Tetrahedron Letters,Vol.25,No.5,pp 519-522,1984
Printed in Great Britain

0040-4039/84 $3.00 + .00

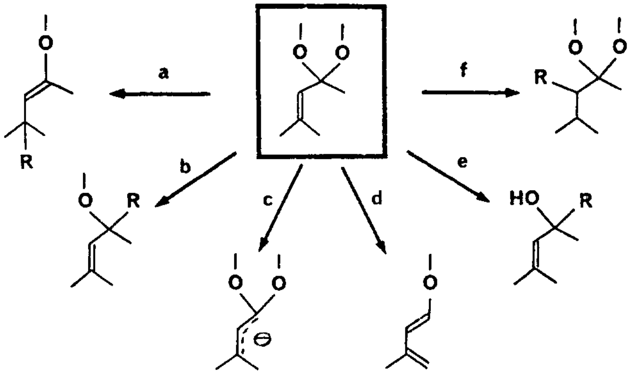
REACTIVITY OF α,β-UNSATURATED ACETALS AND KETALS TOWARD ORGANOLITHIUM REAGENTS IN PENTANE

Charles Mioskowski*
Ecole Nationale Supérieure de Chimie
ERA du CNRS No. 687, Université Louis Pasteur
67008 Strasbourg, France

S. Manna and J.R. Falck*
Department of Molecular Genetics
University of Texas Health Science Center at Dallas
Dallas, Texas 75235 USA

Summary: Depending upon structure and reaction conditions, α,β-unsaturated acetals and ketals react with organolithium reagents in pentane by addition, substitution, or proton abstraction.

Grignard reagents react with α,β-unsaturated acetals and ketals at high temperature (80°-100°C) affording mixtures of vinylic (pathway a) and allylic ethers (pathway b)[1]. Inclusion of copper bromide[2] or titanium tetrachloride[3] allows the selective formation of vinylic (1,4-addition) or allylic (1,2-addition) products, respectively.



In contrast to Grignard reagents, reaction of α,β-unsaturated acetals and ketals with lithium reagents has not been well studied. Exceptions are a brief report of addition[4] to acrolein acetal (pathway b) and its deprotonation[5] (pathway c). Because of our current interest[6] in the preparation of synthetically useful enol ethers[7], we report herein our studies on the reactivity of representative organolithium reagents with α,β-unsaturated acetals and ketals in pentane.

At room temperature, β-unsubstituted ketal or acetals (Table I, entries 1-3) and *trans*-monosubstituted acetals (entry 4) react with a variety of organolithiums via pathway a to give exclusively 1,4-addition products in high yield. The smooth addition of the bulky ^{t}Bu group is particularly noteworthy. The high *trans* stereoselectivity (>90%) with diethyl acetals (entries 2 and 4) complements the *cis* predominance observed by Normant et al[2] using RMgX/CuBr. For dioxolanes, the *trans* selectivity is lower (entry 1). Hydrolysis of the acetal addition products furnishes 3-substituted aldehydes which are otherwise difficult to prepare by cuprate addition to the corresponding α,β-unsaturated aldehyde because of competitive 1,2-addition.

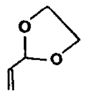
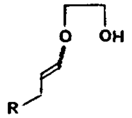
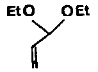
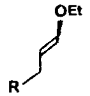
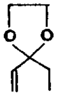
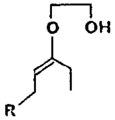
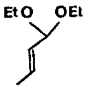
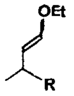
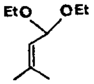
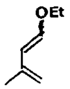
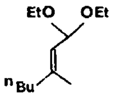
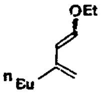
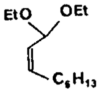
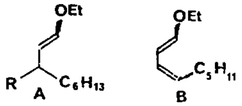
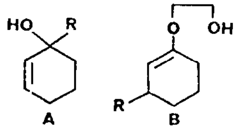
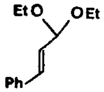
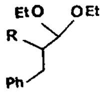
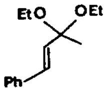
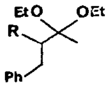
β-Disubstituted acetals (entries 5 and 6) give no evidence of addition and instead undergo apparent regiospecific elimination to 1,4-dienes (pathway d), possibly assisted by chelation of the organolithium with the acetal oxygens. Entry 7 shows that a β-*cis*-monosubstituted acetal is much less reactive than the *trans* isomer (cf. entry 4) and affords a mixture of 1,4-addition and elimination products. Cyclic ketals are also unreactive and behave much like their saturated analogues[8], probably as a consequence of diminished interaction between the ethylene π bond and the C-O bonds. The dioxolane in entry 8 reacts by fragmentation of the ketal leading to the lithium enolate of acetaldehyde and cyclohexenone which then adds alkyllithium (pathway e).

The delicate balance of these reactions can be seen in the case of β-phenyl substituted α,β-unsaturated systems (entries 9 and 10) which favor addition at the α-carbon (pathway f). Similar reactions have been described for styrene systems in which the phenyl can satisfy the resultant negative charge at the benzylic position.

In summary, reaction of α,β-ethylenic acetals and ketals can lead to several types of products depending upon structure and reaction conditions (Scheme I). The order of reactivity of organolithium reagents toward unsaturated acetals and ketals is ^{t}Bu > ^{n}Bu > Ph.

Acknowledgement: Supported in part by a grant-in-aid from the American Heart Association with funds contributed in part by the Texas Affiliate and NATO (RG 158.80).

TABLE 1. Reaction of RLi with α,β-unsaturated Acetals and Ketals in Pentane.

Entry	Substrate	RLi	Equiv	Time, h	Temp. °C	Product	Yield %	E/Z or A/B
1		^{t}Bu	1.1	1	rt		90	76/24
		^{n}Bu	1.1	1	rt		90	78/22
		Ph	1.1	3	rt		80	52/48
2		^{t}Bu	1.3	1	rt		80	92/8
		^{n}Bu	1.3	1	rt		85	92/8
		Ph	1.3	3	rt		87	90/10
3		^{t}Bu	1.1	10	rt		83	
		^{n}Bu	1.5	10	rt		75	
		Ph	1.5	10	rt		68	
4		^{t}Bu	1.1	10	rt		92	97/3
		^{n}Bu	1.3	10	rt		75	90/10
5		^{t}Bu	1.3	3	-5		80	
		^{n}Bu	1.5	1	35		50	
		Ph	1.3	1	35		30	
6		^{t}Bu	2	3	0		85	
		^{n}Bu	1	1	35		70	
		Ph	1	1	35		30	
7		^{t}Bu	2	3	0		70	70/30
		^{n}Bu	2	12	rt		10	10/90
8		^{t}Bu	2.3	3	0		70	75/25
		^{n}Bu	2.3	10	rt		65	100/0
9		^{t}Bu	1.5	2	rt		85	
		^{n}Bu	1.5	2	rt		60	
		Ph	1.5	10	rt		45	
10		^{t}Bu	1.5	2	rt		85	

References:

1. R. Quelet, P. Bergot, and J. D'Angelo, Bull. Soc. Chim. Fr., 3258 (1966); R. Quelet and J. D'Angelo, ibid., 1503 (1967).

2. J.F. Normant, A. Commercon, M. Bourgain, and J. Villieras, Tetrahedron Lett., 3833 (1975); Y. Gendreau and J.F. Normant, Bull. Soc. Chim. Fr., 305 (1979).

3. T. Mukaiyama and H. Ishikawa, Chem. Lett., 1077 (1974).

4. R. Quelet, C. Broquet, and J. D'Angelo, Compt. Rend. Acad. Sci., 264C, 1316 (1967).

5. D. Seyferth, R.E. Mammarella, and H.A. Klein, J. Organometall. Chem., 194, 1 (1980).

6. S. Manna, J.R. Falck, and C. Mioskowski, J. Org. Chem., 47, 5021 (1982).

7. J.E. Baldwin, G.A. Hofle, and O.W. Lever, J. Amer. Chem. Soc., 36, 7125 (1974); C.G. Chavdarian and C.H. Heathcock, ibid., 97, 3822 (1975); E. Wenkert, E. Michelotti, and C.S. Swindell, ibid., 101, 2246 (1979); F.L. Pattison and R.E.A. Dear, Can. J. Chem., 2600 (1963); E. Piers and J.R. Arierson, J. Org. Chem., 42, 3755 (1977); R.K. Boeckman and K.J. Bruza, Tetrahedron Lett., 4187 (1977); O. Riobe, A. Lebouc, and J. Delaunay, Compt. Rend. Acad. Sci., 284C, 281 (1977); T. Mukaiyama and H. Ishikawa, Chem. Lett., 305 (1975).

8. C.H. Heathcock, J.E. Ellis, and R.A. Badger, J. Heterocyclic Chem., 139 (1969).

9. G. Fraenkel and J.M. Geckle, J. Amer. Chem. Soc., 102, 2869 (1980); M.F. Semmelhack, W. Seufert, and L. Keller, ibid., 102, 6584 (1980).

(Received in France 30 September 1983)