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A Novel Rearrangement Induced by the Addition of Organyllithium Reagents to 2,3-Difluoro-4,4-dimethylbut-2-enolide

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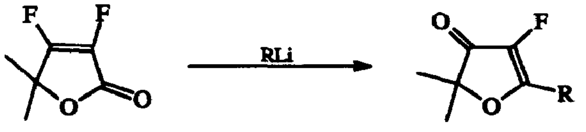
Abstract. Addition of O-nucleophiles and Grignard reagents in the presence of copper(I) bromide-dimethyl sulphide to 2,3-difluoro-4,4-dimethylbut-2-enolide proceeds by 1,4-addition and expulsion of a fluoride anion to give 4-substituted butenolides. Organolithium reagents, however, react to give furan(2H)-3-ones in a novel oxygen rearrangement reaction.

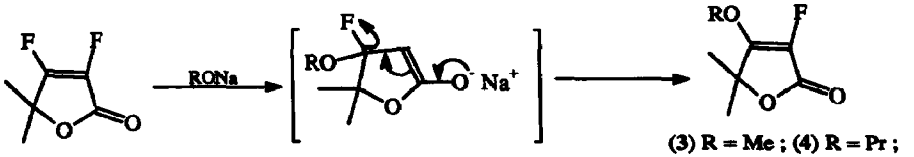
As part of studies targeted to producing fluorine containing chiral lignans by tandem addition methodology[1], we have studied the addition of nucleophiles to the readily available[2], 2,3-difluoro-4,4-dimethylbut-2-enolide (**1**). Consequently we have uncovered a novel rearrangement produced by the action of organolithium reagents on (**1**) and depicted in equation (1).



(**1**) (**2**)

(1)

Oxyanions react with (**1**) to yield monofluorobutenolides such as (**3**) - (**6**) (Table 1), presumably by 1,4-addition followed by fluoride anion expulsion (equation 2). The i.r. and ^{13}C nmr spectra of (**3**) to (**6**) show the presence of the butenolide ring, and the ^{19}F nmr spectra and accurate molecular weight determinations (Table 2) demonstrate the loss of the β-fluorine atom of (**1**) and the addition of the nucleophile



(**1**)

(**3**) R = Me ; (**4**) R = Pr ;
(**5**) R = Bu^t ; (**6**) R = 4-ClC$_6$H$_4$

(2)

We then tested the addition of carbon nucleophiles using copper assisted 1,4-additions of methylmagnesium bromide and phenylmagnesium bromide. These reactions gave butenolides (**7**) and (**8**) as products by 1,4-addition-elimination reactions analogous to those yielding (**3**) to (**6**). (Tables 1,2; equation 3).

(3)

(7) R = Me ; (8) R = Ph .

Table 1

Reactions of (1) with nucleophiles

Exp.	**Nucleophile**	**Product**	**Yield (%)**[a]	**Acc. Mass**
1	MeLi	(2a)	48[b]	144.0587
2	PhLi	(2b)	83[c]	206.0743
3	MeONa	(3)	84[c]	160.0536
4	Pr^{n}ONa	(4)	83[c]	188.0849
5	Bu^{t}ONa	(5)	54[c]	203.1083
6	4-ClC$_6$H$_4$ONa	(6)	72[c]	256.0303
7	MeMgBr.CuBr	(7)	56[c]	144.0587
8	PhMgBr.CuBr	(8)	77[d]	206.0743

[a] All yields are of product purified by distillation[b], l.c.[c], or recrystallisation[d].

Table 2

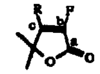
Some spectroscopic data of products (2) to (8)

Compound	δ_F[1]		δ_C[2]		ν_{max}
	C_a	C_b	C_c[3,4]		
(3)	-178.7	164.3	125.2	158.9	1773, 1706
(4)	-177.8	164.5	124.7	158.2	1775, 1703
(5)	-166.5	165.5	122.6	154.8	1773, 1693
(6)	-164.8	163.6	125.6	155.6	1781, 1714
(7)	-153.7	163.9	143.1	142.3	1778, 1744
(8)	-145.2	163.6	142.8	142.1	1776, 1670
(2a)	-187.7	195.2	142.5	173.9	1723, 1642
(2b)	-180.4	195.3	140.9	166.7	1706, 1626

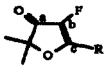
[1] Values in ppm downfield from CFCl$_3$.

[2] Values in ppm downfield from TMS.

[3]

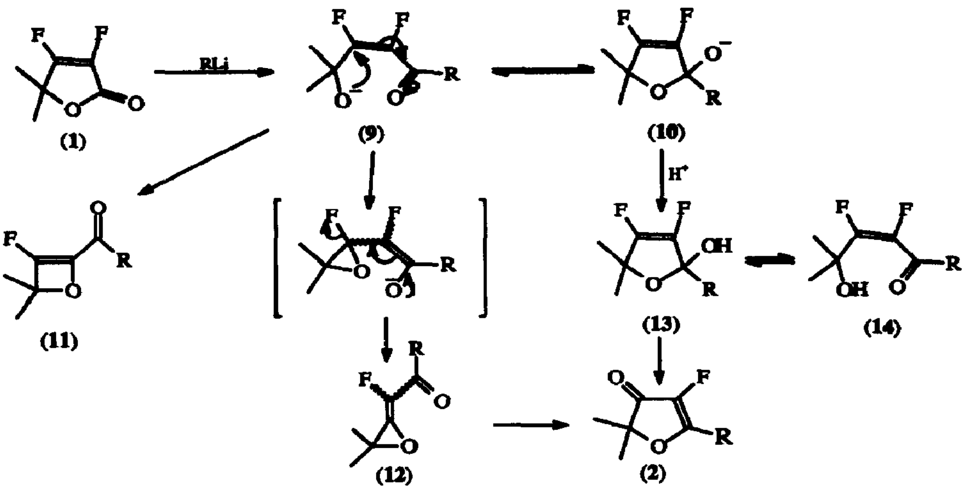


[4]



The reactions of (1) with methyllithium and phenyllithium gave (2a) and (2b) respectively. Compounds (2a) and (2b) were isomeric with products (7) and (8) (Table 1), but did not contain a butenolide ring as shown by the absences of bands at *ca.* 1775-1780cm^{-1} in their i.r. spectra (Table 2). Instead, each contained a ketone group ($\delta_C \sim$ 195 ppm; γ_{max} 1723cm^{-1} (2a), 1706cm^{-1} (2b)). The pattern of the signals in the ^{13}C nmr were similar for the pair (7) and (8) and differed considerably from the pair (2a) and (2b). Attempts to use INADEQUATE experiments to define the connectivity of the chain of four carbon atoms foundered on the long relaxation times and the spread of the signals.

Three types of structure (11), (12) and (2) were considered for products (2a) and (2b) (Scheme 1), all based on 1,2-addition of the organolithium to yield (9) and (10).



Scheme 1

Structures (11) were considered mechanistically less plausible than (12) and were excluded because the ^{19}F nmr signal of (2a) and (2b) corresponded to a fluorine atom α rather than β to the carbonyl group. Compounds (12) would be formed by 1,4-intramolecular oxyanion addition followed by fluoride anion expulsion, similar to the reactions yielding (3) - (6). Protonation of (9) and (10), on work up, would yield (13) and (14). Both (12) and (13) could yield (2) (*vide infra*).

Compounds of general structure (11) (and (12)) correspond to strained enol ethers and would be expected to readily hydrolyse. In fact, the products (2a) and (2b) were unchanged after prolonged reflux with dilute hydrochloric acid in THF. This led us to structures (2a) and (2b), based on the parent structure (2). Eventually compound (2b) was produced as crystals suitable for X-ray analysis, which continued (Figure 1) its structure. The close similarity of (2a) and (2b) allowed the assignment of structure (2a) (equation 1).

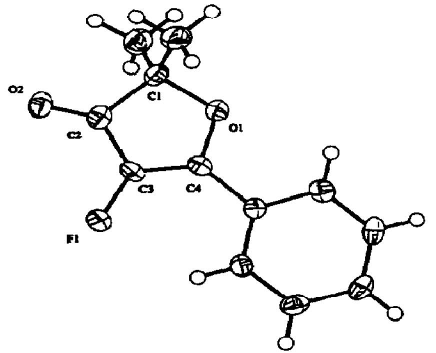
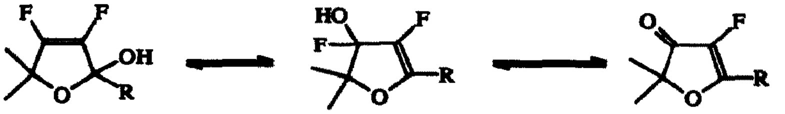


Figure 1

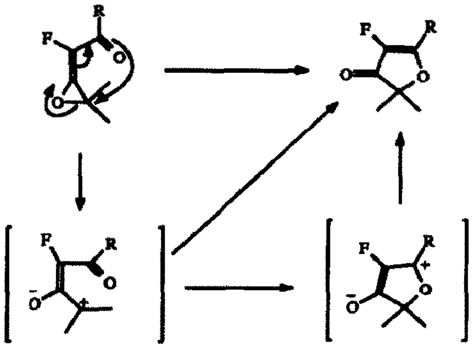
To gather further insight into the plausibility of the pathway leading from (10) to (13) to (2), the reaction mixture derived from the interaction of (1) with phenyllithium was quenched, as usual, with trifluoroacetic acid and then sodium bicarbonate was added immediately afterwards. The mixture was rapidly purified and at once examined by ^{1}H and ^{13}C nmr. It was shown to be a mixture of (13),

(14) and (2b), each readily distinguishable. The nmr tube containing the mixture was allowed to stand for 12h at room temperature, after which the nmr spectra corresponded to (2b) only. Thus compounds of type (13) and (14) can indeed rearrange to those of type (2). The mechanism could involve a precedented[3-5], autocatalytic allylic migration, as shown in equation (4).



(4)

There is also analogy for the rapid rearrangement of alkylidene epoxide (12), which could be produced *during* the reaction, to (2) either by a concerted $[_{\pi}2_s + {}_{\sigma}2_a + {}_{\pi}2_a]$ process or through zwitterionic intermediates (Scheme 2). Similar reactions of butadienylidene epoxides have been studied and used synthetically.[6-11]



Scheme 2

Epoxides such as (12) should be available by the epoxidation of αβ-allenyl ketones and could be studied separately to see whether the postulated rearrangement does, in fact, proceed and if so, *whether it is a new general electrocyclic reaction.*

We are currently attempting to differentiate the various pathways that could lead from (1) to (2).

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References

1. Pelter, A.; Ward, R. S.; Jones, D. M.; Maddocks, P., *J. Chem. Soc., Perkin Trans. 1*, **1993**, 2621.
2. Sendrik, V. P.; Paleta, O.; Dedek, V., *Coll. Czech. Chem. Commun.*, **1977**, *42*, 2350.
3. Sterlin, R. N.; Yatsenko, R. D.; Knunyants, I. L., *Khim. Nauka I. Promy*, **1958**, *3*, 540; *Chem. Abs.* **1959**, *53*, 4195.
4. Tarrant, P.; Johncock, P.; Savory, J., *J. Org. Chem.*, **1963**, *28*, 839.
5. Normant, J. F.; Foulon, J. P.; Masure, D.; Sauvetre, R.; Villieras, J., *Synthesis*, **1975**, 122.
6. Grimaldi, J.; Bertrand, M., *Tetrahedron Lett.*, **1969**, 3269; *Bull. Soc. Chim. Fr.*, **1971**, 957.
7. Bertrand, M.; Dulciere, J.-P.; Gil, G., *Tetrahedron Lett.*, **1977**, 4403.
8. Malacria, M.; Gore, J., *J. Org. Chem.*, **1979**, *44*, 885.
9. Doutheau, A.; Gore, J.; Diab, J., *Tetrahedron*, **1985**, *41*, 329.
10. Kim, S. J.; Cha, J. K., *Tetrahedron Lett.*, **1988**, *29*, 5613.
11. Denmark, S. E., "Comprehensive Organic Synthesis", Ed. Trost, B. M., Fleming, I, Pergamon Press, Oxford, 1991, Vol. 5, p772-775.

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