

EASY CONJUGATE ADDITIONS TO $\Delta^{1(9)}$ -OCTAL-2-ONE AND ITS 10-METHYL DERIVATIVE

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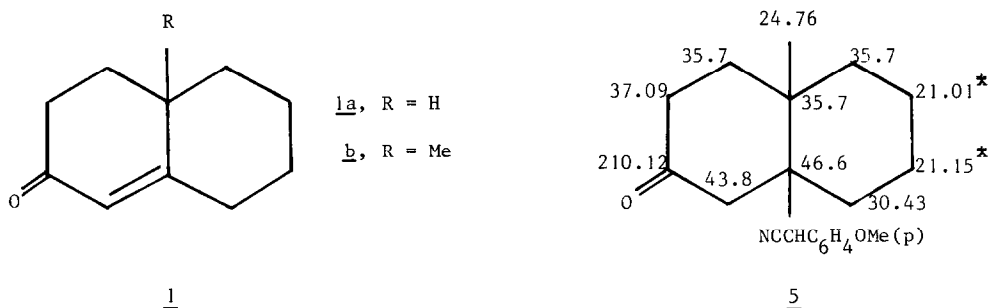
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Summary : Conjugate additions of lithiated arylacetonitriles to 2-octalones give good yields of *cis*-decalone products. The stereochemistry of the adducts is determined by ¹³C NMR spectroscopy.

Conjugate additions of enolates², cuprates³, allylsilanes⁴ and aluminum or zirconium acetylides (via nickel catalysis)⁵ to $\Delta^{1(9)}$ -octal-2-ones (1) are known to take place generally with poor to moderate yield, especially in the case of 10-methylated compounds (e.g. 1b). Since it has been shown that the conjugate addition of lithiated arylacetonitriles to 2-cyclohexenones proceeds easily and in high yield (in THF-HMPA possibly under kinetic control^{6, 7} and in THF under thermodynamic control⁶), a study of the addition of the lithio compounds to octalones 1 was undertaken.

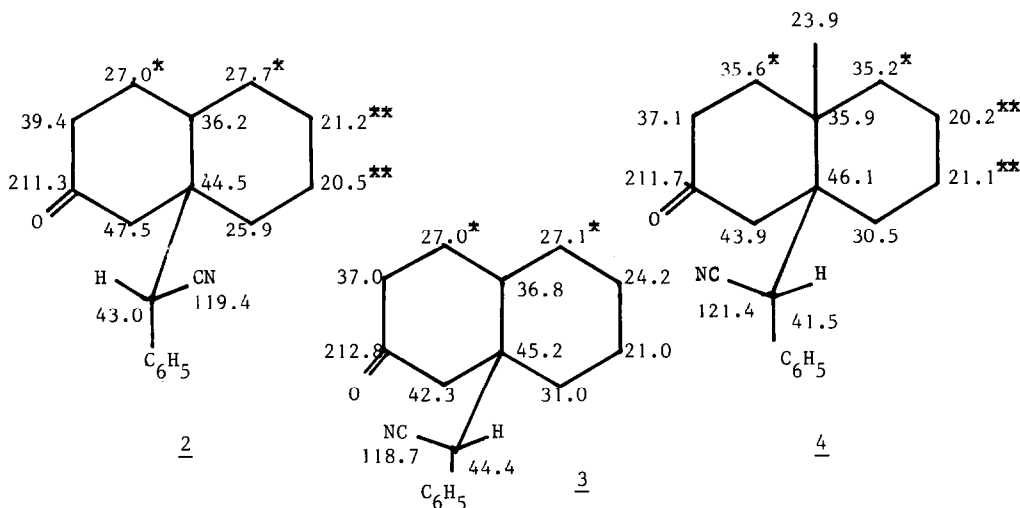


Interaction of 1a with lithio phenylacetonitrile in THF-HMPA (1:1 ratio of reagents) (-40°C, 2h, 60% yield) or in THF (-45°C, 2h, 90% yield) led to adducts 2 (mp 168°C) and 3 (mp 148°C) in 2:3 ratio (separation by T.L.C. on SiO₂ eluent hexane-ether 7/3). Whereas exposure of 1b to lithiated phenylacetonitrile or *p*-methoxyphenylacetonitrile in THF-HMPA under various conditions of reaction time and temperature led only to recovery of starting material,

a reaction in THF (-30°C, 3h, ca. 90% yield) produced diastereoselectively adducts 4 (mp 175°C) and 5 (mp 164°C), respectively.

No significant change in the ^1H NMR spectra of the crude product mixtures of the reactions of 1b and the lithio phenylacetonitriles in THF (-30°C, 3h), when at the end of the reaction HMPA was added and the mixture stirred at -30°C for 1h, indicated that the lack of reactivity of 1b in THF-HMPA was not due to an unfavorable equilibrium in the Michael condensation, but due to steric interference to conjugate addition. ⁸

In analogy with past experience ²⁻⁵ all adducts were cis-decalones, whose stereochemistry was determined by ^{13}C NMR spectroscopy.



The stereochemistry of the ring juncture of decalone 4 is revealed by its methyl shift of 23.9ppm, trans-10-methyl-2-decalone showing a 14.9ppm methyl signal⁹ and related cis-decalones exhibiting angular methyl signals in the 26-28ppm range.¹⁰ The shielding of the methyl group of ketone 4 vis-à-vis other cis-decalones can be attributed to the γ -effect exerted by the sidechain methine, as shown also by the reciprocal shielding of the latter vis-à-vis the same site in the unmethylated ketones 2 and 3. The upfield position of the bridgehead methine of the two ketones, contrasted with the 43.7ppm resonance of the same site in trans-9-methyl-2-decalone⁹, indicates the cis stereochemistry of the unmethylated ketones.

The assignment of the stereochemistry of the cyanobenzyl group in the ketones 2-4 rests on the differentiation of the α -ketomethylenes from the other methylenes by the residual coupling difference and from each other by the difference of coupling behavior, on C(6)

and C(7) being expected to exhibit the highest field signals among the methylenes¹¹, on the assumption of the phenyl group¹² being determinant in the sidechain rotamer population preference and being oriented away from the ring system and on the cyano group exerting a γ -effect on C(1) or C(8).^{13, 14}

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8. The reactions in THF appear to occur under thermodynamic control, as shown by the formation of the lithio allyloxides, i.e. the 1,2-addition products, at -90°C and their conversion into the lithio enolates of 4 and 5 at higher temperature.
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14. The values on formulas 2-4 are in ppm downfield from TMS ; $\delta(\text{TMS}) = \delta(\text{CDCl}_3) + 76.9\text{ppm}$.
The starred and doubly starred values may be interchanged.

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