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ORGANOCUPRATE-INDUCED SUBSTITUTION OF THE ENOL OXYGEN MOIETY IN 2,2-DIFLUORO ENOL PHOSPHATES WITH ALLYL HALIDES: A NOVEL ROUTE TO gem-DIFLUOROOLEFINS FROM CHLORODIFLUOROMETHYL KETONES[1]

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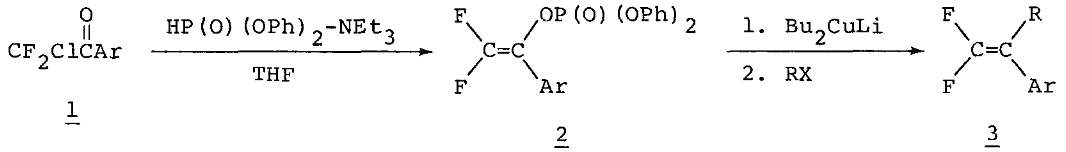
Abstract: 2,2-Difluoro-1-arylethenyl diphenyl phosphates, prepared from chlorodifluoromethyl ketones and diphenyl phosphite, reacted with dibutylcopperlithium and successively with various allyl halides to give allylated *gem*-difluoroolefins in moderate to excellent yields.

The conversion of a ketone into an alkyl-substituted olefin is one of the most important transformations in organic synthesis. Methods developed so far for effecting such a transformation involve catalytic or non-catalytic coupling of enol esters or ethers with organometallic compounds such as organocuprate, organoaluminum, or Grignard reagents.[2,3] In the course of our studies on the synthesis and reactions of fluorinated enols and related compounds,[4] we have found that the reaction of 2,2-difluoro enol phosphates with an organocuprate reagent followed by allylation affords, instead of a coupling product, allylated *gem*-difluoroolefins which are generally synthesized by the difluoromethylenation of aldehydes or ketones using various types of difluoromethylides.[5,6]

This paper describes an effective substitution of the enol phosphate group in 2,2-difluoro enol phosphates with various allyl groups by the use of dibutylcopperlithium. This reaction is, to our knowledge, the first example that provides a novel route to *gem*-difluoroolefins from chlorodifluoromethyl ketones.



When 2,2-difluoro enol diphenyl phosphates 2[7] were treated with dibutylcopperlithium in tetrahydrofuran (THF) containing tetramethylethylenediamine (TMEDA) at -60°C and successively with an excess of allyl halides at the same temperature for 1 h, allylated *gem*-difluoroolefins (3)[8] were obtained in moderate to excellent yields. Among the solvents examined, *i.e.*, THF, diethyl ether, 1,2-dimethoxyethane, and hexane, the highly coordinating THF gave the best results. It was also found that the addition of TMEDA to THF as a cosolvent not

Table I. Preparation of *gem*-Difluoroolefins **3**

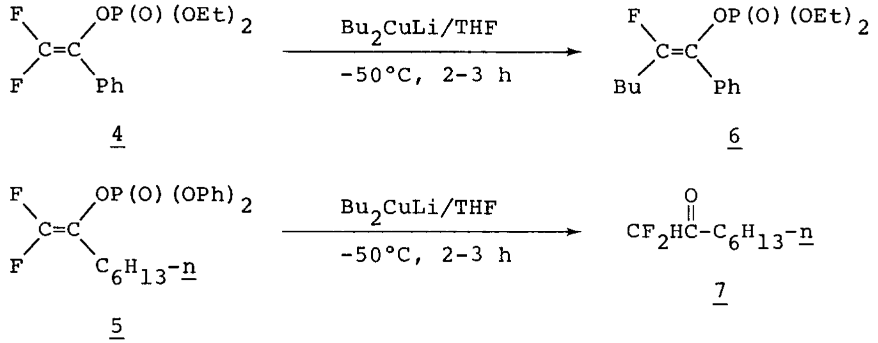
Entry	Ar in **2**	RX	R in **3**	Yield[a] of **3** %
1	C_6H_5	H_2O	H (**3a**)	67
2		$CH_2=CHCH_2Cl$	$CH_2=CHCH_2$ (**3b**)	48[b]
3		$CH_2=CHCH_2Br$	**3b**	79
4		$CH_2=CHCH_2I$	**3b**	88
5		$CH_2=C(CH_3)CH_2Cl$	$CH_2=C(CH_3)CH_2$ (**3c**)	30[c]
6		$CH_2=CHCH(CH_3)Cl$	$CH_3CH=CHCH_2$ (**3d**)	44[d]
7		$CH_3CH=CHCH_2Br$	**3d**	90[b]
8		$PhCH=CHCH_2Br$	$PhCH=CHCH_2$ (**3e**)	70
9		$(CH_3)_2C=CHCH_2Br$	$(CH_3)_2C=CHCH_2$ (**3f**)	73
10	*p*-$CH_3C_6H_4$	H_2O	H (**3g**)	54
11		D_2O	D (**3h**)	53
12		$CH_2=CHCH_2Br$	$CH_2=CHCH_2$ (**3i**)	70

[a] Yields are those of the products purified by column chromatography or distillation. [b] Determined by ^{19}F NMR. [c] The reaction time was 3 h after the addition of methallyl chloride. [d] The product contained a trace amount of the S_N2 product, 1,1-difluoro-3-methyl-2-phenyl-1,4-pentadiene.

only increased the yields of the product **3** but also much improved the reproducibility of the reaction. Out of dibutyl-, dimethyl-, and diphenylcopperlithiums, only dibutylcopperlithium was sufficiently effective for the reaction; neither dimethyl- nor diphenylcopperlithium caused the expected reaction at all, the starting enol phosphates being recovered unchanged. The results of the reaction are summarized in Table I.

To be noted is that no trace of butylated *gem*-difluoroolefins (**3**, R = Bu) was detected in the reaction mixture. This fact is in sharp contrast to those observed in the reaction of fluorine-free enol phosphates or triflates with dialkylcopperlithium, giving alkyl-substituted olefins.[3] Most plausibly, the first step in the present reaction[9] is the formation of a fluorine-containing organocopper intermediate,[10] which can undergo allylation with allyl halides to give the allylated *gem*-difluoroolefin compounds (**3**). The intermediacy of this copper species is also evidenced by the hydrolysis or deuterolysis of the reaction mixture with water or deuterium oxide to produce the corresponding protonated or deuterated product (entries 1, 10, and 11).

For the intermediate-forming reaction to proceed, the stabilization of the carbanionic center due to the aryl and fluorine substituents on the double bond and the sufficient ability of diphenyl phosphate as a leaving group must play an important role. In fact, 2,2-difluoro-1-phenylethenyl diethyl phosphate (4) and 2,2-difluoro-1-hexylethenyl diphenyl phosphate (5) underwent quite different reactions under the same reaction conditions; they gave a high yield of 6[8] and 7,[8] respectively, as shown in the following scheme:



As Table I shows, the yields of the allylated *gem*-difluoroolefins (3) increased in the order: allyl chloride, bromide, and iodide (entries 2-4) as had been expected. More significantly, the allylation reaction was highly regioselective; crotyl, cinnamyl, and prenyl bromide gave the S_N2 product exclusively (entries 7-9), whereas 1-methyl-2-propenyl chloride gave the S_N2' product nearly exclusively (entry 6). The steric hindrance is thought to be the main factor governing the position of attack in the process of allylation; the intermediary organocopper compound attacks the less hindered side of the allyl halides.

The following procedure for entry 3 is typical. Butyllithium (8.2 mmol) in hexane (1.5 M) was added to a solution of cuprous iodide (5.2 mmol) and TMEDA (4.0 mmol) in anhydrous THF (15 ml) under an argon atmosphere at -50°C. To the resulting mixture was dropwise added 2,2-difluoro-1-phenylethenyl diphenyl phosphate (1.0 mmol) in THF (2 ml) at -60°C and, after stirring for an hour, successively allyl bromide (8.0 mmol) at the same temperature. The whole mixture was stirred for an hour. Quenching with a saturated aqueous ammonium chloride solution and a usual workup followed by column chromatography on silica gel gave 1,1-difluoro-2-phenyl-1,4-pentadiene (3b) in 79% yield.

References and Notes

1. Presented at the 10th International Symposium on Fluorine Chemistry, Vancouver, Canada, August 1982, Abstract No. O-52 and at the 3rd Regular Meeting of Soviet-Japanese Fluorine Chemists, Tokyo, Japan, May 1983, Abstract No. 7-1.
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6. The use of 1,1-difluoro-2-oxoalkanephosphonates for preparing *gem*-difluoroolefins has also been described in the reference 5k.
7. A solution of ketone 1 (20 mmol), diphenyl phosphite (20 mmol), and triethylamine (40 mmol) in THF (30 ml) was refluxed for 24 h with stirring. After a usual workup, distillation *in vacuo* or column chromatography on silica gel gave the starting enol phosphates 2 in 75-85% yields.
8. All products were fully characterized on the basis of their spectroscopic analyses.
9. This reaction can be understood as a unique type of exchange between an enol phosphate and an organocuprate reagent, in which an electron transfer may be operative. For the electron transfer in the reaction of organocuprates, see: H. O. House, Acc. Chem. Res., 9, 59 (1976); E. C. Ashby, R. N. DePriest, A. Tuncay, and S. Srivastava, Tetrahedron Lett., 23, 5251 (1982) and see also for the related exchange reactions, H. O. House and M. J. Umen, J. Am. Chem. Soc., 94, 5495 (1972); H. Yamamoto, K. Kitatani, T. Hiyama, and H. Nozaki, ibid., 99, 5816 (1977).
10. The fluorine-containing organocopper intermediate failed to react with alkyl halides or sulfonates in spite of a prolonged reaction time or an elevated temperature (25°C) being used.

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