

# Regioselective Syntheses of Polyalkylated Cyclopentanones

Serge Halazy and Alain Krief\*

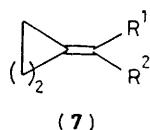
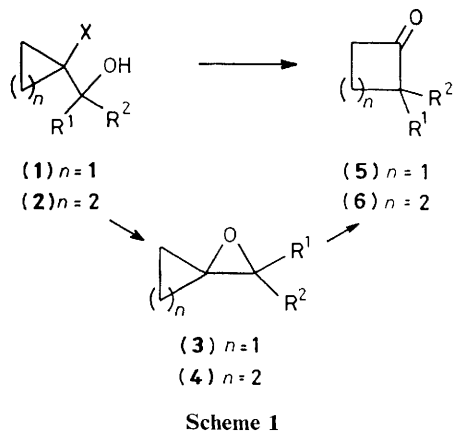
Département de Chimie, Facultés Universitaires Notre-Dame de la Paix, Rue de Bruxelles, 61, B-5000-Namur, Belgium

The title compounds have been regioselectively prepared from carbonyl compounds *via* two ring expansions.

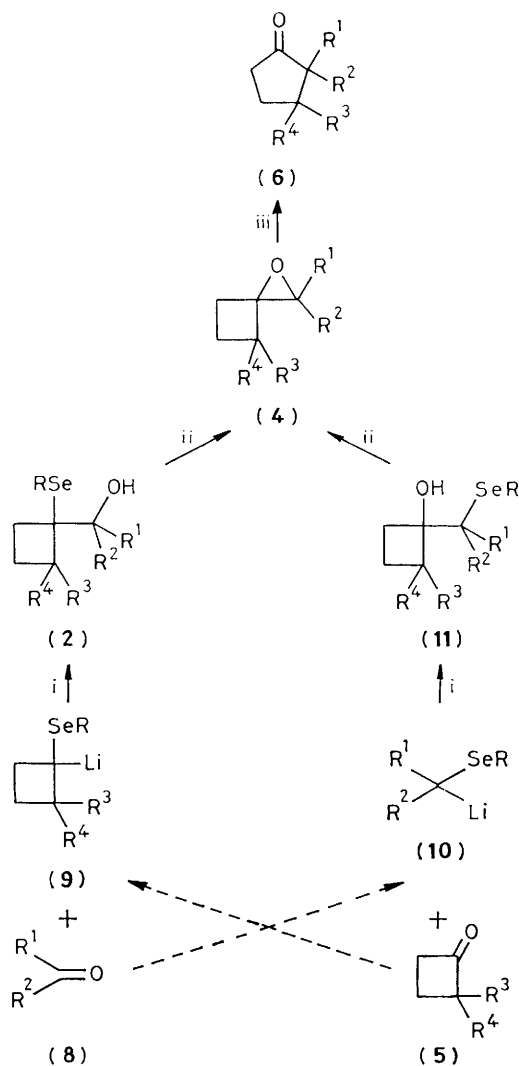
Since the discovery of Trost<sup>1</sup> and Conia,<sup>2</sup> the cyclopropyl derivatives of general formula (1) (Scheme 1) are known<sup>6</sup> to be efficient precursors of the cyclobutanones (5). This ring expansion can be directly achieved from (1) or *via* a preformed oxaspiropentane (3).<sup>3</sup> Few reports<sup>4,5</sup> describe the homologous reaction: the ring expansion of cyclobutane to cyclopentane derivatives. This is due to the lack of methods for synthesizing (2) and to the lower strain in cyclobutyl compounds compared with the cyclopropyl ones so that the ring expansion step is less favoured.

Thus, whereas the cyclopropyl selenides (1) (X = SeMe) lead to the formation of the cyclobutanones (5)<sup>6</sup> on treatment with toluene-*p*-sulphonic acid in wet benzene (1 equiv., 80 °C, 12 h), the higher homologues (2) (X = SeMe) yield exclusively the corresponding alkylidenecyclobutanes (7) under similar conditions.†

The ring expansion from cyclobutanones to cyclopentanones was achieved *via* the oxaspirohexanes (4) (Scheme 2). These were readily prepared from the cyclobutanones (5) and aldehydes or ketones (8) using a set of reactions we have already described for straight chain carbonyl compounds<sup>7</sup> and which appears to work perfectly in the special cases reported herein. Thus, the cyclobutyl selenides<sup>7</sup> (2) and (11) (Scheme 2) obtained from the cyclobutanones (5) and carbonyl compounds (8) were transformed into the epoxides (4) after alkylation with methyl iodide‡ followed by treatment with base



[Bu<sup>t</sup>OK—dimethyl sulphoxide (method A) or 10% aq. KOH—ether (method B)]. The transformation of the epoxides (4) into the cyclopentanones (6) was best achieved with lithium iodide in refluxing methylene chloride (Scheme 2). This isomerisation, first described by Lerverend,<sup>5a</sup> and used by Trost<sup>5b</sup> in a modified version, was exclusively reported for



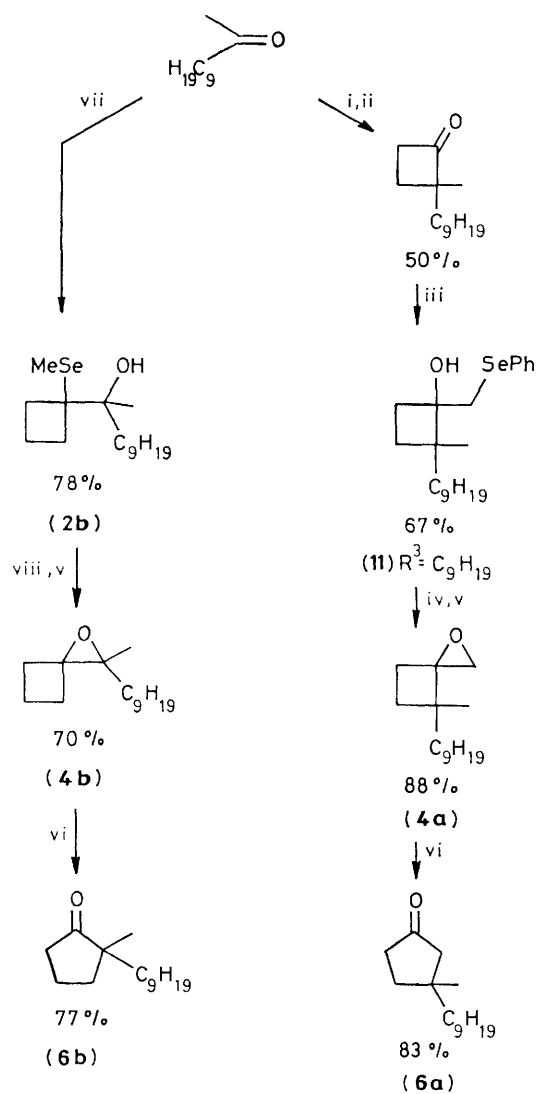
						Product yields (%)		
						(4),	(6)	
R	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	(2)	(11)	(method A)	(B)
Me	H	C <sub>10</sub> H <sub>21</sub>	H	H	90	—	81 (A)	91
Me	Me	C <sub>9</sub> H <sub>19</sub>	H	H	78	—	70 (B)	77
Me	H	C <sub>10</sub> H <sub>21</sub>	H	C <sub>5</sub> H <sub>11</sub>	71	—	71 (A)	87
Me	H	C <sub>10</sub> H <sub>21</sub>	H	C <sub>5</sub> H <sub>11</sub>	71	—	70 (B)	87
Me	H	C <sub>10</sub> H <sub>21</sub>	H	H	—	71	65 (B)	91
Ph	H	H	Me	C <sub>9</sub> H <sub>19</sub>	—	67 <sup>a</sup>	88 (B)	83

† These results will be reported in the full paper.

‡ In some cases, MeI—AgBF<sub>4</sub> has been used instead of MeI alone. The only noticeable difference is that the reaction works faster in the presence of AgBF<sub>4</sub>.

<sup>a</sup> This yield refers to a reaction performed in ether.

Scheme 2. Reagents and conditions: i, tetrahydrofuran (THF), -78 °C, 1 h; ii, MeI, KOH—ether; iii, LiI, CH<sub>2</sub>Cl<sub>2</sub>.



**Scheme 3.** Reagents and conditions: i,  $\text{CH}_2\text{CH}_2\text{C}(\text{SeMe})\text{Li}$ , THF; ii,  $p\text{-MeC}_6\text{H}_4\text{SO}_3\text{H}$ ,  $\text{H}_2\text{O}$ ,  $\text{C}_6\text{H}_6$ ,  $80^\circ\text{C}$ ; iii,  $\text{PhSeCH}_2\text{Li}$ , ether,  $-78^\circ\text{C}$ ; iv,  $\text{MeI-AgBF}_4$ ; v,  $\text{KOH-ether}$ ; vi,  $\text{LiI}$ ,  $\text{CH}_2\text{Cl}_2$ ,  $40^\circ\text{C}$ ; vii,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(\text{SeMe})\text{Li}$ , THF; viii,  $\text{MeI}$ .

oxaspirohexanes bearing two hydrogen atoms on the epoxide ring. We found that this reaction can accommodate one and even two alkyl groups on the epoxide ring. We also found it to be highly regioselective since it occurs by migration of the more highly substituted carbon atom of the cyclobutane ring.

Finally, our method allows the regioselective (100%) synthesis of the two isomeric cyclopentanones (**6a**) and (**6b**) from undecan-2-one (Scheme 3) through the regioselective formation of the two oxaspiro[2,3]hexanes (**4a**) and (**4b**). Since cyclobutanones can be readily prepared from cyclopropyl derivatives<sup>1-3,6</sup> (see also Scheme 1), the synthesis reported herein allows the formation of a cyclopentane ring from a cyclopropane ring by two consecutive ring enlargements.

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### References

- B. M. Trost, D. E. Keeley, H. C. Arndt, and M. J. Bogdanowicz, *J. Am. Chem. Soc.*, 1977, **99**, 3088.
- J. P. Barnier, B. Garnier, C. Gerard, J. M. Denis, J. Salaun, and J. M. Conia, *Tetrahedron Lett.*, 1973, 1747, and references therein; J. Salaun, A. Fadel, and J. M. Conia, *Tetrahedron Lett.*, 1979, 1429.
- T. Hiyama, S. Takehara, K. Kitatani, and H. Nozaki, *Tetrahedron Lett.*, 1974, 3295; M. Braun, R. Damman, and D. Seebach, *Chem. Ber.*, 1975, 2368; B. M. Trost and M. J. Bogdanowicz, *J. Am. Chem. Soc.*, 1973, **95**, 5321.
- A. E. Greene, J. P. Deprès, H. Nagano, and P. Crabbé, *Tetrahedron Lett.*, 1966, 2365; P. Lriverend, *Bull. Soc. Chim. Fr.*, 1973, 3498; M. Larchevêque, P. Mulot, and T. Cuvigny, *C. R. Acad. Sci., Ser. C*, 1975, **280**, 309; T. Cohen, D. Kuhn, and J. R. Falck, *J. Am. Chem. Soc.*, 1975, **97**, 4749; J. D'Angelo, *Bull. Soc. Chim. Fr.*, 1975, 333; A. E. Greene and J. P. Deprès, *J. Am. Chem. Soc.*, 1979, **101**, 4003; S. Knapp, A. F. Trope, and R. M. Ornaf, *Tetrahedron Lett.*, 1980, 4301; K. Ogura, M. Yamashita, M. Suzuki, and G. Tsuchiashi, *Chem. Lett.*, 1982, 93; P. Boontanonda and R. Grigg, *J. Chem. Soc., Chem. Commun.*, 1977, 5830.
- (a) M. L. Lriverend and P. Lriverend, *C. R. Acad. Sci., Ser. C*, 1975, **280**, 791; (b) B. M. Trost and L. H. Latimer, *J. Org. Chem.*, 1978, 1978, **43**, 1031.
- S. Halazy and A. Krief, *J. Chem. Soc., Chem. Commun.*, 1979, 1136.
- A. Krief, *Tetrahedron*, 1980, **36**, 2531; S. Halazy and A. Krief, *Tetrahedron Lett.*, 1980, 1997.