

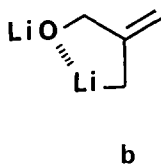
## A SIMPLE WAY TO SOME KETONE HOMOENOLATES

Thérèse CUVIGNY, Marc JULIA, Ludovic JULLIEN and Christian ROLANDO

Ecole Normale Supérieure, Laboratoire de Chimie,  
24 rue Lhomond, 75231 Paris Cédex 05 France.

*Summary:* Under basic conditions 1-alkene-3-ols were converted into ketone homoenolates which led to  $\beta$ -alkylated ketones.

It has recently been shown that treatment of methallyl alcohol or linalool with *n*-BuLi-TMEDA in hexane leads to vinylic metalation a/ whereas in ether-THF, allylic metalation b/ is observed.<sup>1,2</sup>



Under the same reaction conditions 1-decene-3-ol **1a** underwent addition<sup>3</sup> of *n*-BuLi to the double bond. The use of other basic systems were therefore tried. Treatment of the lithium alkoxide of **1a** with *n*-BuLi-*t*BuOK<sup>4,5</sup> led to noticeable amounts of the isomeric ketone **3a**.

Under basic conditions similar isomerisations have been reported<sup>6,7</sup> and interpreted as yet another mode of metalation. A phenyl group in the  $\alpha$  or  $\gamma$  position facilitates the rearrangement<sup>8,3a,9</sup>. Even aldehydes have been obtained by suitable basic treatment of allylic alcohols<sup>10</sup>.

Homoenolates such as **2**<sup>n</sup> arouse considerable interest but they are not easily obtained. Various ways of generating  $\gamma$ -substituted allylic anions as homoenolate equivalents have been proposed<sup>11</sup>.

The possibility of producing useful ketone homoenolates from readily available vinyl carbinols seemed worth investigating. The results are reported in this Letter.

Addition of *n*-BuLi to the potassium alkoxide **2a** or **2b** (M=K) proved to be a convenient basic system and produced an intramolecular Lochmann-Schlosser base. Ether was a more effective solvent than hexane in this case. Addition of TMEDA had no effect on the reaction. Some optimisation of time and temperature (see table) led, after quenching with H<sub>2</sub>O, to 77-70% yields of ketones **3** easily separated from small amounts (11-23%) of unchanged starting alcohol.

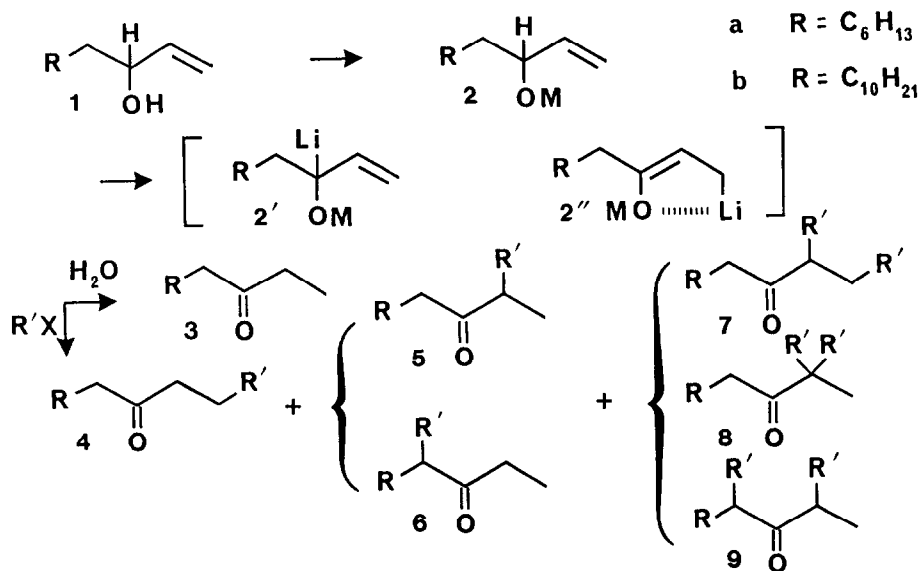
Table : Metalation, hydrolysis or alkylation of the potassium allylic alkoxides <sup>d</sup>.

R	n- BuLi t°C	Metalation R'X t°C	Eq.	Alkylation t°C	Recovered alcohol	Total yield	Distribution of ketones %												
							Total ketones % <sup>b</sup>	3	4	5	6	7	8	9					
C <sub>6</sub> H <sub>13</sub>	1.5	-8/+20	6	H <sub>2</sub> O	11	77	100												
C <sub>10</sub> H <sub>21</sub>	1.5	-8/+20	6	H <sub>2</sub> O	23	70	100												
C <sub>10</sub> H <sub>21</sub>	1.1	-8/+20	0.5	MeI	42	43	23												
C <sub>10</sub> H <sub>21</sub>	1.5	-8/+20	0.5	MeI	28	60	30												
C <sub>6</sub> H <sub>13</sub>	2.5	-8/+20	0.5	MeI	8 <sup>c</sup>	54	13												
C <sub>6</sub> H <sub>13</sub>	1.5	-8/+20	0.5	AllylBr	30	56	-												
C <sub>6</sub> H <sub>13</sub>	1.5	-8/+20	0.5	AllylBr	18	74	18												
C <sub>6</sub> H <sub>13</sub>	1.5	-8/+20	0.5	n-AmylBr	12	78	22												
C <sub>6</sub> H <sub>13</sub>	2.5	-8/+20	0.5	n-AmylBr	11	78	14												
C <sub>10</sub> H <sub>21</sub>	2.5	-8/+20	0.5	n-AmylBr	10	76	8												
C <sub>6</sub> H <sub>13</sub>	1.5	-8/+20	0.5	isoamylBr	25	70	33												
C <sub>6</sub> H <sub>13</sub>	2.5	-8/+20	0.5	isoamylBr	10	82	13												
C <sub>10</sub> H <sub>21</sub>	2.5	-8/+20	0.5	isoamylBr	22	72	19												

<sup>a</sup> all reactions were performed on a 2.5-5 mmol scale <sup>b</sup> isolated products yield <sup>c</sup> 27 % of two unidentified products

<sup>d</sup> polyalkylated ketones <sup>e</sup> unidentified bisalkylated ketones <sup>f</sup> 8 % unidentified isomeric ketones .

The reaction with a number of alkyl halides (see table) was next investigated. With 2.5 equivalents of n-BuLi the saturated halides gave notable amounts of  $\beta$ -alkylated ketones 4 whereas with 1.5 equivalents of  $\alpha$  (5) and  $\alpha'$ (6) substituted isomers were also formed. With allyl bromide, however, 1.5 equiv. of n-BuLi was enough but lower temperature was necessary in order to achieve alkylation.



Some disubstituted ketones 7,  $\alpha,\beta$ , 8,  $\alpha,\alpha$  and 9,  $\alpha,\alpha'$  were also obtained. It is understandable that alkylation of homoenolate 2" should give one of the regioisomeric enolates of ketone 3 and lead after further reaction to 7. If the homoenolate 2" is quenched by a proton donor the resulting enolate of 3 and ketone 3 itself are susceptible to undergo  $\alpha,\alpha'$  alkylation.

In a typical experiment, a solution of 1-decen-3-ol (5mmol,780mg) in 30 ml of anhydrous ether was stirred at 0° under argon with one equiv. of K over a period of ten minutes and the reaction mixture was allowed to warm up to room temperature. When the metal had all disappeared, n-BuLi (2.5 eq.) was added at -8°. After fifteen minutes the bath was removed and the mixture stirred at room temperature for about half an hour. 1-bromo-3-methyl butane (3.5 eq.) was then added at -20° to the well stirred solution which was allowed to warm up to room temperature over twelve hours and poured onto ice-water. After the usual work-up the crude oil was chromatographed on a silica gel column (eluent pentane/ether, gradient of increasing polarity) to give 10% of recovered 1-decen-3-ol, 11% of the isomeric ketone 3 and 71% of the  $\beta$  substituted ketone 4.<sup>12,13</sup>

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## References and Notes.

1. B.M.Trost and D.M.T.Chan, *J.Am.Chem.Soc.* **105**, 2315 (1983)
2. T.Cuvigny, M.Julia and C.Rolando, *J.Chem.Soc. Chem.Comm.*, 8 (1984). See also S.J.Gould and B.D.Remillard, *Tetrahedron Letters*, 4353 (1978); F.K.Meyer, J.G.Drewett and R.M.Carlson, *Synth.Comm.***16**, 261 (1986).
3. a/H.Felkin, G.Swierczewski and A.Tambuté, *Tetrahedron Letters*,707,(1969) b/J.K.Crandall and A.C.Clark, *J.Org.Chem.* **37**, 4236 (1972)
4. L.Lochmann, J. Pospisil and D. Lim, *Tetrahedron Letters*, 257 (1966).
5. M.Schlosser, *J.Organomet.Chem.* **8**, 9 (1967), M.Schlosser and S.Strunk, *Tetrahedron Letters*, **25**, 741 (1984) and references cited therein.
6. J.K.Crandall and L-H.C.Lin, *J.Org.Chem.* **33**, 2375 (1968), J.K.Crandall and M.Apparu, *Organic Reactions*, J.Wiley and Sons, Inc. New-York, **29**, 345 (1983).
7. B.Rickborn and R.P.Thummel, *J.Org.Chem.* **34**, 3583 (1969)
8. M.Tiffeneau, *Bull.Soc.Chim.France*, 4 **1**, 1205 (1907) footnote p.1209 .
9. D.R.Dimmel, W.Y.Fu and S.B.Gharpure, *J.Org.Chem.* **41**, 3092 (1976).
10. H.M.R.Hoffmann, A.Köver and D.Pauluth, *J.Chem.Soc. Chem.Comm.* 812 (1985)
11. D.Hoppe, *Angew.Chem.Int.Ed.* **23**, 932 (1984); H.Roder, G.Helmchen, E.M.Peters, K.Peters and H.G.von Schnering, *ibid.*, **23**, 898 (1984); J.F.Biellmann and J.B.Ducep, *Organic Reactions*, J.Wiley and Sons, Inc.,New-York, **27**, 1 (1982); J.Enda and I.Kuwajima, *J.Am.Chem.Soc.***107**, 5495 (1985); E.Nakamura, H.Oshino and I.Kuwajima, *ibid.* **108**, 3745 (1986); Y.Tamaru, H.Ochiai, T.Nakamura, K.Tsubaki and Z.Yoshida, *Tetrahedron Letters*, **26**, 5559 (1985); E. Nakamura, S.Matsuzawa, Y.Horiguchi and I.Kuwajima, *ibid.* **27**, 4029 (1986); G. Trimitsis, S.Beers, J.Ridella, M.Carlton, D.Cullin, J.High and D.Brutts, *J.Chem.Soc. Chem.Comm.* 1088 (1984).
12. The following ketones were described in the literature: **3a** A.I.Vogel, *J.Chem.Soc.* 610 (1948); **3b** E.E.Blaise and G.Guérin, *Bull. Soc. Chim. France*, 3 **29**, 1208 (1903); **R'=Me**: **4a** J.v.Braun and H.Kröper, *Chem.Ber.* **62**, 2882 (1929), **4b** F.L.Breusch and F.Baykut, *Chem.Ber.* **86**, 684 (1953); **5a** H.H.Morris and R.H.Young Jr., *J.Am.Chem.Soc.* **77**, 6678 (1955); **6a** J.E.Dubois and R.Luft, *Bull.Soc.Chim.France*, 1153 (1954); **7b** W.Schlenk Jr. *Liebigs Ann.Chem.* 1195 (1973); **R'=allyl**: **4a** T.Fujita, S.Watanabe, K.Suga, T.Inaba and T.Takagawa, *J.Appl.Chem.Biotechnol.***28**, 882 (1978); **R'=amyl**: **4a** A.D.Petrov and D.N.Andreev, *J.Gen.Chem.(USSR)* **7**, 570 (1937); **4b** see above **R'=Me**; **R'=isoamyl**: **4b** R.E.Sheads, M.Beroza and E.C.Paşzek, *J.Agric.Food Chem.* **23**, 60 (1975).
13. The spectroscopic data obtained for all new ketones were fully consistent with the assigned structure (<sup>1</sup>H and <sup>13</sup>C NMR, IR and Mass Spectra). The <sup>1</sup>H NMR and mass spectra of ketones **R'=Me**, **a** and **b** : **4**, **5**, **6**; **b** : **7**, **8**, **9** were identical to those of authentic samples prepared by literature methods.

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