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PRELIMINARY NOTE

Regioselective Preparation of Difluoromethyl Allenes [1]

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SUMMARY

The difluoromethylcadmium reagent reacts with primary, secondary, and tertiary propargyl chlorides and tosylates regioselectively to give difluoromethyl allenes in good yields.

Recently, we described the preparation of difluoromethylcadmium via direct reaction of bromo- or iododifluoromethane with acid-washed cadmium powder [2].

$$CF_2HX + 2\ Cd \xrightarrow[\text{RT-55°C}]{\text{DMF}} CF_2HCdX + (CF_2H)_2Cd + CdX_2$$

$X = I, Br$

In contrast to the relative inertness of alkyl or aryl cadmium reagents [3,4], the difluoromethylcadmium reagent reacted readily with allylic halides to afford products of both α- and γ-substitution. The enhanced reactivity of this reagent prompted us to investigate other reactions for the regioselective introduction of the difluoromethyl group.

We became interested in the possible synthesis of difluoromethyl allenes from propargylic substrates. Although organometallic reagents have been widely utilized

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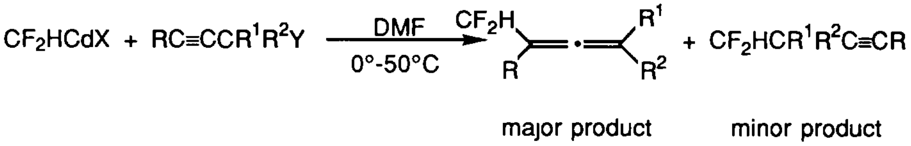
with propargyl substrates to prepare allenes, the only previous report with a perfluorinated organometallic reagent was that of Coe and Milner [5], who reported <10% of 1-(perfluoro-*n*-heptyl)-1,2-propadiene from the reaction of perfluoro-*n*-heptyl copper with propargyl bromide.

However, difluoromethylcadmium reacts with propargyl chlorides or tosylates to regioselectively give difluoromethyl allenes. Table I summarizes our preliminary results.



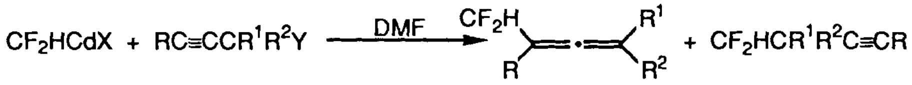
As illustrated in Table I, the major (or exclusive) product of the reaction is substitution at the γ-carbon to give the allene product. Only in the case of 1-bromo-2-butyne, in which steric hindrance to attack at the γ-carbon has been increased, is a significant amount of substitution at the α-carbon (alkyne product) detected. However, even in this example the propensity for γ-attack predominates. The rate of reaction increases with increasing substitution at the α-carbon.

3° propargyl substrates > 2° > 1°

In a typical experimental procedure, a 300 mL three-necked round-bottomed flask fitted with a septum, magnetic stirbar and a nitrogen inlet was charged with an 86 mL aliquot of a 0.70 M difluoromethylcadmium reagent (60 mmol) in DMF. The cadmium reagent was cooled in an ice bath and 10.0 g (68 mmol) of 3-bromo-3-methyl-1-butyne was added dropwise via syringe. After the complete addition of the haloalkyne, the reaction mixture was warmed and stirred overnight at room temperature. The nitrogen inlet was replaced with a vacuum distillation head which was fitted with a 100 mL receiving flask (cooled in liquid nitrogen). The volatile components were removed under vacuum, and washed with an equal volume of ice water. The organic layer was separated, washed with 2 x 100 mL of water and

TABLE I

Reaction of Difluoromethylcadmium Reagent with Propargyl Substrates[a]



I II

R	R^1	R^2	Y	T°C	Yield %[b]	I %	II %
H	H	H	Cl	RT-50°/10 days	41	95	5
H	H	CH_3	Cl	RT/2 days	(84)	100	0
H	H	CH_3	OTs	RT/7 hours	(87)	100	0
H	CH_3	CH_3	Br	0°-RT/O/N[c]	64	100	0
CH_3	H	H	Br	0°-RT/O/N	69	78	22
H	-$(CH_2)_5$-		Cl	0°-RT/O/N	56	70[d]	0

[a] All products gave satisfactory ^{19}F, ^1H, ^{13}C NMR, FT-IR and GC/MS data.

[b] Isolated yields; yields in parentheses are ^{19}F NMR yields.

[c] O/N = overnight.

[d] 30% 3-ethynyl-1-cyclohexene also formed.

dried over 4Å molecular sieves. Distillation through a short path distillation apparatus gave 3.80 g (64%) of 1,1-difluoro-4-methyl-2,3-pentadiene, 100% GLPC purity, bp 77-79°C/atm. pressure. ^{19}F NMR ($CDCl_3$): δ -107.4 ppm (dd, $^2J_{HF}$ =57 Hz, $^3J_{HF}$ =6 Hz); ^1H NMR ($CDCl_3$): δ 1.75 ppm (d, $^5J_{HH}$ =3.0 Hz, 6H), δ 5.21 ppm (td hept; $^3J_{HH}$=6.3 Hz, 1H), δ 6.02 ppm (td, 1H); ^{13}C NMR (neat): $C^aF_2HC^bH{=}C^c{=}C^d(C^eH_3)_2$: δ^a 115.2 ppm (t, $^1J_{CF}$ =236.2 Hz), δ^b 86.6 ppm (t, $^2J_{CF}$ =28.9 Hz), δ^c 204.4 ppm (t, $^3J_{CF}$ =12.4 Hz), δ^d 101.2 ppm (s), δ^e 19.3 ppm (s). FT-IR (CCl_4): 2989 (m), 2948 (m), 2916 (m), 2859 (w), 1978 (m), 1449 (m), 1421 (m), 1367 (m), 1329 (m), 1121 (s), 1055 (s), 1021 (s) cm^{-1}. MS: (m/e, %) M^+, 118 (51.0), 103 (17.8), 97 (12.1), 83 (18.9), 79 (11.8), 77 (32.4), 67 (100.0), 65 (27.3), 57 (12.0), 51 (47.0), 50 (14.2), 41 (55.9).

The ease of preparation of difluoromethylcadmium and the regioselectivity of this reagent in its reactions with propargylic substrates provides a facile entry to difluoromethyl allenes.

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1 G.A. Hartgraves and D.J. Burton, presented in part at the Third Chemical Congress of North America, Toronto, Canada, June 1988, Abstract FLUO #30.
2 G.A. Hartgraves and D.J. Burton, J. Fluorine Chem., 39 (1988) 425.
3 J. Cason and R.J. Fessenden, J. Org. Chem., 22 (1957) 1326.
4 P.R. Jones and S.J. Costanzo, J. Org. Chem., 38 (1973) 3189.
5 P.L. Coe and N.E. Milner, J. Organometal. Chem., 70 (1974) 147.