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A HIGHLY STEREOCONTROLLED SYNTHESIS OF a-HYDROXYCYCLOPROPANES POSSESSING A TRIFLUOROMETHYL GROUP

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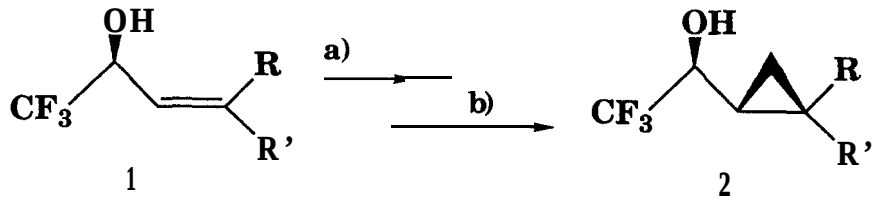
Abstract. The preparation of optically pure syn and anti-α-hydroxy-cyclopropanes possessing a trifluoromethyl group from stereoisomers of optically pure allylic alcohols by samarium-based carbenoids is described.

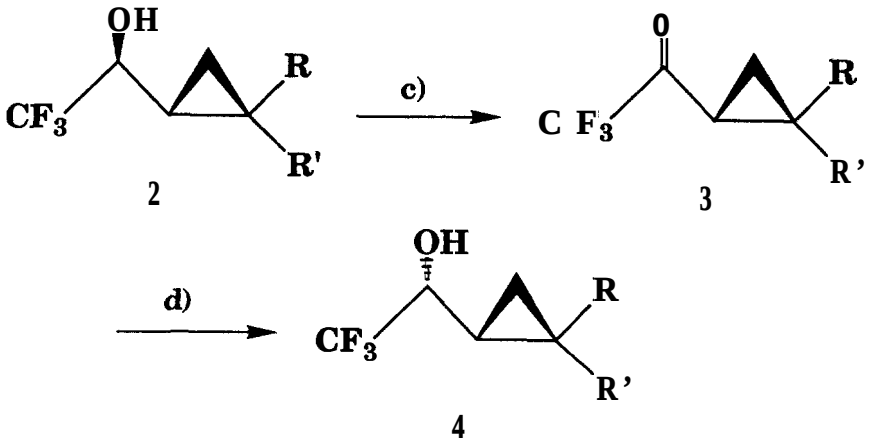
The stereoselective construction of organofluorine compounds is currently of fundamental importance in such fields as the preparation of bioactive materials and ferroelectric liquid crystals[1-5]. In particular, considerable attention is being focussed on the search for synthetic methods for the assembly of contiguous stereocentres with high relative as well as absolute stereocontrol. However, only a few methods are known for the control of stereochemistry of fluorine containing molecules giving the diastereomeric and/or enantiomer anti(erythro) or syn(threo) configuration[6-9].

We report herein the stereocontrolled synthesis of syn and/or anti cyclopropyl carbinols possessing a trifluoromethyl group. We desired a stereochemically controlled synthesis from starting materials of known absolute configuration which would eliminate the need for diastereomeric separation. Therefore, we chose to utilize the hydroxy-directed cyclopropanation[10] of (R)- or (S)-(E)- and/or (R)- or (S)-(Z)-allylic alcohols" possessing a trifluoromethyl group. These substrates were found to have a dramatic effect on diastereoselectivity of the cyclopropanation, giving only syn-isomer via the Houk model shown in Figure I. In our case, we believe that samarium metal is more tightly coordinated with the oxygen atom in the above Houk model, giving rise to the higher diastereoselectivity.

No previous studies have examined the stereocontrolled synthesis of the anti isomers (4). The syn isomers were oxidized with oxalyl chloride-dimethyl sulphoxide, giving the ketones(3) (Scheme). To achieve the desired stereocontrolled conversion to (4), we investigated the transformation of the optically pure cyclopropyl ketones (3), using a variety of reducing reagents. As the consequence, we found that L-selectride gave by far the highest stereoselection. The desired stereocontrolled products were obtained in moderate to good yields (Table).



a) Sm, CH_2I_2, THF, 0°C, 1h b) r.t., 1h



c) $(COCl)_2$, Me_2SO, Et_3N, -50 ⟶ 0°C d) L-selectride, EtOH

Scheme

Table Synthesis of cyclopropyl carbinols

Compd. No (abs)[a]	R	R	Yield (%)	$[\alpha]_D^{20}$ MeOH	NMR chemical shift ^{19}F δ ppm[b]	^1H δ ppm (J : Hz)
2 (R)	H	Ph	87	+57.9 (1.04)	0.82(d)	0.93-l .50(3H,m),2.08(1H,dt,
(S)	H	Ph	60	-46.4 (1.12)		J=6.6,J=5.2), 2.24(1H,d),3.67 (1H,dq,J=12.6),7.25(ArH)
(R)	Ph	H	86	+124.7(1.01)	1.08(d)	0.94-1.29(2H,m),1.46(1H,ddt
(S)	Ph	H	87	-118.9(1.01)		J=6.5,J=8.9,J=8.9),2.12(1H,d), 2.37,3.19(2H),7.29(ArH)
(R)	H	C_6H_{13}	92	+12.2 (1.13)	1.05(d)	0.72-1.57(17H,m),2.48 (1H,
(S)	H	C_6H_{13}	92	-16.7 (1.12)		bs),3.32(1H,J=11.9)
(R)	C_6H_{13}	H	83	+2.90 (1.14)	1.07(d)	0.70-1.89(17H,m),2.28(1H,
(S)	C_6H_{13}	H	89	-2.20 (1.16)		bs),3.52(1H,dq,J=13.1)
4 (S)	H	Ph	46	+13.4 (1.03)	1.03(d)	11.11-1.44(3H,m),2.02-2.12
(R)	H	Ph	38	-9.73 (1,07)		(1H,d,J=5.8),3.58(1H,dq,J= 12.8),7.08-7.32(ArH)
(S)	Ph	H	45	i-23.7 (0.92)	0.75(d)	0.94-l .63(2H,m),1.96(1H,d,J = 4.8),2.39(1H,dt,J=7.5,J=8.3 2.12,3.13(2H),7.37(ArH)
(S)	H	C_6H_{13}	34	+5.70 (0.93)	1.13(d)	0.75-1.68(17H,m),2.49(1H, bs),3.36(1H,dq,J=11.7)
(S)	C_6H_{13}	H	37	+5.31 (1.15)	1.07(d)	0.72-l .85(17H,m)2.43(1H, bs),3.43(1H,dq,J=13.9)

a) absolute configuration at C-l b) δ ppm from ext. CF_3CO_2H in $CDCl_3$

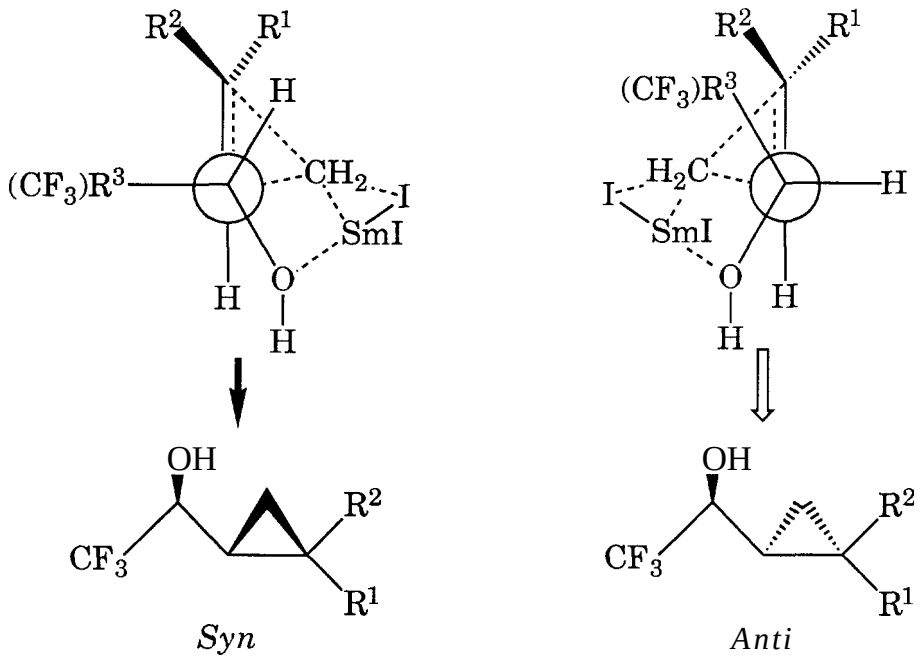


Fig. 1

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