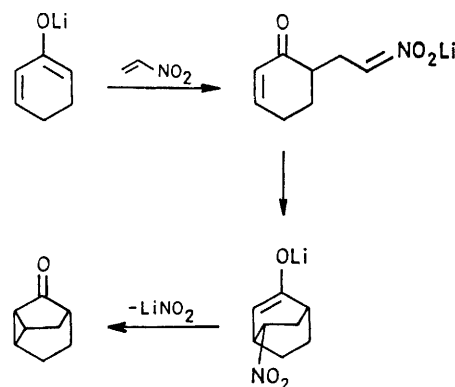


## Bicycloannulation with Nitroethene and 1-Nitropropene. A One-step Synthesis of Tricyclenone

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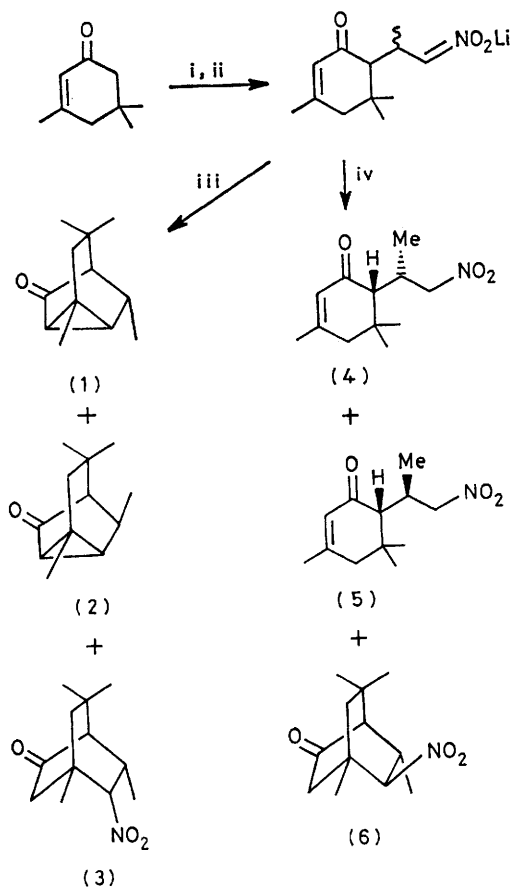
**Summary** Tricyclo[3.2.1.0<sup>2,7</sup>]octan-6-ones and tricyclo[2.2.1.0<sup>2,6</sup>]heptan-3-ones are formed in one step from  $\alpha\beta$ -cyclohexenones and  $\alpha\beta$ -cyclopentenones, respectively, by treatment of their  $\alpha'$ -enolates with nitroethene and 1-nitropropene in tetrahydrofuran and then refluxing the resulting solution with added hexamethylphosphoric triamide.

OLEFINIC bicycloannulation reagents are finding increasing utility in organic synthesis. To the two types developed by us, vinylphosphonium salts<sup>1</sup> and alkenyl sulphones,<sup>2</sup> and that developed by Hagiwara and co-workers,  $\alpha$ -bromo- $\alpha\beta$ -unsaturated esters,<sup>3</sup> we have now added nitro-olefins. The reactions involving these nitro-olefins are viewed as three-stage processes (illustrated in the Scheme for nitroethene) in which the reagent first acts as an acceptor in a conjugate addition by a cyclic cross-conjugated dienolate. The resulting stabilized carbanionic carbon undergoes intramolecular Michael addition to the  $\alpha\beta$ -unsaturated ketone moiety, giving a bicyclic enolate intermediate which then loses, by intramolecular displacement, the group originally responsible for activating the reagent. The final step in this mechanism closes a cyclopropane ring, and the overall reaction thus constitutes an addition of adjoining five- and three-membered rings to the previously existing ring of the substrate. Thus far, the method has been limited to cyclohexenones as substrates.



SCHEME. Nitro-olefin bicycloannulation.

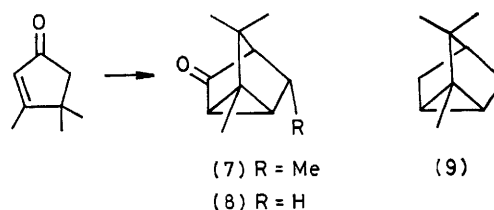
Although conjugate additions of enolates to nitro-olefins and of nitronate anions to enones are both well-known processes,<sup>4</sup> displacement of the nitro group from sp<sup>3</sup> carbon is quite rare.<sup>5</sup> Recently, however, it was reported that highly activated (electron poor) olefins may be cyclopropanated by nitromethane and nitroethane in the presence of potassium *t*-butoxide.<sup>6</sup> Thus, sufficient precedent existed for the use of nitro-olefins in bicycloannulations analogous to those previously mentioned.



*Reagents and conditions:* i, lithium di-isopropylamide at 0 °C; ii, MeCH=CHNO<sub>2</sub> at -78 °C; iii, HMPA, reflux; iv, AcOH at -78 °C.

In the event, addition of 1-nitropropene<sup>7</sup> to a solution of the  $\alpha'$ -enolate<sup>1</sup> from isophorone in tetrahydrofuran (THF) at -78 °C, followed by addition of hexamethylphosphoric triamide (HMPA) (9:1 mole ratio of HMPA to ketone) at room temperature and, finally, refluxing for 16 h produced a remarkable 63% yield of bicycloannulation products, tricyclo-octanones (1) and (2) in a ratio of 12:1. In addition, a small amount (4%) of a partially cyclized product, bicyclo[2.2.2]octanone (3), was also isolated. In contrast with the high stereoselectivity observed here in favour of diastereomer (1), when the mixture of intermediates was quenched at -78 °C by addition of acetic

acid, a 74% yield of the two diastereomeric conjugate addition products (4) and (5) was obtained (approximately equal amounts) along with a small amount of what appears to be the bicyclo[2.2.2]octanone (6), a diastereomer of (3). We believe the most reasonable explanation for this discrepancy is the decreased tendency of (5) to cyclize to (2), relative to the conversion of (4) into (1), as a result of unfavourable steric interactions, but detailed examination of these effects must await further experimentation.



In a similar fashion, reaction between 1-nitropropene and the  $\alpha'$ -enolate from 3,4,4-trimethylcyclopent-2-en-1-one<sup>8</sup> in refluxing THF in the presence of HMPA gave, stereoselectively, a 39% yield of the tricycloheptanone (7). This is the first instance in which this type of bicycloannulation has been extended to a substrate other than a cyclohexenone. Diastereomeric products analogous to adducts (4) and (5) were obtained, again in approximately equal amounts, when the reaction was quenched at -78 °C with acetic acid. Treatment of the same enolate with nitroethene<sup>9</sup> gave tricyclenone (8), but only after a much longer reflux period with added HMPA. Even though the yield of (8) was only 22%, this compares favourably with the overall yield of (8) from a recently reported multistep sequence.<sup>10</sup> Furthermore, since tricyclenone has previously been converted to tricyclene (9),<sup>11</sup> our synthesis of (8) constitutes a formal total synthesis of this naturally occurring<sup>12</sup> monoterpene in two steps from the cyclopentenone.

In view of the relatively high yield and stereoselectivity of the bicycloannulation of isophorone with 1-nitropropene, the synthetic potential of this new bicycloannulation reaction is at least as great as that of previously discovered bicycloannulation procedures.

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