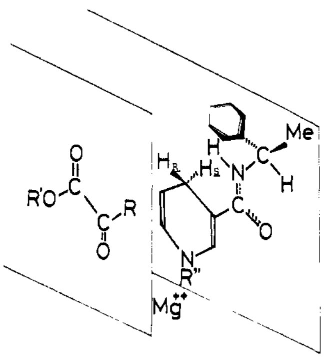

**Figure 1.** Schematic representation for stereochemical interpretation of the reaction.

pro-*R* hydrogen from the pro-*S* counterpart in NAD(P)H and its analog.[25] The stereochemistry of the reactions with the enantiomers of **1** as well as the effect of the prochirality of the $C_4$ hydrogens are currently under investigation in these laboratories.

**Acknowledgment.** The authors thank Dr. M. Fukuyama of SCRC for helpful discussion.

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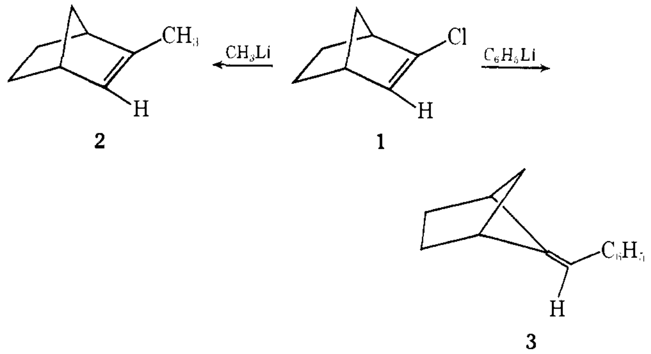
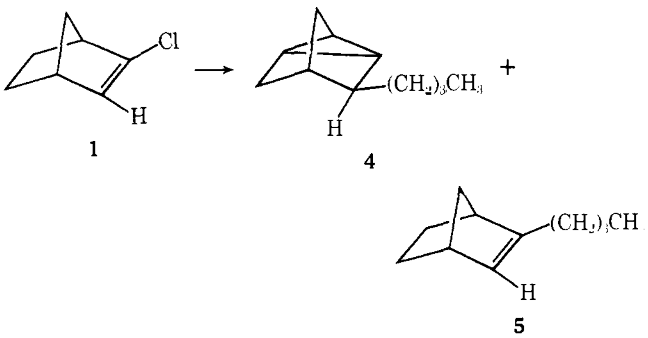
## Norbornyne[1]

*Sir:*

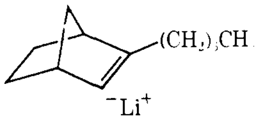
The reaction of organolithium reagents with cyclic vinyl halides has been much discussed as a route to strained cycloalkynes.[2,3] Thus, it was of interest that the reactions of methyllithium and phenyllithium with 2-chlorobicyclo[2.2.1]heptene (**1**) gave 2-methylbicyclo[2.2.1]heptene (**2**)[4] and 5-benzalbicyclo[2.1.1]hexane (**3**)[5] in 73 and 62% yields, respectively. Even more surprising was the observation that optically active **1** gave optically active **2** with retention of stereochemistry.[6] These observations, in particular those associated with the formation of **2**, rule out the intermediacy of a symmetrical intermediate in the reaction of **1** with certain organolithium reagents. The failure of **1** to react with methyllithium to form a cycloalkyne can be rationalized in terms of the large amount of strain which would occur if a triple bond were to be incorporated into the bicyclo[2.2.1]heptyl skeleton. This rationalization would appear to be justified by the difficulty observed in the generation of cyclopentyne from a variety of precursors.[2] With this background in mind, we wish to report that the reaction of **1** with *n*-butyllithium takes yet a different mechanistic pathway, which is best explained by the intermediacy of bicyclo[2.2.1]heptyne (norbornyne).



Treatment of a solution of **1** with 4–5 equiv of *n*-butyllithium in tetrahydrofuran[7] at 25° for 2 hr, followed by quenching with water, gave 80% of a 1:1.6 mixture of 3-*n*-butyltricyclo[2.2.1.$0^{2,6}$]heptane (**4**) and 2-*n*-butylbicyclo[2.2.1]heptene (**5**). In order to elucidate the mechanistic pathway from **1** to **4** and **5**, three sets of labeling experiments were carried out. In the first of these studies, the reaction mixture was quenched with deuterium oxide instead of with water. This gave an 88% yield of a 1:1.6 mixture of **4** (no deuterium incorporation) and **5**. Both mass



spectral and NMR measurements indicated that the 2-*n*-butylbicyclo[2.2.1]heptene, which was formed, was 87% deuterated in the 3-position.[8] This demonstrated the presence of the anion **6** prior to quenching. The less than quantitative incorporation of deuterium indicated that more than one mechanism might be involved in the formation of **5**.



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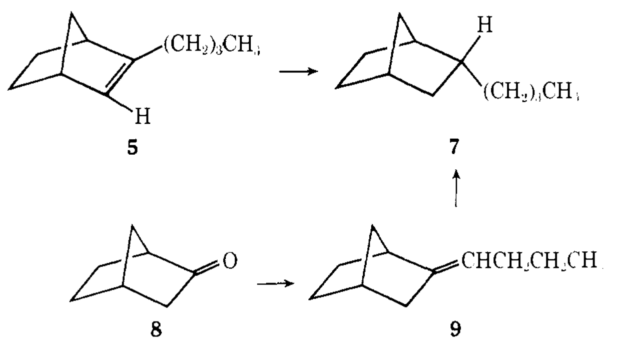
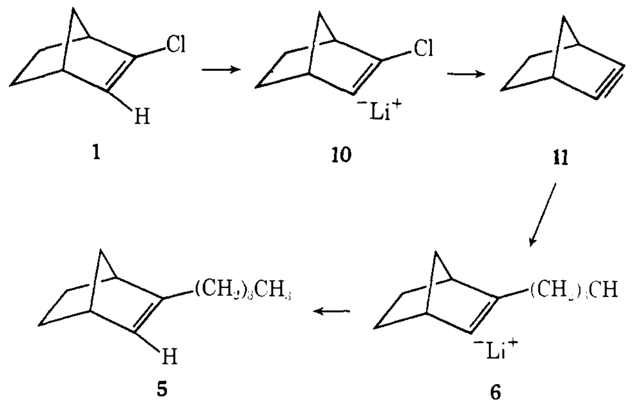
In a second study involving isotopic labeling, **1** (81% deuterium[9] at C-3) was treated with excess *n*-butyllithium in tetrahydrofuran. This produced 86% of a 16:1 mixture of **4** (89% deuterium at C-3) and **5** (15% deuterium at C-3). Several aspects of this experiment merit discussion. First, a large change in product ratio was noted. This indicated that *at least* two different mechanisms were involved in the reaction of **1** with *n*-butyllithium. Furthermore, it provided strong evidence that the rate-determining step in the formation of the major portion of **5** involved removal of the deuterium at C-3 of **1**. The retention of 15% of deuterium at C-3 of **5** was consistent with the observations in the deuterium oxide quenching experiment. Again, strong support for the formation of **5** by two competing mechanisms was obtained.

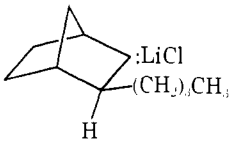
The last experiment involved the use of optically active (+)-(1*S*)-2-chlorobicyclo[2.2.1]heptene (**1**), $[\alpha]^{25}\text{D}$ +0.91 ± 0.10° (*c* 3.7, $CHCl_3$), which was prepared from (+)-(1*S*)-bicyclo[2.2.1]heptan-2-one, $[\alpha]^{25}\text{D}$ +5.0 ± 0.1° (*c* 21.0, $CHCl_3$) according to the method of McDonald and Steppel.[10] Treatment of (+)-**1** with *n*-butyllithium under the conditions described above gave a 1:1.6 mixture of (−)-(2*R*)-3-*n*-butyltricyclo[2.2.1.0$^{2,6}$]heptane (**4**), $[\alpha]^{25}\text{D}$ −8.1 ± 0.1° (*c* 3.1, $CHCl_3$)[11] and (+)-(1*S*)-2-*n*-butylbicyclo[2.2.1]heptene (**5**) $[\alpha]^{25}\text{D}$ +2.06 ± 0.10° (*c* 3.3, $CHCl_3$). In order to determine the absolute configuration of **5** and the extent of retention (or inversion) of configuration, a sample of optically active **8**, identical in rotation with that used in the preparation of (+)-**1**, was treated with butylidenetriphenylphosphine. This gave (+)-(1*S*)-2-butylidenebicyclo[2.2.1]heptane (**9**), $[\alpha]^{25}\text{D}$ +21.6 ± 1° (*c* 10.6, $CHCl_3$). Catalytic reduction of **9** gave (−)-(1*S*)-*endo*-2-*n*-butylbicyclo[2.2.1]heptane (**7**), $[\alpha]^{25}\text{D}$ −0.89 ± 0.10° (*c* 4.0, $CHCl_3$). Similar catalytic reduction of the sample of (+)-**5** obtained from (+)-**1** gave (−)-**7**, $[\alpha]^{25}\text{D}$ −0.23 ± 0.10° (*c* 2.5, $CHCl_3$). This indicated that most of **5** was formed via a mechanism which resulted in racemization. Within experimental error, the retention of optical activity in **5** was equivalent to the percentage of retention of deuterium in the reaction of deuterated **1** with *n*-butyllithium and to the percentage of C-3 protium retention in the deuterium oxide quenching experiment.



The three labeling experiments described above are all consistent with the intermediacy of a symmetrical species in the formation of ca. 85% of **5**.[12] The large deuterium isotope effect on the product ratio implies that the first step in the formation of this symmetrical intermediate was the removal of the vinylic proton to produce **10**. The only obvious route from **10** to a symmetrical intermediate is via loss of chloride to give **11**. *We feel that the accumulated data provide overwhelming evidence that norbornyne* (**11**) *is present* as a major intermediate in the reaction of **1** with *n*-butyllithium. Norbornyne would be expected to be a highly reactive intermediate. Addition of *n*-butyllithium to **11** under the reaction conditions should give **6**, which on quenching would produce **5**.



The inversion of stereochemistry in the formation of **4**[11] was consistent with the addition of the *n*-butyllithium to **1** followed by α-elimination to give **12**. Insertion of the carbenoid intermediate across the ring would then produce **4**. This mechanism is also consistent with the total retention of deuterium from labeled **1** and the failure of **4** to incorporate deuterium in the deuterium oxide quenching experiment.



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In summary, we have shown that 2-chlorobicyclo-[2.2.1]heptene can react with a strong base such as *n*-butyllithium to the extent of 52% to produce norbornyne. We believe that this is probably the most strained acetylene prepared thus far.[13] Our studies in this area are being continued.

**Acknowledgment.** We are indebted to the National Science Foundation for a grant which supported this investigation.

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(12) The mechanism whereby the other 15% is derived remains to be elucidated. Presumably this occurs through some type of direct coupling reaction since retention of stereochemistry is observed.

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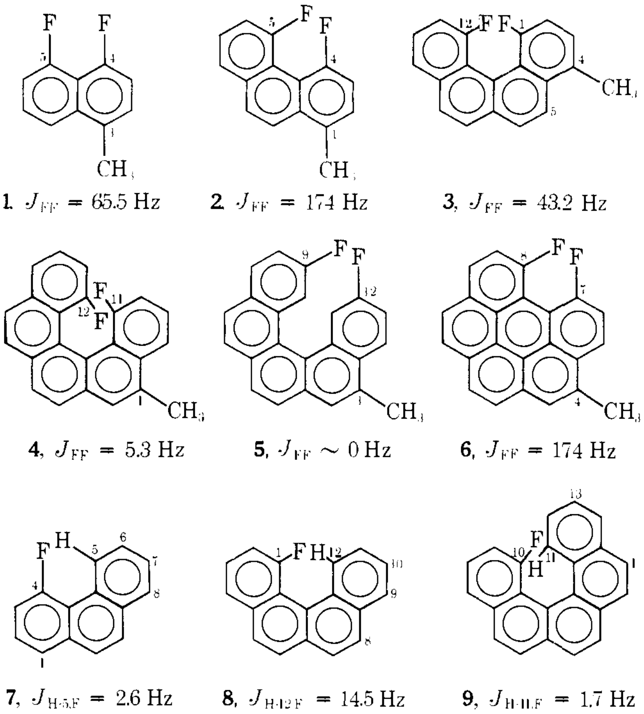
## Nuclear Spin–Spin Coupling via Nonbonded Interactions. III. Effects of Molecular Structure on Through-Space Fluorine–Fluorine and Hydrogen–Fluorine Coupling[1]

*Sir:*

The concept[2] that certain intramolecularly crowded atoms can experience nuclear spin-spin coupling predominantly via through-space (or direct) nonbonded interactions of the two atoms, as opposed to interactions involving the intervening bonds, continues to receive considerable attention. Many examples have been reported for both FF[3,4] and HF[2a,5] coupling, and several theoretical treatments have appeared.[1a,6] Some initial findings of the systematic investigations we are undertaking of through-space coupling in polynuclear aromatic systems are presented in Chart I.[7,8]

The values of $J_{FF}$ observed for **1–6**[9] support the idea that the magnitude of through-space FF coupling depends on the internuclear distance. For example, the FF distance in the difluorophenanthrene **2** obviously is shorter than that in the difluoronaphthalene **1**, which accounts for $J_{FF}$ being much larger for **2** than for **1**. In the series of difluoro compounds **2–5**, the sharply decreasing values of $J_{FF}$ (**2**, 174 Hz;[10] **3**, 43.2 Hz;[11] **4**, 5.3 Hz;[12] **5**, ca. 0 Hz) are consistent with the expectation that out-of-plane distortions in these helical molecules give rise to increasing FF distances in the sequence **2** < **3** < **4** < **5**. The observation of the same $J_{FF}$ value of 174 Hz for both the benzo[*ghi*]perylene derivative **6**[12] and the phenanthrene derivative **2** reflects the similar spatial relationship of the two fluorines in these compounds.

Chart I. Through-space FF and HF coupling constants for compounds 1–9.



1, $J_{FF}$ = 65.5 Hz
2, $J_{FF}$ = 174 Hz
3, $J_{FF}$ = 43.2 Hz
4, $J_{FF}$ = 5.3 Hz
5, $J_{FF}$ ~ 0 Hz
6, $J_{FF}$ = 174 Hz
7, $J_{H\text{-}5,F}$ = 2.6 Hz
8, $J_{H\text{-}12,F}$ = 14.5 Hz
9, $J_{H\text{-}11,F}$ = 1.7 Hz

Coupling between bay hydrogen and fluorine nuclei in 4-fluorophenanthrenes has apparently not been reported previously. In addition to the value of 2.6 Hz[13] for the coupling between H-5 and F-4 in 4-fluorophenanthrene (**7**) itself, we find the following values of $J_{54}$ for seven different substituted derivatives of **7**:[14] 8-methyl, 2.9 Hz; 8-chloro, 3.8 Hz; 6-fluoro, 3.8 Hz; 6-chloro, 4.4 Hz; 6-bromo, 4.4 Hz; 6-methoxy, 4.6 Hz; and 7-fluoro-1-methyl, 4.6 Hz. To our knowledge, the value of 14.5 Hz[12] for the coupling between H-12 and F-1 in 1-fluorobenzo[*c*]phenanthrene (**8**) exceeds in magnitude all previously reported values for through-space HF coupling via nonbonded interactions.[15] We also find the following values of $J_{12,1}$ for four different substituted derivatives of **8**:[7] 9-methoxy, 14.6 Hz; 9-bromo, 14.7 Hz; 9-cyano, 15.3 Hz; and 10-fluoro-8-methyl, 14.3 Hz. A value of 1.7 Hz is found for the coupling constant for H-11 and F-10 in 10-fluorodibenzo[*c*,*g*]phenanthrene (**9**) and also in its 13-fluoro-1-methyl derivative.

The patterns of our FF and HF coupling results show one striking and instructive feature as illustrated graphically in Figure 1: the magnitudes of the HF coupling constants in **7–9** run qualitatively parallel to those of the FF coupling constants in **1–3**, respectively, and there is no such parallelism for what might have been regarded as the structurally more comparable systems **7–9** and **2–4**, respectively. For example, the largest value of $J_{FF}$ in the series **1–4** is found in the phenanthrene system **2**, whereas the largest value of $J_{HF}$ in the series **7–9** is found not in the corresponding phenanthrene system **7** but rather in the benzo[c]phenanthrene system **8**. We believe this provides evidence for the concept that the nonbonded interactions of importance for through-space HF coupling are not those between F and H