

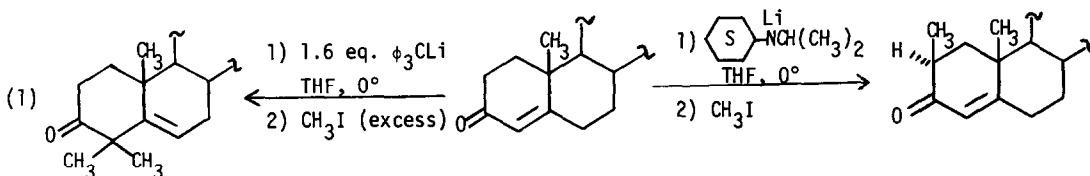
ANOMALOUS REACTIONS OF TRITYL BASES

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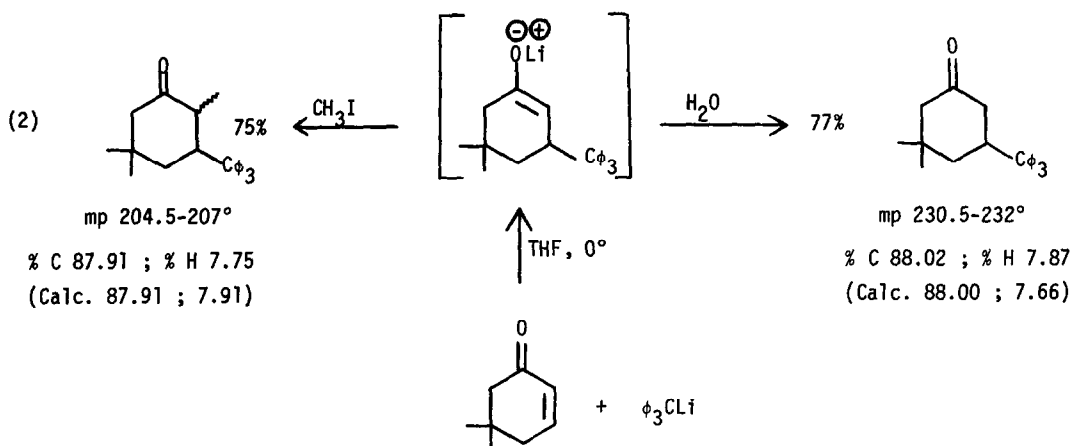
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In the course of developing a procedure for the specific  $\alpha'$ -alkylation of  $\alpha,\beta$ -unsaturated ketones,<sup>1</sup> we were puzzled by the fact that very different results were obtained using lithium 2°-amides and trityllithium bases. This is illustrated below for the characteristic case of a steroidal  $\Delta^4$ -ene-3-one.

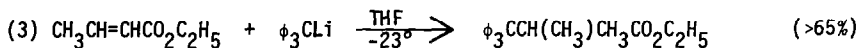


We first considered the possibility that enolate anion equilibration was taking place during the trityllithium reaction - either before or during the alkylation step. Since trityllithium is known to effect selective kinetic enolate formation in the case of saturated ketones,<sup>2,3</sup> equilibration prior to alkylation seemed unlikely. Indeed, House has noted<sup>3</sup> that lithium enolates may take 30 min. or more to come to equilibrium in the presence of as much as 20 mole % excess ketone.<sup>4</sup> If, on the other hand, equilibration occurred during the methylation step, a preventive mechanism to account for its absence in the 2°-amide promoted reactions was clearly necessary. One possibility was that the 2°-amine formed from the amide base acted in some way (eg. by increasing the rate of alkylation or retarding proton transfer) to prevent equilibration. However, addition of an equivalent of isopropylcyclohexylamine to the enone conjugate base generated by the trityllithium reaction failed to change the course of the methylation reaction.

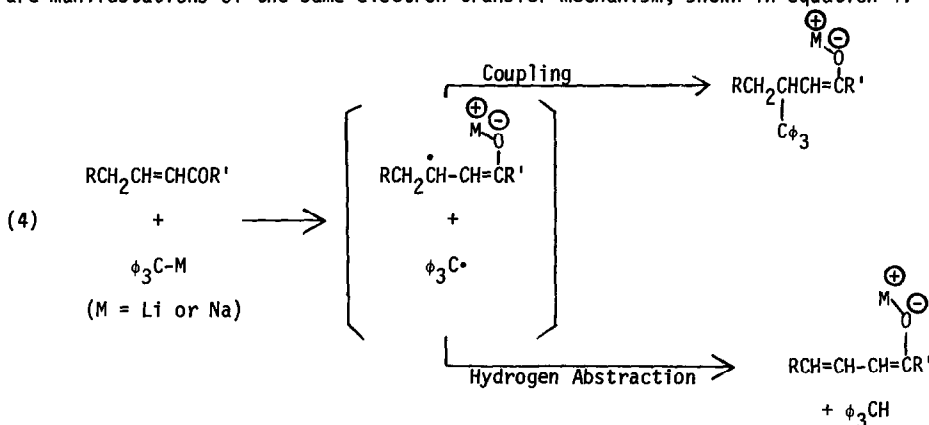
At this point we became convinced that one of these two strong bases (ie. trityllithium or the lithium 2°-amide) was behaving in an anomalous manner toward  $\alpha,\beta$ -unsaturated ketone substrates. Our suspicion was then directed at the trityl base, as a consequence of the unexpected conjugate addition observed in its reaction with 5,5-dimethylcyclohex-2-ene-1-one (equation 2).



Conjugate addition reactions involving tritylsodium or trityllithium are rare. Four such examples were reported in 1943 by Michael and Soffer<sup>5</sup> (to cinnamate esters) and McPhee and Lindstrom<sup>6</sup> (to methyl acrylate and ethyl crotonate). Of the unsaturated esters studied by these workers only ethyl crotonate offers the possibility of an alternative proton transfer reaction, and it is interesting to note that the two research groups disagreed on the course of its reaction with tritylsodium. We find that trityllithium gives extensive conjugate addition to ethyl crotonate in THF solution at -23°, thereby supporting the report of McPhee and Lindstrom.

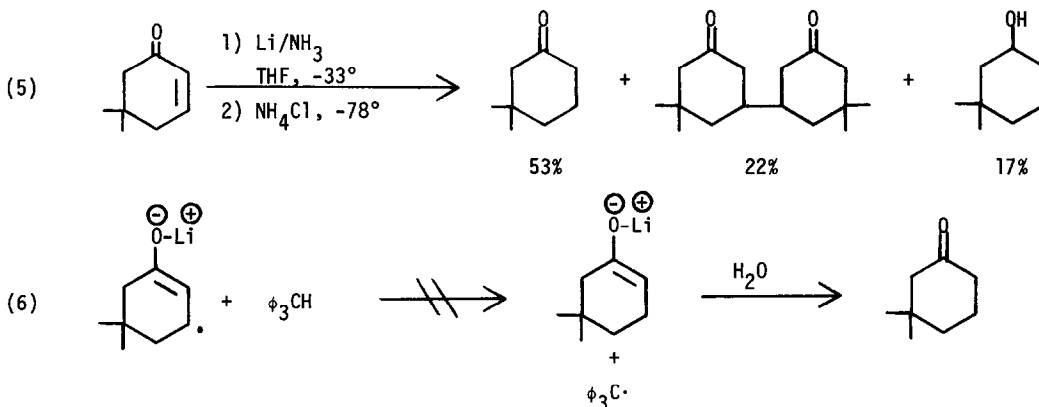


We now propose that the trityl base promoted  $\alpha$ -alkylation reactions of  $\alpha,\beta$ -unsaturated ketones and the infrequent conjugate additions of trityl bases to unsaturated carbonyl compounds are manifestations of the same electron transfer mechanism, shown in equation 4.



The resulting enolate anions can, of course, be alkylated or protonated as desired.

In an effort to support this mechanism we have attempted to obtain independent evidence for the ketyl intermediate. Since unsaturated ketyls having hydrogen atoms  $\alpha$  to the  $\pi$  electron system are known to be highly unstable,<sup>7</sup> our difficulties in this endeavor were not unexpected. When reaction (2) was conducted in the presence of an excess of the unsaturated ketone, none of the dimeric product anticipated by analogy with the corresponding lithium in ammonia reduction (equation 5) was obtained. Similarly, reactions carried out with a large excess of triphenylmethane (triphenylstannane is not suitable<sup>8</sup>) gave no saturated ketone, as proposed in equation 6.



These results indicate that the ketyl intermediate, if it exists, is so reactive that most of it fails to escape the solvent cage before reacting with the triphenylmethyl radical. However, esr and CIDNP<sup>9</sup> experiments suggest that small amounts of ketyl apparently do manage to escape or decompose by some alternative pathway. When our dimethylcyclohexenone was added to an argon blanketed THF solution of trityllithium held at  $-78^\circ$  in the resonance cavity of an E-4 Varian ESR Spectrometer, the characteristic resonance pattern of the triphenylmethyl radical immediately appeared. This persisted up to  $0^\circ$ , but vanished at  $25^\circ$ . No other resonance signals were observed.

Proton magnetic resonance measurements conducted at  $-78^\circ$  during the addition of unsaturated ketone to a THF solution of trityllithium disclosed CIDNP emission from the solvent. However, no emission or absorption was observed when  $d_8$  THF was used as the solvent.

Apparently, some of the ketyl is destroyed by solvent reactions, and the surviving triphenylmethyl radicals were observed in our esr experiment. Unfortunately, no direct evidence for the proposed ketyl intermediate has yet been obtained.

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### References

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