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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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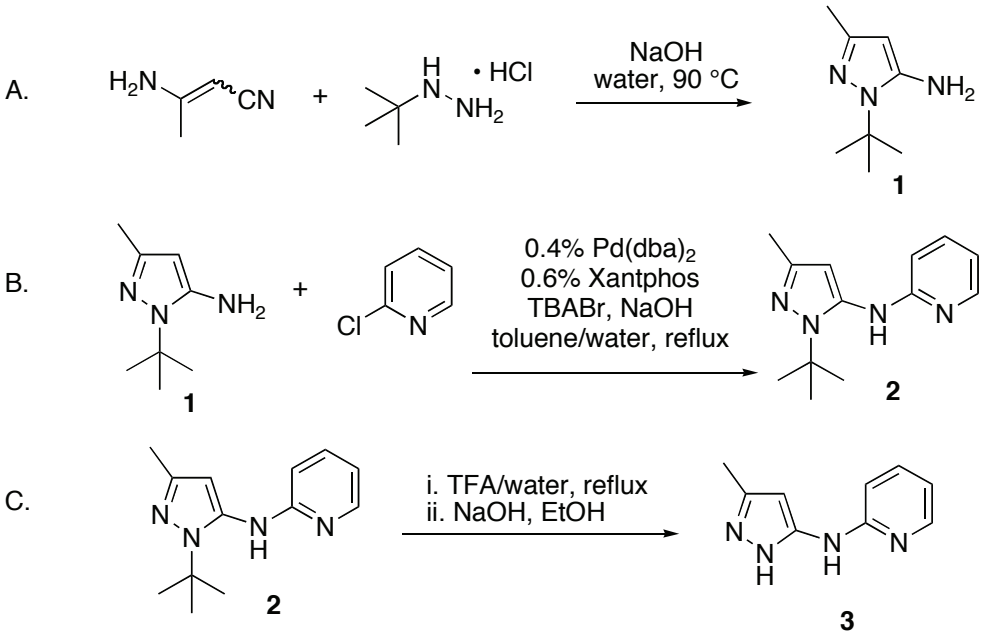
t-Butyl as a Pyrazole Protecting Group: Preparation and Use of 1-*tert*-Butyl-3-Methyl-1*H*-Pyrazole-5-Amine



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Checked by Scott W. Roberts and Margaret Faul.

1. Procedure

A. *1-tert-Butyl-3-methyl-1H-pyrazol-5-amine*. A 250-mL three-necked round-bottomed flask is equipped with a large oval stir bar (3.75 cm x 0.75 cm) and placed in an oil bath. Using a large plastic funnel, the flask is charged with solid *tert*-butylhydrazine hydrochloride (25.00 g, 98%, 196.6 mmol) (Note 1) and 2 M NaOH (98.3 mL, 2 M, 196.6 mmol) (Note 2) is added. Stirring is started at ambient temperature. When a complete solution has formed (approx. 10 min), 3-aminocrotononitrile (16.82 g, 96%, 196.6 mmol) (Note 3) is added through the funnel, and the stirring is continued. The funnel is replaced with a thermocouple (Note 4), an air-cooled reflux condenser is fixed to the flask, the third joint is sealed with a glass stopper, and the top of the condenser is connected to an ambient pressure nitrogen line (Note 5). The slurry is then heated to 90 °C (internal reaction temperature) with vigorous stirring for 22 h. After 22 h, the yellow/orange biphasic mixture is cooled to 57 °C, the glass stopper removed, and a ~2 mL aliquot of the well-stirred biphasic mixture is

removed with a pipette and placed in a 10-mL round-bottomed flask containing a small stir bar (1/2" x 1/8"). The 10 mL flask is then immersed in a dry ice/acetone bath for several minutes until completely frozen. The 10-mL flask is then removed from the bath and allowed to warm up slowly over a magnetic stirplate with the stirring on. As the mass melts, a slurry of seed crystals is formed (Note 6). With the bulk of the reaction being held and stirred vigorously at 57 °C, the seed slurry is introduced by pouring it through the empty joint into the 250-mL flask in a single portion. Crystallization is evidenced by the formation of large clear globules, and when this is apparent, the heating is turned off and the oil bath is removed. Vigorous stirring is continued, as the mixture cools to ambient temperature, and when the internal temperature is <30 °C, the slurry is immersed in an ice-water bath for one hour, during which time the tan solids adopt a more granular appearance. A 500-mL filter flask is fitted with a 7 cm porcelain filter funnel containing a paper filter, which is wetted with 2-3 mL of water. The slurry is filtered, and the cold filtrate (Note 7) is used to rinse the flask out and ensure maximum recovery of product (Note 8). The tan solids are allowed to suck dry on the filter for at least 5 min, and then scraped out onto a large piece of filter paper and any chunks are broken up with a spatula. The solids are then transferred into a tared 250-mL beaker, covered with a laboratory wipe, which is secured with a rubber band, and placed in vacuum oven at ambient temperature for 3 days (Note 9) to afford a light tan granular solid. The mass of the dried product is 27.0 g that was confirmed to be 97% purity by quantitative NMR. KF of the isolated solids is 3.7%, which affords a corrected yield of 87% (Notes 10, 11, 12, 13 and 14).

B. *N-(1-tert-Butyl-3-methyl-1H-pyrazol-5-yl)pyridin-2-amine.* To a 250-mL three-necked round-bottomed flask is added 2-chloropyridine (10.00 g, 99%, 87.2 mmol) (Note 15), and the flask is then equipped with an oval magnetic stir bar (3.75 cm x 0.75 cm), a water-cooled reflux condenser open to the air, an oil bath, a thermocouple (Note 4) and a plastic funnel. To the flask are then added **1** (14.46 g, estimated 97% potency, 91.5 mmol), *tetra*-butylammonium bromide (1.42 g, 99%, 4.40 mmol) (Note 16), toluene (100 mL) (Note 17) and a commercial solution of NaOH (110 mL, 2 M, 220.2 mmol) (Note 2). The funnel is replaced with a rubber septum, stirring started, and a six inch stainless steel syringe needle connected to a nitrogen source is inserted through the septum and placed below the level of the liquid in order to sparge the solution and headspace with a vigorous stream of nitrogen. Nitrogen is bubbled through the solution for 5 min, after which

time $Pd(dba)_2$ (0.20 g, 0.35 mmol) and Xantphos (0.31 g, 0.5 mmol) (Notes 18 and 19) are added as solids by removing the septum rapidly, pouring in the solids, and then quickly replacing the septum. Nitrogen is then bubbled through the mixture for two additional minutes, after which time the top of the condenser is attached to a static-pressure nitrogen source. The mixture is heated to vigorous reflux (internal temperature 87 ºC) (Note 20) with stirring for 24 h (Notes 21, 22, and 23). After 24 h, the oil bath is turned off and removed, and the mixture is cooled to <30 °C by immersion into a cool water bath. A 500-mL filter flask is equipped with a 7 cm porcelain funnel and a filter paper. The paper is wetted with water, and the solids are isolated by filtration (Note 24). The flask is rinsed with toluene (25 mL) and this is used to rinse the solids on the filter. The solids are washed with water (25 mL) and then EtOH (25 mL) (Note 25) and allowed to suck dry for >5 min. The solids are scraped off the filter paper with a spatula onto a large piece of filter paper and any solids are broken up. The solids are placed in a tared 250-mL beaker and covered with a laboratory wipe, which is secured with a rubber band, and placed in vacuum oven at 50 °C under full house vacuum for 17 h to afford 20.0 g of light yellow/green solids (100%) (Notes 26 and 27).

C. *N-(3-Methyl-1H-pyrazol-5-yl)pyridin-2-amine.* A 250-mL three-necked round-bottomed flask is charged with **2** (10.00 g, 43.4 mmol) and equipped with a magnetic stir bar (3.75 cm x 0.75 cm), oil bath, water-cooled reflux condenser open to the air (Note 28), thermocouple (Note 4), and plastic funnel. Deionized water (100 mL) is added, followed by trifluoroacetic acid (9.9 mL, 99%, 127.0 mmol) (Note 29). The mixture is then heated to 95 °C, and a clear light green solution is formed, with some dark solids observed floating in the solution. Once the mixture has reached 95 °C, it is held at that temperature with stirring for three hours. After three hours, the oil bath is turned off and removed, and the solution is cooled to <60 °C, at which time EtOH (50 mL) is added (Note 25). The solution is then further cooled to <30 °C using a cool water bath. A second 250-mL three-necked round-bottomed flask is equipped with two stoppers and a 4-cm coarse-fritted Büchner funnel (30 mL volume size) containing dry Celite™ (4.00 g). A few mLs of water is used to wet the Celite™ in order to form a filter pad. The Celite™ filter pad is washed until the filtrate is no longer cloudy and then the collection flask is connected to the funnel. The reaction mixture is carefully filtered through the pad into the second 250 mL flask using gentle vacuum (Note 30). The reaction flask is rinsed with water

(10 mL), which is then used to rinse the walls of the filter funnel and filter pad (Note 31). The filter and stoppers are removed, a pH probe is inserted through one of the unused side joints, and a Teflon stir paddle with a glass stir shaft assembly are introduced through the center joint and connected to an overhead stirrer (Note 32). A commercial solution of 5 N NaOH (25 mL) (Note 2) is then added via pipette rapidly at first and more slowly once pH 7 is reached, and the titration is continued until a final pH of 8-10 is reached (Notes 33, 34, 35, and 36). Upon neutralization, the solution gradually turns cloudy over a few minutes, and crystallization ensues. The slurry is placed in an ice-water bath for one hour with stirring. A 250-mL filter flask is equipped with a 5 cm porcelain funnel and filter paper. The paper is wetted with water (1-2 mL) and the product is isolated by vacuum filtration. To the flask is added water (25 mL) and any residual solids in the flask are rinsed onto the filter cake. After 2-3 minutes on vacuum, the solids are then washed with additional water (25 mL), and then sucked dry for 5 minutes. The solids are scraped onto a large piece of filter paper, broken up with a spatula, placed into a tared 250-mL beaker and covered with a laboratory wipe, which is secured with a rubber band, and placed in vacuum oven at 50 °C under full house vacuum for 15 h to afford the product (g, 6.73 g, 89%) as a pale tan powdery solid (Note 37).

2. Notes

1. *tert*-Butylhydrazine hydrochloride (98%) was obtained from Aldrich Chemical Co. Inc. and used as received.

2. Sodium hydroxide (2 M) was purchased from Fluka Analytical. Sodium hydroxide (5 M) was purchased from Sigma Aldrich. A 2 M solution prepared using NaOH pellets and water also works well.

3. 3-Aminocrotononitrile was obtained from Aldrich Chemical Co. Inc. (96%) and used as received.

4. The temperature of all reactions was controlled using a programmable J-KEM™ temperature controller.

5. If desired, the ammonia evolved from the reaction can be scrubbed by washing the outlet of the nitrogen line with diluted HCl.

6. This method of seed crystal generation is not necessary once the reaction has been run one time, as the isolated product is suitable to induce crystallization.

7. It is very important to only use the cold filtrate to wash the product, as the pyrazole is highly soluble in pure water, and the recovery is greatly reduced if plain water is used.

8. If a ring of product has formed in the flask or if large clumps of product have crystallized around the stir bar or thermocouple, a spatula is used to loosen them, and they are rinsed into the funnel with cold filtrate.

9. House vacuum was used (measured to be 10-20 mbar). Temperatures higher than ambient occasionally resulted in sublimation of the product and yield reduction. It was determined that after three days, the solids were reliably dried to a constant mass (less than 100 mg loss/day).

10. The solids have been shown by single crystal X-Ray crystallography to be a 1/3 hydrate, which is in theory 3.8% water by mass; in some cases additional surface water can yield higher KF data. When the reaction was performed at one-half scale, the isolated yield was 13.0 g (86%).

11. Pyrazole **1** is commercially available in small quantities, and larger amounts can be custom made. A 1 kg batch was obtained at great cost, but its purity and physical properties were vastly inferior to material produced by this method.

12. An HPLC potency method was developed by determination of the potency of a reference standard of material by quantitative ^{1}H NMR, and these results agreed well when combined with the KF data (mass balance of >99%).

13. The reactions can be monitored by HPLC using the conditions as described: Zorbax SB C8 column (Part Number 866953-906), 4.6 x 75 mm, 3.5 μm particle size; 1.0 mL/min flow, 40 °C column temperature, detection at 215 nm; Solvent A = 1 mL/L TFA in HPLC grade water, Solvent B = 1 mL/L TFA in HPLC grade CH_3CN; Gradient Elution (min): T(0) = 5% B to 80% B at T(7), hold at 80% B until T(8), to 5% B at T(8.1), hold at 5% B until 10.5 min. HPLC samples were prepared using 5% ACN (0.1% TFA):95% water (0.1% TFA) and a 5.0 μL injection volume.

14. Properties of Pyrazole **1**: mp 70–71 °C; IR (neat) cm^{-1}: 3435, 3331, 3228, 2976, 2937; ^{1}H NMR (400 MHz, DMDO-d_6) δ: 1.48 (s, 9 H), 1.95 (s, 3 H), 4.71 (brs, 2 H), 5.18 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 29.6, 58.2, 93.9, 145.3, 145.6; HRMS (ESI) calcd for $C_8H_{16}N_3$ ($M+H^+$): 154.1344, found: 154.13335, δ = 3.4 ppm; KF = 3.4-3.7%; weight % by quantitative ^{1}H NMR (triphenyl methane (Aldrich, 99%) used as internal

standard) = 97%; purity determined by HPLC method described by submitter (Note 13) = 100.0% at 230 nm, HPLC retention time = 3.10 min.

15. 2-Chloropyridine (99%) was purchased from the Aldrich Chemical Co. Inc and used as received.

16. *tetra*-Butylammonium bromide (99%) was purchased from Aldrich Chemical Co. Inc. and used as received.

17. Toluene (reagent grade) was purchased from Aldrich Chemical Co. Inc. and used as received.

18. The $Pd(dba)_2$ CoA for the $Pd(dba)_2$ used for this study reports carbon = 71.8%, Pd = 18.0% and Xantphos (97%) were purchased from the Aldrich Chemical Co. Inc. and used as received. They were weighed out in air, and no special precautions were taken.

19. All attempts to perform the coupling reaction *via* S_NAr reaction in the absence of palladium met with failure.

20. The azeotropic boiling point of the reaction mixture has been observed to be 87–89 °C; the set point of the temperature controller was set to 95 °C to ensure a very vigorous reflux, which improves mixing and is crucial to the success and reproducibility of the reaction.

21. During the reaction, the upper walls of the flask can become coated with a thin film of black precipitate, presumably Pd(0). Furthermore, a solid precipitate of product is observed to form a suspension between the water and toluene layers.

22. The reaction may be monitored effectively by removing the oil bath to stop the reflux, and stopping stirring to allow the reaction mixture to settle. Using a long syringe needle, a small amount of the upper toluene solution is removed (no solids should be drawn up), and one drop of the solution is placed in an HPLC vial, and diluted with 1 mL of 3A EtOH (3 µL HPLC injection). After sampling, the stirring is started again and the oil bath is replaced.

23. These amination conditions are somewhat unconventional. Due to the extreme insolubility of the product these conditions were the most satisfactory that we surveyed, as the product forms an easily stirred suspension. The reaction using K_2CO_3 in *t*-amyl alcohol resulted in an extremely thick mixture, which could not be effectively stirred and also resulted in an incomplete reaction.

24. This filtration is somewhat slow and each step requires approximately 5 min ensuring that the majority of the liquid is removed from the solids before the next wash solvent is introduced.

25. EtOH (200 proof) was purchased from Decon Labs, Inc.

26. The solids are contaminated with some gray particles, which are presumed to be Pd(0) (Note 33). The submitters report that the gray material along with a small amount of insoluble green impurity can be removed by magnetically stirring the solids (5.00 g) with 25 mL water and 25 mL EtOH at ambient temperature while 37% HCl (5.35 mL, 3 equiv) is added over a few minutes to afford a hazy solution. Filtration of the mixture through a pad of Celite™ (2 g, wetted with water) afforded a clear and nearly colorless solution. This solution was then neutralized by the addition of 50% NaOH (3.44 mL, 3 equivalents) over five min with stirring, which afforded a thick white slurry. Filtration of the solids, washing with water (100 mL), and drying *in vacuo* resulted in pure white **2** (4.77 g, 95%, mp = 229.4–230.5 °C).

27. When the reaction was performed at one-half scale, the isolated yield was 10.2 g (100%). Properties of pyrazole **2**: mp 229–231 °C (DSC); IR (neat) cm^{-1}: 2926, 1585, 1553, 1414; ^{1}H NMR (400 MHz, AcOH-d_4) δ: 1.62 (s, 9 H), 2.27 (s, 3 H), 6.13 (s, 1 H), 6.79 (d, J = 9.0 Hz, 1 H), 7.06 (t, J = 6.5 Hz, 1 H), 7.96 (ddd, J = 1.6, 7.2, 7.2 Hz, 1H), 8.28 (d, J = 5.3 Hz, 1 H), 11.81 (s, 1 H); ^{13}C NMR (100 MHz, AcOH-d_4) δ: 12.62, 29.2, 60.3, 104.8, 110.8, 114.6, 135.3, 139.3, 144.2, 147.0, 154.6; HRMS (ESI) calcd for $C_{13}H_{19}N_4$ ($M+H^+$): 231.1610, found: 231.16062, δ = 0.9 ppm; purity determined by HPLC method (Note 13): purity = 100.0% at 230 nm, HPLC retention time = 3.88 min.

28. It was observed that the reaction was slower when it run under a nitrogen atmosphere, this may be due to the more efficient removal of iso-butylene from the system when it is open to the air. A nitrogen sweep could also be employed.

29. Trifluoroacetic acid (99%) was purchased from Sigma-Aldrich. While the deprotection can be accomplished using aqueous HCl, we chose to develop the less volatile and corrosive trifluoroacetic acid method at hand. A 5–8 °C exotherm was observed during the fast addition of TFA into the water/pyrazole slurry.

30. The clear yellow filtrate was observed to have a tendency to foam, and caution must be used in order to ensure that none of the solution is sucked into the vacuum line and lost.

31. The filtration removes the black solids as well as dark green material, which is possibly related to the Xantphos ligand from step two and affords a clear, yellow/green solution.

32. While magnetic stirring can be used during the neutralization, the mixture becomes very thick and difficulties in maintaining the stirring can be encountered when using magnetic stirring.

33. The residual palladium levels were 4200 ppm in **2** and 31 ppm in **3** as measured by ICP-ICP/MS. Further palladium rejection studies were not conducted on this system.

34. The theoretical amount of NaOH required is 26.1 mL; typically 25 mL is required to adjust the pH to the desired level as some TFA is lost presumably to evaporation.

35. Normally the color of the solution fades to nearly colorless towards the end of the NaOH addition, if the pH becomes >11, a pink color has been observed, which can be neutralized by adjustment of the pH back to 8–10 with a few drops of TFA.

36. An exotherm of 5–10 °C is normally observed during the neutralization and can be controlled by the use of a cool water bath.

37. When the reaction was performed at one-half scale, the isolated yield was 3.16 g (84%). Properties of pyrazole **3**: mp 153–154 °C; IR (neat) cm^{-1}: 3076, 2918, 1603, 1573, 1435, 1316; ^{1}H NMR (400 MHz, AcOH-d_4) δ: 2.31 (s, 3H), 5.95 (s, 1 H), 7.08 (t, J = 6.7 Hz, 1 H), 7.44 (d, J = 9.0 Hz, 1 H), 8.03 (dt, J = 7.6, 1.0 Hz, 1 H), 8.20 (d, J = 6.1 Hz, 1 H), 11.77 (brs, 2 H); ^{13}C NMR (100 MHz, AcOH-d_4) δ: 11.8, 96.5, 116.4, 116.6, 137.8, 143.4, 145.6, 149.6, 151.8; HRMS (ESI) calcd for $C_9H_{11}N_4$ ($M+H^+$): 175.0984, found: 175.09738, δ = 2.5 ppm; purity determined by HPLC method (Note 13): purity = 100.0% at 230 nm, HPLC retention time = 3.27 min.

Safety and Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academies Press; Washington, DC, 2011.

3. Discussion

5-Aminopyrazoles are ubiquitous throughout pharmaceutical and agricultural chemistry and many currently marketed products contain this residue.[2] The introduction of the unprotected aminopyrazole moiety is frequently accomplished without incident, but in some cases the use of a protected variant is required to overcome unselective reactions or to

facilitate product isolation and purification. We sought to develop the large-scale single-step preparation of a suitably protected aminopyrazole that could be coupled efficiently with a chloropyridine derivative and then cleanly deprotected. A previous synthesis of a protected pyrazole in our laboratories utilized three chemical steps to generate a mono-substituted hydrazine, which was then condensed with a β–keto nitrile. The unprotected 5-aminopyrazole is inexpensive and commercially available, but many protection methods either failed altogether, or suffered from poor chemo and regioselectivity. In our hands, the analogous Boc-protected 5-aminopyrazole[3] was thermally and hydrolytically unstable to the amination reaction conditions. Our efforts turned back to ring synthesis, and a brief survey of commercially available mono-substituted hydrazines quickly lead us to *tert*-butylhydrazine hydrochloride as an inexpensive, relatively non-toxic, easily handled solid, stable, and safe masked hydrazine. The use of 3-aminocrotononitrile is noteworthy in that our previous synthesis had relied upon *in situ* generation of α-cyanoacetone from methylacetate and acetonitrile; the aminonitrile is an inexpensive and convenient synthon for aminopyrazole preparation. The use of the *tert*-butyl protection group is also noteworthy, as the *tert*-butyl group on the 5-aminopyrazole system seems to exhibit unusual lability; other *tert*-butylpyrazoles in our laboratories have not exhibited the same relative ease of deprotection. The *tert*-butyl group is an atom economic protecting group, the byproduct being *iso*-butylene (C_4H_8).

Pyrazole **1** has previously been prepared by Giori *et al*. in a similar fashion in refluxing EtOH using triethylamine as base.[4] Giori's procedure employs an aqueous extraction to isolate the product, which we found difficult given the high water solubility of the product. We have developed this modified procedure, which uses no organic solvent and an inorganic base, as an environmentally friendly alternative. Furthermore, the product isolation is extremely facile, affording crystalline material directly from the reaction mixture. The byproduct from the hydrochloride neutralization-NaCl, is important in achieving high product recovery. It was found that the solubility of **1** in pure water was *ca.* 100 mg/mL, where as its solubility in NaCl solution (10 g NaCl diluted with 100 mL water, approximately what is generated under these reaction conditions) was *ca.* 30 mg/mL at ambient temperature. We believe that this salting-out effect is responsible for the ability to isolate the product in high yield as demonstrated. The isolated material contains water, NaCl, and possibly some NaOH, but is relatively

free of organic impurities. Methods of further purification include vacuum sublimation, chromatography, or vacuum distillation.

The Buchwald-Hartwig amination has recently become an extremely popular method of aryl C-N bond formation.[5] We have found that the biphasic conditions as described above are very convenient in this case due to the extreme insolubility of the product. More conventional conditions using alcohol/carbonate bases afforded mixtures that could not be stirred and stalled reactions. The conditions described above use a low loading of transition metal, are simple to implement, and have proven to be robust in our hands. Both $Pd(dba)_2$ and $Pd_2(dba)_3$ work well for the reaction and we chose the former for stoichiometry determination convenience. We did not extensively screen phosphine ligands, but we found Xantphos to be convenient due to good reactivity, ease of use, and ready commercial availability. The addition of TBABr was introduced in order to act as a phase transfer agent and pull hydroxide base into the organic layer, as we had observed some reaction stalling, which we attributed to the organic layer being starved of base. The observation that a vigorous reflux is beneficial is likely due to additional deoxygenation of the solvent that is accomplished with the reflux, as well as improved mixing provided by the boiling action. The use of excess base in conjunction with the phase transfer catalyst and vigorous refluxing has resulted in a highly robust process.

Giori[4] demonstrated removal of the *tert*-butyl group in hot formic acid solvent. We wanted to identify an acid that could be used at lower stoichiometry and hence reduce the amount of base required for neutralization. We have found that many aqueous acids (including HCl and sulfuric) are competent at removal of the *tert*-butyl group, but TFA was convenient in that the volatility of TFA accomplishes a continuous washing of the sides of the reaction vessel during the course of the deprotection and avoids the formation of solids on the vessel walls, which has been observed with related systems.

This convenient three-step sequence highlights the efficiency with which **1** can be prepared and isolated. The utility of **1** is then demonstrated in a C-N bond formation to afford pyrazole **2**. Finally the ease with which the *tert*-butyl group can be removed is showcased with the aqueous acid deprotection and isolation of pyrazole **3**.

1. Chemical Product Research and Development, Lilly Research Laboratories, Lilly Corporate Center, Eli Lilly and Company, Indianapolis, IN 46285; k_cole@lilly.com.
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Appendix
Chemical Abstracts Nomenclature; (Registry Number)

tert-Butylhydrazine hydrochloride; (7400-27-3)
3-Aminocrotononitrile; (1118-61-2)
1-*tert*-Butyl-3-methyl-1H-pyrazol-5-amine; (141459-53-2)
2-Chloropyridine; (109-09-1)
$Pd(dba)_2$: bis(dibenzylideneacetone)palladium; (32005-36-0)
4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene; (161265-03-8)
Tetra-*n*-butylammonium bromide; (1643-19-2)
Trifluoroacetic acid; (76-05-1)

Kevin Cole was born in 1979 in St. Paul, Minnesota. He obtained a Ph.D. in chemistry in 2005 from the University of Minnesota Twin Cities campus, and worked in the laboratories of Professor Richard Hsung. In 2007, he completed postdoctoral studies in the laboratory of Professor K.C. Nicolaou at The Scripps Research Institute in San Diego, CA. In 2007, Kevin joined Eli Lilly and Company in Indianapolis, Indiana and works in Chemical Product Research and Development.

Patrick Pollock was born in Chicago, Illinois and grew up in San Diego, California. He attended the University of Washington and then San Diego State University working under the direction of Professor Mikael Bergdahl. He earned an M.S. in Chemistry in 2001 and then joined the Chemical Product Research and Development group at Eli Lilly and Company in Indianapolis, Indiana.

Scott W. Roberts was born in Ojai, California. He obtained a Ph.D. in Chemistry in 2007 from the University of Utah, where he worked under the direction of Professor Jon D. Rainier. In 2007, he completed postdoctoral studies under the direction of Professor Larry E. Overman. In 2009, Scott joined the department of Chemical Process Research and Development at Amgen Inc. in Thousand Oaks, California.