosphere. Trifluoromethanesulfonic acid (5.0 mg, 0.033 mmol) was added to the solution via syringe at 0 °C, and the tube was capped and shaken to yield a light yellow solution that proved stable indefinitely at room temperature. ^{1}H NMR (300 MHz) δ 2.5 (br s, 12 H), 1.9 (br s, 12 H), −3.46 (br s, 1 H). ^{13}C NMR (22.49 MHz) 19.3 (t), 41.6 (t), 139.3 (d, J_{C-H} = 47 Hz). Solutions of the corresponding chloride and trifluoroacetate salts were prepared similarly, and all showed identical NMR spectra. An infrared spectrum was taken of the trifluoromethanesulfonate salt: FTIR (CH_2Cl_2) 2113 cm^{-1}. The chloride salt showed an identical absorption.

***in*-Bicyclo[4.4.4]-1-tetradecenylium Acetate (3-Acetate).** Alkene **5** (5.0 mg, 0.025 mmol) was dissolved in 0.5 mL of neat CD_3COOD. NMR analysis revealed a 1:1 mixture of cation **3** and starting alkene **5**.

***in*-Deuteriobicyclo[4.4.4]-1-tetradecenylium Triflate (19-Triflate).** Deuterated cation **19** was prepared identically to **3** substituting **18** for **5**. ^{2}D NMR (100 MHz) δ −3.36. FTIR (chloride salt, CH_2Cl_2) 1558 cm^{-1}.

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Atom Transfer Addition and Annulation Reactions of Iodomalonates

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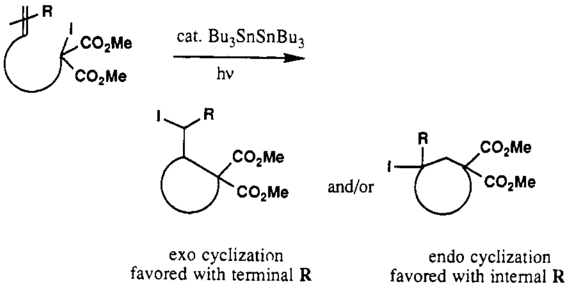
Abstract: Atom transfer addition and annulation reactions of iodomalonates with alkyl- and phenyl-substituted alkenes are described. For example, sunlamp irradiation of dimethyl methyliodomalonate and 1-hexene in the presence of 10% hexabutylditin provides dimethyl 2-methyl-2-(2-iodohexyl)malonate in 69% yield. Treatment of this reaction mixture with tributyltin hydride prior to workup provides dimethyl 2-methyl-2-hexylmalonate in comparable yield. Good yields of adducts are observed with terminal alkenes, and in addition to γ-iodomalonates and reduced products, lactones (resulting from intramolecular substitution) and alkenes (resulting from elimination of HI) can also be formed in many cases. When allyl- or progargyliodomalonates are used, annulated products are formed in a single step. For example, sunlamp irradiation of propargyliodomalonate and 1-hexene in the presence of 10% hexabutylditin provides 3,3-dicarbomethoxy-1-(iodomethylene)cyclopentane in 52% yield. Mechanistic considerations that will allow the design of successful annulation reactions with electrophilic radicals like iodomalonates are presented.

Malonates and related 1,3-dicarbonyl compounds are central functional groups in organic synthesis because they are rapidly assembled by classical alkylation reactions (the malonic ester synthesis[2]) and modern organometallic reactions [Pd(0)-promoted allylic alkylations[3]], and because they are readily transformed into other functional groups. We have recently shown[4] that iodomalonates, a hitherto little-known class of molecules,[5] are readily prepared and are excellent substrates for radical cyclizations conducted by the atom transfer method (see eq 1).[4,6] We now



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report that atom transfer addition and annulation[7] reactions of

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