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THE ADDITION OF ALKYLLITHIUM REAGENTS TO *trans*-CYCLOOCTENE. THE FACILE ELIMINATION OF LITHIUM HYDRIDE IN THE CYCLOOCTYL RING

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Summary

The addition of s-butyllithium and t-butyllithium to *trans*-cyclooctene has been shown to occur very readily. The facile elimination of lithium hydride from s-cyclooctyllithium compounds affording cyclooctenes is also reported.

The addition of alkyllithiums to conjugated olefins has been known for many years [1]. More recently, these compounds have been shown to add to acetylenes [2], aromatic hydrocarbons [3] and norbornadiene [4]. Alkyllithium reagents will also add to allylic alcohols [5] or to unconjugated double bonds that contain a dimethylamino or thioether group β to the double bond [6]. However, with the exception of ethylene, addition of alkyllithium compounds to isolated, unconjugated carbon—carbon double bonds does not occur readily. Thus, alkenes such as cyclopentene, cyclohexene, *cis*-cyclooctene and 1-hexene have been shown to be unreactive to t-butyllithium, but secondary and tertiary alkyllithium compounds readily add to ethylene [7].

In contrast, RLi addition to several isolated unconjugated alkenes that are highly strained has been observed. For example, the addition of phenyllithium to cyclopropene [8] and of n-butyllithium to diphenylmethylenecyclopropane [9] have been reported. t-Butyllithium has also been observed to add to the strained double bond of norbornene [10]. The addition of alkyllithiums to several other strained bicyclic systems also has been studied [7, 11].

The increased reactivity of norbornene to alkyllithiums has been attributed to angle strain in the double bond [10]. The purpose of the present study was to examine the addition of alkyllithium reagents to the strained, unconjugated alkene, *trans*-cyclooctene (I). The strain in this alkene is due principally to out-of-plane deformation of the double bond. Theoretical considerations suggest that it should be reactive towards alkyllithium reagents. The strain energy of norbornene has been calculated to be 23.62 kcal/mol, while that of *trans*-cyclo-

TABLE 1

THE ADDITION OF RLi TO *trans*-CYCLOOCTENE (I) IN ETHER AND PENTANE[a]

RLi[b]	Reaction time (h)	Solvent	*cis*--Cyclooctene[c]	% Polymer[d]	% Addition[c]	Ratios of adducts formed		
						(III)	(IV)	(V)
t-BuLi	18	Et_2O	8	0	44	7	7	86
t-BuLi	72	Pentane	10	0	89	78	18	4
s-BuLi	72	Pentane	8	25	30	87	10	3
n-BuLi	72	Pentane	15	38	< 1			

[a] All 72 h reactions utilized 3.8 mmol of I at room temperature; the 18 h reaction used 2.3 mmol of I.

[b] t-BuLi, 2.00 *M* in hexane; s-BuLi, 1.20 *M* in hexane, n-BuLi, 2.37 *M* in hexane.

[c] These values are an average of at least two experiments and are obtained by comparison to cyclooctane internal standard upon separation of the crude reaction mixture on an NMPN gas chromatography column.

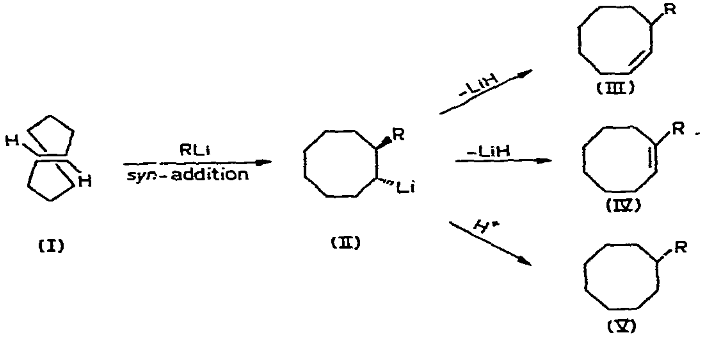
[d] These values are an average of at least two experiments and represent non-volatiles not chromatographable on a 15% SE 30 gas chromatography column at 120°C.

[e] These values are the result of at least two experiments and are obtained by summation of the three adduct peaks after comparison with the cyclooctane internal standard as separated on a SE 30 gas chromatography column.

octene is 17.85 kcal/mol. [12]. However, the reactivity of these alkenes should be a function of relief of strain on addtiton of RLi rather than ground state strain inherent in the alkene.

We now report that s-butyllithium and t-butyllithium will add to the double bond in *trans*-cyclooctene. We also report the interesting observation that the resulting alkyl-substituted secondary cyclooctyllithium compound II undergoes a facile elimination of lithium hydride at room temperature, affording the substituted *cis*-cyclooctenes III and IV (Scheme 1).

SCHEME 1



(IIa) R = t-Bu, (IIb) R = s-Bu
(IIIa) R = t-Bu, (IIIb) R = s-Bu
(IVa) R = t-Bu, (IVb) R = s-Bu
(Va) R = t-Bu, (Vb) R = s-Bu

In a typical experiment, an excess of the alkyllithium was added to *trans*-cyclooctene (I) in pentane under argon. The reaction mixture was stirred at room temperature and, after hydrolytic work-up, the ratio of unreacted I, addition products, substitution products, and *cis*-cyclooctene to an internal standard was determined by gas chromatography (GLC). Control experiments established that *cis*-cyclooctene (VI), formed by isomerization of I, was unreactive toward the alkyllithium, and that III is not being formed from IV under the reaction conditions. Our results, which are summarized in Table 1, show significant addition of s-butyllithium and t-butyllithium to I. However, the reaction of I with n-butyllithium in pentane for 72 h resulted in $< 1\%$ addition. In pentane solvent, the percent addition is in accord with what would be anticipated on the basis of the reactivity of the carbanion of the alkyllithium (i.e., tert $>$ sec $>$ n). In ether solvent, t-butyllithium readily added to *trans*-cyclooctene affording as the major product, the saturated hydrocarbon Va. This difference in product distribution reflects the greater acidity of ether toward secondary alkyllithiums since quenching the reaction with D_2O did not result in incorporation of a detectable amount of deuterium. The failure to observe addition of methyllithium or phenyllithium to I in ether solvent is also consistent with the reactivity trend noted in pentane solvent.

The reaction products of I with t-butyllithium have been isolated and identified. Hydrogenation of the crude reaction mixture in glacial acetic acid using a platinum oxide catalyst effected complete conversion of IIIa to Va and partial hydrogenation of the hindered trisubstituted alkene IVa affording IVa and Va in a ratio of 8/92. The spectral properties of IIIa, IVa and Va are in complete accord with their assigned structure. Similarly, IIIb, IVb, and Vb have been isolated and identified from the reaction of I with s-butyllithium. The addition of RLi to I very likely proceeds by a *syn*-mechanism affording the *trans* adduct II, since the back side of the double bond in I is sterically hindered. Competition experiments have established that I is ~ 17 times more reactive than norbornene toward t-butyllithium in pentane. These data suggest that considerable relief of strain in the transition state for addition to I must be attained. However, the difference in reactivity could also reflect the greater steric interactions involved in the *exo-cis*-addition to norbornene than to I

The elimination products III and IV obviously arise by the remarkably facile room temperature elimination of LiH from II. This is an unusual observation since the elimination of LiH from alkyllithiums is usually accomplished at elevated temperatures [14]. For example, n-butyllithium [15] decomposes slowly at 100° and t-butyllithium [16] affords LiH and isobutylene above 140°. The elimination of LiH from s-butyllithium [17] at 80° has been reported but a reaction time was not given. The driving force for elimination of LiH from II is very likely the relief of transannular strain upon formation of a double bond in a medium ring. Theoretical calculations [12] indicate that *cis*-cyclooctene is 2.7 kcal/mol less strained than cycloctane. These data therefore suggest that other medium ring alkyllithiums should also readily eliminate LiH. A four center mechanism for this elimination has been proposed [15].

Finally, the above data suggest that elimination of LiH from II in ether must be fairly slow relative to reaction of II with the solvent to afford the saturated hydrocarbon V as the major product. These results were anticipated since the half-life of n-butyllithium in ethyl ether at room temperature is 153 h while that of cyclohexyllithium is only 0.5 h [13].

Experimental

Addition of RLi to trans-cyclooctene in pentane

A. t-Butyllithium

A dry 50 ml round bottom flask equipped with a stirring bar was flushed with dry argon. To the flask was added 0.5 g of a 5/1 (w/w) mixture of *trans*-cyclooctene (I) (3.8 mmol) and cyclooctane (GLC internal standard) and 12 ml of dry pentane. The flask was fitted with a serum stopper. To the flask was added 3.0 ml of t-butyllithium solution (2.00 *M* in hexane, Ventron). The reaction mixture was stirred for 72 h and quenched by addition of 5 ml of H_2O in the cold. The crude product was analyzed by GLC (12 ft 10% SE 30 on Chromosorb W and 8 ft 25% 3-nitro-3-methylpimelonitrile (NMPN)on Chromosorb P). The product peak areas were measured by triangulation and compared to that of the cyclooctane internal standard. The chromatogram exhibited 1% of I, 10% of *cis*-cyclooctene (VI), and 89% addition with IIIa, IVa and Va, in a ratio of 78/18/4 respectively. Repetition of this experiment gave 1% of I; 10% of VI, and 89% addition with IIIa, IVa, and Va in a ratio of 78/18/4 respectively.

Repetition of the above process on a larger scale using 11.02 g (0.10 mol) of *trans*-cyclooctene (I) and 125 ml (0.25 mol) of t-butyllithium solution yielded 12.3 g of reaction product after distillation at 80°C (20 mm). Analysis of the distillate by GLC indicated the presence of IIIa, IVa, and Va in a ratio of 79/12/9 respectively.

Products IIIa, IVa, and Va were isolated from the crude reaction mixture by liquid column chromatography on a 20% $AgNO_3$ on neutral alumina solid phase. The saturated hydrocarbon Va was eluted first with pentane solvent and IVa and IIIa were eluted, in that order, with 10% Et_2O/pentane solvent.

The NMR data obtained for 3-t-butylcyclooctene (IIIa) are (CCl_4) δ 5.5 (m, 2, vinyl H), 2.5-1.1 (m, 2, 11), 0.87 ppm (s, 9, t-butyl). IR (neat) 3010 cm^{-1} (vinyl) m, 2930 (CH_3, CH)s, 1650 (C=C) 2, 1450 (CH_3, CH_2) m, 1395 (CH_3)m, 1370 (methine)s, 1235 (CH_2)m, 710 (*cis*-1,2-disubstituted olefin)m. Mass spectrum (70 eV) *m/e* (rel. intensity) 166(6.5), 110(25), 109(7), 108(5), 95(13), 83(7), 82(16), 81(12), 80(6), 70(7), 69(14), 68(6), 58(5), 57(100), 55(19), 54(5), 53(5). (Anal.: Found: C, 86.77; H, 13.40. $C_{12}H_{22}$ calcd.: C, 86.67; H, 13.33%.)

The NMR data obtained for 1-t-butylcyclooctene (IVa) are (CCl_4)δ 5.40 (t, 1, *J* 8 Hz, vinyl), 2.4-1.8 (m, 4, allylic), 1.48 (m, 8), 1.03 ppm (s, 9, t-butyl). IR (neat) 3025 cm^{-1} (vinyl)w, 2920 (CH_3CH_2CH)s, 1650 (C=C)2, 1470 (CH_2)s, 1450 (CH_3)m, 1390 (CH_3)w, 1360 (methine)m, 845 (trisubstituted C=C)2. Mass spectrum (70 eV) *m/e* (rel. intensity) 166(28), 151(13), 138(19), 109(62), 96(20), 95(74), 85(17), 83(70), 82(24), 81(59), 80(19), 79(16), 70(15), 69(52), 68(15), 67(63), 57(100), 55(65), 53(17). The presence of an *M*—15 peak in IVa and the absence of this peak in IIIa is worthy of note. (Anal.: Found: C, 86.79; H, 13.22 $C_{12}H_{22}$ calcd.: C, 86.67; H, 13.33%.)

The NMR data obtained for t-butylcyclooctane (Va) are (CCl_4)δ 2.0-1.0 (m, 15), 0.81 ppm (s, 9, t-butyl). IR (neat) 2920 (CH_3, CH_2CH)s, 1475 (CH_2)m, 1445 (CH_3)m, 1390 (CH_3)m, 1365 (methine)s. Mass spectrum (70 eV) *m/e* (rel. intensity) 168(1), 111(47), 110(36), 97(6), 95(5), 83(7), 82(26), 81(11), 70(5), 69(91), 68(7), 67(14), 66(8), 58(100), 57(95), 56(52).

B. s-Butyllithium

The above procedure, using 0.5 g of a mixture of I (3.8 mmol) and cyclooctane, 5 ml of s-butyllithium solution (1.20 *M* in hexane, Ventron) and 12 ml of dry pentane (reaction time 72 h), gave 37% of I, 8% of VI, and 30% addition with IIIb, IVb, and Vb in a ratio of 87/10/3, respectively. The remaining I (25%) was polymerized to a white amorphous solid. The products were isolated from the crude reaction mixture by liquid chromatography on a 20% $AgNO_3$ silica gel solid phase. Elution with pentane gave Vb, IVb, and IIIb in that order.

The NMR data obtained for 3-s-butylcyclooctene IIIb are (CCl_4) δ 5.4 (m), 2.5-1 (m), 1.0-0.7 ppm (m). IR (neat) 3005 cm^{-1} (vinyl)m, 2925 (CH_3, CH_2, CH)s, 1650 (C=C)2, 1450 (CH_3, CH_2)m, 1380 (methine)m, 775m, 715 (*cis*-1,2-disubstituted olefin)m. Mass spectrum (70 eV) *m/e* (rel. intensity) 166(11), 138(12), 137(18), 110(52), 109(73), 96(32), 95(38), 81(70), 67(100), 55(75). (Anal.: Found: C, 86.57; H, 13.03. $C_{12}H_{22}$ calcd.: C, 86.67; H, 13.33%.)

The NMR data obtained for 1-s-butylcyclooctene IVb are (CCl_4) δ, 5.3 (t, *J* 6.5 Hz), 2.3-1.8 (m), 1.48 (m), 1.1-0.6 ppm (m). IR (neat) 2920 cm^{-1} (CH_3, CH_2, CH)s, 1660 (C=C)2, 1470 (CH_2)s, 1450 (CH_3)s, 1375 (CH_3)m, 900 m, 890 m, 845 m, 835 (trisubstituted C=C)m. Mass spectrum (70 eV) *m/e* (rel.

intensity) 166(28), 138(36), 137(28), 110(17), 109(75), 96(19), 95(72), 81(100), 67(70), 55(70). (Anal.: Found: C, 86.37; H, 13.21. $C_{12}H_{22}$ calcd.: C, 86.67; H, 13.33%.) s-Butylcyclooctane (Vb) had mass spectrum (70 eV) *m/e* (rel. intensity) 168(1), 111(100), 110(12), 97(3), 95(8), 83(9), 82(13), 81(11). Insufficient sample was available for further analysis.

C. n-Butyllithium

The above procedure, using 0.5 g of a mixture of I (3.8 mmol) and cyclooctane, 2 ml of n-butyllithium solution (2.37 *M* in pentane, Ventron), and 12 ml of dry pentane (reaction time 72 h), gave 48% of I, and 16% of VI. Less than 1% addition occurred, affording three products with GLC retention times similar to those of III, IV and V in a ratio of 58/31/11 respectively. A repetition of this experiment gave 46% of I, 14% of VI, and < 1% addition, with three products in a ratio of 60/29/11, respectively. Each of these experiments yielded a white solid that was insoluble in pentane, CCl_4, $CHCl_3$, CH_2Cl_2, Et_2O, MeOH, H_2O, and alkaline MeOH. This solid decomposed slowly in concentrated chromic acid solution and was assumed to be the high molecular weight polymer of I.

Addition of RLi to I in diethyl ether

The above procedure using 0.30 g of a mixture of I (2.3 mmol) and cyclooctane, 1.5 ml of t-butyllithium solution and 5 ml of dry Et_2O (reaction time 18 h) gave 47% of I, 8% of VI, and 45% addition with IIIa, IVa, and Va in a ratio of 7/7/86, respectively. Repetition of this experiment gave 48% of I, 7% of VI, 45% addition and IIIa, IVa, and Va in a ratio of 6/6/88, respectively. Each of these reactions was quenched with D_2O. However, no deuterium incorporation in Va was found by mass spectral analysis.

Relative rate of addition of RLi to I and norbornene

Employing the above procedure, 0.5 g of a mixture of I (1.8 mmol), norbornene (1.8 mmol) and cyclooctane, 2 ml of t-butyllithium solution (4.0 mmol) and 5 ml of dry pentane was stirred at room temperature for 4.5 h. GLC analysis showed that the ratio of *exo*-2-t-butylnorborane VII [11a] to the addition products of I was 6/100. The addition of I had occurred to the extent of 25% and products IIIa, IVa, and Va were formed in a ratio of 83/10/7, closely paralleling the product ratios observed at longer reaction times. A duplicate experiment gave essentially identical results.

Hydrogenation of the mixture of IIIa, IVa, and Va

To a Parr hydrogenator was added 3.0 g of the adduct mixture, 50 ml of glacial acetic acid and 1.0 g of platinum oxide. After 72 h at 50 psi of hydrogen pressure, the pentane extracts were dried ($MgSO_4$), concentrated, and distilled (82—85°, 20 mm) to give 1.9 g of clear liquid. GLC analysis (15 ft 20% SE 30 on Chromosorb W, *T* 145°) showed IIIa to be entirely gone and a IVa/Va ratio of 8/92. NMR (CCl_4) showed only minor absorptions in the olefinic region 6.0—5.0, 2.0—1.1(m), 1.05(s) and 0.82(s) ppm. The singlet at δ 0.87 has disappeared. The ratio of the singlets for compounds IVa and Va was now 8/92. Attempts to reduce these compounds in absolute ethanol were not successful.

Determination of the reactivity of cis-cyclooctene to RLi in ether and pentane

To a dry round bottom flask equipped with a stirring bar was added 1 g of a mixture of 0.5 g of cyclooctane and 0.5 g of *cis*-cyclooctene and 25 ml of dry ether and subsequently 3.0 ml (5 mmol) of methyllithium solution (1.67 *M* in diethyl ether). The reaction mixture was stirred for 16 h and was hydrolyzed. The aqueous phase was separated and the organic phase was analyzed by GLC (8 ft 25% NMPN on Chromosorb P, *T* 90°). The ratio of the internal standard cyclooctane to *cis*-cyclooctene was measured by integration of the GLC peak areas. Before reaction, the mixture had a ratio of cyclooctane to *cis*-cyclooctene of 53.3/46.7. After treatment with MeLi solution the ratio was 53.1/46.9, suggesting that *cis*-cyclooctene was stable under the reaction conditions.

Similar results were obtained with phenyllithium, n-butyllithium, s-butyllithium and t-butyllithium in both ether and pentane solvents.

Attempted isomerization of IVa

To 0.05 g of the above hydrogenation mixture (~ 0.3 mmol IVa) in 0.5 ml of dry pentane was added 0.4 ml of t-butyllithium solution (0.8 mmol). After 45 min at r.t. the reaction mixture was quenched in the usual manner. GLC analysis of the crude reaction mixture revealed no change in ratio of IVa to Va and no generation of IIIa. A repetition of this experiment gave the same result.

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