Stereospecific Protonative Deconjugation of Alkyl 3-Trimethylstannylalk-2-enoates

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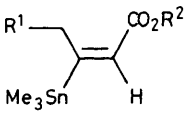
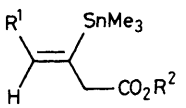
Treatment of the β-trimethylstannyl α,β-unsaturated esters (**3**)—(**8**) with lithium di-isopropylamide in tetrahydrofuran (THF) [(**3**)—(**5**)] or THF–hexamethylphosphoramide [(**6**)—(**8**)], followed, in each case, by transfer of the resultant solution to a cold (−98 °C) solution of acetic acid in ether, provides *exclusively* the alkyl 3-trimethylstannylalk-3-enoates (**9**)—(**14**), respectively.

In connection with a research programme involving the preparation of bifunctional conjunctive reagents and their use in organic synthesis,[1] we have investigated the protonative deconjugation of geometrically isomeric β-trimethylstannyl α,β-unsaturated esters. We report herein that these transformations are *highly stereospecific*. Thus, deconjugation of the (*E*)-esters (**3**)—(**5**) affords *exclusively* the alkyl (*Z*)-3-trimethylstannylalk-3-enoates (**9**)—(**11**), respectively, while the (*Z*)-esters (**6**)—(**8**) give only the products (**12**)—(**14**), respectively.

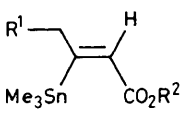
$R^1CH_2C{\equiv}CCO_2R^2$

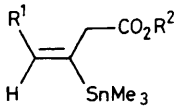
(**1**) $R^1 = CH_2CH_2OSiMe_2Bu^t$, R^2 = Et
(**2**) $R^1 = Pr^c$, R^2 = Me





(**3**) R^1 = Me, R^2 = Et (**9**)
(**4**) $R^1 = CH_2CH_2OSiMe_2Bu^t$, R^2 = Et (**10**)
(**5**) $R^1 = Pr^c$, R^2 = Me (**11**)





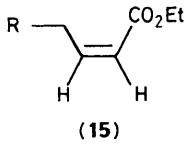
(**6**) R^1 = Me, R^2 = Et (**12**)
(**7**) $R^1 = CH_2CH_2OSiMe_2Bu^t$, R^2 = Et (**13**)
(**8**) $R^1 = Pr^c$, R^2 = Me (**14**)

Pr^c = cyclopropyl

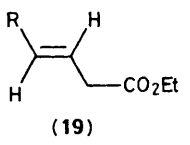
Successive treatment of a tetrahydrofuran (THF) solution of 5-t-butyldimethylsiloxypent-l-yne† with methyl-lithium and ethyl chloroformate provided the ester (**1**) (89%). On the other hand, when a solution of the dianion of propynoic acid (formed by treatment of the parent acid with 2 equiv. of Bu^nLi) in THF–HMPA (hexamethylphosphoramide) was allowed to react with cyclopropylmethyl bromide (1.05 equiv., room temperature, 24 h) and subsequently with methyl iodide (4 equiv., room temperature, 24 h), methyl 4-cyclopropylbut-2-ynoate (**2**) was produced directly (53%). Reaction of the two α,β-acetylenic esters (**1**) and (**2**) with lithium (phenylthio)(trimethylstannyl)cuprate[2a] under appropriate reaction conditions[2b] provided the required β-trimethylstannyl α,β-unsaturated esters (**4**), (**5**), (**7**), and (**8**).

When ethyl (*E*)-3-trimethylstannylpent-2-enoate (**3**)[2b] was allowed to react with lithium di-isopropylamide (LDA) (2.3 equiv.) in THF (−78 °C, 0.5 h; 0 °C, 1 h) and the resulting solution (recooled to −78 °C) was transferred (cannula) to a cold (−98 °C) solution of acetic acid in ether, ethyl (*Z*)-3-trimethylstannylpent-3-enoate (**9**) was produced exclusively (82% yield of purified, distilled product). In similar fashion, the (*E*)-esters (**4**) and (**5**) were converted cleanly and efficiently into the β,γ-unsaturated esters (**10**) (83%) and (**11**) (79%). Careful analysis of the crude products of these reactions showed the complete absence of the geometrically isomeric esters (**12**)—(**14**).

† All compounds reported herein exhibit spectra consistent with assigned structures. New compounds were spectrally characterized and gave satisfactory molecular mass determinations (high resolution mass spectometry).



(15)



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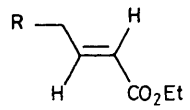
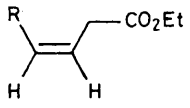


(16) R = Me
(17) R = Pr^n
(18) R = Pr^i

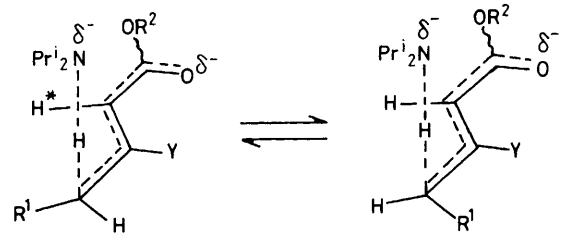


(20)
(21)
(22)

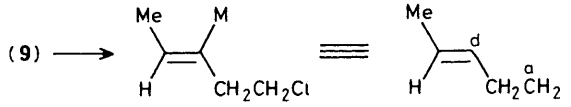
Protonative deconjugation of the (*Z*)-esters (**6**)—(**8**) also occurred with complete stereoselectivity, producing exclusively the alkyl 3-trimethylstannylalk-3-enoates (**12**)—(**14**), respectively (isolated yields 77—87%). The procedure employed for these reactions was very similar to that used for the (*E*)-esters (**3**)—(**5**), except that deprotonation was done with 1.5 equiv. of LDA in THF containing 1.5 equiv. of HMPA. Again, none of the geometrically isomeric deconjugated esters (**9**)—(**11**) could be detected in the crude products.‡

Recently, it was shown,[4] *inter alia*, that protonative deconjungation of ethyl (*Z*)-alk-2-enoates (**15**) produces, highly stereoselectively, the (*E*)-esters (**19**). In contrast, however, it was found that the stereoselectivity associated with deconjugation of (*E*)-alk-2-enoates [*e.g.* (**16**)—(**18**)] decreases markedly as the size of the R group increases. For example, although substrate (**16**) produces exclusively the ester (**20**), deconjugation of (**17**) and (**18**) provides, in each case, a mixture of the possible isomeric products [(**17**) → (**21**) (81%) + (**19**) (R = Pr^n) (13%); (**18**) → (**22**) (62%) + (**19**) (R = Pr^i) (35%)].[4b] Thus, although our results on the deconjugation of esters (**3**)—(**5**) correlate well with those obtained earlier[4] with the structurally simpler substrates (**15**), it is clear that the stereoselectivity associated with the deconjugation of alkyl (*Z*)-3-trimethylstannylalk-2-enoates [*cf.* (**6**)—(**8**)] is more consistent and, in most cases, much higher than that connected with deconjugation of the corresponding esters [*cf.* (**16**)—(**18**)] lacking the Me_3Sn group. This latter difference may be rationalized as follows. It can be (reasonably) assumed that deprotonation of (**6**)—(**8**) and (**16**)—(**18**) occurs *via* one or both of two possible transition states, one of which [represented by (A)] would eventually lead to the products (**12**)—(**14**) and (**20**)—(**22**), while the other [represented by (B)] would ultimately provide the corresponding geometric isomers. When R is small and Y = H [*e.g.* (**16**)], (A) is evidently of lower energy than (B).[4b] However, as R becomes relatively more bulky [*e.g.* (**17**), (**18**)], the non-bonded steric strain between R and H* [see (A)] becomes increasingly important and deprotonation *via* transition state (B) (Y = H) competes significantly with deprotonation *via* (A) (Y = H). In contrast, when Y = $SnMe_3$, the steric strain between R and H* in (A) is offset by non-bonded repulsion between R and Y (= $SnMe_3$) in (B). Thus, apparently, even when R is relatively bulky, deprotonation occurs exclusively by way of transition state (A) (Y = $SnMe_3$) and substrates (**6**)—(**8**) are converted cleanly into the β,γ-unsaturated esters (**12**)—(**14**), respectively.

‡ The stereochemistry of the esters (**9**)—(**14**) was established by means of ^1H n.m.r. spectroscopy (see ref. 3).

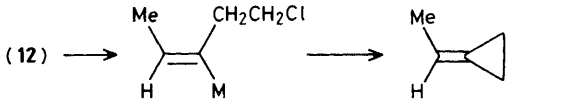


(A) (B)



(23) M = $SnMe_3$
(24) M = Li
(25) M = MgBr

(C)



(26) M = $SnMe_3$
(27) M = Li

(28)

Conversion of the esters (**9**) and (**12**) into the chlorides (**23**) and (**26**), respectively, can be accomplished efficiently *via* standard reactions. Transmetallation (MeLi, THF, −78 °C) of (**23**) affords (**24**), which may be transformed ($MgBr_2$) into the Grignard reagent (**25**). Both (**24**) and (**25**) serve effectively as conjunctive reagents which are synthetically equivalent to the (*E*)-d^3,a^5-pent-2-ene synthon (C). For example, copper(I)-catalysed conjugate addition of (**25**) to enones and subsequent intramolecular alkylation of the resultant products form the basis of a new (*Z*)-ethylidenecyclopentane annulation method.[5] Interestingly, although transmetallation of (**26**) also occurs smoothly, the resultant lithio reagent (**27**) is very unstable and, even at low temperatures (−78 °C), it self-annihilates rapidly to give ethylidenecyclopropane (**28**).[5]

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