Communications to the Editor

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PALLADIUM(0)-CATALYZED REACTIONS OF TRIFLUOROMETHYLATED ALLYLIC ESTER DERIVATIVES: SYNTHESIS OF TRIFLUOROMETHYLATED CHRYSANTHEMIC ACID ESTER

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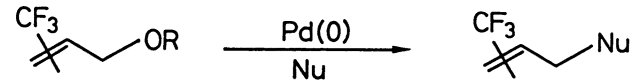
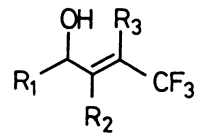
Reactions of the esters of trifluoromethylated allylic alcohol derivatives (1, 2, 3, and 4) with malonate anion in the presence of palladium catalyst and their use in synthesizing trifluoromethylated chrysanthemic acid are described.

KEYWORDS — π -allyl complex; palladium catalyst; trifluoromethyl group; crysanthemic acid; C-C bond formation

Recent advances in the chemistry of carbon-carbon bond-forming reactions of allylic alcohol derivatives with nucleophiles in the presence of a palladium catalyst have indicated new possibilities in the field of synthetic chemistry.[1] The easy availability of trifluoromethylated allylic alcohol derivatives either in racemic or optically active form[2] prompted us to examine the reactivity and the effects of the trifluoromethyl group of trifluoromethylated allylic alcohol derivatives on palladium-catalyzed nucleophilic reactions. In this report, we describe the reactions of the esters (acetate, diethyl phosphate, ethyl carbonate and/or tosylate) of trifluoromethylated allylic alcohols (1, 2, 3 and 4) with sodium dimethyl malonate in the presence of palladium catalyst [$(Ph_3P)_4Pd$ or $(DPPE)_2Pd$], and the synthesis of the trifluoromethylated chrysanthemic acid analog. The results are summarized in Table I.





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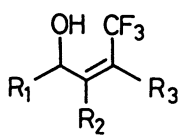

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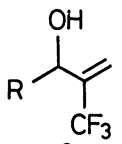

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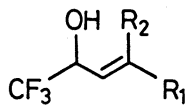


4

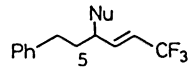
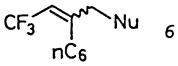
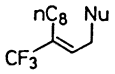
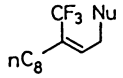
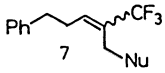
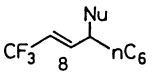
	R_1	R_2	R_3
a:	Ph∼	H	H
b:	H	nC_6H_{13}	H
c:	H	H	nC_8H_{17}

	R_1	R_2	R_3
a:	Ph∼	H	H
b:	H	nC_6H_{13}	H
c:	H	H	nC_8H_{17}

R = Ph∼

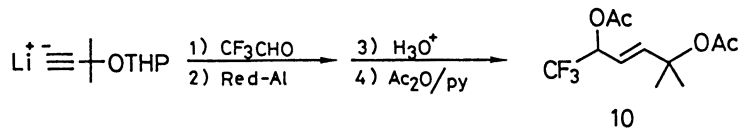
	R_1	R_2
a:	nC_6H_{13}	H
b:	H	nC_6H_{13}

Table I. Reactions of Trifluoromethylated Allylic Esters with $NaCH(COOMe)_2$ in the Presence of Palladium Catalyst[a)]

Entry	Substrate	Ligand	Time(h)	Temp.	Product[c)]	Ratio[d)]	Yield(%)
1	1a(OAc)	PPh_3	0.5	50 °C	 5		91
2	1a(OAc)	DPPE	6	Room temp.	5		93
3	1b(OAc)	PPh_3	53	Room temp.	 6	16/1	90
4	1c(OAc)	PPh_3	30	Reflux			84
5	2a(OAc)	PPh_3	2	50 °C	5		93
6	2a(OAc)	DPPE	6	Room temp.	5		91
7	2b(OAc)	PPh_3	24	Room temp.	6	1/22	94
8	2c(OAc)	PPh_3	15	Reflux			63
9	3(OAc)	PPh_3	2	50 °C	 7	4/1	78
10	3(OAc)	DPPE	3	Room temp.	7	2/1	92
11	4a(OAc)	PPh_3	13	Reflux	No reaction		
12	4a(OAc)	DPPE	7	Reflux			70
13	4a(OCOEt)[b)]	PPh_3	5	Reflux	No reaction		
14	4a(OCOEt)	DPPE	7	Reflux	8		90
15	4a[OP(OEt)$_2$]	PPh_3	1	Reflux	8		92
16	4a[OP(OEt)$_2$]	DPPE	6	Room temp.	8		96
17	4a(OTs)	PPh_3	1	Room temp.	8		99
18	4b[OP(OEt)$_2$]	PPh_3	3	Reflux	8		68

a) A Pd catalyst (5 mol%) in THF was used. The ratio of the substrate to the nucleophile [$NaCH(COOMe)_2$] was 1:1. b) No base was used for generating the malonate anion. c) Stereochemistry was determined by NMR studies (coupling constants of olefinic protons and NOE study). See also ref. 3). Nu; $CH(COOMe)_2$ d) The E/Z ratio was determined by integrating ^{19}F-NMR signals.

The nucleophile attacks the non-trifluoromethylated and less hindered carbon. The regioselectivity reflects the electron withdrawing effect of the trifluoromethyl group in the π -allylic palladium complex.[4] The stereochemistry of the double bond in the product indicates the exclusive or favored formation of the E-isomer, except in the case of the trisubstituted compound (entries 7 and 8). These facts indicate that , in the π -allylic palladium complex, the positive charge leans on the non-trifluoromethylated carbon owing to the electron withdrawing effect of the trifluoromethyl group. It should be mentioned that all of the reaction did not proceed without a palladium catalyst. The effects of the ligand of the palladium catalyst and the ester group are quite evident in the case of allylic alcohol 4 (entries 11-17). This different trend of 4 from that of the others is probably due to the enhanced strength of the carbon-oxygen bond directly bound to the electronegative trifluoromethyl group. Similar observation as to the reactivity of the trifluoromethylated allylic alcohols has been made in the case of the Claisen rearrangement in which allylic alcohols 1, 2, 3 but not 4 underwent rearrangement.[5]



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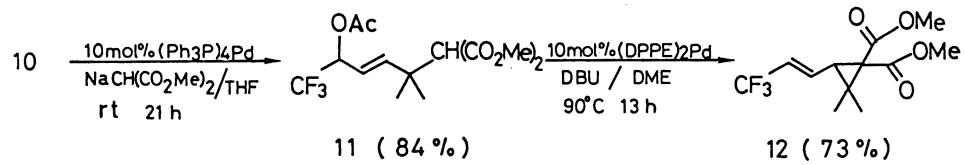
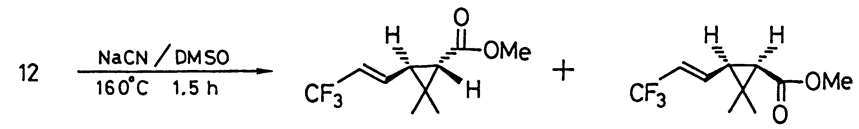


11 (84 %) 12 (73 %)



9a 9b

47 % (1 : 1)

These results were applied to the synthesis of the trifluoromethylated chrysanthemic acid ester (9).[6] Treating diacetate (10) obtained by reacting the lithium acetylide of 2-methyl-3-butyn-2-ol tetrahydropyranyl ether with trifluoroacetaldehyde at -78°C and subsequent trans reduction (Red-Al, THF) and acetylation, with sodium dimethyl malonate in the presence of tetrakis(triphenylphosphine)palladium [$(Ph_3P)_4Pd$] in tetrahydrofuran at room temperature gave a monosubstituted product (11) in 84% yield, as expected.[7] Treating 11 with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) in the presence of bis[1,2-bis(diphenylphosphinoethane)]palladium [$(DPPE)_2Pd$] at 0 °C gave a cyclopropane derivative (12)[8] in 73% yield. Conversion of 12 to 9[9] in 47% yield

was achieved by treatment with sodium cyanide in dimethyl sulfoxide at 160 °C.[10] This synthesis of 9 made it possible to prepare a series of trifluoromethylated chrysanthemic acid derivatives in optically active form, because of the easy availability of optically active trifluoromethylated allylic alcohol.[2] We are now preparing an optically active 9 and other fluoro analogs of crysanthemic acid.

REFERENCES AND NOTES

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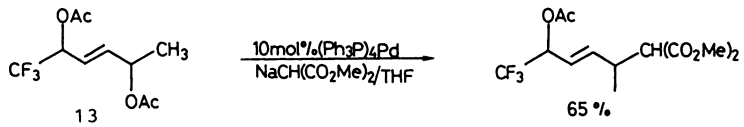
3) Y. Hanzawa, K. Kawagoe, N. Kimura and Y. Kobayashi, Chem. Pharm. Bull., 34, 3953 (1986) and references cited therein.

4) For the regiochemical study of methyl compound; E. Keinan and M. Sahai, J. Chem. Soc., Chem. Commun., 1984, 648.

5) Y. Hanzawa, K. Kawagoe, A. Yamada and Y. Kobayashi, Tetrahedron Lett., 26, 219 (1985) and the unpublished result.

6) P. D. Bently, R. Cheetham, R. K. Huff, R. Pascoe and J. D. Sayle, Pestic. Sci., 11, 156 (1980). The synthesis of chrysanthemic acid derivatives using a palladium catalyzed allylic substitution has been reported. J. Genet, M. Balabane and F. Charbonnier, Tetrahedron Lett., 23, 5027 (1982) and references cited therein.

7) To secure the regioselectivity of 10, we have also examined the following reaction using diacetate 13.



13 65 %

8) ^{1}H-NMR spectrum ($CDCl_3$) δ ; 1.23 (s, 3H, 2-Me), 1.33 (s, 3H, 2-Me), 2.40 (d, 1H, J=10.1, 3-H), 3.74 (s, 3H, OMe), 3.76 (s, 3H, OMe), 5.87 (dq, 1H, J=15.6Hz, J_{H-F}=10.1, 5-H), 6.25 (ddq, 1H, J=15.6 and 10.1Hz, J_{H-F}=2.1, 4-H).

9) A mixture of trans- and cis-isomer (9a and 9b) was obtained in a ratio of 1:1; it was separated by flash column chromatography (CH_2Cl_2:hexane =1:9). 9a: ^{1}H-NMR spectrum ($CDCl_3$) δ ; 1.23 (s, 3H, 2-Me), 1.28 (s, 3H, 2-Me), 1.72 (d, 1H, J=5.3Hz, 1-H), 2.10 (dd, 1H, J=9.3 and 5.3Hz, 3-H), 3.69 (s, 3H, OMe), 5.77 (dq, 1H, J=15.5Hz, J_{H-F}=6.4Hz, 5-H), 6.08 (ddq, 1H, J=15.5 and 9.3Hz, J_{H-F}=2.1Hz, 4-H). 9b: ^{1}H-NMR spectrum ($CDCl_3$) δ ; 1.24 (s, 3H, 2-Me), 1.31 (s, 3H, 2-Me), 1.82 (dd, 1H, J=9.4 and 8.3Hz, 3-H), 1.86 (d, 1H, J=8.3Hz, 1-H), 3.67 (s, 3H, OMe), 5.75 (dq, 1H, J=15.7Hz, J_{H-F}=6.5Hz, 5-H), 6.77 (ddq, 1H, J=15.7 and 9.4Hz, J_{H-F}=2.1Hz, 4-H).

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