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REACTION OF t-BUTYLLITHIUM WITH 1-PHENYLCYCLOALKENES

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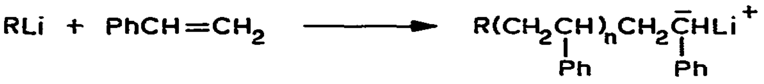
Summary

The course of reaction of 1-phenylcycloalkenes, $Ph\overline{C{=}CH(CH_2)_n}$ with t-butyllithium in the presence of THF or TMEDA is found to vary with ring size as follows: $n = 2$, polymerization; $n = 3$, allylic deprotonation and addition to the double bond; $n = 4$, allylic deprotonation only; $n = 5$, metalation of the aromatic ring. These results are in accord with the stereochemistries of starting olefins.

Introduction

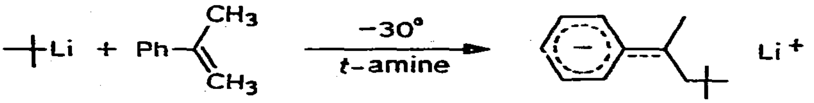
The reaction of organolithium compounds with styrenes leads to anionic polymers [1]:



$$RLi + PhCH{=}CH_2 \longrightarrow R(CH_2\underset{Ph}{CH})_nCH_2\underset{Ph}{\bar{C}H}Li^+$$

(I)

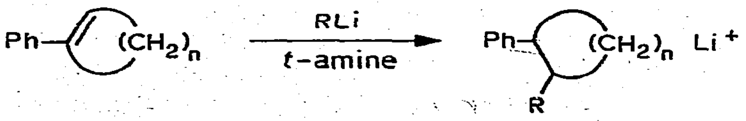
or under certain conditions such as in eq. 1 to 1/1 adducts:



(1)

(II)

which appear to contain conjugated benzylic anions [2—8]. Analogously to eq. 1 let us consider the possible addition of t-butyllithium to 1-phenylcycloalkanes,



(2)

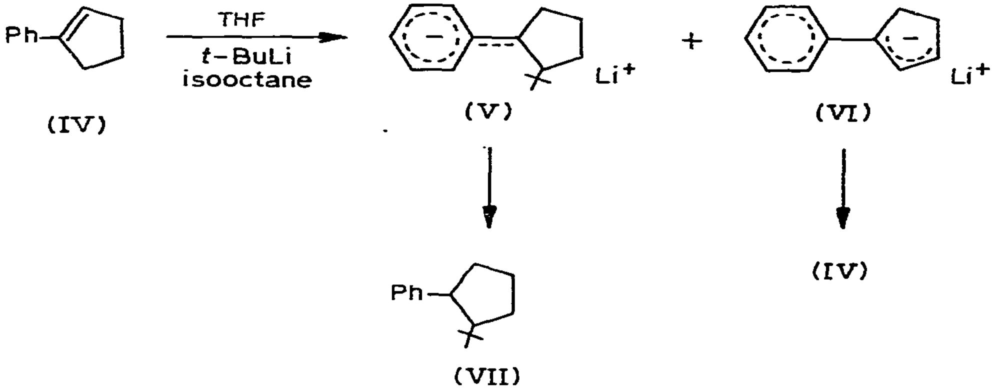
(III)

The extent to which the benzyl carbon participates in the π electron system will depend on the structure in the loop about benzyl. If this situation is unfavorable to sp^2 hybridization at the benzyl carbon there may be some covalent bonding to carbon [9]. These effects could be monitored using ^{13}C NMR [10].

It will be shown below that the reactivities of 1-phenylcycloalkanes with t-butyllithium are so different that the qualitative nature of the reaction changes among substrates as well as experimental conditions.

Results and discussion

When 1-phenylcyclopentene (IV) is treated at 0° C with t-butyllithium in isooctane containing two equivalents of THF, the NMR spectrum of IV is entirely replaced by that shown in Fig. 1. Hydrolysis of this reaction mixture gave compounds IV and VII. Hence, the spectrum in Fig. 1 is evidently due to a mixture of the benzylic lithium compound, V, with 1-phenylcyclopentenyllithium (VI):



(3)

TABLE 1

PRODUCTS FROM REACTION 3

T(°C)	VII	IV
0	50	30
—15	80	20
—30	95	5

However, when the reaction is carried out at −30° C the product consists almost entirely of V, see the proton NMR spectrum shown in Fig. 2. The ^{13}C and proton parameters for V using computer program LACOON [1], are listed in Table 2.

It should be noticed that all five hydrogens in the aromatic ring in V are magnetically non-equivalent. These results closely resemble those for t-benzyllithium compounds published previously [2] which were concluded to exist as solvent separated ion pairs, since the NMR data were independent of ligand and counterion.

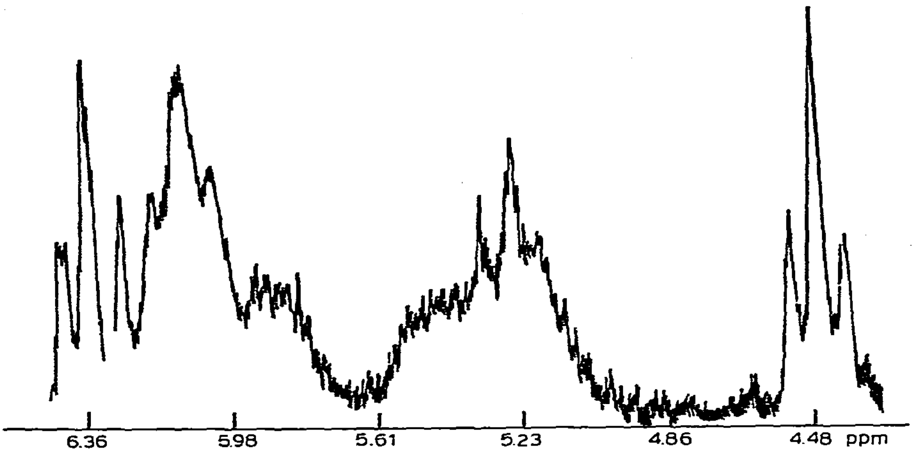


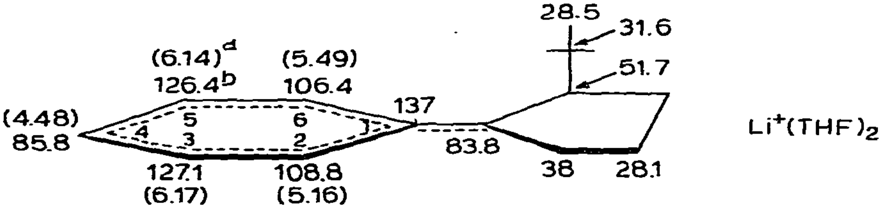
Fig. 1. Proton NMR spectrum (90 MHz) of the unsaturated parts V and VI (1 *M* in THF/pentane at 27°C).

The carbon-13 shifts, see structure heading Table 2, support this conclusion. An estimate of the effect of charge [10] on shift in V can be obtained by using the results for hydrolysate VII as neutral model shifts, (except for C-benzyl). A reasonable estimate for a neutral shift of an sp^2 benzyl carbon would be 142 ppm. Subtracting the π carbon shifts of V from the neutral ones gives a total shift increment of 149—148 ppm. This treatment does not consider other contributions to the carbon shift. However, the result is not far from the 160 ppm e^- [12] usually observed and supports the conclusion that V exists mainly as separated ion pairs containing a conjugated benzylic anions.

Hydrolysis of this adduct of 1-phenylcyclopentene with t-butyllithium, obtained at —30°C in THF/pentane, gave two products VIIa and VIIb in ratio

TABLE 2

NMR PARAMETERS



(V)

$J_{X,Y}$(Hz) [c]

X, *Y*	*J*	*X*, *Y*	*J*
2, 3	8.9	3, 5	—2.4
2, 4	—1.2	3, 6	—0.1
2, 5	—0.1	4, 5	6.5
2, 6	2.8	4, 6	—1.2
3, 4	6.5	5, 6	8.9

[a] Protol shift, ppm/TMS. [b] ^{13}C shift, ppm/TMS. [c] Proton, proton coupling constants.

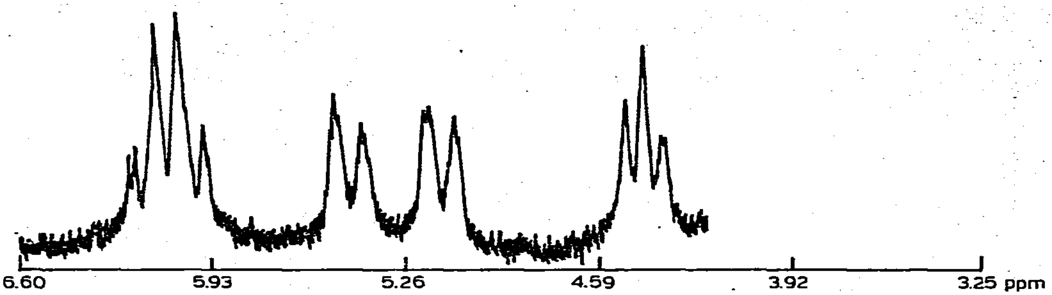
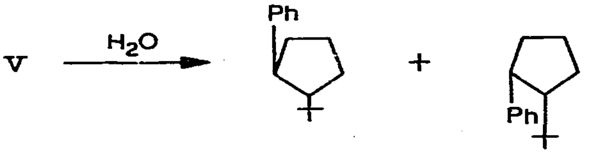


Fig. 2. Proton NMR spectrum (90 MHz) of the unsaturated ring in 1-t-butyl-2-lithio-2-phenylcyclopentane (1.0 *M* in THF/cyclopentane at 0° C).

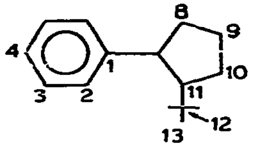
2/1. The major isomer is assigned *trans* on the basis that proton shifts of groups *cis* to phenyl are always shielded with respect to the corresponding protons in the *trans* structures [13]. Furthermore, the methylene carbon-13 resonances in the minor isomer (*cis*) are all shielded with respect to those in the *trans* isomer. This is consistent with that is known about steric compression effects in five-membered rings [14]. Table 3 lists the ^{13}C and proton shifts for VII, *trans* and *cis*.



(VIIa) (VIIb)

TABLE 3

NMR SHIFTS FOR VII [a]



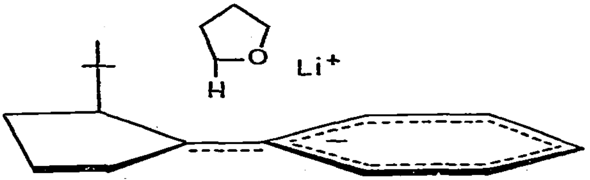
(VII)

δ (ppm) [b]	^{13}C		^{1}H	
	trans-VIIa	*cis*-VIIb	*trans*-VIIa	*cis*-VIIb
1	149.2	147.1		
2	128.1	129.3		
3	127.1	127.9	7.22	7.19
4	125.4	125.6		
7	48.0	47.5	2.84	3.24
8	39.0	34.5	1.65	1.83
9	25.8	22.9		
10	28.2	25.1	1.93	1.83
11	57.3	57.5	1.68	1.83
12	33.5	32.4		
13	28.2	28.8	0.78	0.67

[a] 0.25 *M* in $CDCl_3$, 30° C. [b] ppm/TMS.

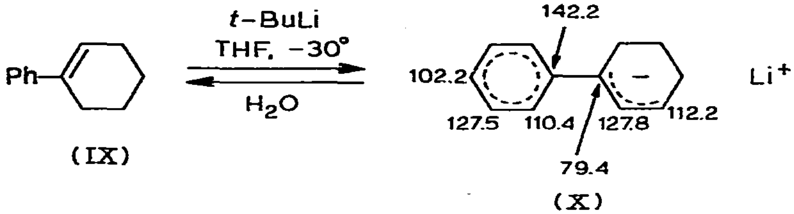
In contrast to the above results treatment with D_2O of a sample of V, prepared at −30° C, that had been stored for five months at 0° C gave a product which contained no deuterium and consisted almost entirely of VII *trans*. Thus, on protracted storage V had deprotonated THF in a stereoselective manner.

This must have come about by approach of THF from the same side as t-butyl (VIII). The alternative route (*trans* to t-butyl) would move phenyl *cis* to the t-butyl group. Clearly, in this system THF as a proton acid has severe steric requirements compared to water.



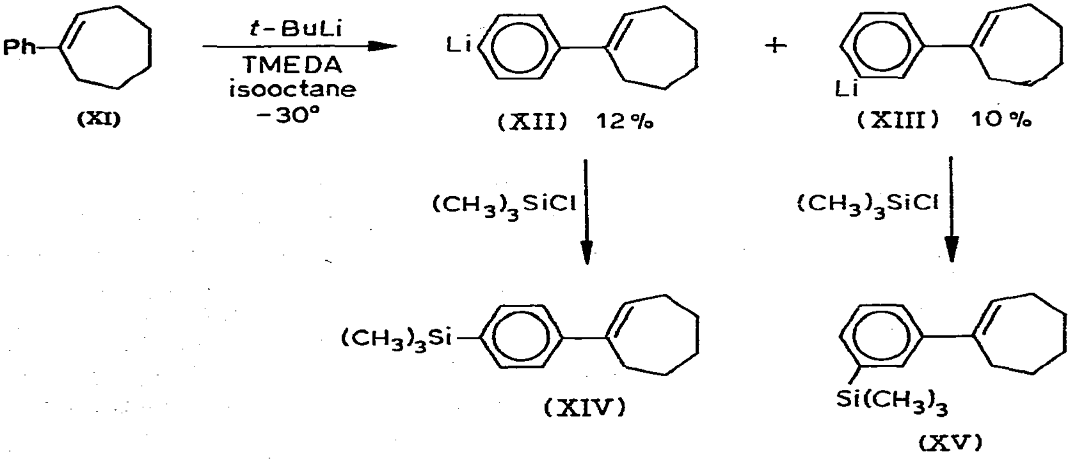
(VIII)

Increasing ring size causes drastic changes in the chemistry of the 1-phenylcycloalkenes. Thus, 1-phenylcyclohexene-1 and t-butyllithium in pentane with THF (eq. 4) gave almost entirely allylic deprotonation, over the range 0 to 45° C, (X). The carbon-13 shifts obtained for this species strongly support the assignment of a conjugated ionic structure.

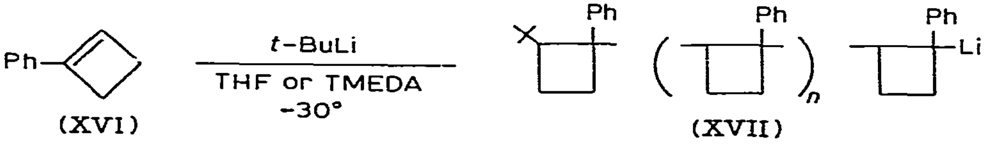


(4)

The behavior of 1-phenylcycloheptene (XI) with t-butyllithium in iso octane/TMEDA is again different from the results described so far. Under the conditions used for V and IX only 22% of starting materal, XI, reacted and that undergoes metalation on the aromatic ring. Proton NMR of the product mixture shows, together with strong peaks for XI, resonance at τ 2.1 ppm indicative of hydrogen *ortho* to lithium. Reaction of this product mixture with trimethylchlorosilane gives the two silyl phenylcycloheptenes XIV and XV.



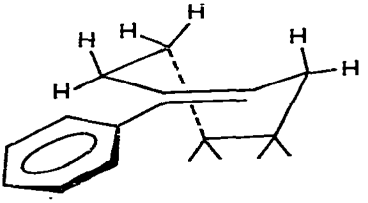
When 1-phenylcyclobutene was treated with 1 to 3 equivalents of t-butyllithium at −30°C (in pentane/THF or pentane/TMEDA) the reaction mixture immediately turned red but no benzylic anion could be detected with NMR. Hydrolysis yielded only polymers. Running these reactions at temperatures between 0 and 45°C gave the same results. Evidently now, due to the compressed angle about C-benzyl in the four-membered ring, the organolithium terminus of XVII reacts faster with 1-phenylcyclobutene than does t-butyllithium.



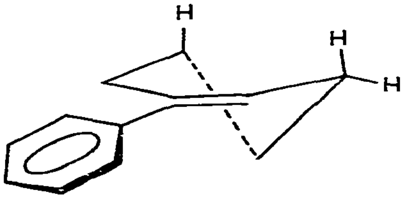
(XVI) (XVII)

The seemingly disparate course which the reactions of 1-phenylcycloalkanes with t-butyllithium take may be better understood by considering the stereochemistry of cycloalkene compared to the hypothetical adduct or allylic lithium compound.

In the 4- and 5-membered 1-phenylcycloalkenes approach perpendicular to the double bond is not impeded and addition is observed. In contrast 1,3 interactions in 1-phenylcyclohexane, most likely in the half chair form XVIII, would seriously hinder addition to the double bond. However, allylic deprotonation at C(3) in V and IX is not hindered and the C—H bonds are already normal to the C(1)—C(2)—C(3) plane, see XVIII.



(XIX)



(XVIII)

Finally, in the case of 1-phenylcycloheptene XI (boat form) steric effects militate against both addition to the double bond (perpendicular) and allylic deprotonation since there there is no axial-like C—H bond. Then, the slower metalation of the aromatic ring becomes evident.

Experimental

Solvents and chemicals

Tetrahydrofuran, ethyl ether and dimethyoxymethane were dried with and distilled from n-butylmagnesium bromide. When the commercial ethers were too wet to allow Grignard preparation directly, prior distillation from calcium hydride eliminated this problem. *N,N,N',N'*-Tetramethylethylenediamine was fractionally distilled from potassium hydroxide pellets. The center cut was stored over CaH_2 and distilled from this reagent directly before use. Pentane and 2,2,4-trimethylpentane (isooctane) were washed with concentrated sulfuric acid, water and 10% sodium bicarbonate solution, dried over anhydrous potassium carbonate, stored over calcium hydride and distilled from this reagent directly before use. All solvents used in anion preparations and organometallic preparations were distilled under argon either directly into the reaction vessel or into a dry side-arm flask and transferred through syringes equipped with stopcocks and stainless steel needles. The equipment was baked at 120°C for at least one hour prior to use.

The 1-phenylcyclopentene and 1-phenylcyclohexene came from the Aldrich Chemical Company; 1-phenylcyclobutene was obtained by the method of Burger and Bennet [15] and its precursors from published methods [16]. Finally, 1-phenylcycloheptene came from the acid dehydration of 1-phenylcycloheptanol [17].

Apparatus

All product mixture analyses and separations by vapor phase chromatography were carried out using a Varian Aerograph A-700. Columns were either a five foot by 1/2 inch 20% SE-30 on firebrick (Column A) or a fifteen foot by 1/4 inch 20% SE-30 on Chrom P (Column B). Operations requiring an inert atmosphere were carried out in either a Kewaunee Scientific Equipment 2C281-20 glove box or a Vacuum Atmospheres HE-43 glove box. Continuous wave proton spectra were obtained on the Varian A-60A (60 MHz), HA-100 (100 MHz) and Bruker HX-90 (90 MHz) spectrometers. Carbon spectra were obtained using a Bruker HX-90 spectrometer at 22.63 MHz in the Fourier transform mode. Auxiliary equipment used in obtaining the Fourier transform spectra included a Nicolet BNC-12 computer containing 20,480 20-bit words of memory and a Diablo movable head disk storage unit. Disks were IBM low density 600 K word capacity.

Reactions of phenylcycloalkenes with t-butyllithium, 1-lithio-1-phenyl-2-t-butylcyclopentane (V) (Method A)

A 10 ml vial equipped with a "stopcock adapter" (2 mm straight bore stopcock attached to a male ground glass joint) was charged by syringe with 1-phenylcyclopentene (1.3 g, 9 mmol) and 2 ml isooctane. The solution was outgassed by passing argon through it via a stainless steel needle. The reaction vessel was a 50 ml roundbottom flask equipped with a "stopcock adapter", a side-arm fitted with a 2 mm straight bore stopcock both protected by rubber serum caps and a magnetic stirring bar. The reaction vessel was charged with t-butyllithium in pentane (0.95 *M*, 10 ml, 9.5 mmol). The pentane was removed by passing a current of argon over the rapidly stirred solution and 2 ml of isooctane added. The reaction vessel was immersed in a dry ice/isopropanol bath at − 50°C and TMEDA (1.16 g, 10 mmol) was added. The bath temperature was allowed to rise to −30°C and the deoxygenated 1-phenylcyclopentene/isooctane solution prepared as described above was added dropwise to the rapidly stirred t-butyllithium/TMEDA slurry over 30−60 min. The temperature of the bath was maintained at −30°C ± 5°C during the addition. The resulting dark red solution was allowed to warm to 0°C and stirred at this temperature for 30 minutes completing the reaction. The yield was 95% by NMR analysis.

cis- and trans-1-t-Butyl-2-phenylcyclopentane (VII) (method B)

A sample of 1-phenylcyclopentene (1.37 g, 9.5 mmol) mixed with 6 ml of dry THF was deoxygenated with a stream of argon as described above.

The reaction vessel (same as in A) was charged with t-butyllithium in pentane (1.33 *M*, ml, 9.9 mmol, 10% excess) and immersed in a dry ice/isopropanol bath at − 50° C. THF (1.0 ml) was added and the temperature of the bath allowed to rise to −30° C. The deoxygenated styrene/THF solution prepared as described above was added dropwise to the rapidly stirred t-butyllithium/THF solution over 30–60 min. The temperature of the bath was maintained at −30° C ± 5° C during the addition. The resulting dark red solution was allowed to warm to 0° C and stirred at this temperature for 30 minutes completing the reaction. With rapid stirring this solution was treated with water (2.0 g, 11.1 mmol). The organic phase was diluted with 50 ml of pentane and washed with 5% aqueous hydrochloric acid (25 ml, 5 times), water (25 ml, once) and saturated aqueous sodium bicarbonate (25 ml, once). Filtration through a cone of anhydrous magnesium sulfate, flash evaporation of solvents and distillation at reduced pressure using a short-path distillation head gave a 60/40 mixture of VIIa and VIIb, respectively, overall yield 90%, b.p. 95—105° C at 0.5 Torr, *m/e* obs. 202.1724786, calcd. 202.7721412. The two isomers were separated by vapor phase chromatography on column B at 165° C, the major isomer (*trans*) eluting first. The proton and carbon NMR data are listed in Table 3.

1-Phenyl-cyclohexenyllithium (X)

Using method B a solution of 1-phenylcyclohexene (1.4 g, 8.9 mmol) in 3 ml of tetrahydrofuran was treated with a solution of t-butyllithium in pentane (0.95 *M*, 10.0 ml, 9.5 mmol) at − 30° C. NMR analysis indicated that X had formed in greater than 95% yield. Hydrolysis of this solution yielded only 1-phenylcyclohexene. NMR data are indicated around structure X.

Metalation of 1-phenylcycloheptene

Following method A, 1-phenylcycloheptene (1.05 g, 6.2 mmol) and t-butyllithium (7.5 mmol; 6 ml, 1.24 *M*) were allowed to react at −30° C in 5 ml of isooctane containing 0.7 g TMEDA. After 4 h at −30° C the mixture was warmed to room temperature and allowed to stir for an additional hour. A sample was removed by syringe for NMR analysis. The remaining product mixture was treated with trimethylchlorosilane (0.78 g, 7.2 mmol), hydrolyzed with water and organic components extracted into ether. The latter phase was dried ($MgSO_4$) and the ether removed by rotary evaporation. The residue was separated on a Varian Aerograph GC using a column packed with 50% SE-30 on firebrick (200° C). There resulted three main fractions: 1-phenylcycloheptene (0.75 g), 1-(4-trimethylsilylphenyl)cycloheptene (XIV), 0.18 g, 12%, *m/e* obs. 244.1652435, calcd. 244.1647194, proton NMR, δ, 0.26 (CH_3Si), 7.52 (arom. $H_{3,5}$), 7.36 (arom. $H_{2,6}$) and 6.17 (olefinic), 1-(3-trimethylsilylphenyl)-cycloheptene (XV), 0.5 g, 10%, *m/e* obs. 244.1657435, calcd. 244.1657194, proton NMR, δ, 0.54 (CH_3Si), 7.4 (arom. H_2), 7.67—7.51 (arom. $H_{4,6}$) and 6.38 (olefinic).

Reaction of t-butyllithium with 1-phenylcyclobutene

Using method A, 1-phenylcyclobutene (0.91 g, 7.0 mmol), t-butyllithium (6.5 ml, 7.4 mmol, 1.24 *M*), 5 ml isooctane and 0.8 g TMEDA were stirred for 4 h at − 30°C under an argon atmosphere. Warming to room temperature followed by hydrolysis and the usual work up gave only polymer, as indicated by NMR. The same results ensued using one, two and three equivalents of t-butyllithium in isooctane/THF at −15°C, −30 and −45°C and using 1—3 equivalents of t-butyllithium in isooctane/TMEDA at the same temperatures. Under no circumstances was 1/1 addition detected either chemically or with NMR methods.

Acknowledgement

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