

VICINAL ALKYLATION OF ALKYNES. A SHORT ROUTE TOWARD
 $\Delta^{\alpha,\beta}$ BUTENOLIDES, FURANS AND CYCLOPENTENONES.

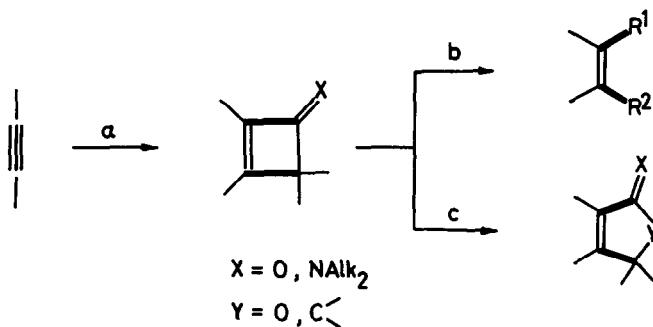
C. Schmit, S. Sahraoui-Taleb, E. Differding, C.G. Dehasse-De Lombaert and L. Ghosez*

Laboratoire de Chimie Organique de Synthèse
Université Catholique de Louvain, Place L. Pasteur, 1
B-1348 LOUVAIN-LA-NEUVE, BELGIUM.

Summary : Cyclobutenones 1 which are readily prepared from alkynes and keteniminium salts 2 were regiospecifically converted into $\Delta^{\alpha,\beta}$ butenolides 4 or cyclopentenones 7. Reaction of 4 with diisobutylaluminum hydride yielded the corresponding substituted furans.

A methodology leading to the regio- and stereoselective addition of carbon chains to an acetylenic bond should be extremely useful. We have considered that this vicinal alkylation could possibly be achieved by a two-step sequence (Scheme 1) involving a [2+2] cycloaddition of a ketene or a keteniminium salt to an alkyne (step a) followed by cleavage of the C¹-C⁴ bond (step b) or, alternatively, the regiospecific insertion of an atom Y in that bond (step c).

Scheme 1. : Vicinal Alkylation of Acetylenes

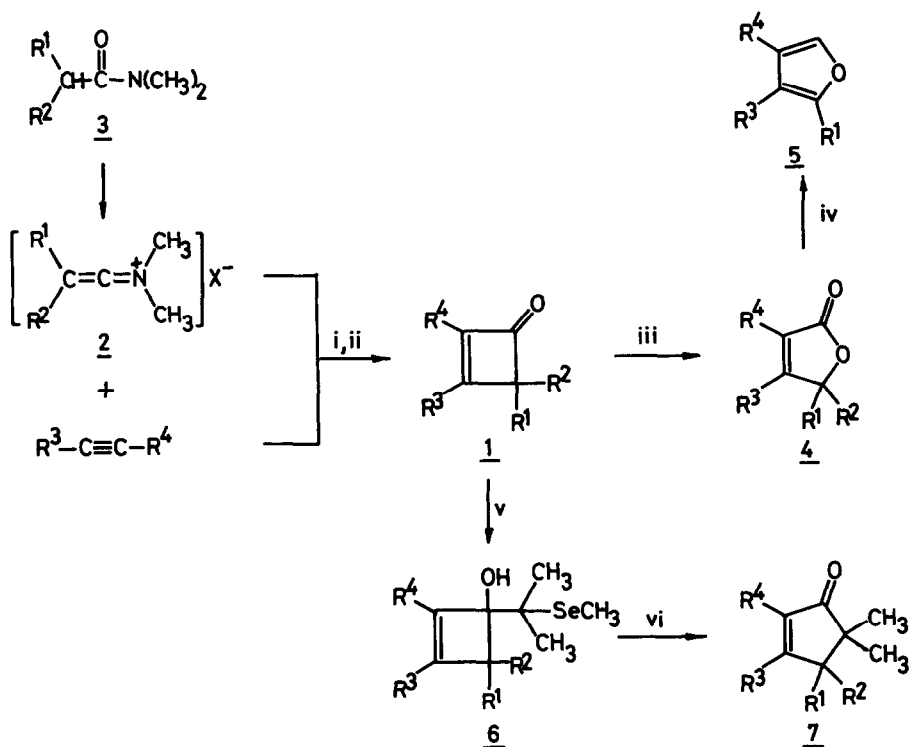


A demonstration of the utility of sequence a-c is the subject of this communication.

Previous studies¹ have shown that unactivated alkynes are rather poor ketenophiles. On the other hand we have shown that tetramethylketeniminium salts readily cycloadd to alkyl- and arylacetylenes². This reaction has now been developed into an efficient and general method of synthesis of cyclobutenones 1.

The results are shown in Scheme 2 and Table 1. When $R^1=R^2=CH_3$, the keteniminium salt **2** was generated from the readily available **3** tetramethyl- α -chloroamine and $TiCl_4$. When R^1 or (and) R^2 are H, **2** was formed in situ from the appropriate tertiary amide **3**, trifluoromethanesulfonic anhydride and collidine in refluxing dichloromethane **4**. Hydrolysis of the crude adducts gave good yields of cyclobutenones **1**. Yields were good even in the case of the more sensitive trimethylsilylacetylene.

Scheme 2.



Experimental Conditions : i. CH_2Cl_2 , $-40^\circ C$ ($X=TiCl_5^-$) **2** or reflux ($X=CF_3SO_3^-$) **4**; ii. 0,1 N NaOH- CH_2Cl_2 ; iii. m CPBA (1.6 equiv.), $NaHCO_3$ (6.6 equiv.) in CH_2Cl_2 ; iv. Dibal (1.5 equiv.), THF, $-20^\circ C$; v. $(CH_3)_2C(SeCH_3)Li$ (1 equiv.) in $(C_2H_5)_2O$, $-78^\circ C$, then NH_4Cl ⁷; vi. KOH 50% - $CHCl_3$ - $C_6H_5CH_2NEt_3Cl$ (entry 7g) or $TlOC_2H_5$ in $CHCl_3$ (entry 7h) ⁷.

Table 1 : Yields of Compounds 1, 4, 5, 6 and 7

Entry	R ¹	R ²	R ³	R ⁴	Yields ^a , (%)				
					<u>1</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>
a	CH ₃	CH ₃	C ₆ H ₅	C ₆ H ₅	82 ^b	57 ^d			
b	CH ₃	CH ₃	CH ₃	CH ₃	70 ^b	51 ^e			
c	CH ₃	CH ₃	(CH ₃) ₃ C	H	61 ^b	66 ^e			
d	CH ₃	H	C ₆ H ₅	H	70 ^c	52 ^d			
e	CH ₃	H	(CH ₃) ₃ C	H	69 ^c	61 ^e			
f	H	H	(CH ₃) ₃ C	H	32 ^c	53 ^e	57 ^e		
g	CH ₃	CH ₃	(CH ₃) ₃ Si	H	88 ^b	76 ^e	77 ^e	44 ^e	58 ^e
h	CH ₃	H	(CH ₃) ₃ Si	H	89 ^c	98 ^e		52 ^e	70 ^e

^a Yields refer to pure isolated compounds which were fully characterized by spectral data.

^b From tetramethyl- α -chloroamine

^c From amides 3.

^d Purified by recrystallisation

^e Purified by chromatography on silicagel

The success of our strategy rested upon the regioselectivity of the ring-expansion reaction. Baeyer-Villiger oxidations of cyclohexenones and other α,β unsaturated ketones normally occur with preferential migration of the vinyl group over the alkyl group⁵. However we anticipated that this sequence of migratory aptitudes could be reversed in cyclobutenones 1 as a result of the allylic character of C-4. Indeed the reaction of 1 with *m*-chloroperbenzoic acid exclusively yielded the $\Delta^{\alpha,\beta}$ butenolides 4. These were readily transformed by a known procedure⁶ into the corresponding derivatives of furan 5.

Finally, using Krief's method⁷ for the ring enlargement of cyclic ketones, we have been able to convert 1 into cyclopentenones 7 via the intermediate β -hydroxyselenide 6. The ring expansion also occurred with preferential migration of the allylic C¹-C⁴ bond over the C¹-C² vinylic bond.

Thus a two-step method to effect the vicinal alkylation of alkynes is now available. The mild conditions required for the reactions, the total regioselectivity, the ease of operation and good yields combine to make this a practical method of synthesis of $\Delta^{\alpha,\beta}$ butenolides or substituted furans or cyclopentenones.

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