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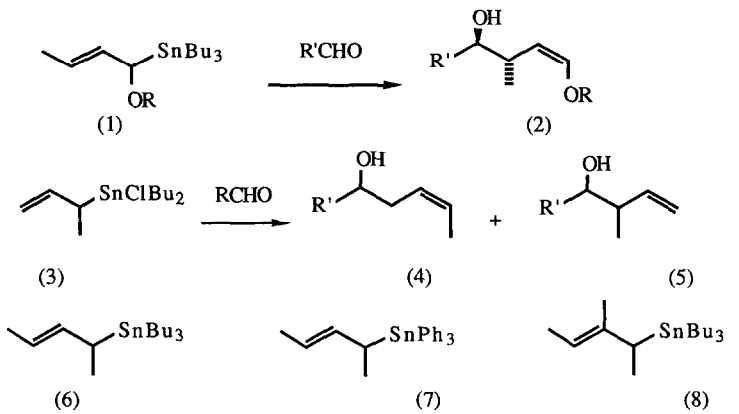
Stereoselective Synthesis of Z-Alkenes from α-Methylcrotylstannanes and Aldehydes

Caroline Hull, Simon V. Mortlock, and Eric J. Thomas*

The Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, U.K.

α-Methylcrotylstannanes (6) - (8) and aldehydes react stereoselectively on heating to give anti-5-hydroxy-4-methyl-Z-pent-2-enes (9) and (10).

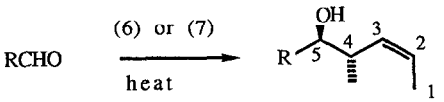
Allylmetal reagents are finding widespread use in organic synthesis.[1] In particular crotylstannanes react stereoselectively with aldehydes to provide syn or anti adducts, the stereoselectivity depending on the conditions.[2] In some cases for α-substituted allyl- and crotylstannanes the newly formed double bond is also introduced stereoselectively, e.g. α-alkoxycrotylstannane (1) on heating with aldehydes gives Z-enol ethers (2),[3] and treatment of aldehydes with the α-methylallylstannane (3), generated in situ from crotyltri-n-butylstannane and n-Bu_2SnCl_2, gave mixtures of adducts (4) and (5) containing predominantly the Z-alkenes (4).[4] We now report analogous reactions of α-methylcrotylstannanes (6) - (8), which provide rapid, highly stereoselective access to anti-5-hydroxy-4-methyl-Z-pent-2-enes (9) and (10).



(1) (2) (3) (4) (5) (6) (7) (8)

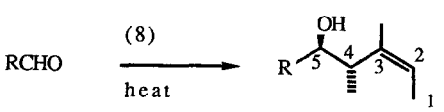
α-Methylcrotylstannanes (6)[5] and (7) were prepared from crotonaldehyde by sequential treatment with MeMgBr, $SOCl_2$, and the corresponding trialkyltin lithium, the trimethylallylstannane (8) being similarly obtained from tiglic aldehyde. The tri-n-butylstannanes (6) and (8) were non-polar oils purified by distillation, b.p.'s 120°C/0.8 mm (6) and 128°C/0.5 mm (8), whereas the triphenylstannane (7) was a crystalline solid purified by flash chromatography and recrystallization from pentane, m.p. 44 - 47°C.

Thermal reactions of stannanes (6) and (7) with aromatic and secondary aliphatic aldehydes and isopropyl glyoxalate, were carried out using a small excess of the stannane at temperatures between 80 - 150°C, neat for stannane (6), or with a small amount of toluene as solvent for stannane (7). Flash chromatography then gave the purified products in the yield shown in the Table. In all cases the reactions were highly stereoselective giving the anti-Z-alkenes (9) containing less than 1% of any other isomer as judged by high field ^1H n.m.r. Examination of the crude reaction mixture from the reaction with benzaldehyde confirmed that essentially just the one anti-Z-alkene (9a) had been formed.



(9a) R = Ph
(9b) R = p-$O_2NC_6H_4$
(9c) R = p-ClC_6H_4
(9d) R = cyclohexyl
(9e) R = i-Pr
(9f) R = i-PrO_2C
(9g) R = PhCH=CH

Benzaldehyde, p-nitrobenzaldehyde, and isobutyraldehyde were similarly reacted with the trimethylallylstannane (8). Again the reactions were very stereoselective (>98%) giving in each case a single product identified as the corresponding anti-Z-alkene (10) after flash chromatography. Qualitatively the trimethylallylstannane (8) was judged to be ca. 10 times as reactive as stannanes (6) and (7).

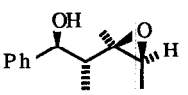


(10a) R = Ph
(10b) R = p-$O_2NC_6H_4$
(10c) R = i-Pr

Table

Aldehyde RCHO R	Stannane	Reaction Conditions Temp. °C	Time. h	Product	Isolated Yield (%)
Ph	(6)	150	18	(9a)	72
p-$O_2NC_6H_4$	"	80	"	(9b)	87
p-ClC_6H_4	"	110	"	(9c)	70
cyclohexyl	"	150	"	(9d)	62
i-Pr	"	150	"	(9e)	55
i-PrO_2C	"	90	"	(9f)	50
Ph	(7)	150	18	(9a)	74
p-$O_2NC_6H_4$	"	80	"	(9b)	80
PhCH=CH	"	150	"	(9g)	67
Ph	(8)	150	18	(10a)	89
p-$O_2NC_6H_4$	"	80	"	(10b)	69
i-Pr	"	150	"	(10c)	50

Structures were assigned to products (9) and (10) on the basis of spectroscopic data and chemical correlation. The cis double-bond geometry of alkenes (9) was supported by the coupling constant across the double-bond ($J_{2,3}$ 11 Hz), and was confirmed by n.O.e. data, e.g. for the benzaldehyde adduct (9a) irradiation of H(1) resulted in 5.1 and 1.8 % enhancements of H(4) and H(5), respectively, but had no effect on H(3). For the trisubstituted alkenes (10) the double-bond geometry was established by n.O.e. studies on epoxide (11) obtained stereoselectively[6] (selectivity ca. 8:1) from the benzaldehyde adduct (10a) by treatment with t-BuOOH/VO(acac)$_2$. The anti-stereochemistry of adducts (9) and (10) at C(4) and C(5) was initially assigned by analogy,[3] and was confirmed for the benzaldehyde adduct (9a) by conversion to the known anti-hydroxy-ester (12)



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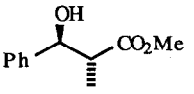
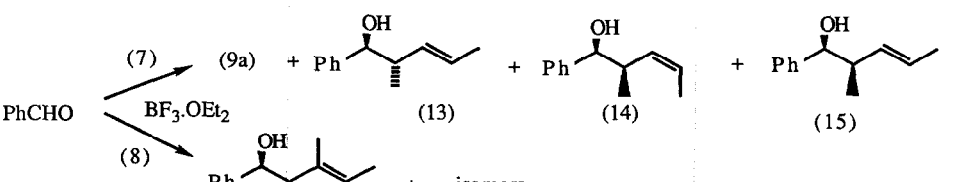
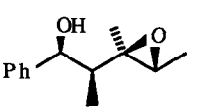


(12)

Lewis acid catalysed reactions of stannanes (6) - (8) and benzaldehyde were also investigated. With $BF_3.Et_2O$ as catalyst, the α-methylcrotylstannanes (6) and (7) gave good yields (60-80%) of products under mild conditions (-78°C, 2h). However these reactions were less stereoselective than the uncatalysed reactions had been, e.g. with (7) a mixture of adducts (9a), (13) - (15) containing predominantly the syn-E-isomer (15), was obtained [(9a):(13):(14):(15) = 6:6:15:73, respectively];[5] other catalysts gave lower yields and/or stereoselectivity. The $BF_3.Et_2O$ catalysed reaction of the trimethylallylstannane (8) and benzaldehyde gave predominantly the syn-E-adduct (16), which accounted for ca. 75% of the product mixture, together with the other three diastereoisomers as minor components. The double-bond geometry of adduct (16) was established by n.O.e. studies on the epoxide (17) prepared stereoselectively using t-BuOOH/VO(acac)$_2$, and ozonolysis gave hydroxyketone (18) which was distinctly different from the anti-hydroxyketone (19) obtained by ozonolysis of thermal adduct (10a). This synthesis of ketones (18) and (19) shows how addition of stannane (8) followed by ozonolysis provides stereoselective routes to ketone aldol products.





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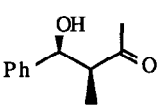

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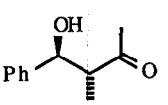
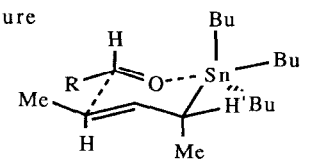


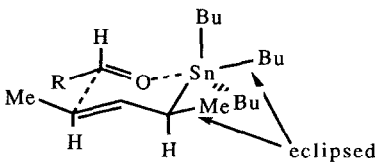
(19)

The stereoselectivity of the uncatalysed reactions between stannanes (6) - (8) and aldehydes is consistent with a six-membered, chair-like, cyclic transition state in which the α-methyl substituent adopts a pseudo-axial position. Analogous stereoselectivity has been observed before for certain α-substituted allylic organometallic reagents including allylboron reagents[7] and the allylstannanes (1)[3] and (3).[4] For α-substituted allylboranes, the stereoselectivity depends upon the nature of the boron and α-substituents,[7,8] with rather low stereoselectivity being observed for an α-methyl group,[9] and has been explained in terms of steric effects involving the boron substituents. Related effects were also invoked to explain the selectivity exhibited by α-methylallylstannane (3) and it was tentatively suggested that the tin is trigonal bipyramidal in the transition state for addition so producing an eclipsed interaction between the α-methyl group and the chlorine substituent on tin if the α-methyl group were to adopt an equatorial position.[4] A similar explanation may be responsible for the stereoselectivity exhibited by stannanes (6) - (8), see Figure, but confirmation of this awaits more detailed knowledge of reaction pathways on tin.[10] However the high stereoselectivities of the uncatalysed reactions between allylstannanes (6) - (8) and aldehydes, simultaneously forming both anti-adducts and cis-disubstituted or Z-tri-substituted double-bonds, suggests that these reactions will find use in synthesis.

Figure



Axial α-methyl leading to Z-alkene product



Equatorial α-methyl leading to E-alkene product

Acknowledgements

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