

**CONVERGENT SYNTHESSES
IN THE SESQUICARENE SERIES USING
A C₇-VINYLALKYNYLCARBENE**

M. FRANCK-NEUMANN, P. GEOFFROY, M. MIESCH, F. ZARAGOZA DÖRWALD
Laboratoire de Chimie Organique Synthétique, Associé au CNRS
Institut de Chimie, Université Louis Pasteur
1 rue Blaise Pascal 67008 - Strasbourg - France

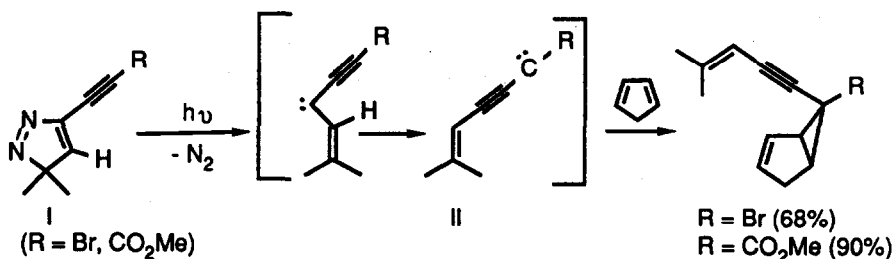
Dedicated to Professor Wolfgang Kirmse on the occasion of his 60th birthday.

Summary : *The possibility of achieving convergent syntheses with elaborate carbenes is illustrated by the isobutenylalkynylcarbene II (R = Br). By reaction with 3-cyclohexen-1-one, the endo cyclopropanic adduct IIIa is formed as a major product. Metalation with MeLi, followed by reaction with MeI, proceeds with inversion of configuration (-> sesquicarene skeleton, XI), or, after protection of the ketofunction, with retention of configuration (-> isosesquicarene VIII).*

Active interest in carbene chemistry has been growing steadily, and distinct progress has been made in many areas of this field. Its application to synthetic organic chemistry, *as far as intermolecular reactions are concerned*, seems however to be limited to the use of simple carbenes like methylene, mono- and dihalomethylenes or mono- and dialkoxycarbonylmethylenes. Little synthetic work dealing with more elaborate carbenes is known, in spite of the fact that many syntheses would become more convergent. This is probably a consequence of the great tendency to undergo intramolecular stabilization (1), limiting *a priori* the use of elaborate carbenes in intermolecular cycloadditions.

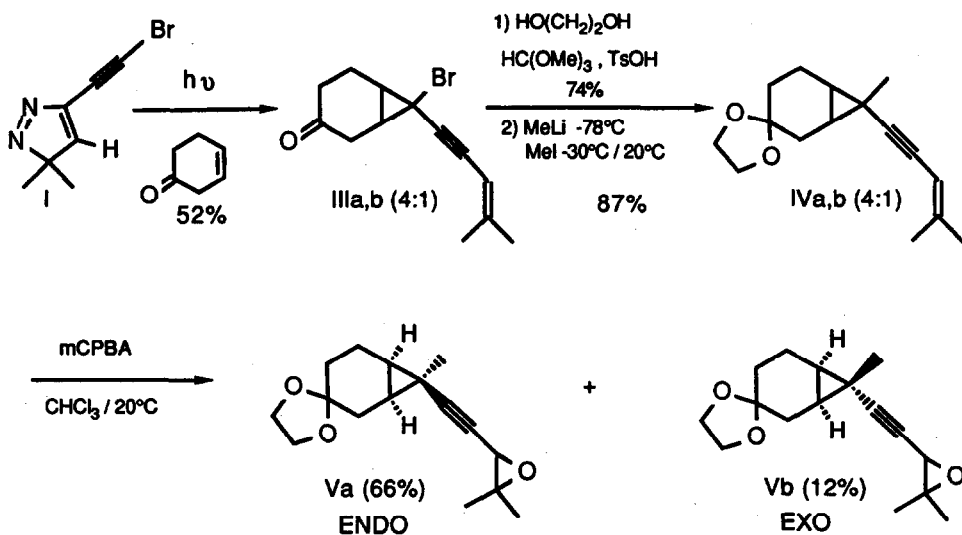
Relatively complex carbenes could however be used for convergent syntheses, provided that their structures preclude a rapid intramolecular deactivation. To illustrate the validity of this proposal, we describe here our results with a C₇-vinylalkynyl carbene in the sesquicarene series.

The vinylcarbenes generated by photolysis of 3,3-dimethyl-5-alkynyl 3H-pyrazoles of type I react preferentially with olefins as the rearranged form II. No intramolecular cyclization to cyclopropenes is observed, and with cyclopentadiene endo (2) cyclopropanic adducts are obtained with good yields (3) :

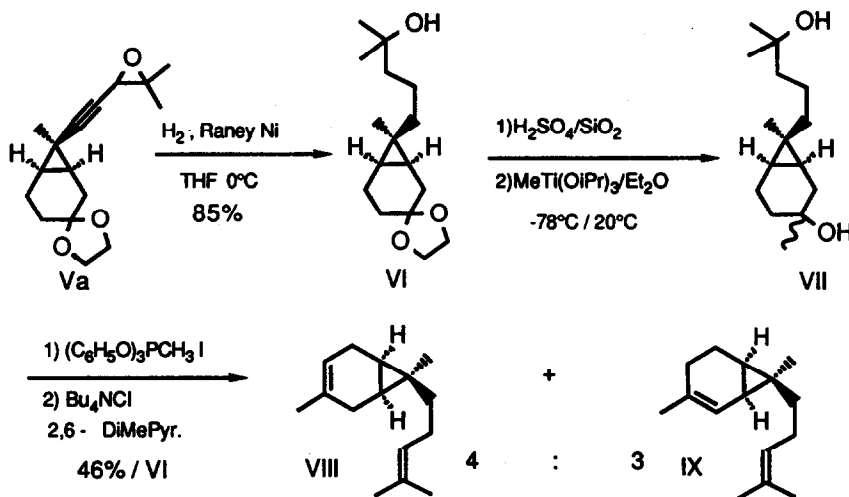


This interesting reactivity and the fact that propargylic cyclopropylic lithiated carbanions can exist either as pyramidal or planar species, depending on the solvent (4), led us to investigate the possibility of using the carbene II (R = Br) as a common precursor of the sesquicarene and isosesquicarene series.

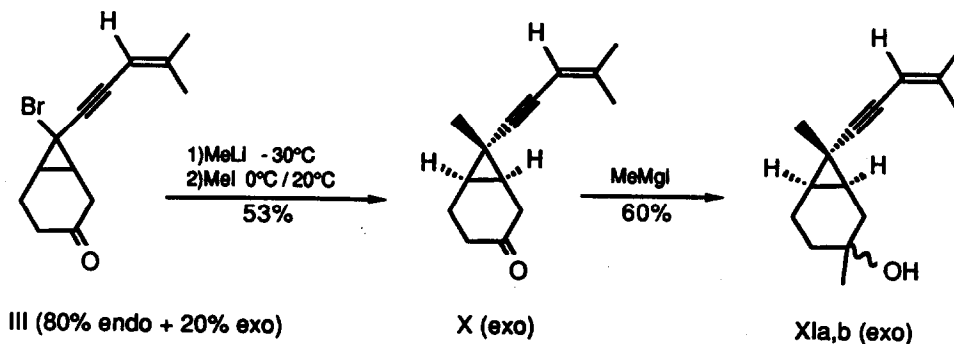
The carbene acceptor has necessarily to be a cyclohexene derivative in this case. As 1-methyl 1,3-cyclohexadiene and 1-methyl 1,4-cyclohexadiene did not lead selectively to the desired cyclopropanic adducts, we chose to start from 3-cyclohexen-1-one. The photolysis (5) of the 3H-pyrazole I (R = Br) in a 25 % methylene chloride solution of this cyclohexenone (6) led to a 4 to 1 diastereomeric mixture of the cyclopropanic adducts IIIa and IIIb with more than 50 % yield. A separation by column chromatography over silica gel was not possible and the three following steps were performed on the mixture. After protection of the carbonyl group by formation of dioxolanes (74 %), the bromine was replaced by a methyl substituent (IVa, IVb, 87 %) without modification of the isomeric ratio (4:1). Selective hydrogenation of the triple bond proved however to be very difficult at this stage. To reduce the acetylenic substituent of the cyclopropane ring we proceeded first by the epoxidation of the isobutenylic double bond. This led to the epoxides Va and Vb (7) which could be separated by a simple chromatography over silica gel (66 % and 12 % yield).



The hydrogenation of the triple bond of the major isomer Va proceeded with opening of the oxirane ring to the tertiary alcohol VI (69 %). After quantitative deprotection, the ketone was transformed into a tertiary alcohol, for which methyl-triisopropoxy-titanium proved to be the most adequate reagent. Conversion of the bis-tertiary alcohol into the corresponding diiodide followed by elimination gave finally a mixture of mainly two diolefins, VIII and IX (4:3, 46 % from VI). Gas chromatography coupled with mass spectrometry and $^1\text{H-NMR}$ allowed us to identify the major component as isosesquicarene (8), the minor component being the cyclohexene double bond isomer.



It is also possible to introduce the methyl substituent directly by treating the mixture of the ketones IIIa and IIIb with methyllithium followed by methyl iodide. Surprisingly, no reaction occurred on the carbonyl function and only substitution of the bromine with formation of the exo (2) derivative X (7) was observed. The ketone X, the dioxolane of which was identical with IVb, was the very major product in this case (70 %, isolated pure 53 %). By treatment with methylmagnesium iodide, two epimeric tertiary alcohols *with the complete carbon skeleton of sesquicarene* were formed (XIa, XIb : 60 %).



Our guess concerning the access of either sesquicarene or isosesquicarene derivatives starting from the same brominated cyclopropanic intermediate proved to be right. In view of these facts, it seems reasonable to suggest that the major carbenic adduct, IIIa, has the endo configuration, in agreement with our previous observations (3), and that the substitution of the bromine via a carbanionic species proceeds with retention of configuration (9) when the ketone is protected and with inversion of configuration when a lithioenolate can be formed.

These first results show that isobutenyl alkynylcarbenes, the precursors of which are easily obtained, can be used for convergent syntheses of cyclopropanic products.

The access, in three steps only, to the complete carbon skeleton of the sesquicarene, starting from one of our precursors (I \rightarrow XI), well illustrates this possibility.

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REFERENCES and NOTES

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2. endo and exo is referred to the CEC triple bond substituent.
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4. G. Köbrich, D. Merkel, *Liebigs Ann.*, **761**, 50 (1972) ;
G. Köbrich, D. Merkel, K. Imkampe, *Chem. Ber.*, **106**, 2017 (1973).
5. Photolysis conditions : 15° C, pyrex-glass vessel ($\lambda > 290$ nm), medium pressure mercury lamp Philips HPK 125.
6. Easily obtained from the commercial 1-methoxy 1,4-cyclohexadiene :
D.S. Noyce, M. Evett, *J. Org. Chem.*, **37**, 394 (1972).
7. Va : M^+ 262 ; RMN (200 MHz, $CDCl_3/TMS$) ; δ = 0,95 (ddd, 1H, 8.0, 6.0 et 2.0 Hz), 1.10 (dddd, 1H, 9.0, 8.5, 3.5 et 1.0 Hz), 1.25 (d, 1H, 1.0 Hz), 1.32 (s, 3H), 1.44 (d, 3H, 2.0 Hz), 1.45 (dddd, 1H, 13.0, 4.0, 3.0 et 1.5 Hz), 1.68 (dd, 1H, 14.5 et 3.5 Hz), 1.70 (ddd, 1H, 13.0, 7.0 et 4.0 Hz), 2.07 (ddd, 1H, 14.5, 9.0 et 3.0 Hz), 1.90-2.20 (m, 2H), 3.26 (s, 1H), 3.94 (m, 4H).
X : ν (cm⁻¹) = 2200 (C≡C), 1715 (C=O), 1630 (C=C) ; δ = 1.15 (s, 3H), 1.50-1.72 (m, 2H), 1.76 (broad s, 3H), 1.85 (broad s, 3H), 2.61 (dd, 1H, 18.5 et 7.5 Hz), 2.00-2.50 (m, 5H, 5.20 (m, 1H).
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This 20 step synthesis starts from tropone and leads also in the last step to a mixture of diolefins, which have to be separated by gas-phase chromatography.
9. Cf. : H.M. Walborsky, F.J. Impastato, A.E. Young, *J. Am. Chem. Soc.*, **86**, 3283 (1964) ;
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