Stannyl cyclopropanes by diastereoselective cyclopropanations with (tributylstannyl)-diazoacetate esters catalyzed by Cu(I) *N*-heterocyclic carbene†

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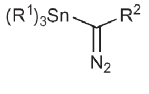
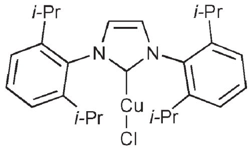
Received (in Bloomington, IN, USA) 15th July 2005, Accepted 23rd August 2005
First published as an Advance Article on the web 19th September 2005
DOI: 10.1039/b509958g

Catalyzed cyclopropanations of alkenes with $Bu_3SnC(=N_2)CO_2R$ (R = Et, *t*-Bu) have been achieved in good yield with excellent diastereoselectivity to make stannyl cyclopropanes having two or three stereocenters, one of which is quaternary.

Cyclopropylstannanes are useful building blocks for organic synthesis, with applications such as tin–lithium exchange reactions, tin–halogen exchanges, cross-couplings, and ring opening reactions.[1] Methods of preparation that are summarized in a recent review include cyclopropanation of vinylstannanes, additions of tin compounds across the double bond of cyclopropenes and methylenecyclopropanes, among others.[1] *Of the methods outlined for the preparation of cyclopropylstannanes in this review, addition of stannyl carbenes to alkenes is clearly the least developed.* The best examples cited are the photochemical decompositions of $Me_3SnC(=N_2)CO_2Et$, **1a**, reported to go in 40–70% yields by Schöllkopf *et al.* in 1972.[2] In the only example reported for a *cis* alkene, diastereoselectivity was poor: with *cis*-2-butene, a 53 : 47 diastereomer ratio (dr) was obtained in 60% combined yield. Our own search of the literature uncovered the rhodium acetate catalyzed addition of $Me_3SnC(=N_2)Ph$, **1b**, to electron-rich alkenes, reported in a 1990 PhD thesis.[3] Since this process produces cyclopropanes having a quaternary stereocenter suitable for further elaboration, it has significant potential for producing new building blocks for organic synthesis.[4,5] As part of a program investigating stereogenic organolithium compounds obtainable by tin–lithium exchange, we decided to reinvestigate cyclopropanations with stannyl carbenes using a transition metal catalyst. Herein, we report that cyclopropanations with $Bu_3SnC(=N_2)CO_2Et$, **1c**, and $Bu_3SnC(=N_2)CO_2t\text{-Bu}$, **1d**, give good yields and 82–⩾95% diastereoselectivity with a variety of alkenes, when catalyzed by Cu(I) *N*-heterocyclic carbene (NHC) **2**.[6–8]



1a: R^1 = Me; R^2 = CO_2Et
1b: R^1 = Me; R^2 = Ph
1c: R^1 = Bu; R^2 = CO_2Et
1d: R^1 = Bu; R^2 = CO_2t-Bu



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Stannyl diazoacetates **1c/d** were prepared by the reaction of commercially available ethyl and *tert*-butyl diazoacetate esters with diethylamino(tributyl)stannane in 87% yield, according to the procedure of Lorberth.[9] Initially, we screened a number of catalysts, solvents, *etc.*, for efficacy in causing carbene addition to olefins, with poor results. Reaction of **1c** with styrene, dihydrofuran, or ethyl vinyl ether, in the presence of $Rh_2(OAc)_4$, $Cu(OTf)_2/PhN_2H_3$, or $PdCl_2$ under a variety of conditions, gave little or no cycloadduct.

Copper carbene complex **2** has been used to catalyze conjugate reductions of α,β-unsaturated ketones and esters,[6] and for the reductive silylation of ketones,[7] and was very recently reported to catalyze O–H and N–H insertions and cyclopropanations using ethyl diazoacetate with no diazo coupling (dimerization) side reactions.[8] Diastereoselectivities in cyclopropanations were low, affording 68 : 32 and 73 : 27 drs with styrene and cyclooctene, respectively. Curiously, **2** did not catalyze the decomposition of ethyl diazoacetate in the absence of substrate (olefin, amine, or alcohol), perhaps indicating an unusual mechanism in which **2** is not the active catalyst.

We chose to optimize the conditions for cycloaddition using styrene as a substrate. Under the conditions reported by Fructos, *et al*, (CH_2Cl_2, rt, 3 h),[8] no reaction occured. Optimization studies revealed that both a chlorinated solvent and elevated temperature are required. Thus, when **1c** is allowed to react with 4 mol% **2** in the presence of styrene (**3**, R = H) and dichloroethane at 80 °C for 3 h, a 67% yield of cycloadduct is formed as a 93 : 7 ratio of diastereomers, eqn (1). The relative configuration of the major diastereomer was determined by 2D NOESY NMR, which revealed cross peaks between the butyl protons and the aromatic protons, and no cross-peaks between the ester methylene and benzylic methine protons. When a 3 : 1 mixture of diastereomers **4** and *epi*-**4** (R = Et, R′ = H) is treated with DibalH, only the major diastereomer is reduced to **5** (72% corrected yield, plus 32% recovered *epi*-**4**), which can be protected as its MOM derivative **6** (81% yield). In both **5** and **6**, NOESY crosspeaks between the OCH_2 protons and the benzylic cyclopropyl proton further confirmed the configurational assignment.

Using these optimized conditions, several other styrenes and vinyl ethers were tested, with the results shown in Table 1. Cyclopropanation of styrene worked equally well with either the ethyl (**1c**) or *tert*-butyl (**1d**) (tributylstannyl)diazo esters, but with somewhat lower diastereoselectivity in the latter case. To evaluate electronic effects, four *para*-substituted styrenes were evaluated with **1c**. All gave reasonable yields of cyclopropanes. Two styrenes, **3** (*p*-CH_3,and *p*-CF_3) gave similar diastereoselectivities. With *para*-methoxystyrene, only one diastereomer was detectable

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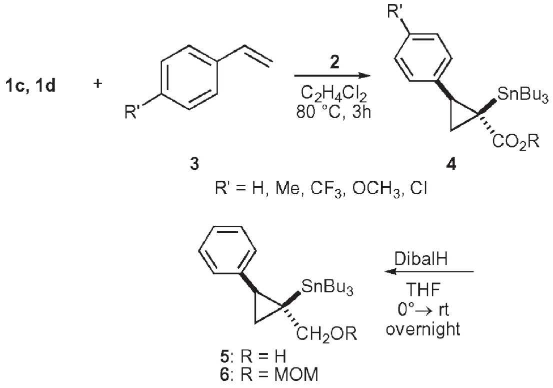
† Electronic supplementary information (ESI) available: Further experimental details. See http://dx.doi.org/10.1039/b509958g



(1)

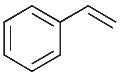
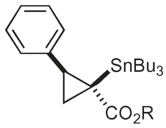
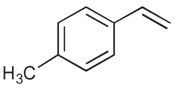
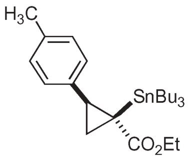
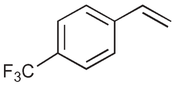
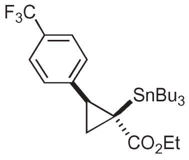
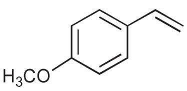
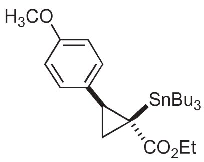
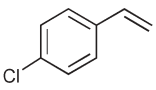
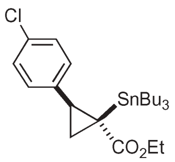
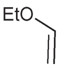
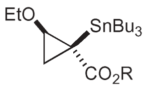
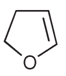
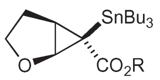
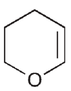
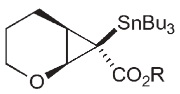
by NMR; *para*-chlorostyrene gave lower selectivity (83 : 17). These drs are subject to some error due to inaccuracies in NMR integration, and small differences should not be overinterpreted.

Three vinyl ethers were tested, with the results summarized in entries 7–12. Consistent with the fact that *para*-methoxystyrene showed high diastereoselectivity, only a single diastereomer could be detected in the cyclopropanation of these substrates. Note that similar yields and diastereoselectivities were recorded for additions of either **1c** and **1d** to the three vinyl ethers (entries 7–12).

In all cases, the major diastereomer had the aryl or alkoxy substituent *cis* to the tributylstannyl group, as determined by crosspeaks in the NOESY NMR.

In conclusion, we have shown that copper NHC catalyst **2** effects cyclopropanation of tributylstannyl diazo acetate esters. Noteworthy in these experiments is the complete suppression of diazo couplings, such that slow addition of diazo ester is not necessary, and that high diastereoselectivities are achieved. The cyclopropanes produced have two or three stereocenters, one of which is quaternary and suitable for electrophilic substitution.

Table 1 Cyclopropanations of stannyl diazoesters catalyzed by Cu(I) NHC carbene **2**‡. Diastereomer ratios (drs) were determined by NMR and are ±5%

Entry	Diazo	Alkene	Product	Yield	dr
1 **2**	**1c** **1d**			67 (R = Et) 65 (R = *t*-Bu)	93 : 7 82 : 18
3	**1c**			65	90 : 10
4	**1c**			58	82 : 18
5	**1c**			64	⩾95 : 5
6	**1c**			50	83 : 17
7 **8**	**1c** **1d**			71 (R = Et) 66 (R = *t*-Bu)	⩾95 : 5 ⩾95 : 5
9 **10**	**1c** **1d**			56 (R = Et) 58 (R = *t*-Bu)	⩾95 : 5 ⩾95 : 5
11 **12**	**1c** **1d**			63 (R = Et) 62 (R = *t*-Bu)	⩾95 : 5 ⩾95 : 5

This work was supported by the US National Institutes of Health (GM 56271). Core facilities were funded by the NIH (P20 R15569) and the Arkansas Biosciences Institute. We are grateful to Professor Steve Nolan (University of New Orleans) for a helpful discussion and for a gift of catalyst **2**.

Notes and references

‡ General experimental procedure: A mixture of **2** (19 mg, 0.04 mmol), **1** (1 mmol), 2 mL alkene, and 0.5 mL $ClCH_2CH_2Cl$ were heated at 80 °C (bath temperature) for 3 h. After concentration at reduced pressure, the product(s) were isolated by silica gel chromatography using 50 : 1 hexane–ethyl acetate as eluent. All compounds were characterized by 1D ^1H and ^{13}C, HMQC, DEPT-135, COSY, and NOESY NMR, IR, MS, and combustion analysis.

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