

A Publication of Reliable Methods for the Preparation of Organic Compounds

Working with Hazardous Chemicals

The procedures in Organic Syntheses are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full accessed text can be free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

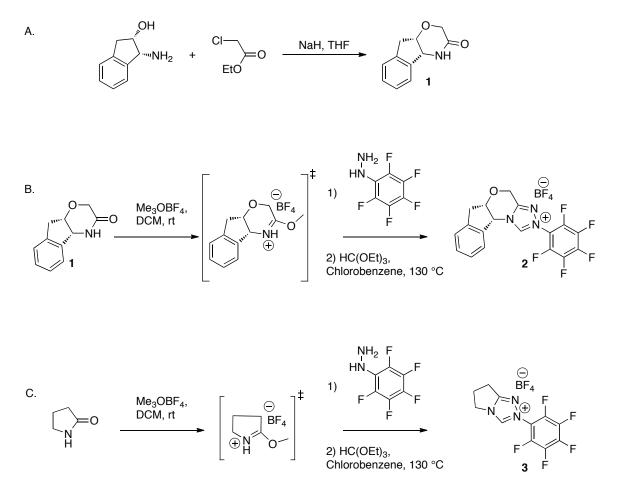
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.,* its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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.

Copyright © 2010 Organic Syntheses, Inc. All Rights Reserved

PREPARATION OF CHIRAL AND ACHIRAL TRIAZOLIUM SALTS: CARBENE PRECURSORS WITH DEMONSTRATED SYNTHETIC UTILITY



Submitted by Harit U. Vora, Stephen P. Lathrop, Nathan T. Reynolds, Mark S. Kerr, Javier Read de Alaniz, and Tomislav Rovis.¹ Checked by Spandan Chennamadhavuni and Huw M. L. Davies.

1. Procedure

A. 4,4a,9,9a-Tetrahydro-1-oxa-4-aza-fluoren-3-one (1). A 2.0 L, single-necked, round-bottomed flask fitted with a magnetic stir bar (1 ¹/₄ inch x 5/8 inch egg shaped), and a rubber septum with a needle inlet is flame dried and then cooled under an argon atmosphere. The septum is removed and the flask is charged with sodium hydride (3.48 g, 60% in mineral oil, 87.15 mmol, 1.3 equiv) (Note 1) via a powder funnel, followed by *n*-pentane *Org. Synth.* 2010, *87*, 350-361 Published on the Web 6/15/2010

(300 mL) (Note 2). The septum is then replaced and the heterogeneous mixture is subjected to an argon atmosphere by means of a needle in the septum followed by agitation for 20 min. Agitation is stopped and the sodium hydride is allowed to settle out of solution for 30 min. *n*-Pentane is removed via cannula by increasing the positive pressure of argon in the flask. Residual mineral oil present in sodium hydride is removed by washing with an additional 100 mL of pentane as above. The combined pentane solutions containing residual sodium hydride are quenched with isopropanol (Note 3). The septum is briefly removed to add anhydrous tetrahydrofuran (1.0 L) (Note 4) by means of an addition funnel followed by replacement of the septum and refilling the reaction flask with argon. The reaction flask is placed in a -10 °C ice-brine bath (Note 5) with agitation and allowed to cool for 30 min. The septum is then replaced with a powder funnel and (1R, 2S)-(-)-cis-1-amino-2-indanol (5 g, 33.52 mmol) (Note 6) is added followed by refilling of the reaction flask with argon. Within 10 min, the reaction mixture turns heterogeneous and the color changes to light purple. The septum is then replaced with a powder funnel and a further batch of (1R, 2S)-(-)-cis-1-amino-2-indanol (5 g, 33.52 mmol) (Note 6) is added followed by refilling of the reaction flask with argon. The flask is then fitted with a reflux condenser and the stirred reaction mixture is heated in a 70 °C oil bath for 40 min under an argon atmosphere. The solution is then placed into a -10 °C ice-brine bath and allowed to cool for 1 h while stirring. Ethyl chloroacetate (8.38 g, 7.32 mL, 68.37 mmol, 1.02 equiv) (Note 7) is added via syringe over 5 min. The reaction flask is removed from the ice-brine bath and the mixture is stirred for 30 min at room temperature. The solution is then placed in an oil bath heated to 70 °C and stirred for 1 h under argon. After cooling to room temperature, brine (30 mL) is slowly added to the reaction flask to quench the reaction, and then THF is removed under reduced pressure using a rotary evaporator. The homogeneous deep purple reaction mixture is then poured into a 2.0-L separatory funnel and brine (200 mL) is added. The reaction mixture is extracted using ethyl acetate (2 x 200 mL) (Note 8). The combined organic layers are then dried using anhydrous MgSO₄ (50 g) (Note 9) followed by vacuum filtration through a coarse fritted funnel. The resultant purple solution is transferred into a 1.0-L roundbottomed flask in approx. 500 mL portions and concentrated in vacuo to dryness. To the 1.0-L round bottomed flask containing the crude light brown solid is added a stir bar and hexanes (300 mL) (Note 10). The sides of the round-bottomed flask are scraped with a metal spatula to ensure that all of the crude solid material rests at the bottom of the flask. The flask is fitted with a reflux condenser left open to the atmosphere and the heterogeneous mixture is stirred vigorously in an oil bath heated to 70 °C for a period of 2 h. After cooling to room temperature, vacuum filtration affords an off-white solid which is transferred into a 100-mL round-bottomed flask by means of a powder funnel and dried under vacuum (2 mmHg) in an oil bath heated to 70 °C for 1 h, affording 10.21–10.95 g (80–86%) of 1 (Note 11).

B. 2-Pentafluorophenyl-6,10b-dihydro-4H,5aH-5-oxa-3,10c-diaza-2azonia-cyclopenta[c]fluorene; tetrafluoroborate (2). To a flame-dried 1.0-L single-necked, round-bottomed flask with magnetic stir bar (1 1/4 inch x 5/8 inch egg shaped) is added morpholinone 1 (10.00 g, 52.85 mmol, 1.0 equiv) by means of a powder funnel. The flask is then evacuated and back-filled with argon. Methylene chloride (300 mL) (Note 12) and trimethyloxonium tetrafluoroborate (7.82 g, 52.85 mmol, 1.0 equiv) (Note 13) are then added via powder funnel and the flask is fitted with a septum and a needle connected to an argon line. The heterogeneous mixture is stirred at room temperature until the reaction is homogeneous (Note 14). Pentafluorophenylhydrazine (10.47 g, 52.85 mmol, 1.0 equiv) (Note 15) is added in a single portion by means of a powder funnel followed by replacement of the powder funnel with a septum and a needle connected to an argon line, and then the reaction mixture is stirred for 4 h (Note 16). The magnetic stir bar (Note 17) is removed followed by removal of the solvent in *vacuo*. The 1.0-L flask is then placed in an oil bath heated to 100 °C for 1 h under vacuum (2 mm Hg). A magnetic stir bar, chlorobenzene (300 mL) (Note 18) and triethyl orthoformate (19.58 g, 21.97 mL, 132.13 mmol, 2.5 equiv) (Note 19) are then added using a syringe, and the flask is fitted with a reflux condenser, placed in an oil bath heated to 130 °C and stirred for 24 h open to the atmosphere. Triethyl orthoformate (19.58 g, 21.97 mL, 132.13 mmol, 2.5 equiv) (Note 18) is then added via syringe followed by continued agitation for 24 h. A third portion of triethyl orthoformate (19.58 g, 21.97 mL, 132.13 mmol, 2.5 equiv) (Note 19) is added via syringe followed by continued agitation for 24 h. After removal of the reaction flask from the oil bath and cooling to room temperature, the solution is added to a 1.0-L round-bottomed flask containing toluene (300 mL) (Note 20) that is agitated with a magnetic stir bar. The reaction flask is then rinsed with toluene (50 mL) (Note 20) followed by addition of the heterogeneous mixture to the 1-L flask containing the crude product. The slurry is stirred for 10 min followed by vacuum filtration. The filtrate is rinsed with toluene

(200 mL) (Note 20) and hexane (200 mL) (Note 10). The solid is then transferred to a 125-mL Erlenmeyer flask containing a stir bar by means of a powder funnel, triturated with ethyl acetate (20 mL) (Note 8) and methanol (5 mL) (Note 21) and stirred vigorously for 30 min. The slurry is then filtered through a medium frit funnel and the filter cake is washed with cold ethyl acetate (15 mL) (Note 8) via a glass pipette to yield **2** as an off-white solid. The off-white solid is transferred to a 100-mL round-bottomed flask by means of a powder funnel, placed in an oil bath heated to 100 °C and subjected to vacuum (2 mmHg) for 1 h, affording 15.06–15.79 g (61–64%) of **2** (Note 22).

C. 2-Pentafluorophenyl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-2-ium; tetrafluoroborate (3). Into a flame-dried 1.0-L flask equipped with a magnetic stir bar is added 2-pyrrolidinone (5.00 g, 58.75 mmol, 1.0 equiv) (Note 23). The flask is then evacuated and back-filled with argon. Methylene chloride (300 mL) (Note 12) and trimethyloxonium tetrafluoroborate (8.69 g, 58.75 mmol, 1.0 equiv) (Note 13) are added by means of a powder funnel and the flask is then fitted with a septum and a needle connected to an argon line. The heterogeneous mixture is stirred at room temperature until the solution is homogeneous (Note 14). Pentafluorophenylhydrazine (11.64 g, 58.75 mmol, 1.0 equiv) (Note 15) is added in a single portion by means of a powder funnel followed by replacement of the powder funnel with a septum and a needle connected to an argon line. The reaction mixture is stirred for 4 h (Note 16). The magnetic stir bar is removed (Note 17) followed by removal of the solvent in vacuo. The 1.0-L flask is then placed in an oil bath heated to 100 °C for 1 h under vacuum (2 mmHg). A magnetic stirring bar, chlorobenzene (300 mL) (Note 18) and triethyl orthoformate (17.41 g, 19.54 mL, 117.5 mmol, 2.0 equiv) (Note 19) are then added via syringe and the flask is fitted with a reflux condenser, placed in an oil bath heated to 130 °C and stirred for 24 h open to the atmosphere. Triethyl orthoformate (17.41 g, 19.54 mL, 117.5 mmol, 2.0 equiv) (Note 19) is then added via syringe followed by continued agitation for 24 h. After removal of the reaction vessel from the oil bath and cooling to room temperature, the reaction mixture is added to a 1.0-L round-bottomed flask containing toluene (300 mL) (Note 20) that is agitated with a magnetic stir bar for 1 h. The reaction flask is then rinsed with toluene (50 mL) (Note 20) followed by addition of the heterogeneous mixture to the 1-L round-bottomed flask containing the crude product. The slurry is stirred for 10 min followed by vacuum filtration. The filtrate is rinsed with toluene (200 mL) (Note 20) and

hexanes (200 mL) (Note 10). The crude brown solid is then transferred to a 125-mL Erlenmeyer flask containing a magnetic stir bar by means of a powder funnel. The solid is triturated with ethyl acetate (20 mL) (Note 8) and methanol (3 mL) (Note 20) and stirred vigorously for 30 min. The heterogeneous mixture is then filtered through a medium fritted funnel under vacuum (120 mmHg). The filter cake is then washed with cold ethyl acetate (15 mL) via a glass pipette to yield **3** (15.91–16.13 g) as an off-white powder. The off-white solid is transferred to a 100-mL round-bottomed flask by means of a powder funnel, placed in an oil bath heated to 100 °C and subjected to vacuum (2 mmHg) for 1 h, affording 15.91–16.13 g (74–76%) of **3** (Note 24).

2. Notes

1. Sodium hydride (60% dispersion in mineral oil) was purchased from Aldrich. It was determined that removal of the mineral oil in the reaction resulted in higher yields of the desired product.

2. Pentane (99.0%) was purchased from Fisher Scientific and used as received.

3. Isopropanol was purchased from Aldrich Chemical Co., and used without further purification.

4. THF (HPLC grade, $H_2O = 0.003\%$) was purchased from Fisher Scientific Company and purified by pressure filtration under argon through activated alumina. The checkers found that the reaction gave similar results with freshly distilled THF over sodium benzophenone ketyl.

5. It was observed that cooling the reaction with an ice-brine bath resulted in an increase in chemoselectivity for the *N*-acylation product to give a higher yield of the desired regioisomer. It is crucial to maintain the reaction temperature between -10 °C and -15 °C in order to obtain a single regioisomer of the product. The checkers monitored the internal temperature of the reaction mixture using a digital thermometer.

6. (1R,2S)-(+)-*cis*-1-Amino-2-indanol (99%) was purchased from Aldrich, and used without further purification.

7. Ethyl chloroacetate (99%) was purchased from Aldrich and used without further purification.

8. Ethyl acetate (99.9%) was purchased from Fischer Scientific and used without further purification.

9. Anhydrous magnesium sulfate was purchased from Fischer Scientific.

10. Hexanes (HPLC grade, $H_2O = 0.0005\%$) was purchased from Aldrich and used as received.

11. The spectral data for 4,4a,9,9a-tetrahydro-1-oxa-4-aza-fluoren-3one (1) are as follows: $R_f = 0.18$ (EtOAc); Mp 180–183 °C (dec.); $[\alpha]_D^{23}$ -17.3 (*c* 1.08, MeOH); IR (neat) 3179, 3050, 2910, 1681, 1646, 1484, 1417 cm⁻¹; ¹H NMR (400 MHz, acetone-d₆) δ : 2.97 (d, *J* = 16.8 Hz, 1 H), 3.23 (dd, *J* = 16.6, 4.9 Hz, 1 H), 3.89 (d, *J* = 16.2 Hz, 1 H), 4.05 (d, *J* = 16.2 Hz, 1 H), 4.57 (t, *J* = 4.6 Hz, 1 H), 4.82 (t, *J* = 4.0 Hz, 1 H), 7.23-7.29 (m, 3 H), 7.46-7.49 (m, 1 H), 8.21 (br s, 1 H); ¹³C NMR (101 MHz, acetone-d₆) δ : 38.2, 59.4, 67.1, 77.1, 124.7, 125.7, 127.6, 128.4, 140.8, 143.1, 168.5; HRMS (APCI+) *m*/*z* calcd. for C₁₁H₁₂NO₂ (M⁺) 190.0863; found 190.0862; Anal. calcd. for C₁₁H₁₁NO₂: C, 69.83; H, 5.86; N, 7.40; found: C, 69.68; H, 5.83; N, 7.33.

12. Methylene chloride (99.9%) was purchased from Fischer Scientific and purified by pressure filtration under argon through activated alumina. A Karl-Fisher Titrator was used to determine the water content in methylene chloride (<20 ppm/mL).

13. Trimethyloxonium tetrafluoroborate (95%) was purchased from Aldrich Chemical Co. The bottles were stored in the refrigerator at -15 °C and a freshly opened bottle was used for each reaction. Direct contact of with skin trimethyloxonium tetrafluoroborate must be avoided because of its caustic nature and alkylating properties. It is absolutely critical to add only one equivalent of trimethyloxonium tetrafluoroborate. Excess of this reagent will result in lower yields and the product may not precipitate out. The checker also found that it is essential to add trimethyloxonium tetrafluoroborate under an argon atmosphere because of its highly hygroscopic nature.

14. Upon complete dissolution of the trimethyloxonium tetrafluoroborate an aliquot is removed from the reaction vessel and concentrated in vacuo. The oil is then dissolved in acetone- d_6 and ¹H NMR is used to verify the consumption of morpholinone. It usually takes 1–2 h for the reaction mixture to turn completely homogenous.

15. Pentafluorophenylhydrazine (97%) was purchased from Aldrich Chemical Co. and used without further purification.

16. Disappearance of activated amidate (typically \sim 4 h) could also be observed by measuring the ¹H NMR of an aliquot.

17. The magnetic stir bar was removed, because otherwise it will stick firmly to the bottom of the flask and will not stir during the next sequence of the procedure.

18. Chlorobenzene (99%) was purchased from Aldrich Chemical Co. and used without further purification.

19. Triethylorthoformate (98%) was purchased from Acros Organics, and used without further purification.

20. Toluene (99.9%) reagent grade was purchased from Fisher Scientific and used without further purification.

21. Methanol (99.9%) was purchased from Fischer Scientific and used without further purification.

22. The spectral data for 2-pentafluorophenyl-6,10b-dihydro-4H,5aH-5-oxa-3,10c-diaza-2-azoniacyclopenta[c]fluorine, tetrafluoroborate (2) are as follows: $R_f = 0.22$ (3:1; CH₂Cl₂:acetone); Mp 223–226 °C; $[\alpha]_D^{23}$ -130.80 (c MeCN); IR(neat) 3147, 3106, 3028, 2967, 1595, 1530, 1517, 1487, 1.28 1461, 1056, 1046, 998 cm⁻¹; ¹H NMR (400 MHz, acetone-d₆) δ : 3.28 (d, J = 17.2 Hz, 1 H), 3.55 (dd, J = 17.1, 4.9 Hz, 1 H), 5.19 (t, J = 4.5 Hz, 1 H), 5.25 (d, J = 16.4 Hz, 1 H), 5.39 (d, J = 16.4 Hz, 1 H), 6.33 (d, J = 4.0 Hz, 1 H), 7.34 (t, J = 7.3 Hz, 1 H), 7.43 (g, J = 7.4 Hz, 2 H), 7.63 (d, J = 7.6 Hz, 1 H), 11.09 (br s, 1 H); ¹³C NMR (101 MHz, acetone-d₆) δ: 37.9, 60.8, 63.5, 78.2, 125.2, 126.4, 128.1, 130.4, 136.2, 141.7, 147.1, 152.5; HRMS (APCI+) m/z calcd. for C₁₈H₁₁N₃OF₅ (M⁺) 380.0817; found 380.0816; Anal. calcd. for C₁₈H₁₁BF₉N₃O: C, 46.28; H, 2.37; N, 9.00; found: C, 45.95; H, 2.23; N, 9.03. Based on the observed analytical results we propose the salt to be between anhydrous and a half-hydrate. Anal. calcd. for C₁₈H₁₁BF₉N₃O•1/2H₂O: C, 45.41; H, 2.54; N, 8.83. The checker's efforts to get an elemental analysis of an anhydrous sample were unsuccessful.

23. 2-Pyrrolidinone (\geq 99%) was purchased from Aldrich Chemical Co, and used without further purification.

24. The spectral data for 2-pentafluorophenyl-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium; tetrafluoroborate (**3**) are as follows: $R_f = 0.13$ (3:1; CH₂Cl₂:acetone); Mp 242–245 °C; IR (neat) 3145, 3097, 2983, 1655, 1604, 1524, 1499, 1028, 994, 875 cm⁻¹; ¹H NMR (400 MHz, acetone-d₆) δ : 3.00 (ddd, *J* = 15.0, 7.7, 7.7 Hz, 2 H), 3.42 (t, *J* = 8.0 Hz, 2 H), 4.76 (t, *J* = 8.0 Hz, 2 H), 10.19 (s, 1 H); ¹³C NMR (101 MHz, acetone-d₆) δ : 22.6, 27.6, 49.5, 137.8, 140.4, 142.9, 143.3, 144.5, 145.6, 145.8, 165.8; HRMS (APCI+) *m/z* calcd. for C₁₁H₇N₃F₅ (M⁺) 276.0555; found 276.0556; Anal.

calcd. for $C_{11}H_7BF_9N_3$: C, 36.40; H, 1.94; N, 11.58; found: C, 36.45; H, 1.76; N, 11.54.

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, 1998.

3. Discussion

In recent years, *N*-heterocyclic carbenes have attracted significant attention as catalysts in facilitating umpolung reactivity.² Ukai's utilization of a thiazolium salt as a carbene precursor in the benzoin reaction³ and Breslow's elucidation of the mechanism⁴ of this reaction displayed the potential use of these nucleophilic carbene precatalysts. These early reports led to the subsequent development of carbene precatalysts to facilitate a multitude of Umpolung reactions. In 1996, Enders and coworkers demonstrated the asymmetric benzoin reaction with a triazolium salt as the carbene precursor in moderate yield and enantioselectivity.⁵ Bicyclic triazolium carbene precursors were next studied to see if greater asymmetric induction could be obtained in various Umpolung reactions.

The aminoindanol-derived carbene scaffold introduced by us in 2002 has proven to be one of the most general for these carbene precursors.⁶ In subsequent work, we noted that the electronic nature of the N-aryl substituent has a profound effect on reactivity and control of enantioselectivity in the Stetter reaction. This led to the development of triazolium precatalyst 2. Application of triazolium 2 in the asymmetric Stetter reaction generates quaternary stereocenters in high enantiomeric excess and very good chemical yields.⁷ The umpolung reactivity with triazolium precatalyst 2 can also be extended towards the desymmetrization of cyclohexadienones to yield hydrobenzofuranones in excellent enantioselectivities and chemical yields.⁸ Extension of this work to vinylphosphine oxides and vinylphosphonates as the Michael acceptor can be achieved to generate keto phosphonates and keto phospine oxides in excellent enantioselectivities and yields.⁹ The application of precatalyst **2** towards the rapid assembly of the tetracyclic core of natural product FD-838 was accomplished.¹⁰ The asymmetric synthesis of α -chloro esters via an acyl anion redox reaction was also accomplished with precatalyst 2 to yield the respective enantioenriched aryl esters.¹¹

- 1. Department of Chemistry, Colorado State University, Fort Collins, CO, 80523, USA.
- (a) Enders, D.; Niemeier, O; Hensler, A. Chem. Rev. 2007, 107, 5606– 5655. (b) Moore, J. L.; Rovis, T. Top. Curr. Chem. 2009, 290, 77-144.
- **3.** Ukai, T.; Tanaka, R.; Dokawa, T. J. Pharm. Soc. Jpn. **1943**, 63, 296-300.
- 4. Breslow, R. J. Am. Chem. Soc. 1958, 80, 3719-3726.
- 5. Enders, D.; Breuer, K.; Teles, J. H. *Helv. Chim. Acta* **1996**, 79, 1217-1221.
- 6. Kerr, M. S.; Read de Alaniz, J.; Rovis, T. J. Am. Chem. Soc. 2002, 124, 10298-10299.
- (a) Kerr, M. S.; Rovis. T.; *J. Am. Chem. Soc.* 2004, 126, 8876-8877. (b) Moore, J. L.; Kerr, M. S., Rovis, T. *Tetrahedron* 2006, 128, 2552-2553. (c) Read de Alaniz, J.; Kerr, M. S.; Moore, J. L.; Rovis, T. *J. Org. Chem.* 2008, 73, 2033-2040. (d) Read de Alaniz, J.; Rovis, T. *Syn. Lett.* 2009, 1189-1207.
- (a) Liu, Q.; Rovis, T. J. Am. Chem. Soc. 2006, 128, 2552-2553. (b) Liu, Q.; Rovis, T. Org. Proc. Res. Dev. 2007, 11, 598-604.
- 9. Cullen, S. C.; Rovis, T. Org. Lett. 2008, 10, 3141-3144.
- 10. Orellana, A.; Rovis, T. Chem. Comm. 2008, 730-732.
- 11. Reynolds N. T.; Rovis, T. J. Am. Chem. Soc. 2005, 127, 16406-16407.

Appendix Chemical Abstracts Nomenclature; (Registry Number)

4,4a,9,9a-Tetrahydro-1-oxa-4-azafluoren-3-one: Indeno[2,1-*b*]-1,4-oxazin-3(2*H*)-one, 4,4a,9,9a-tetrahydro-, (4a*R*,9a*S*)-; (862095-79-2)
(1*R*, 2*S*)-(+)-*cis*-1-Amino-2-indanol; (136030-00-7)
Ethyl chloroacetate; (105-39-5)
2-Pentafluorophenyl-6,10b-dihydro-4*H*,5a*H*-5-oxa-3,10c-diaza-2-azoniacyclopenta[*c*]fluorene; tetrafluoroborate; (740816-14-2)
Trimethyloxonium tetrafluoroborate; (420-37-1)
Pentafluorophenylhydrazine; (828-73-9)

Triethyl orthoformate: Ethane, 1,1',1"-[methylidynetris(oxy)]tris-; (122-51-0)

2-Pentafluorophenyl-6,7-dihydro-5*H*-pyrrolo[2,1-*c*][1,2,4]triazol-2-ium; tetrafluoroborate; (862095-91-8)

2-Pyrrolidinone; (616-45-5)



Tomislav Rovis was born in Zagreb in the former Yugoslavia but was largely raised in Southern Ontario, Canada. Following his undergraduate studies at the University of Toronto, he earned his Ph.D. degree at the same institution in 1998 under the direction of Professor Mark Lautens. From 1998-2000, he was an NSERC postdoctoral fellow at Harvard University with Professor David A. Evans. In 2000, he began his independent career at Colorado State University and was promoted in 2005 to Associate Professor and in 2008 to Professor. He currently holds the John K. Stille Chair in Chemistry.



Harit U. Vora was born in 1979 in Calcutta, India and raised in Tobyhanna, PA. He received his undergraduate education at the University of Pittsburgh where he carried out research under the guidance of Professor Paul E. Floreancig. He then obtained a position with the Medicinal Chemistry division at Roche in Palo Alto, CA. He is now pursuing his graduate studies at Colorado State University where his research under the guidance of Professor Tomislav Rovis involves the development of new synthetic methods involving *N*-heterocyclic carbenes.



Stephen P. Lathrop was born in Indianapolis, Indiana in 1982. He received his BS degree in Chemistry in 2005 from Indiana University. Upon graduation, he began his doctoral work at Colorado State University with Tomislav Rovis. His graduate research has focused on the intramolecular Stetter reaction and its applications towards natural product synthesis.



Nathan T. Reynolds was born in 1977 in Ithaca, New York. After graduating from the State University of New York at Binghamton, he obtained his PhD in 2006 at Colorado State University under the direction of Professor Tomislav Rovis, where he worked on the preparation and synthetic applications of *N*-heterocyclic carbenes. He is currently a Senior Research Scientist at AMRI.



Mark S. Kerr was born in Duluth, Minnesota in 1978. He received his Bachelor of Arts in Chemistry from Coe College in Cedar Rapids, IA in 2000. That year he began his doctoral studies at Colorado State University under Professor Tomislav Rovis. His graduate work focused on the development of a family of chiral nucleophilic carbenes as catalysts for the intramolecular Stetter reaction. Upon completion of his PhD. in 2006, he joined the laboratory of professor David W. C. MacMillan at the Merck Center for Catalysis at Princeton University, working on the implementation of organocascade catalysis in natural product synthesis. He is currently a Scientist at Eli Lilly.



Javier Read de Alaniz was born and raised in Las Vegas, New Mexico. He received his B.S. degree from Fort Lewis College in 1999 where he conducted undergraduate research under the direction of Professor William R. Bartlett. His Ph.D. degree was obtained under the direction of Tomislav Rovis at Colorado State University in 2006. During that time he was the recipient of an NIH Ruth L. Kirschstein minority predoctoral fellowship. From 2006-2009, he was a University of California President's Postdoctoral Fellow with Larry E. Overman at the University of California, Irvine. He is currently an Assistant Professor of Chemistry at University of California, Santa Barbara.



Spandan Chennamadhavuni received his BS degree in chemistry (2000) from Kakatiya University (India), and earned his MS degree in organic chemistry (2002) from Osmania University (India). He worked as research assistant for Jon C. Antilla at University of Mississippi for three years where he carried out methodological studies on Bronsted acid catalytic amidation of imines, amidation of enones and developed enantio and diastereoselective versions of imine amidation. He moved to SUNY Buffalo to pursue doctoral studies under the supervision of Professor Huw M. L. Davies. He moved to Emory University along with rest of the Davies group to continue his PhD studies. His current project includes synthesis of various pharmaceutical agents utilizing rhodium carbenoid chemistry.