Regioselective Germyl–Stannylation of α,β-Acetylenic Esters

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Palladium(0)-catalysed addition of $Bu^n_3SnGeMe_3$ to α,β-acetylenic esters (**1a**—**f**) affords predominantly the (*E*)-2-tri-n-butylstannyl-3-trimethylgermylalk-2-enoates (**2a**—**f**), which serve as effective precursors of synthetically useful, stereochemically defined, tetrasubstituted alkenes.

In connection with our interest in the preparation and synthetic uses of 2,3-dimetallo α,β-unsaturated esters and related substances, in this communication we report that treatment of α,β-acetylenic esters (**1**) with $Bu^n_3SnGeMe_3$ in the presence of a Pd^0 catalyst provides primarily the addition products (**2**) and that the latter materials are effective precursors of stereochemically homogeneous, tetrasubstituted alkenes that are useful intermediates for organic synthesis.

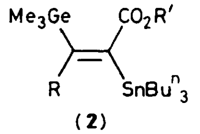
Treatment (neat, 85 °C, 24 h) of ethyl but-2-ynoate (**1a**) with $Bu^n_3SnGeMe_3$†‡ (1.3 equiv.) in the presence of $(Ph_3P)_4Pd$ (0.04 equiv.), followed by column chromatography (silica gel) of the resultant product mixture, afforded compounds (**2a**)§ (61%) and (**3a**) (19%). In similar fashion the α,β-acetylenic esters (**1b**—**f**) were transformed into (**2b**—**f**) (isolated yields 48—56%) and (**3b**—**f**) (14—16%). In each case, the two products were readily separated by column chromatography on silica gel.

The constitution and stereochemistry of (**2**) and (**3**) could be shown by appropriate ^1H n.m.r. decoupling and nuclear Overhauser enhancement (n.O.e.) difference experiments. For example, in the case of (**2b**), irradiation at δ 2.08 (doublet due to Me_2CH) caused collapse of the Me_2CH multiplet (δ 2.33) to a singlet (with satellite peaks due to Sn–H coupling) and showed that $^4J_{Sn-H}$ for the latter signal is 9 Hz, a value typical of coupling between an α-Sn and a *cis* γ-H in an α,β-unsaturated ester. Furthermore, irradiation at δ 0.33 ($GeMe_3$) resulted in enhancement of the signals at δ 3.64 (CO_2Me) and 2.08 (d, Me_2CH), while irradiation at δ 3.64 (CO_2Me) increased the intensity of the $GeMe_3$ singlet (δ 0.33). Similar decoupling and n.O.e. difference experiments showed that in (**3b**) the Bu^n_3Sn and $GeMe_3$ groups have a *cis* relationship, with the latter moiety situated adjacent to the CO_2Me function.

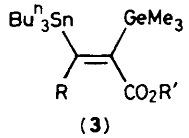
Treatment (THF, −98 °C, 20 min) of (**2a**) with 1.2 equiv. of Bu^nLi effected *clean* transmetallation of the Bu^n_3Sn moiety. Alkylation (MeI, −98 °C, 45 min) of the resultant anion provided the ester (**4a**) (77%). Similarly, use of $H_2C{=}CHCH_2I$, $Me_2C{=}CHCH_2Br$, and $I[CH_2]_3Cl$ as alkylating agents afforded the products (**4b**—**d**), in yields of 81%, 74%,

$R{-}C{\equiv}C{-}CO_2R'$

(**1**)



(**2**)



(**3**)

a; R = Me, R′ = Et
b; R = Pr^i, R′ = Me
c; R = cyclohex-3-enylmethyl, R′ = Me
d; R = $THPO[CH_2]_3$, R′ = Me
e; R = $Cl[CH_2]_5$, R′ = Me
f; R = $Bu^tMe_2SiO[CH_2]_4$, R′ = Me
THP = tetrahydropyran-2-yl

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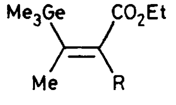
† This reagent was prepared (89%) by reaction of Bu^n_3SnH with lithium di-isopropylamide (LDA) in tetrahydrofuran (THF) (−20 °C), followed by addition of Me_3GeBr.

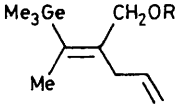
‡ All compounds reported herein exhibited spectra consistent with structural assignments and new compounds gave satisfactory molecular mass determinations (high resolution mass spectrometry).

§ It is highly likely that the geometric isomer of (**2a**) is the initially formed 2-tri-n-butylstannyl-3-trimethylgermylbut-2-enoate. However, this substance would be expected to isomerise to (**2a**) under the reaction conditions (see ref. 1).



(4)

a; R = Me
b; R = $H_2C{=}CHCH_2$
c; R = $Me_2C{=}CHCH_2$
d; R = $Cl[CH_2]_3$



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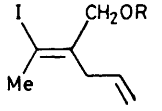
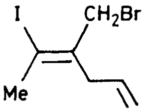


(6)

a; R = H
b; R = $MeOCH_2$



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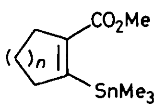
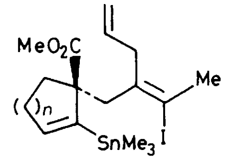
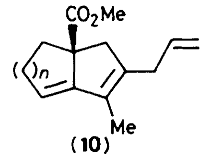


(8)



(9)



(10)

a; n = 1
b; n = 2
c; n = 3

and 42%, respectively. Reduction (Bu^i_2AlH, Et_2O) of (**4b**) gave the alcohol (**5a**) (99%). Reaction of the corresponding methoxymethyl ether (**5b**) with iodine (CH_2Cl_2, room temperature)[2] produced, cleanly and efficiently (83%), the tetrasubstituted alkene (**6b**).¶ On the other hand, treatment of the alcohol (**5a**) with I_2 in CH_2Cl_2 gave (**6a**) (72%), which was readily transformed (Ph_3P, Br_2, CH_2Cl_2, −20 °C to room temperature) into the bromide (**7**).

Alkylation (LDA, THF–hexamethylphosphoramide, −20 °C) of each of the cyclic α,β-unsaturated esters (**8a**—**c**)[1] with the allylic bromide (**7**) gave, in good yields, the corresponding products (**9a**—**c**). Treatment of acetonitrile, solutions of the latter substances with $Pd(OAc)_2$ (5 mol %)–Et_3N (2 equiv.)–Ph_3P (10 mol %) afforded, after reaction times (refluxing MeCN) of 2.5—4 h, the bicyclic triene esters (**10a**—**c**).[3] Interestingly, even the cyclisation of (**9a**) to the notably strained bicyclo[3.3.0]octa-3,5-diene (**10a**) was quite efficient (55%). The yields of (**10b**) and (**10c**) were >80%. While many extensions and modifications to this chemistry can be envisaged, it is already clear that a variety of bicyclic substances possessing highly functionalized heteroannular diene systems are readily prepared *via* the methods described herein. With respect to the possibility of applying these methods to the total synthesis of natural products, the syntheses of functionalized bicyclo[5.3.0]decadienes [*e.g.* (**10c**)] and bicyclo[3.3.0]octadienes [*e.g.* (**10a**)] are particularly noteworthy.

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¶ In a n.O.e difference experiment (^1H n.m.r.), irradiation at δ 2.56 (vinyl Me group) caused enhancement of the signals (m, δ 5.01—5.08, 2H; ddt, δ 5.70—5.82, 1H) due to the vinyl protons.

References

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