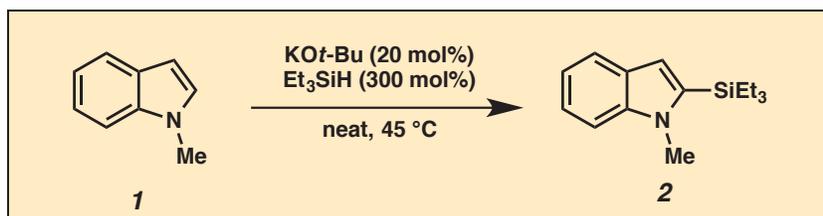


## Potassium *tert*-Butoxide–Catalyzed Dehydrogenative Cross-Coupling of Heteroarenes with Hydrosilanes

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Checked by Jose M. Medina and Neil K. Garg



### Procedure

A. *1-Methyl-2-(triethylsilyl)-1H-indole* (2). An oven-dried 100-mL round-bottom Schlenk flask is equipped with a Teflon-coated magnetic stir bar (25 x 8 mm) and capped with a rubber septum (Note 1). The side arm of the flask is connected to Schlenk line and the flask is cooled to room temperature under vacuum and back-filled with nitrogen. Potassium *tert*-butoxide (1.34 g, 12.0 mmol, 0.2 equiv) is added to the flask under positive nitrogen flow (Notes 2 and 3), and then the flask is evacuated and back-filled with nitrogen three times. *N*-Methylindole (7.48 mL, 7.86 g, 60.0 mmol, 1.0 equiv) and triethylsilane (28.6 mL, 20.82 g, 179.5 mmol, 3.0 equiv) are added sequentially via syringe through the septum, resulting in a yellow heterogeneous mixture (Figure 1). After the septum is replaced with a glass stopper (Note 4), the reaction mixture is degassed (Note 5) and stirred at 45 °C for 76 h (Note 6), resulting in a dark purple solution. The heating bath is removed and the reaction mixture is allowed to cool to ambient temperature (~25 °C), then anhydrous diethyl ether (30 mL) is added



Figure 1. Reaction vessel prior to degassing

slowly while stirring (Note 7). The reaction mixture is filtered through a silica pad (Note 8) into a 500-mL round-bottom flask as a clear yellow solution. The reaction flask is rinsed with diethyl ether (3 x 10 mL) and transferred to the top of a silica pad. The silica pad is washed with diethyl ether (3 x 40 mL) and the combined filtrates are concentrated *in vacuo* using a rotary evaporator to give an orange liquid (Note 9). This liquid is transferred to a 50-mL round-bottom flask, and diethyl ether (3 x 5 mL) is used to assist the transfer. The resulting solvents are concentrated *in vacuo* using a rotary evaporator (Note 9) and put under high vacuum (ca. 0.03 mmHg) for 30 min. An egg-shaped magnetic stir bar (16 x 6 mm) is added to this flask



Figure 2. Vacuum distillation apparatus

and a distillation apparatus with a thermometer installed at the distillation head is attached (Figure 2). The product 1-methyl-2-(triethylsilyl)-1*H*-indole 2 (10.34–10.55 g, 70–72% yield) is isolated by vacuum distillation as a pale yellow oil (Figure 3) (Notes 10 and 11).

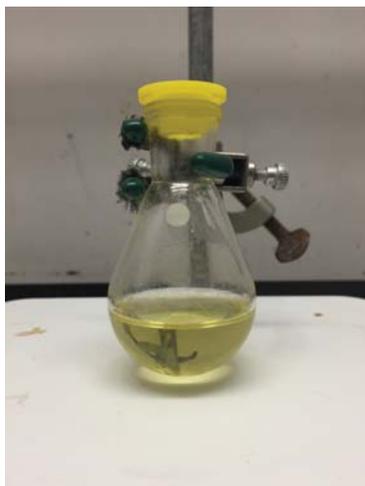


Figure 3. Product (2), a pale yellow oil

## Notes

1. The flask and stir bar are dried in a 120 °C oven for 2 days before use. To limit the possibility of contamination from adventitious transition metal species, a brand-new stir bar is used for each reaction.
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3. Potassium *tert*-butoxide (KO*t*-Bu) is hygroscopic and kept in a desiccator or a glove box. It should be manipulated as quickly as possible to avoid hydrolysis.
4. The Schlenk flask is uncapped and quickly capped with a lightly greased glass stopper (oven-dried and cooled down in a desiccator) under a positive stream of nitrogen.

- Freeze-pump-thaw cycles (x 4 times) are used for degassing: 1) close the sidearm stopcock and leave the attached hose of the Schlenk line on vacuum; 2) put this flask into liquid nitrogen until the mixture is frozen, open the stopcock to vacuum and pump off atmosphere for 10 min; 3) close the stopcock and thaw the mixture in an *i*-PrOH bath until it just melts; 4) repeat steps (2) – (3) for 4 cycles, and 5) fill the flask with nitrogen gas.
- An oil bath is used for heating. The mixture is stirred at 800 rpm throughout the reaction.
- Caution:* Gas bubbles through the liquid vigorously.
- Silica pad (diameter: 4 cm, height: 3 cm) is packed with silica gel (10 g). The silica gel is purchase from Silicycle (SilaFlash P60, 60 Å, 40–63 μm).
- Rotary evaporation is performed at 25 mmHg and 25 °C.
- Vigorous stirring (700 rpm) and full vacuum are maintained throughout the distillation. The condenser is cooled with ice-water (using a circulating ice-water pump), and a liquid nitrogen cold trap is connected between the distillation apparatus and high vacuum pump (see Figure 2 for setup). The checkers used chilled water (from the fume-hood faucet) to cool the condenser. Distillation procedure: 1) The oil bath is heated to 85 °C slowly. When the vacuum stabilizes around 0.24 mmHg (submitters pressure reading = 0.1 mmHg), a forerun comes off as a colorless liquid and the thermometer reads 23–28 °C.; 2) When the drip rate decreases, the heating bath is increased to 140 °C and more undesired liquid comes over at 0.24 mmHg (submitters pressure reading = 0.08 mmHg) when the thermometer reads ~70 °C; 3) Again, as the drip rate decreases, the heating bath is increased to 165 °C, and when the vacuum is lowered to 0.23 mmHg (submitters pressure reading = 0.07 mmHg), desired 1-methyl-2-(triethylsilyl)-1*H*-indole (**2**) product is isolated in a separate receiving flask (100–110 °C) as a pale yellow oil (Figure 3).
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## Discussion

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We have established a method for such a dehydrogenative cross-coupling reaction using potassium *tert*-butoxide as a catalyst that provides a unique way to access a wide array of heteroarylsilanes.<sup>14,15</sup> As described above, the desired silylation product **2** was obtained in good yield (70–72%). This procedure features readily available and inexpensive starting materials, mild reaction conditions, and good functional group tolerance.

The procedure reported here is applicable to a range of heteroarenes and hydrosilanes, giving access to synthetically valuable heteroarylsilanes on multi-gram scales.<sup>14,15</sup>

## References

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### Appendix

#### Chemical Abstracts Nomenclature (Registry Number)

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Brian M. Stoltz was born in Philadelphia, PA in 1970 and obtained his B.S. degree from the Indiana University of Pennsylvania in Indiana, PA. After graduate work at Yale University in the labs of John L. Wood and an NIH postdoctoral fellowship at Harvard with E. J. Corey, he took a position at the California Institute of Technology. A member of the Caltech faculty since 2000, he is currently Professor of Chemistry. His research interests lie in the development of new methodology for general applications in synthetic chemistry.



Robert H. Grubbs obtained his B.S. degree from the University of Florida. After receiving his Ph.D. from Columbia University under the supervision of Professor Ronald Breslow, he joined the lab of James P. Collman as an NIH Postdoctoral Fellow at Stanford University. Then he started his academic career as an assistant professor in chemistry at Michigan State University in 1969. He moved to California Institute of Technology in 1978 and currently, he is the Victor & Elizabeth Atkins Professor of Chemistry.



Jose M. Medina was born in Peru. He received his Bachelor's Degree in Chemistry from CSU Channel Islands in 2012. He is currently pursuing his Ph.D. in organic chemistry in the laboratory of Professor Neil K. Garg at the University of California, Los Angeles. His graduate research has focused on harnessing cyclic alkynes for the synthesis of heterocyclic compounds and the development of nickel-catalyzed C-C bond forming reactions from amides.



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Anton A. Toutov was born in Kiev, Ukraine. He obtained his B.S. degree in chemistry in 2011 from Queen's University in Kingston, Canada, where he developed new heterocyclic lithiation chemistries under the supervision of Victor Snieckus. He then moved to Caltech where he is currently a 5<sup>th</sup> year Ph.D. candidate in the laboratory of Robert H. Grubbs. His research focuses on using Earth-abundant elements in the development of efficient and sustainable chemical reactions.



Wen-Bo Liu was born in China and he received his Bachelor's Degree in Chemistry from the Nankai University in 2006. He obtained his Ph.D. in organic chemistry (2011) from the Shanghai Institute of Organic Chemistry (SIOC) under the supervision of Professor Li-Xin Dai and Professor Shu-Li You. Then he joined the laboratory of Professor Brian M. Stoltz at Caltech as a postdoctoral scholar, working on asymmetric catalysis and sustainable chemistry.



Brian M. Stoltz was born in Philadelphia, PA in 1970 and obtained his B.S. degree from the Indiana University of Pennsylvania in Indiana, PA. After graduate work at Yale University in the labs of John L. Wood and an NIH postdoctoral fellowship at Harvard with E. J. Corey, he took a position at the California Institute of Technology. A member of the Caltech faculty since 2000, he is currently Professor of Chemistry. His research interests lie in the development of new methodology for general applications in synthetic chemistry.

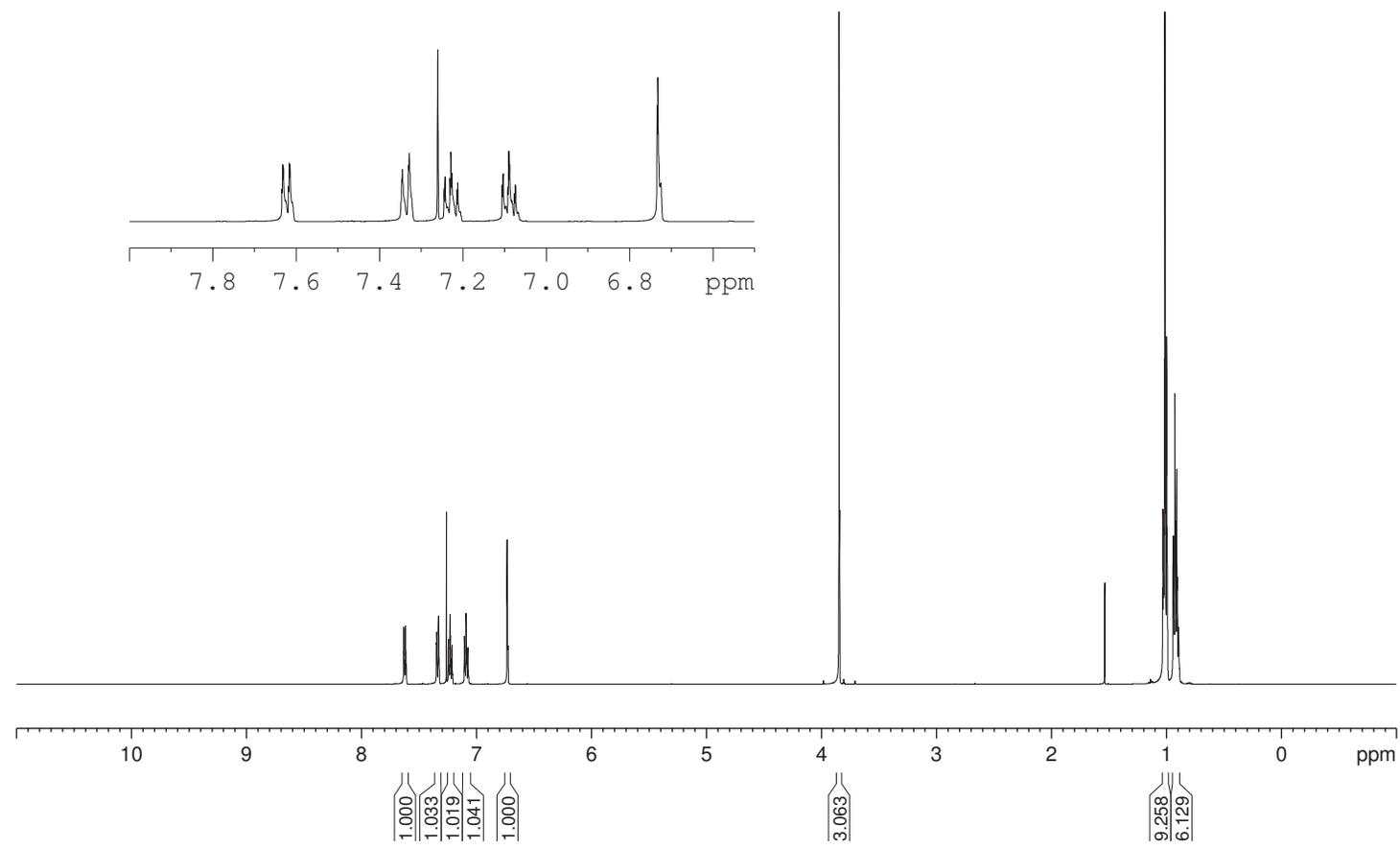
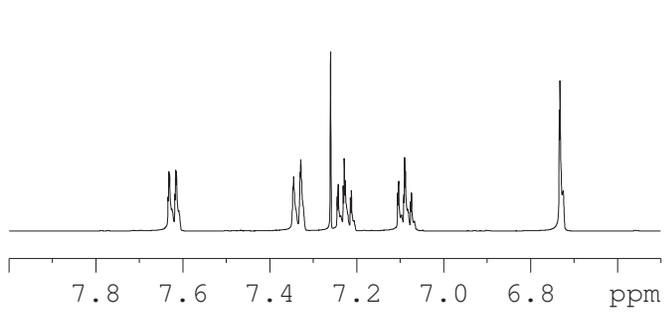
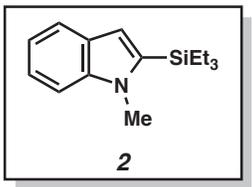
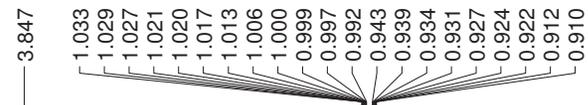
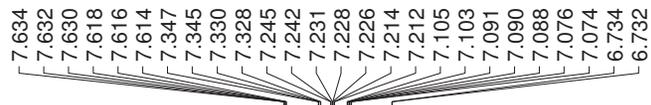


Robert H. Grubbs obtained his B.S. degree from the University of Florida. After receiving his Ph.D. from Columbia University under the supervision of Professor Ronald Breslow, he joined the lab of James P. Collman as an NIH Postdoctoral Fellow at Stanford University. Then he started his academic career as an assistant professor in chemistry at Michigan State University in 1969. He moved to California Institute of Technology in 1978 and currently, he is the Victor & Elizabeth Atkins Professor of Chemistry.



Jose M. Medina was born in Peru. He received his Bachelor's Degree in Chemistry from CSU Channel Islands in 2012. He is currently pursuing his Ph.D. in organic chemistry in the laboratory of Professor Neil K. Garg at the University of California, Los Angeles. His graduate research has focused on harnessing cyclic alkynes for the synthesis of heterocyclic compounds and the development of nickel-catalyzed C-C bond forming reactions from amides.

1H NMR spectra for compound (2)

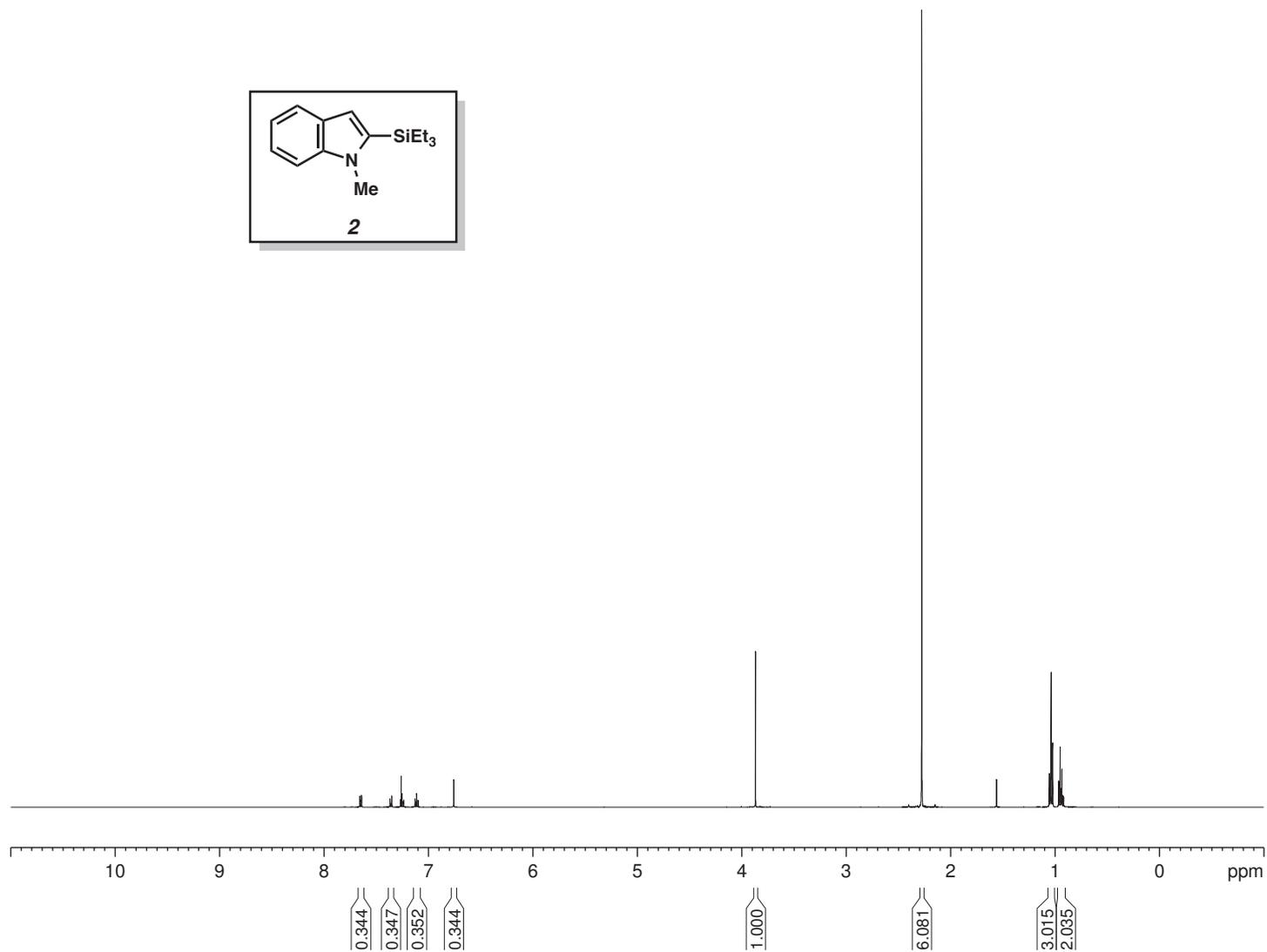
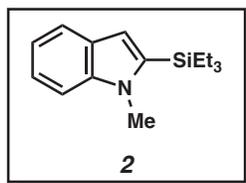


<sup>1</sup>H qNMR for compound (2) with Hexamethylbenzene 99+% as the standard

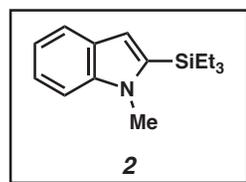
7.655 7.639 7.367 7.366 7.351 7.349 7.267 7.265 7.253 7.251 7.248 7.237 7.234 7.128 7.126 7.113 7.111 7.099 7.097 6.757 6.756

3.867

2.275 1.057 1.054 1.051 1.037 1.023 1.021 0.966 0.962 0.950 0.947 0.945 0.935 0.933 0.929 0.919 0.915



13C NMR for compound (2)



140.299  
138.375  
128.647  
121.947  
120.660  
119.118  
113.041  
109.135

33.100

7.659  
4.114

