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September 2014: The paragraphs above replace the section “Handling and Disposal of Hazardous Chemicals” in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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Pd(0)-CATALYZED DIAMINATION OF TRANS-1-PHENYL-1,3-BUTADIENE WITH DI-TERN-BUTYLDIAZIRIDINONE AS NITROGEN SOURCE

A. Di-tert-butylurea (I). A 5-L Erlenmeyer flask equipped with a mechanical stirrer and an internal thermometer is charged with tert-butylamine (85.2 mL, 791 mmol, 6.6 equiv), triethylamine (127 mL, 900 mmol, 7.5 equiv), and toluene (2000 mL) (Note 1). The mixture is cooled to an internal temperature of 5 °C in an ice bath and triphosgene (36.3 g, 120 mmol, 1.0 equiv) (Note 2) is added in small portions over a period of 20 min (Note 3). The mixture is warmed to room temperature and stirred for 24 h. The reaction mixture is quenched with water (500 mL), transferred to a separatory funnel, and the aqueous phase is discarded. The organic layer is washed with water (4 x 500 mL) and the white solids are collected by suction filtration (water aspirator) (Note 4 and 5). The combined white solids are washed with water (2000 mL) (Note 6), and dried at 65 °C under vacuum (74 mmHg) for 12 h to give 49.7 g (80%) of di-tert-butylurea as a white solid (Notes 7 and 8).

B. Di-tert-butylidiaziridinone (2). A 500-mL, one-necked, round-bottomed flask equipped with a Teflon-coated magnetic stir bar (length:...
3.3 cm) and a rubber septum is charged with di-tert-butylurea (30.0 g, 174 mmol, 1.0 equiv) and Et₂O (200 mL) (Note 9). The reaction vessel is protected from light and tert-butyl-hypochlorite (20.8 g, 192 mmol, 1.1 equiv) (Note 10) is added to the slurry over a period of 10 min. The resulting pale yellow solution is stirred for an additional 30 min, cooled to 5 °C in an ice bath, and treated with potassium tert-butoxide (25.4 g, 226 mmol, 1.3 equiv) (Note 11) in small portions over a period of 20 min (Note 12). The resulting solution is warmed to room temperature and stirred for 5 h (Note 13). The reaction mixture is diluted with hexanes (200 mL), transferred to a 2-L separatory funnel, and washed with water (3 x 150 mL). The organic phase is dried over anhydrous K₂CO₃ (30.0 g) (Note 14) by stirring over 5 h, filtered, and concentrated by rotary evaporation (25 °C, 18 mmHg) (Note 15). The crude material is purified by fractional distillation under vacuum (7 mmHg) using a vigreux column (length 10.5 cm) fitted with a short path distillation head (Note 16). The oil bath temperature is gradually increased from 24 °C to 70 °C to give 22.6 g (76%) of di-tert-butylidiaziridinone as a colorless liquid (Notes 17, 18, 19, and 20).

C. trans-1,3-Di-tert-butyl-4-phenyl-5-vinyl-imidazolidin-2-one (3). A 25-mL, one-necked, round-bottomed flask equipped with a Teflon-coated magnetic stir bar (length: 1.3 cm) and a rubber septum is charged with freshly distilled (E)-1-phenyl-1,3-butadiene (2.60 g, 20.0 mmol, 1.0 equiv) (Note 21) and tetrakis(triphenylphosphine)palladium (0.462 g, 0.400 mmol, 0.02 equiv) (Notes 22 and 23). The flask is evacuated and back-filled with argon three times. The mixture is placed in a preheated (65 °C) oil bath and di-tert-butyl-diaziridinone (3.75 g, 22.0 mmol, 1.1 equiv) is added over 3 h via syringe pump (Note 24). The resulting red mixture is stirred for an additional 1 h (Note 13), cooled to room temperature, and diluted with 5 mL of a hexanes/Et₂O (5:1) solution. The solution is loaded onto a wet-packed silica gel column (305 g SiO₂, diameter: 6.5 cm, height: 22 cm, pretreated with hexanes/diethyl ether, 5:1 (Note 25). The product is eluted with hexanes/diethyl ether, 5:1) to give 5.78 g (96%) of trans-1,3-di-tert-butyl-4-phenyl-5-vinyl-imidazolidin-2-one as a yellow oil (Notes 26 and 27).

2. Notes

1. tert-Butylamine (98%, Alfa Aesar), triethylamine (99%, Fisher Chemicals), and toluene (99.9%, Fisher Chemicals, ACS grade) were used as received.
2. Triphosgene (98%) was purchased from Alfa Aesar and used as received.
3. The addition was carried out at such a rate that an internal temperature of 15 °C was not exceeded.
4. The solids are suspended in the organic phase.
5. The filtrate was concentrated to give an additional 2.35 g of di-tert-butylurea.
6. It is imperative to wash the solids extensively with water to remove any residual Et$_3$N-HCl, which may decrease the yield for the subsequent step.
7. Working at 50% scale, the checkers obtained 23.1 g (76%).
8. The product has the following physicochemical properties: White solid, mp 245–246 °C; $^1$H NMR (300 MHz, DMSO-$_d_6$) $\delta$: 1.18 (s, 18H), 5.45 (s, 2H); $^{13}$C NMR (75 MHz, DMSO-$_d_6$) $\delta$: 29.3, 48.8, 157.0; IR (ATR) 3349, 1633 cm$^{-1}$; MS (EI+) $m/z$ 172 (M$^+$, 26), 157 (67), 57 (100); HRMS (EI+) $m/z$ calcd for C$_9$H$_{20}$N$_2$O 172.1576, found 172.1569; Anal. Calcd for C$_9$H$_{20}$N$_2$O C, 62.75; H, 11.70; N, 16.26; Found C, 63.02; H, 11.94; N, 16.16.
9. Diethyl ether (ACS grade) was purchased from Fisher Chemicals and dried by distillation over sodium/benzophenone under an argon atmosphere.
10. tert-Butyl hypochlorite was prepared according to a literature procedure: Teeter, H. M.; Bell, E. W. *Org. Synth.* 1952, 32, 20.
11. Solid potassium tert-butoxide (97%) was purchased from Alfa Aesar and used as received.
12. Upon complete addition the reaction vessel does not need to be protected from light.
13. The progress of the reaction can be monitored by $^1$H NMR analysis of aliquots taken directly from the reaction mixture.
14. Anhydrous K$_2$CO$_3$ (ACS grade) was purchased from Fisher Chemicals and used as received.
15. The tert-butanol generated in the reaction should be completely removed to prevent interference with the subsequent distillation.
16. The dimensions of the distillation head are as follows. Single piece construction with inlet for vacuum/inert gas, 10/18 thermometer joint on top, 14/20 joints for distillation and collection flasks, approx. 35 mm length of condenser x 65 mm height (head).
17. Di-tert-butylidiaziridinone is collected at 47–49 °C (7 mmHg) and stored away from light.
18. The submitters reported a bp of di-tert-butylidiaziridinone of 60–64 °C (7 mmHg).
19. Working at 50% scale, the checkers obtained 11.1 g (75%).
20. The product has the following physicochemical properties: bp 47–49 °C /7 mmHg; \(^1\)H NMR (300 MHz, benzene-\(d_6\)) \(\delta\): 1.07 (s, 18 H); \(^{13}\)C NMR (75 MHz, benzene-\(d_6\)) \(\delta\): 27.2, 59.3, 159.3; IR (ATR) 1929, 1875, 1856 cm\(^{-1}\); MS (EI\(+\)) \(m/z\) 170 (M\(^+\), 5), 157 (67), 131 (15), 84 (40), 57 (100); HRMS (EI\(+\)) \(m/z\) calcd for C\(_9\)H\(_{18}\)N\(_2\)O 170.1419, found 170.1420; Anal. Calcd for C\(_9\)H\(_{18}\)N\(_2\)O C, 63.49; H, 10.66; N, 16.45; Found C, 63.61; H, 10.79; N, 16.17.

21. (E)-1-Phenyl-1,3-butadiene was prepared according to a literature procedure: Grummitt, O.; Becker, E. I. Org. Synth. 1950, 30, 75; or Wittig, G.; Schoellkopf, U. Org. Synth. 1960, 40, 66. Similar results were obtained for step C using the diene prepared from either protocol.

22. Tetrakis(triphenylphosphine)palladium (9% min. palladium) was purchased from Pressure Chemical Co. and used as received.

23. Reaction is performed neat.

24. The submitters added di-tert-butyl-diaziridinone via a 10-mL addition funnel. The checkers observed more consistent results using a syringe pump.

25. Silica gel 40–63 D (60 Å) (Silicycle, Quebec City, Canada) was used.

26. Working at 50% scale, the checkers obtained 2.86 g (95%).

27. The product has the following physicochemical properties: \(^1\)H NMR (300 MHz, benzene-\(d_6\)) \(\delta\): 1.36 (s, 9 H), 1.39 (s, 9 H), 3.55 (dm, \(J = 8.4\) Hz, 1 H), 4.05 (d, \(J = 1.2\) Hz, 1 H), 4.86 – 4.95 (m, 2 H), 5.92 (ddd, \(J = 17.1, 10.2, 8.4\) Hz, 1 H), 7.07-7.16 (m, 3 H), 7.27 (dm, \(J = 6.9\) Hz, 2 H); \(^{13}\)C NMR (75 MHz, benzene-\(d_6\)) \(\delta\): 29.1, 29.2, 53.7, 53.9, 63.8, 65.5, 115.6, 126.5, 129.4, 141.8, 145.1, 159.2; IR (ATR) 1682 cm\(^{-1}\); MS (EI\(+\)) \(m/z\) 300 (M\(^+\), 55), 285 (100), 229 (81), 132 (60); HRMS (EI\(+\)) \(m/z\) calcd for C\(_{19}\)H\(_{28}\)N\(_2\)O 300.2202, found 300.2191; Anal. Calcd for C\(_{19}\)H\(_{28}\)N\(_2\)O C, 75.96; H, 9.39; N, 9.32; Found C, 76.01; H, 9.60; N, 9.31.

**Safety and Waste Disposal Information**

All hazardous materials should be handled and disposed of in accordance with “Prudent Practices in the Laboratory”; National Academy Press; Washington, DC, 1995.
3. Discussion

The diamination of olefins provides an attractive and efficient approach to biologically and chemically important vicinal diamines.\textsuperscript{5} To date, various metal-mediated\textsuperscript{6} or catalyzed\textsuperscript{7} diaminations have been developed. Recently, we reported that conjugated dienes and trienes can be regio- and stereoselectively diaminated using Pd(0)\textsuperscript{8} or Cu(I)\textsuperscript{9} as the catalyst and di-\textit{tert}-butyldiaziridinone (2) or related compounds as a convenient nitrogen source. When Pd(0) is used as the catalyst, the diamination occurs regioselectively at the internal double bond (Scheme 1).\textsuperscript{8a}

This diamination can be applied to various alkyl and aryl-substituted dienes as well as electron-rich and electron-deficient dienes (Table 1).\textsuperscript{8a} When the diamination is carried out under solvent-free conditions as described herein, the amount of Pd(PPh\textsubscript{3})\textsubscript{4} catalyst can be further reduced.\textsuperscript{10}
Table 1. Pd(0)-Catalyzed Diamination of Conjugated Dienes and Trienes

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<th>Entry</th>
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<th>Product (5)</th>
<th>Yield (%)</th>
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<td>R = p-MeOPh</td>
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<td>R = 2-Furyl</td>
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<td>6</td>
<td>R = OMe</td>
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</table>

*All reactions were carried out with di-tert-butylidiaziridinone (2) (1.0 equiv), diene or triene (1.2 equiv), and Pd(PPh₃)₄ (0.1 equiv) in benzene-d₆ in an NMR tube at 65 °C under argon for 0.25 to 5 h.*

A possible catalytic cycle for this diamination is shown in Scheme 2.²⁺ All reactions were carried out with di-tert-butylidiaziridinone (2) (1.0 equiv), diene or triene (1.2 equiv), and Pd(PPh₃)₄ (0.1 equiv) in benzene-d₆ in an NMR tube at 65 °C under argon for 0.25 to 5 h.

Oxidative insertion of Pd(0) into the N-N bond of diaziridinone 2 generates four-membered Pd(II) species 6. This intermediate then reacts with diene 4 to form π-allyl Pd complex 8, which undergoes a reductive elimination to release 5 and regenerate the Pd(0) catalyst.
When a chiral ligand is used, the diamination proceeds with high enantioselectivity. Chiral diamines can be obtained upon deprotection and the double bonds contained in the diamination products can be elaborated into other functionalities.  

Scheme 2

1. Department of Chemistry, Colorado State University, Fort Collins, CO 80523; yian@lamar.colostate.edu.
2. Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260, USA; pwipf@pitt.edu.
6. For metal-mediated diaminations, see: (a) Gomez Aranda, V.; Barluenga, J.; Aznar, F. Synthesis 1974, 504. (b) Chong, A. O.; Oshima,


The detailed studies will be described elsewhere.

Appendix

Chemical Abstracts Nomenclature; (Registry Number)

Di-tert-butyurea: Urea, N,N'-bis(1,1-dimethylethyl)-; (5336-24-3)

 tert-Butylamine: 2-Propanamine, 2-methyl-; (75-64-9)

Triethylamine: Ethanamine, N,N-diethyl-; (121-44-8)

Triphosgene: Methanol, 1,1,1-trichloro-, 1,1'-carbonate; (32315-10-9)

Di-tert-butyldiaziridinone: 3-Diazipiridinone, 1,2-bis(1,1-dimethylethyl)-;

(19656-74-7)
tert-Butyl-hypochlorite: Hypochlorous acid, 1,1-dimethylethyl ester; (507-40-4)
Potassium tert-butoxide: 2-Propanol, 2-methyl-, potassium salt (1:1); (865-47-4)
trans-1,3-Di-tert-butyl-4-phenyl-5-vinyl-imidazolidin-2-one: 2-Imidazolidinone, 1,3-bis(1,1-dimethylethyl)-4-ethenyl-5-phenyl-, (4R,5R)-rel-; (927902-91-8)
(E)-1-Phenyl-1,3-butadiene: Benzene, (1E)-1,3-butadienyl-: (16939-57-4)
Tetrakis(triphenylphosphine)palladium; (14221-01-3)

Yian Shi was born in Jiangsu, China in 1963. He obtained his B.Sc. degree from Nanjing University in 1983, M.Sc. degree from University of Toronto with Professor Ian W.J. Still in 1987, and Ph.D. degree from Stanford University with Professor Barry M. Trost in 1992. After a postdoctoral study at Harvard Medical School with Professor Christopher Walsh, he joined Colorado State University as assistant professor in 1995 and was promoted to associate professor in 2000 and professor in 2003. His current research interests include the development of new synthetic methods, asymmetric catalysis, and synthesis of natural products.

Haifeng Du was born in Jilin, China in 1974. He received his B.Sc. degree in 1998 and M.Sc. degree in 2001 from Nankai University. He then moved to Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, and obtained his Ph.D. degree in 2004 under the supervision of Professor Kuiling Ding. In the fall of 2004, he joined the Department of Chemistry at Colorado State University as a postdoctoral fellow with Professor Yian Shi. His research interests include the development of novel synthetic methodology and asymmetric synthesis.
Baoguo Zhao was born in Hubei, China in 1973. He received his B.Sc. degree from Wuhan University in 1996 and M.Sc. degree from Nanjing University in 2002 under the supervision of Professor Jianhua Xu. After completing his Ph.D. degree under the supervision of Professor Kuiling Ding at Shanghai Institute of Organic Chemistry, Chinese Academy of Science in 2006, he joined Department of Chemistry at Colorado State University as a postdoctoral fellow with Professor Yian Shi. His current research interests include the development of novel synthetic methodology and asymmetric synthesis.

Eric Buck was born in 1985 in Fairmont, West Virginia. He graduated from the University of Minnesota with his B.Sc. in 2006. During his freshman year he entered the laboratory of Professor Thomas R. Hoye where he pursued the synthesis of petromyzonamine disulfate analogs with a focus on 5-β petromyzonamine disulfate. While attending the U of M he was supported by the David A. and Merece H. Johnson Scholarship. In 2007 he moved to Pittsburgh, Pennsylvania where he is currently a graduate student under the direction of Professor Peter Wipf. His current research interests include asymmetric synthesis and the synthesis of natural products.
di-tert-butylurea

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NUC1
13C
P1
9.00 usec
PL1
2.00 dB
PL1W
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SFO1
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--- CHANNEL f2 ---
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1H
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PL12
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PL13
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WDW
EM
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0
LB
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GB
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PC
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di-tert-butylidiaziridinone
trans-1,3-Di-tert-butyl-4-phenyl-5-vinyl-imidazolidin-2-one 13C
di-tern-butylurea
di-tert-butyl-diaziridinone
trans-1,3-di-tert-butyl-4-phenyl-5-vinyl-imidazolidin-2-one

N N

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