

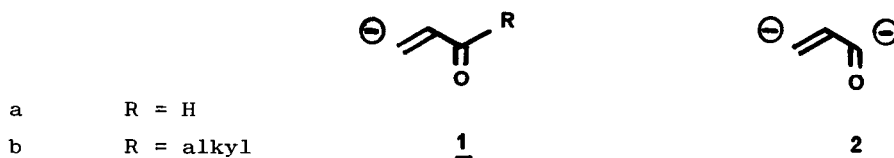
A NEW SIMPLE STEREOSELECTIVE SYNTHESIS  
OF TRANS- $\alpha$ ,  $\beta$  UNSATURATED CARBONYL COMPOUNDS.

Jean Claude CLINET and Gérard LINSTRUMELLE

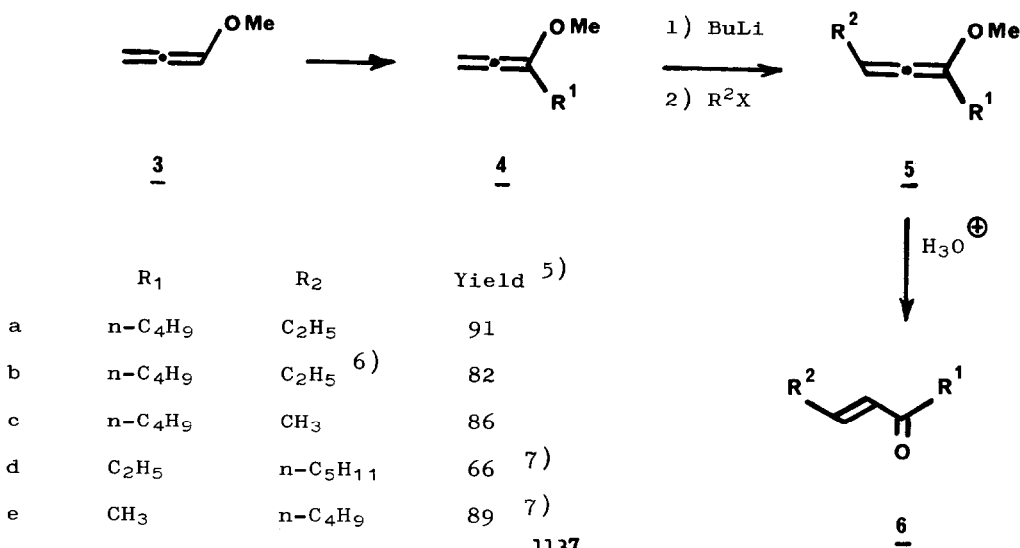
E.R. 12 du C.N.R.S., Laboratoire de Chimie de l'Ecole Normale Supérieure,  
24, rue Lhomond, 75231 Paris Cedex 05, France.

(Received in UK 4 January 1978; accepted for publication 3 February 1978)

Much interest has been devoted to the polarity inversion (umpolung) of the carbonyl reactivity <sup>1)</sup>. Several methods which formally transfer a vinylous acyl anion to an electrophilic center have been described <sup>2)</sup>.



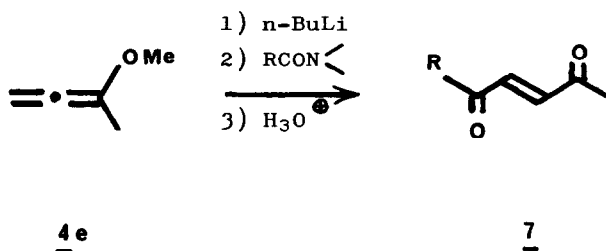
Our studies on allenic lithium reagents <sup>3)</sup> led us to investigate the reactivity of the easily obtainable <sup>4)</sup> allenic ethers.



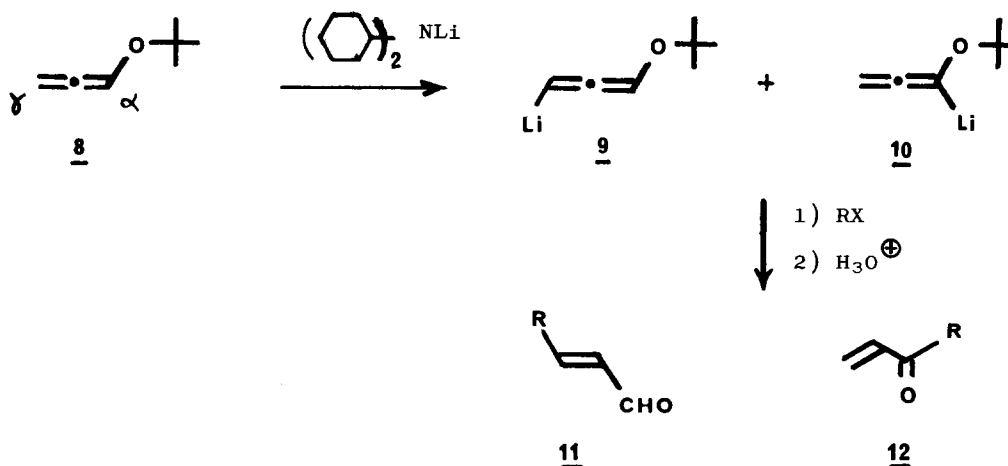
We have found that the ethers 4<sup>4)</sup> were metalated by n or t-butyllithium and alkylated by iodides or bromides without the formation of isomeric acetylenic by-products. A mild acid hydrolysis of the crude product gave pure trans conjugated ketones 6 in high yields<sup>5)</sup>. The trans geometry of 6 was confirmed by i r ( $970\text{ cm}^{-1}$ ) and n m r ( $J_{\text{trans}} = 16 - 18\text{ Hz}$ ) analyses.

The ethers 4 d and 4 e, prepared from 3 in THF, cannot be easily separated from the solvent. However, further metalation and alkylation provide a "one pot" synthesis of ketones 6 d and 6 e in good overall yield.

The lithiated derivatives of the ethers 4 can also be utilized in other nucleophilic reactions. Thus, when treated with dimethyl amides 3<sup>c)</sup> at  $-78^\circ$  for 2hr, trans unsaturated  $\gamma$ -diketones 7<sup>8)</sup> were obtained.



Alkoxy allenes are known to be lithiated in the  $\alpha$  position<sup>4,9)</sup>. However, by reaction of a more hindered allenic ether with a bulky amide, terminal metalation might be expected. The allenic lithium reagent 9 represents a useful synthetic equivalent of the anion 1 a.



Thus, 1-t-butoxy-1,2-propadiene <sup>10)</sup> 8, treated sequentially with lithium dicyclohexylamide and an alkyl iodide <sup>11)</sup>, gave after acid hydrolysis 80 % of trans -  $\alpha, \beta$  - unsaturated aldehyde 11 containing a small amount (5-6%) of ketone 12. Filtration through silica gel gave pure aldehyde 11 in 68 to 73 % yield.

#### TYPICAL PROCEDURES.

(E) - 3 - nonen - 5 - one 6a :

2.52 g (20 mmol) of 3-methoxy-1-2-heptadiene 4 a <sup>4)</sup> in THF (30 ml) were treated with n-butyllithium (1 eq.) at - 50° for 2 hr, then with ethyl iodide (3.12g, 1 eq.) from - 78° to -20° during 2 hr. The resulting mixture was then hydrolyzed with cold brine and extracted with ether. The organic extracts were combined, washed with water and stirred overnight with 5 % sulfuric acid (30 ml). Work-up in the usual manner followed by distillation gave 2.55g (91 %) of pure (E)-3-nonen-5-one 6 a.

(E) - 2 - heptenal 11 (R = n-C<sub>4</sub>H<sub>9</sub>) :

2.4g (21 mmol) of t-butoxyallene <sup>10)</sup> in THF (5 ml) were added dropwise into a solution of lithium dicyclohexylamide <sup>12)</sup> (21 mmol) in THF (40 ml) at - 55°. After 15 mn, 2.3 ml (20 mmol) of n-butyl iodide was added. The mixture was allowed to warm to -20° over 3 hr, hydrolyzed with cold brine and extracted with ether. The organic extracts were combined, washed with water and stirred overnight with 5 % sulfuric acid (30 ml). Work-up in the usual manner gave 1.90 g (80 %) of aldehyde 11 (R = n - C<sub>4</sub>H<sub>9</sub>) containing 5 % of 1-hepten-3-one. Chromatography through silica gel (pentane-ether 98.5 : 1.5) gave 1.52 g (68 %) of pure (E) - 2 - heptenal.

The authors thank Dr Sylvestre JULIA for interest and the Centre National de la Recherche Scientifique for financial support.

#### References and Notes

- 1) For recent reviews, see : D. Seebach and M. Kolb, Chemistry and Industry, 687 (1974) ; O.W. Lever, Jr., Tetrahedron, 32, 1943 (1976) ; B.T. Gröbel and D. Seebach, Synthesis, 357 (1977).
- 2) E.J. Corey, B.M. Erickson and R. Noyori, J. Amer. Chem. Soc., 93, 1724 (1971) ; Y. Leroux and R. Mantione, Tetrahedron Letters, 591 (1971) ; K. Hirai and Y. Kishida, ibid., 2743 (1972) ; T. Hayashi, ibid., 339

- T. Nakai, H. Shiono and M. Okamora, Tetrahedron Letters, 3625, (1974); I. Hori, T. Hayashi and H. Hidorikawa, Synthesis, 727 (1975); K. Kondo and T. Tunemoto, Tetrahedron Letters, 1007, 1397 (1975); M. Julia and B. Badet, Bull. Soc. Chim. Fr. 1363 (1975); K. Oshima, H. Yamamoto and H. Nozaki, Bull. Chem. Soc. Japan, 48, 1567 (1975); T. Cohen, D.A. Bennet and A.J. Mura jr., J. Org. Chem., 41, 2506 (1976); B. Corbel et J.P. Paugam, M. Dreux et P. Savignac, Tetrahedron Letters 835 (1976); M. Wada, H. Nakamura, T. Taguchi and H. Takei, Chemistry Letters, 345 (1977);
- 3) a) G. Linstrumelle and D. Michelot, J. Chem. Soc. Chem. Comm., 561 (1975)  
b) D. Michelot and G. Linstrumelle, Tetrahedron Letters, 275 (1976);  
c) J.C. Clinet and G. Linstrumelle, Nouveau Journal de Chimie, I, 373 (1977).
  - 4) S. Hoff, L. Brandsma and J.F. Arens, Recueil Trav. Chim. Pays-Bas, 87, 916 (1968).
  - 5) The yields given are for distilled products except otherwise indicated. All new compounds exhibited satisfactory spectral and physical properties.
  - 6) With  $R_2X = n-C_4H_9Br$ ; reaction time : 5 hr from  $-78^\circ$  to  $+20^\circ$ , then overnight at room temperature.
  - 7) Overall yield from 3 in a "one pot" procedure. In the case of the ketone 6 d, purification by chromatography through silica gel (elution pentane - ether 97 : 3) was performed.
  - 8) Overall yield from 3 in a "one pot" procedure after filtration through silica gel (elution pentane - ether 96 : 4) : 68% ( $R = CH_3$ ), 48% ( $R = (CH_3)_2CHCH_2$ ).
  - 9) Y. Leroux and C. Chantal, Tetrahedron Letters, 2585, 1973.
  - 10) This compound was the starting material for a new synthesis of  $\gamma$ - ketoaldehydes : B. Cazes and S. Julia, Bull. Soc. Chim. Fr., 1977 (in press).
  - 11) Butyl bromide gave 68% of aldehyde 11 containing 12% of ketone 12.
  - 12) Prepared by treatment of dicyclohexylamine with n-butyllithium in hexane at  $0^\circ$  and left at room temperature for 1 hr.