

Direct Metallation of Isoprene

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Treatment of isoprene with an excess of the couple potassium t-butoxide–lithium tetramethylpiperidide in tetrahydrofuran, followed by addition of a higher alkyl bromide or oxirane, gives the dienes $\text{H}_2\text{C}=\text{CHC}(\text{=CH}_2)\text{CH}_2\text{R}$ ($\text{R} = \text{alkyl}$ or $-\text{CH}_2\text{CH}_2\text{OH}$) in reasonable yields.

Recently¹ we showed that the combination of butyl-lithium and potassium t-butoxide in tetrahydrofuran (THF) can be successfully used to metallate propene and isobutene under mild conditions. Attempts to convert isoprene into the potassium salt $\text{H}_2\text{C}=\text{CHC}(\text{=CH}_2)\text{CH}_2\text{K}$ using this system gave only oligomers. A similar negative result was obtained by Gordon *et al.*^{2,3} using the same couple in an apolar solvent. This report³ prompts us to communicate successful experiments concerning the metallation of isoprene.

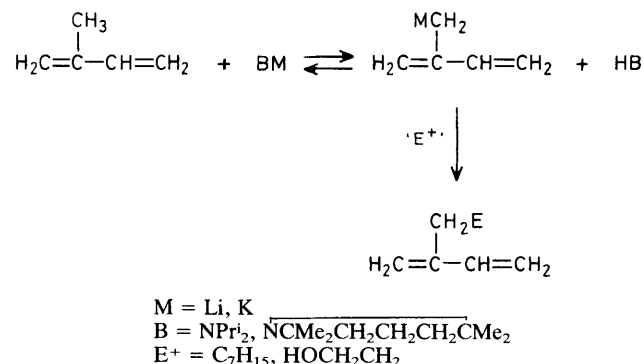
Our experiments were based upon the consideration that a sterically hindered base with a sufficiently high thermodynamic as well as kinetic basicity would be required. An extensively exploited property of bases such as lithium di-isopropylamide (LDA) is their decreased tendency to add across multiple bond systems. Reaction at *ca.* -70°C of isoprene with a 100% excess of LDA, followed by addition of a corresponding excess of bromoheptane and allowing the temperature to rise to 0°C gave no trace of the desired alkylation product. Oligomerisation, however, had occurred to a slight extent only. The low yield of the desired product thus may be largely ascribed to an unfavourable deprotonation equilibrium (Scheme 1).

A significant improvement (42% yield) was attained by carrying out the metallation with a 50% excess of the couple LDA– Bu^tOK (prepared *in situ* by adding a THF solution of Bu^tOK to the LDA solution), other conditions being similar to the preceding experiment. It appeared, however, that in this case dehydrohalogenation of bromoheptane had occurred. If, prior to carrying out the alkylation, an equivalent amount of anhydrous lithium bromide in THF was added, no alkylation product at all was obtained. This experiment strongly suggests that the negative result in the attempt

described above, is not due to a very low rate of deprotonation by LDA.

In a recent paper of Fraser and Mansour⁴ *pK* values of a number of sterically hindered secondary amines have been reported. The commercial availability of tetramethylpiperidine (TMP)⁵ and its higher *pK* value (37.3) than that of di-isopropylamine (35.7) prompted us to repeat the experiments with the combination $\text{LiTMP-Bu}^t\text{OK}$, under conditions similar to those in the LDA– Bu^tOK experiments and it was found that the alkylated isoprene was formed in yields up to *ca.* 60%. Reaction with an excess of oxirane gave the expected alcohol in 75% yield.

Interaction between LiTMP (without Bu^tOK) and isoprene, followed by addition of a higher alkyl bromide and



Scheme 1

raising the temperature to 35–40 °C, gave only the alk-1-ene (as a result of dehydrohalogenation) and unconverted alkyl bromide. The presence of Bu^tOK during the interaction between isoprene and LDA or LiTMP is thus essential.

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