Regioselective Syntheses of Polycylic Compounds by Carbanion-Mediated Polycyclisation of Olefins.

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Abstract: This paper reports straightforward syntheses of 1-aryl-bicyclo-[n.1.0]-alkanes, 1aryl-bicyclo-[3.3.0]-alkanes and of 1-phenyl-1,4-dimethyl-cyclopentane from unsaturated benzylselenides which involve the organolithiums-mediated cyclisation of olefins and poly-olefins.

Although intra- and inter-molecular additions of carbenium ions ¹⁻⁷ and radicals ⁸⁻¹⁰ to non functionalized olefins have been increasingly used for the synthesis of complex organic molecules, those involving organometallics have been restricted to the synthesis of polymers or of rather simple hydrocarbons.¹¹⁻¹⁸ The later approach would however offer the unique advantage not only to control the stereochemistry of the product by means of the metal but also to provide a novel organometallic species which is able to take part in further reactions.

We have been active in this field, over the past few years and have shown that benzyllithiums bearing an olefinic side chain cyclise to produce 1-aryl-2-lithiomethyl cycloalkanes ^{19,20} and that benzyllithiums ^{20,21} and α -selenobenzyllithiums ²² react with ethylene and functionalized ethylenes to provide respectively two-carbon-homologated organolithiums and aryl cyclopropane derivatives in reasonably good yields. We now disclose that benzyllithiums are able to initiate polyolefin-cyclisation and that α -selenobenzyllithiums efficiently produce 1-aryl bicyclo-[n.1.0]-alkanes <u>6</u> (Scheme 1).



Thus 1,1(bis)-methylseleno-1-phenyl-5-hexene <u>2a</u>, readily available on reaction of 1,1(bis)methylseleno-1-phenyl-methylpotassium [from 1,1-(bis)-methylseleno-1-phenyl-methane and KDA, THF,-

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78°C, 0.25hr] with 5-bromo-1-pentene [THF,-78°C, 0.5 hr, 81% yield], reacts with n-butyllithium in THF at -78°C to provide almost immediately 1-methylseleno-1-phenyl-5-hexenyl-1-lithium <u>3</u> (Scheme 1). The later proved stable at this temperature and can be protonated or allylated on reaction with methanol or allyl bromide to provide the benzylselenides <u>4</u> in good yields [MeOH, -78°C, 0.5 h, 95% yield or 1.2 equiv. allyl bromide, -78°C to 20°C, 0.5h, 82% yield, Scheme 1 - route a]. If, however, the reaction medium is allowed to reach 0°C without any electrophile added [-78°C to 20°C, 0°.5h], 1-phenyl-[3.1.0]-bicyclohexane <u>6a</u> is obtained in very good yield (Scheme 1 - route b). The whole process has been successfully applied to analogous selenoacetals bearing for example a substituted phenyl group or possessing an hexenyl side chain (Scheme 1 - route b) and has allowed, in the latter case, the high yield synthesis of the bicyclo-[4.1.0]-heptane derivative <u>6b</u>.

The cyclisation does not take place with 6-methyl-1-methylseleno-1-phenyl-5-heptenyl-1-lithium <u>3d</u> (Scheme 2 - R=Me) which possesses a tri-substituted carbon-carbon double bond even when the reaction is carried out under the same conditions but for longer time. In this case, 6-methyl-1-methylseleno-1-phenyl-5-heptene <u>4d</u> resulting from protonation of the corresponding benzyllithium is produced (82% yield).

We envisaged that the cuprate 23,24 resulting from the addition of 1 equiv. of CuI : Me₂S complex on the α -selenobenzyllithium would perhaps initiate the cyclisation reaction but this proved unsuccessful. We found in fact that, under these conditions, the organometallic intermediate couples at around -40°C as already described for α -selenoalkyl cuprates 23 to produce 2,13-dimethyl-7,8-diphenyl-2,7,12tetradecatriene <u>7d</u> in 83% yield as a 30/70 mixture of stereoisomers (Scheme 2). It is also interesting to notice that 1-methylseleno-1-phenyl-5-hexenyl-1-lithium <u>3a</u> which exhibits the high propensity to cyclise to 1-phenyl-[3.1.0]-bicyclohexane <u>6a</u> reported above, exclusively produces 6,7-diphenyl-1,6,11-dodecatriene <u>7a</u> when the reaction is carried out in the presence of copper iodide [1 equiv. of CuI:Me₂S, -78°C, then -78°C to 20°C, 1.5 hr, 53% yield, Scheme 2].





In the course of this work, we have also found that the benzylselenide $\underline{4a'}$ bearing two olefinic double bonds in a suitable position, reacts at -78°C, with n-Buli in THF to provide, after heating to room temperature and hydrolysis, the bicyclo-[3.3.0]-octane derivative $\underline{11}$ in reasonably good yield [45% as a 75/25 mixture of stereoisomers, Scheme 3]. Apparently, the benzyllithium <u>8</u> intermediary produced, promotes a very facile poly-cyclisation reaction.



The inter-molecular version of this polyolefin addition-cyclisation process is even more spectacular. We found for example, that 2-phenyl-4-pentenyl-2-lithium <u>13</u>, readily available from acetophenone and allyl bromide [(i) 2 equiv. MeSeH, 0.35 eq. TiCl₄, CCl₄, -50° C, 0.25h; 20°C, 2h (ii) n-Buli, -78° C, 0.2h (iii) allyl bromide -78° C to 20°C, 0.1h (iv) n-Buli, -78° C, 0.2h], which is not prone to cyclise to 1-methyl-1-phenyl-2-lithiomethyl cyclopropane <u>14</u> (Scheme 4 - route a), reacts with ethylene to provide after hydrolysis 1,3-dimethyl-1-phenyl cyclopentane <u>18</u> in modest but not yet optimized yield [35%, as a one to one mixture of stereoisomers, Scheme 4 - route b]. This product probably results from the addition of the benzyllithium to ethylene followed by cyclisation of the resulting alkenyllithium <u>16</u> on the suitably positioned carbon-carbon double bond.

Scheme 4



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We have therefore shown with a few examples that carbanion mediated poly-olefin addition is a viable process which can be applied to non functionalized olefins and which can be used for the construction of relatively complex carbon frameworks. Particular mention has to be made of the fact that all the cyclic compounds described in this paper derive in a connective fashion from aromatic aldehydes or ketones by the concomitant formation of at least two novel carbon-carbon bonds from the benzylic carbon (Schemes 1-4). These reactions therefore allow the geminal di-alkylation of the carbonyl group of aromatic aldehydes or ketones ²⁶. We are currently determining their scope and limitations.

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