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A New Palladium-Catalyzed Phenyl-Alkene Bond Formation

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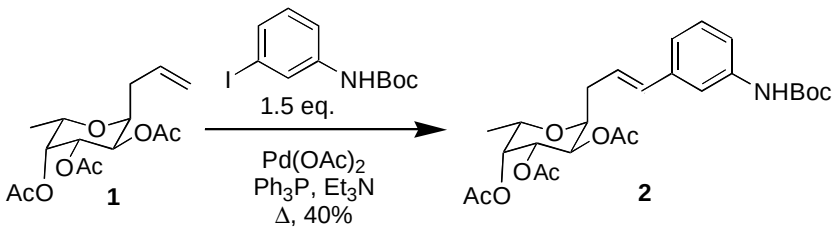
Abstract: A new method of palladium-catalyzed phenyl-alkene bond formation is reported. This reaction involves transfer of all three phenyl groups from triphenylantimony onto alkenes containing allylic protons.

Keywords: C-C bond formation, palladium catalysis.

Introduction

During the course of ongoing activities toward the preparation of the inflammatory sialyl Lewis-X peptidomimetics [1], it became desirable to accomplish the transformation of alkene **1** [2] into the substituted compound **2**, obtained in moderate yield via a Heck reaction (Scheme 1). During attempts to optimize the yield by changing the catalyst and the ligand, unexpected products were obtained. This report describes a previously unreported outcome of the Heck reaction in the presence of triphenylantimony.

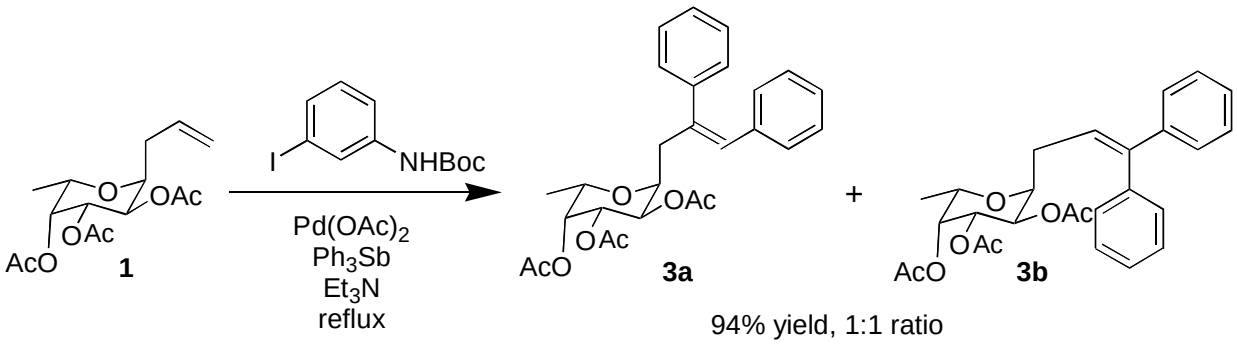
Scheme 1



Results and Discussion

In an attempt to improve the yield of the above transformation the triphenylphosphine ligand was replaced by either triphenylarsenic or triphenylantimony. The reaction with triphenylarsenic gave no significant products; when, however, the reaction was performed with triphenylantimony a new, unexpected product was obtained in high yield (94%), which was found to involve transfer of phenyl groups from the antimony to the alkene (Scheme 2).

Scheme 2

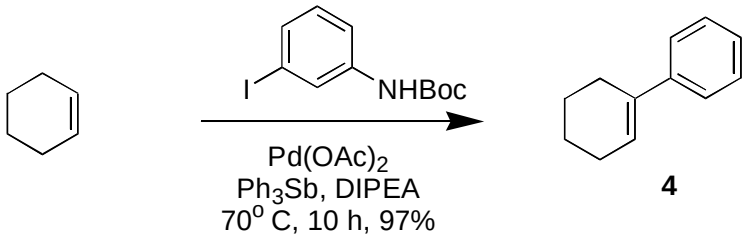


The structures of the products were elucidated by ^{1}H-NMR and mass spectral analysis. The use of a catalytic amount of triphenylantimony in the first attempt gave low yields, while stoichiometric quantities gave systematically higher yields. No mono-substituted compounds were detected. Using substoichiometric amounts of triphenylantimony resulted in formation of diphenyl-compounds **3a** and **3b** in nearly quantitative yield (based upon the triphenylantimony), thus suggesting the possible transfer of all three phenyl groups. The geometrical configuration of the products results (presumably) from an initial *trans* mono-phenylation, with the second phenyl group then being added at either remaining position.

This transformation is not completely without precedent, as examples of phenyl transfer from phosphorus [3-4], arsenic [5] and antimony [6] have all been reported, albeit usually with specially generated pentacoordinated species. However, this process seems to be unique in its chemoselectivity and ease of implementation.

In order to further explore the usefulness of this reaction, we then examined its application to other substrates, finding that it could not be applied to alkenes not bearing an allylic hydrogen, such as styrenes. It was also surprising to find that the 3-iodo-*N*-Boc-aniline, while not present in the product, was required for the reaction to proceed, and is consumed in the reaction. In a simpler example cyclohexene was treated under these conditions to yield the known compound 1-phenyl-1-cyclohexene (**4**) in excellent yield (Scheme 3). Comparison of the data for **4** with published spectral data [7] confirmed the authenticity of the product.

Scheme 3



To the best of our knowledge, this constitutes the first transfer of phenyl groups from antimony onto an unactivated alkene under such conditions. A procedure published by Kawamura *et al*. [3] provides a similar transformation, but under more stringent conditions, with reaction only on terminal alkenes and with very poor yields, and the reactions are accompanied by various rearrangement products. Treatment of cyclohexene under the conditions of Kawamura *et al*. gave no reaction after 24 h.

Conclusions

We have presented a simple method for introduction of phenyl groups onto unactivated alkenes in high yield. The scope and further applications of this process are under investigation.

Experimental

General

^{1}H- and ^{13}C-NMR spectra were obtained using a Bruker AMX 500 NMR and were recorded at 500 and 125 MHz respectively. All reagents and chemicals were obtained from Aldrich Chemical Company (Canada) and were used as received unless otherwise noted.

Preparation of **3a** *and* **3b**: Compound **1** (10.5 mg, 0.0335 mmol) was treated with triphenylantimony (23.7 mg, 0.067 m mol, 2 eq.), 3-iodo-*N*-Boc-aniline (16.0 mg, 0.0503 mmol), $Pd(OAc)_2$ (0.8 mg, 3.5 μmol), and triethylamine (1 mL), and refluxed for 5 hours. The reaction mixture was evaporated under reduced pressure, and the residue chromatographed on silica gel, using 4:1 hexane-ethyl acetate as eluent, giving 14.7 mg (94%) of a colorless oily semi-solid. ^{1}H-NMR showed it to be a 1:1 mixture of the 2',3'- and the 3',3'-disubstituted isomers. An excess of 3-iodo-*N*-Boc-aniline was used since this reaction was intended to provide Heck coupling, thus requiring stoichiometric amounts of the aryl halide. *Spectral Data:* MS (ESI) for $C_{27}H_{30}O_7$: 467 (M+H); **3a**: ^{1}H-NMR ($CDCl_3$) δ: 7.4-7.0 (10H, m, Ar-H), 6.75 (1H, s, H-3'), 5.26 (1H, dd, $J_{1,2}$ = 8.8 Hz, $J_{2,3}$ = 10.3 Hz, H-2), 5.15 (1H, dd, $J_{3,4}$ = 3.3 Hz, $J_{4,5}$ = 0.8 Hz, H-4), 5.05 (1H, dd, $J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 3.4 Hz, H-3), 4.21 (1H, m, H-1), 4.02 (1H, dq, $J_{4,5}$ = 0.8 Hz, $J_{5,6}$ = 6.4 Hz, H-5), 3.10 (1H, dd, $J_{1,1'}$ = 10.6 Hz, $^{2}J_{1',1'}$ = 14.7 Hz, H-1'), 2.85 (1H, dd, $J_{1,1'}$ = 3.6 Hz, $^{2}J_{1',1'}$ = 14.8 Hz, H-1'), 2.12, 1.95, 1.91 (9H, 3s, CO-CH_3), 1.13 (3H, d, $J_{5,6}$ = 6.4 Hz) (Note:

certain assignments may be reversed); ^{13}C-NMR ($CDCl_3$) δ: 170.5, 170.0, 169.9 (C=O), 144.0, 142.1, 139.7 (4º C=C), 130.9 (C-3'), 129.6, 128.5, 128.4, 127.3, 127.2, 126.0 (Ar-C), 73.2 (C-1), 70.7 (C-2), 70.6 (C-4), 70.4 (C-3), 65.9, (C-5), 26.5 (C-1'), 20.8, 20.6, 20.6 ($COCH_3$), 16.1 (C-6); **3b**: ^{1}H-NMR ($CDCl_3$) δ: 7.4-7.0 (10H, m, Ar-H), 6.2-6.0 (1H, m, H-2'), 5.26 (1H, dd, $J_{1,2}$ = 8.7 Hz, $J_{2,3}$ = 10.3 Hz, H-2), 5.15 (1H, dd, $J_{3,4}$ = 3.3 Hz, $J_{4,5}$ = 0.8 Hz, H-4), 5.05 (1H, dd, $J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 3.4 Hz, H-3), 4.33 (1H, m, H-1), 3.63 (1H, dq, $J_{4,5}$ = 0.8 Hz, $J_{5,6}$ = 6.4 Hz, H-5), 2.7-2.4 (2H, m, H-1'), 2.03, 1.92, 1.88 (9H, 3s, CO-CH_3), 1.09 (3H, d, $J_{5,6}$ = 6.4 Hz); ^{13}C-NMR ($CDCl_3$) δ: 170.4, 170.0, 169.6 (C=O), 142.9, 139.8, 137.7 (4º C=C), 128.5, 128.4, 128.1, 127.2, 126.9, 125.4 (Ar-C), 124.4 (C-2'), 71.9 (C-1), 68.5 (C-3), 68.4 (C-2), 68.1 (C-4), 65.6 (C-5), 25.9 (C-1'), 20.7, 20.6, 20.5 ($COCH_3$), 15.2 (C-6).

1-Phenyl-1-cyclohexene (**4**): A screw-cap test tube was charged with cyclohexene (0.5 mL), diisopropylethylamine (0.5 mL), triphenylantimony (63.3 mg, 0.179 mmol, 0.537 mmol phenyl groups), palladium acetate (10.1 mg, 0.045 mmol), and 3-iodo-*N*-Boc-aniline (17.1 mg, 0.0535 mmol). The tube was sealed and heated at 70° C on a water bath for ten hours. The resulting black suspension was then carefully evaporated under reduced pressure, and the residue brought up in pentane (20 mL). The pentane phase was then washed with 6 N HCl (2 x 20 mL), dried over sodium sulfate, filtered and carefully evaporated to a yellow oil. The oil was then chromatographed on silica gel using pentane as eluent to give **4** (83 mg, 97 % based on triphenylantimony) as a clear, colorless oil. The NMR and mass spectra of this oil matched those published in the literature for **4** [7]

References and Notes

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Sample Availability: Available from the authors.