Organic Syntheses

Synthesis of the Isocyanide Building Block Asmic, anisylsulfanylmethylisocyanide

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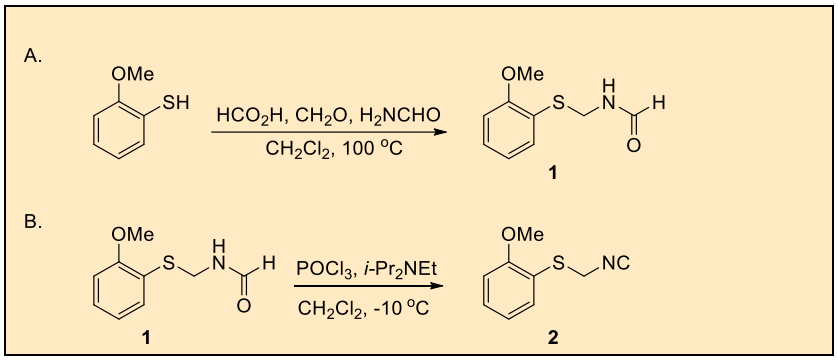

Procedure (Note 1)

A. *Preparation of N-((2-methoxyphenylthio)methyl)formamide (**1**).*
A 3-neck, 500 mL round bottom flask (note 2), equipped with a magnetic stir bar (PTFE-coated, cylindrical, 3 cm, Figure 1a) was charged with paraformaldehyde (17.7 g, 589 mmol, 4.1 equiv), formamide (43 mL, 48.6 g, 1.08 mol, 7.6 equiv), formic acid (27 mL, 33 g, 716 mmol, 5 equiv), and 2-methoxybenzenethiol (17.4 mL, 20 g, 143 mmol, 1 equiv, note 3, Figure 1b).

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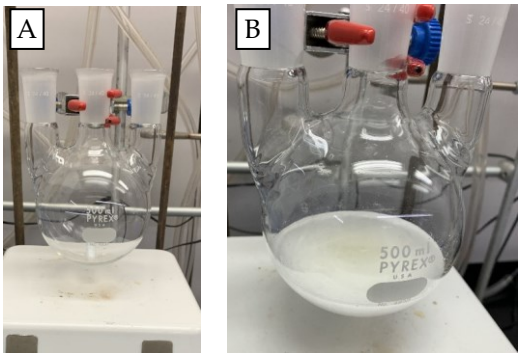


Figure 1. (a) Flask with stir bar (b) Flask with stir bar and reagents

The left and right necks are stoppered with a 24/40 rubber septum and the middle neck is connected to a reflux condenser stoppered with a 24/40 rubber septum that is pierced with an 18-gauge disposable needle open to the atmosphere (Figure 2).

Figure 2. Reaction set-up prior to heating.

The flask was immersed in an oil bath that was gradually heated to 100 °C over 1 h; the temperature was then maintained at 100 °C for an additional 3 h (note 4, Figure 3a-c).

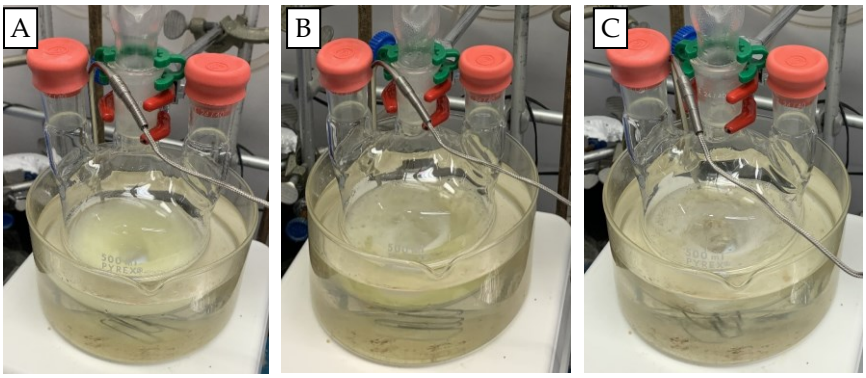


Figure 3. (a) Reaction mixture at 91 °C (b) Reaction mixture at 100 °C (c) Reaction mixture after 3h at 100 °C

The reaction was monitored by silica gel thin layer chromatography with both 5% (5:95) EtOAc-hexanes as the eluent to check for the presence of 2-methoxybenzenethiol and 75% (3:1) EtOAc-hexanes as eluent to monitor the formation of the formamide **1**. The TLC plate was visualized with UV light (note 5, Figure 4a). The reaction mixture was then allowed to cool to room temperature (Figure 4b).

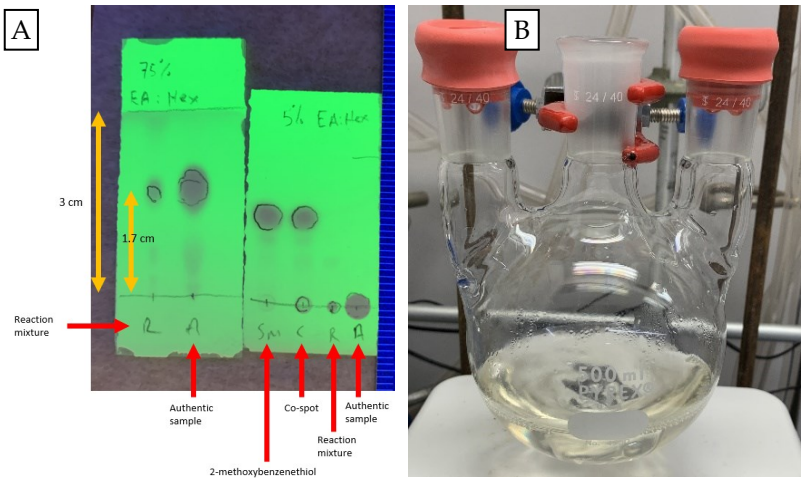


Figure 4. (a) TLC analysis after 3 h at 100 °C (b) Reaction mixture after cooling to rt.

Distilled water (200 mL) and dichloromethane (80 mL) were added to the crude reaction mixture (note 6, Figure 5).

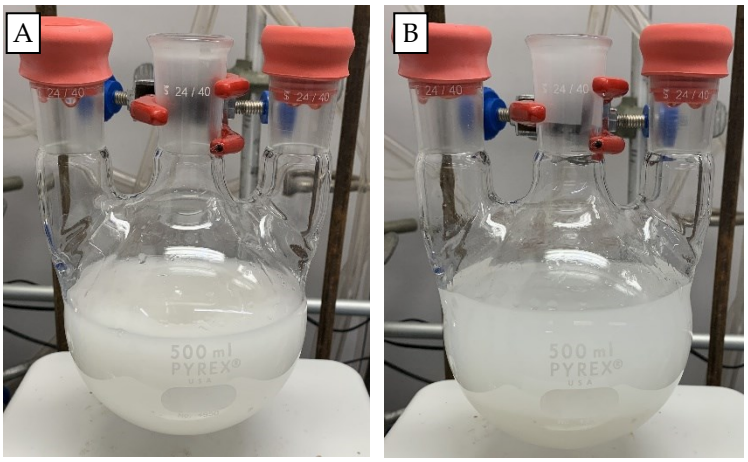


Figure 5. (a) The reaction mixture after the addition of water (b) The reaction mixture after the addition of dichloromethane.

The contents of the flask were transferred to a 1 L separatory funnel (Figure 6a). The phases were separated, and then the aqueous phase was extracted with dichloromethane (100 mL x 3). The combined organic extract was

washed with brine (200 mL, Figure 6b), dried for 10 min over sodium sulfate (Na_2SO_4, 80 g,) and concentrated to afford the crude formamide as a clear, pale yellow viscous oil (Figure 6c).

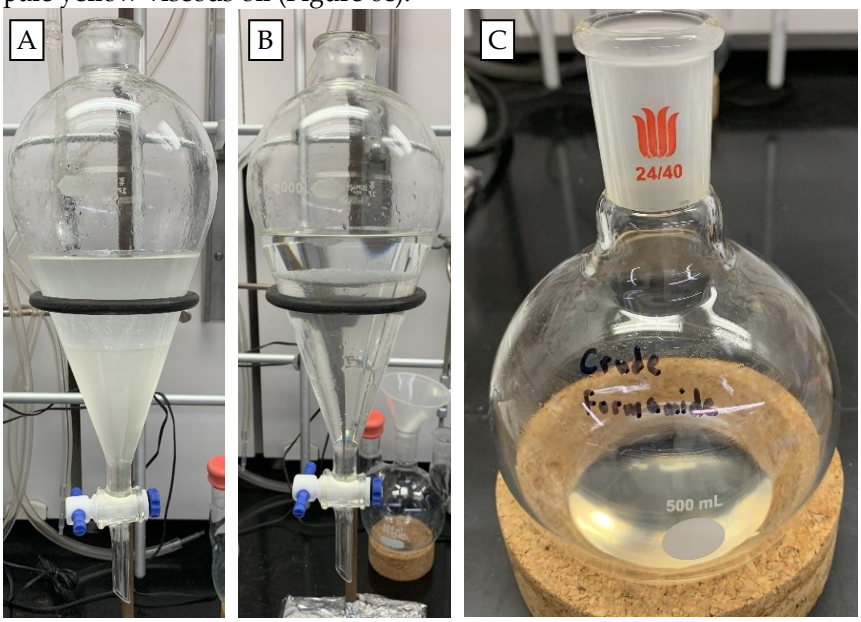


Figure 6. (a) Crude reaction mixture (b) The crude reaction mixture after aqueous washing with brine (c) The crude formamide

The formamide was purified by precipitation from a dichloromethane solution through the addition of hexane. The crude formamide was dissolved in dichloromethane (75 mL) to which hexanes was added portion-wise until no further precipitation was observed (note 7, Figure 7). The resultant suspension was placed in a -20 °C freezer.

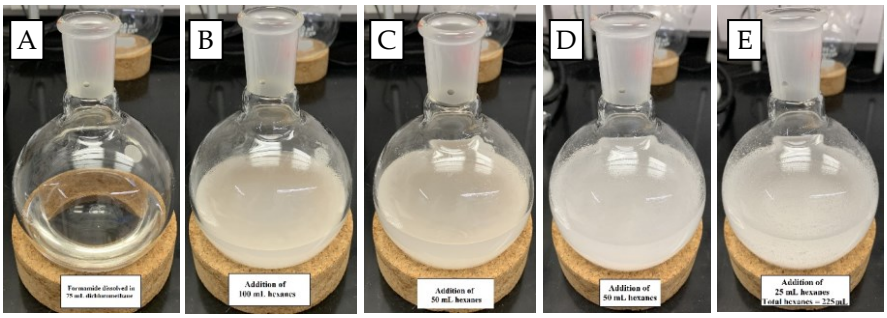


Figure 7. (a) Dissolution of the crude formamide in CH_2Cl_2 (b) Addition of 100 mL of hexanes (c) Addition of a further 50 mL of hexanes – 150 mL total (d) Addition of a further 50 mL of hexanes – 200 mL total (e) Addition of a further 25 mL of hexanes – 225 mL total.

After 19 h, the white solid (Figure 8a) was isolated by filtration through a 500 mL medium porosity, sintered Buchner funnel (Figure 8b). The solid on the frit was washed with cold (0 °C) hexanes (25 mL x 2). The solid was collected, dissolved in 50 mL of CH_2Cl_2 and then precipitated with hexanes (200 mL, note 8). The white solid was filtered, washed with cold (0 °C) hexanes (25 mL x 2). The solid was again collected, dissolved in 50 mL of CH_2Cl_2, precipitated with hexanes (200 mL), filtered, and washed with cold (0 °C) hexanes (25 mL x 2). The white solid was then dried under vacuum (1 mmHg) for 1 h at room temperature to afford 21.1 g (75% yield) of formamide **1** as a white solid (Figure 8c, note 10).

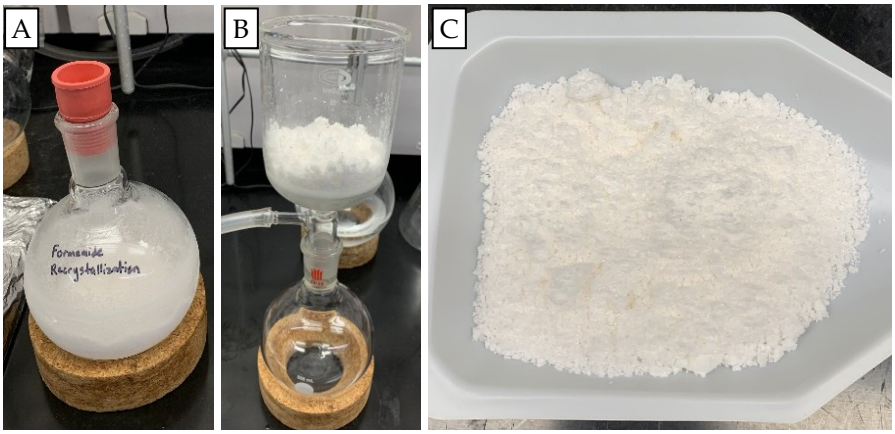


Figure 8. (a) Formamide **1** after 19 h at -20 °C (b) Formamide **1** after filtration (c) Formamide after third precipitation

B. *Preparation of Anisylsulfanylmethylisocyanide (Asmic)*

A 3-necked, 500 mL-round bottomed flask, equipped with a magnetic stir bar (PTFE-coated, cylindrical, 3 cm, note 2) was charged with *N-((2-methoxyphenylthio)methyl)formamide* (20 g, 101 mmol, 1 equiv, note 9); the left and right necks of the flaks were stoppered with 24/40 rubber septa (Figure 9a). Dichloromethane (120 mL, note 11) was added at room temperature (20 °C, Figure 9b). After the formamide was completely dissolved, diisopropylethylamine (88 mL, 65.5 g, 507 mmol, 5 equiv, note 12) was added from a graduated cylinder through the middle neck (note 13).

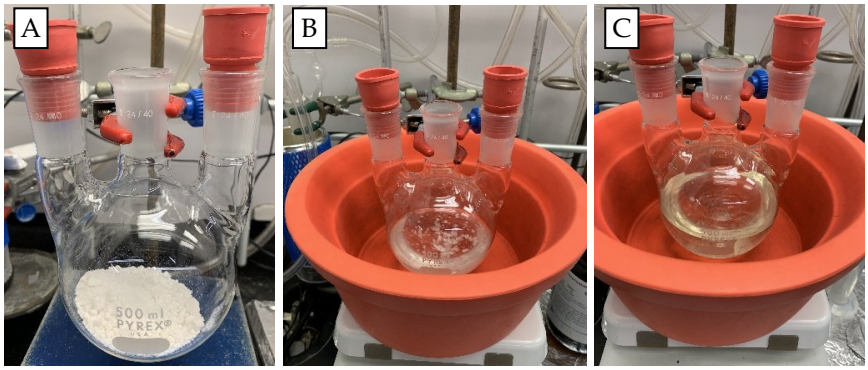


Figure 9. (a) Reaction set-up with formamide **1** (b) Dissolution of formamide **1** in CH_2Cl_2 (c) Reaction mixture after addition of diisopropylethylamine

After 10 minutes, the middle neck was equipped with a 100 mL, pressure-equalizing addition funnel capped with a septum pierced with an 18-gauge needle open to the atmosphere (Figure 10). The two side necks were capped with septa that were each pierced with an 18-gauge needle open to the atmosphere. The reaction mixture was immersed in an ice-salt bath that was cooled to -10 °C (note 14, Figure 10a). The addition funnel was charged with $POCl_3$ (19 mL, 31 g, 203 mmol, 2 equiv, note 15) that was added, dropwise, over 20 min; the reaction temperature was maintained between -12 to -9 °C during the addition (note 16, Figure 10b and 10c).

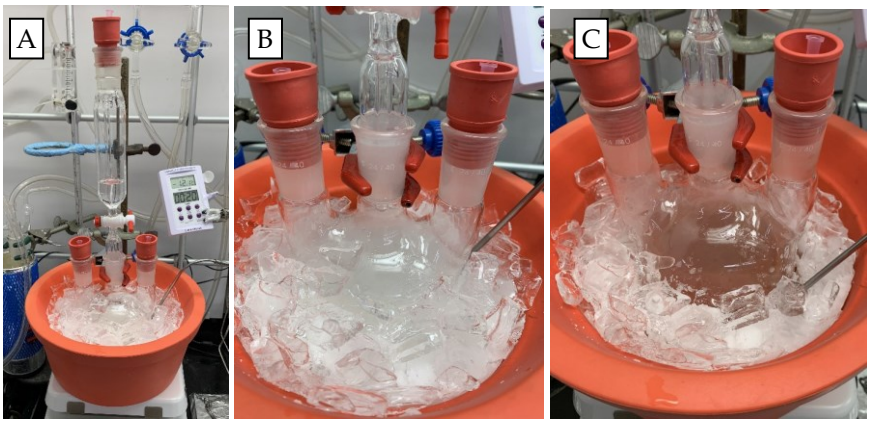


Figure 10. (a) Reaction mixture at -12 C with $POCl_3$ charged in the addition funnel (b) The reaction mixture 20 min after the addition of $POCl_3$ (c) The reaction mixture 90 min after the addition of $POCl_3$.

The reaction was monitored by thin layer chromatography on silica gel with both 1:9 EtOAc-hexanes and 3:1 EtOAc-hexanes as eluent and visualized under UV light (note 17, Figure 11). After 1.5 h, TLC analysis indicated that the reaction was complete.

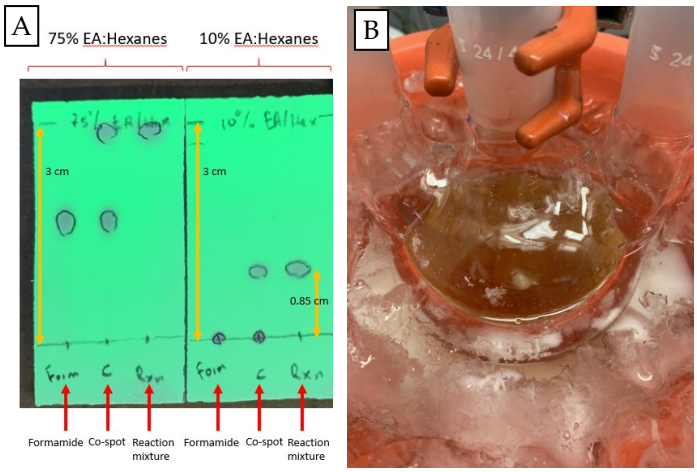


Figure 11. (a) TLC analysis of the reaction after 1.5 h (b) The crude reaction mixture after 1.5 h

The light brown reaction mixture was diluted with dichloromethane (100 mL), transferred to a 2-L Erlenmeyer flask equipped with a magnetic stir bar (PTFE-coated, cylindrical, 3 cm), and then cooled in an ice bath (Figure 12a). A cold (0 °C), saturated, aqueous solution (750 mL) of $NaHCO_3$ was slowly added down the side of the flask via pipette into the stirred reaction mixture until the initially vigorous reaction subsided; the remaining $NaHCO_3$ solution was added by slowly pouring the remaining $NaHCO_3$ solution into the reaction flask (note 18, Figure 12b) until the solution reached a pH = 8 (note 19, Figure 12c).

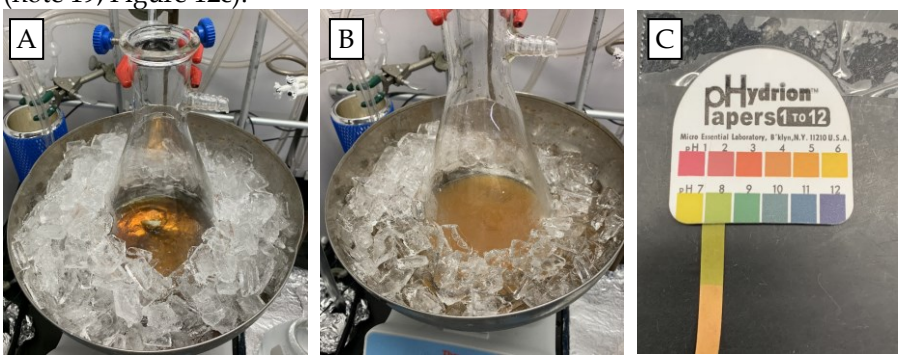


Figure 12. (a) The reaction mixture after dilution with CH_2Cl_2 (b) The reaction mixture after neutralization (c) The pH after addition of saturated, aqueous $NaHCO_3$.

The crude reaction mixture was allowed to warm to room temperature (Figure 13a) and then transferred to a 1-L separatory funnel (Figure 13b). The phases were separated (note 20), the organic layer was collected, and the aqueous phase further extracted with dichloromethane (1 x 100 mL, Figure 13c).

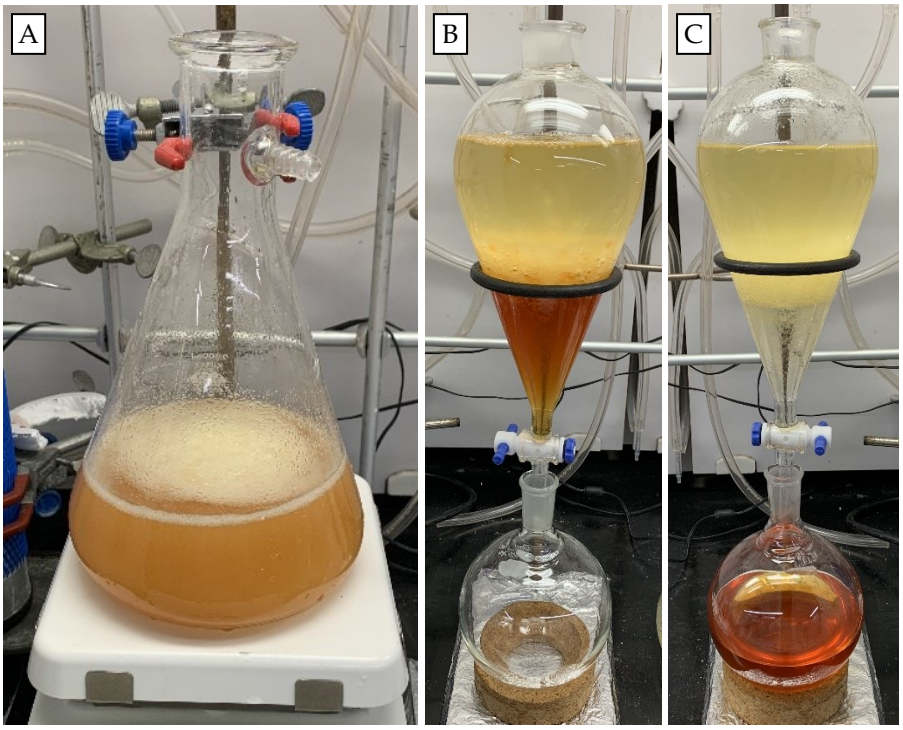


Figure 13. (a) The crude reaction mixture at room temperature (b) the reaction mixture after transfer to the separatory funnel (c) the CH_2Cl_2 extract of the aqueous phase.

The combined organic phase was concentrated by rotary evaporation (30 ° C, 20 mm Hg) to give an amber oil (Figure 14a). The crude oil was dissolved in ethyl acetate (400 mL) and then washed with brine (4 x 250 mL, Figure 14b and c).

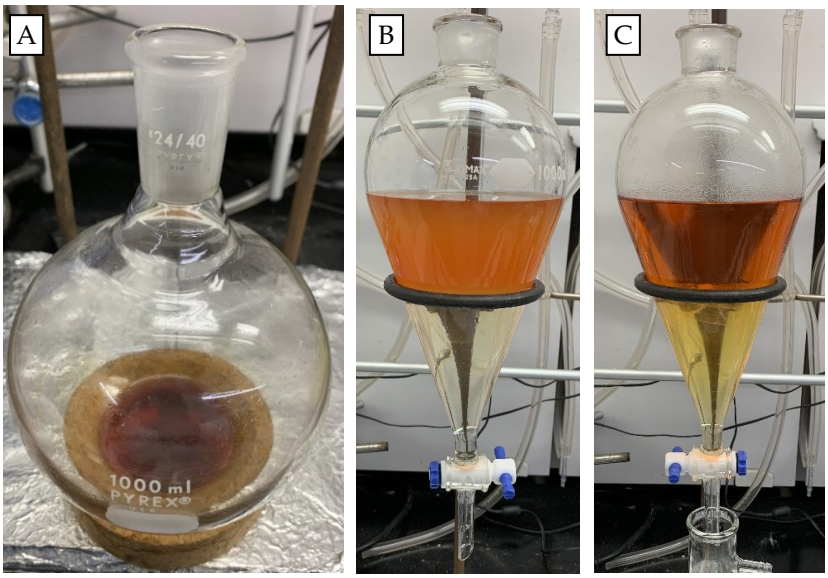


Figure 14. (a) Appearance of crude reaction mixture after concentration (b) Dissolution of crude Asmic in EtOAc followed by washing with brine (c). Crude Asmic after the fourth wash with 250 mL brine

The phases were separated and then the organic phase was combined (Figure 15a). The crude solution of Asmic was dried for 10 min over Na_2SO_4 (40 g, Figure 15b), filtered (Figure 15c), and then concentrated by rotary evaporation (30 ° C, 20 mmHg). Crude Asmic was subjected to a high vacuum (20 °C, 0.1 mmHg) for 15 min which gave a viscous amber oil in 18.05 g, 99% yield (Figure 15d). Asmic obtained at this stage is sufficiently pure for many applications without requiring further purification.

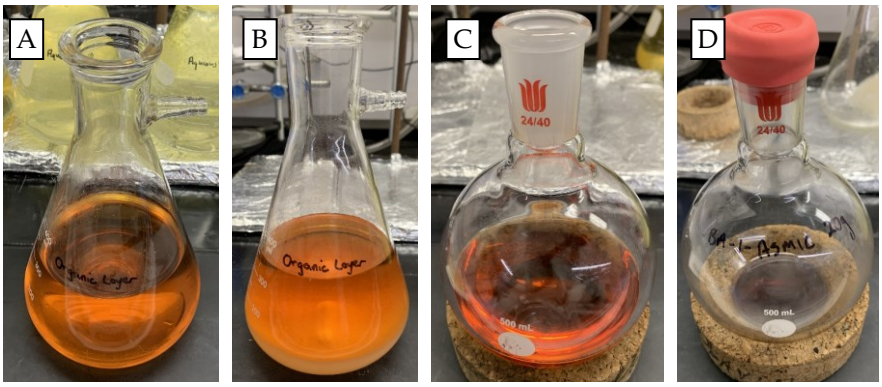


Figure 15. (a) The combined organic phase after extraction (b) The dried organic phase over Na_2SO_4 (c) The dry, filtered organic phase (d) Crude Asmic after removal of the solvent.

Asmic (18.05 g) was purified by dissolving in 100 mL CH_2Cl_2 and adsorbing onto 22 g Celite (note 21). The solvent was removed by rotary evaporation (30 ° C, 20 mmHg) and high vacuum (20 ° C, 0.1 mmHg) for 30 minutes. The adsorbed material (Figure 16) was then charged on a column (6 x 12 cm) of 125 g of silica gel (note 22) pre-equilibrated with hexane (Figure 17) and eluted with 2 L of 10% Ethyl acetate-hexanes (1:9 Ethyl acetate:hexanes). After 450 mL of solvent had eluted, 25 mL fractions were collected, and the elution continued for 56 fractions. Pure Asmic was obtained in fractions 7-53 (Figure 18) that were concentrated by rotary evaporation (30 ° C, 20 mmHg) and then under high vacuum (20 ° C, 0.1 mmHg) for 15 minutes to afford a clear oil. The oil was stored in a -20 °C freezer for 12 h resulting in 15.05 g (83% yield) of an off-white crystalline solid (note 23, Figure 19). Asmic is stable for at least 9 months when stored at -20 °C.

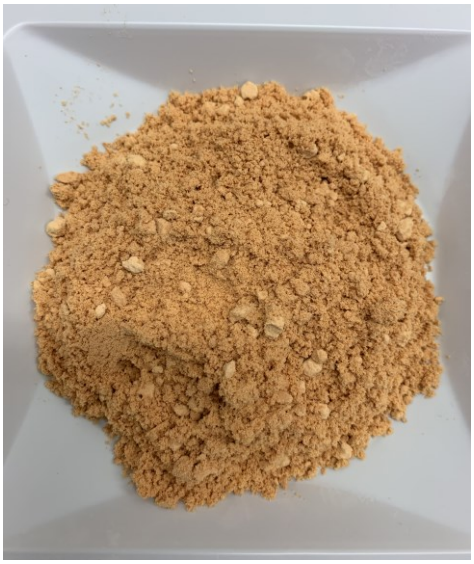


Figure 16. Asmic adsorbed on Celite.

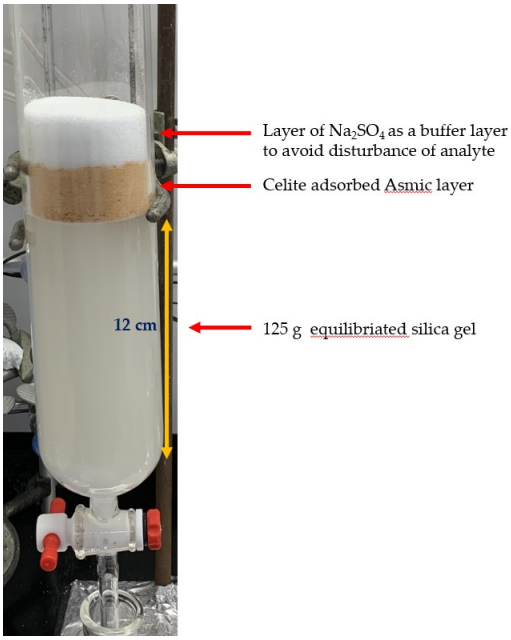


Figure 17. Silica gel column setup with adsorbed Asmic.

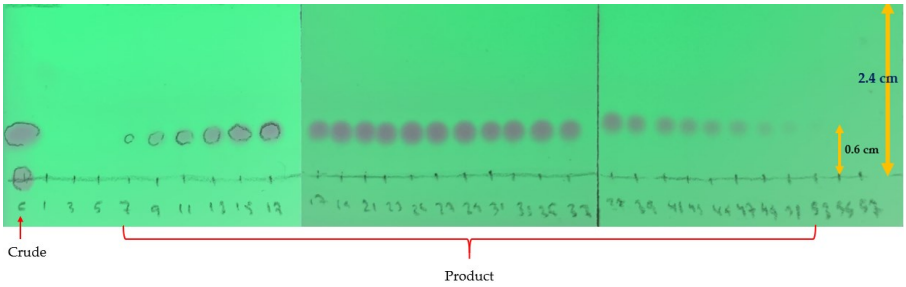


Figure 18. TLC of fractions 7-53 containing product.

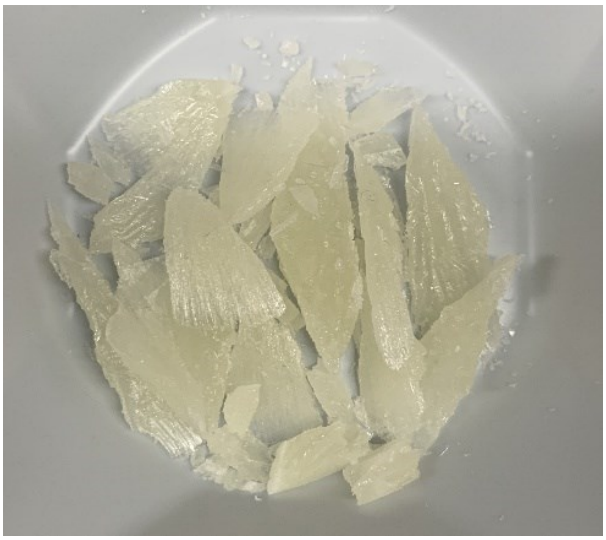


Figure 19. Off-white crystalline Asmic after rotary evaporation, high vacuum, and storage in a -20 °C freezer for 12 h.

Notes

1. Prior to performing each reaction, a thorough hazard analysis and risk assessment should be carried out with regard to each chemical substance and experimental operation on the scale planned and in the context of the laboratory where the procedures will be carried out. Guidelines for carrying out risk assessments and for analyzing the hazards associated

with chemicals can be found in references such as Chapter 4 of "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at https://www.nap.edu/catalog/12654/prudent-practices-in-the-laboratory-handling-and-management-of-chemical. See also "Identifying and Evaluating Hazards in Research Laboratories" (American Chemical Society, 2015) which is available via the associated website "Hazard Assessment in Research Laboratories" at https://www.acs.org/content/acs/en/about/governance/committees/chemicalsafety/hazard-assessment.html. In the case of this procedure, the risk assessment should include (but not necessarily be limited to) an evaluation of the potential hazards associated with paraformaldehyde, formic acid, formamide, 2-methoxybenzenethiol, N,N-diisopropylethylamine, phosphorous oxychloride, sodium hydrogen carbonate hexane, dichloromethane, ethyl acetate, silica gel, Celite, as well as the proper procedures for solvent evaporation and the application of high vacuum.

2. All glassware was dried in an oven (120 °C) for 1 h prior to use.
3. Paraformaldehyde (96%), formic acid (97%), formamide (high purity) and 2-methoxybenzenethiol (95%) were purchased from Acros, Alfa Aesar, VWR, and Oakwood Chemicals, respectively, and used as is without purification. Formamide and formic acid are used in excess as they serve as the solvent for the reaction. The Process Mass Intensity, PMI, is 71, considerably less than the industry standard of 200.
4. Upon heating, the reaction mixture changed from an initial white heterogeneous suspension of paraformaldehyde (Figure 3a), to a yellow suspension (Figure 3b), to a clear yellow solution at 100 °C after 3 h (Figure 3c). Upon cooling to rt, a clear, very pale, yellow solution of formamide **1** is formed (Figure 4d).
5. An aliquot (0.1 mL) is removed and diluted with CH_2Cl_2 (3 mL) to analyze the reaction mixture via TLC.
6. The reaction mixture may appear white and cloudy due to some precipitation of the desired formamide. If significant precipitation is observed, the solid can be filtered and the remaining solution subjected to the precipitation procedure described. The best result is obtained when the reaction mixture is diluted with dichloromethane and washed as described.
7. Portion-wise addition of hexane is recommended as direct rapid addition of hexane sometimes results in an oil that is unable to be precipitated.

8. The first recrystallization results in a white powder that may require iterative recrystallizations to obtain white crystalline solid formamide.
9. The material was dried for 1 h under high vacuum (0.1 mmHg) before performing the dehydration.
10. The precipitated formamide was used directly for the synthesis of Asmic. The formamide can be recrystallized as follows: Formamide (24 g) is dissolved in 50 mL of hot (60 °C) isopropyl alcohol which is then allowed to cool to room temperature (22 °C) over 12 h to afford 14.1 g (50% yield) of an off-white, crystalline solid (m.p. 82-84 °C). At 25 °C, two rotamers, one major and one minor, of the formamide are observed in the NMR spectra: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 1.5 Hz, 1H, major), 7.73 (d, J = 11.7 Hz, 1H, minor), 7.42 (dd, J = 7.9, 1.7 Hz, 1H, minor), 7.40 (dd, J = 7.6, 1.7 Hz, 1H, major), 7.35 (ddd, J = 8.3, 7.5, 1.7 Hz, 1H, minor), 7.29 (ddd, J = 8.2, 7.5, 1.7 Hz, 1H, major), 6.92 (m, 3H, major + minor), 6.18 (s, N-H, major), 6.05 (s, N-H, minor), 4.68 (d, J = 6.1 Hz, 2H, major), 4.55 (d, J = 7.0 Hz, 2H, minor), 3.91 (s, 6H, major+minor); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 160.7, 159.5, 158.6, 136.3, 133.4, 131.0, 129.6, 121.5, 121.3, 121.1, 119.1, 111.5, 111.3, 56.0, 56.0, 46.3, 40.9. IR (ATR) 3276, 3063, 3008, 2938, 2865, 2837, 1659.
11. Dichloromethane (ACS grade) was purchased from Fisher Scientific and used as is without purification.
12. *N*, *N*-diisopropylethylamine (99%) was purchased from Oakwood Chemicals and used as is. Excess *N*, *N*-diisopropylethylamine was employed to minimize hydrolysis by maintaining a basic medium throughout.
13. Precipitation may be observed after addition of *N*,*N*-diisopropylethylamine but this is not detrimental to the overall reaction.
14. The temperature is maintained below -9 °C during the course of the reaction.
15. Phosphorus oxychloride ($POCl_3$, 99%) was purchased from ACROS Organics and used as is without purification.
16. The addition commenced slowly at -12 °C to modulate a rapid exotherm that results in an initial, slight elevation in the reaction temperature. The temperature was maintained between -12 ° and -9 °C throughout the addition.
17. An aliquot (0.2 mL) was removed from the reaction mixture, diluted with CH_2Cl_2 (3 mL) and carefully quenched with saturated, aqueous $NaHCO_3$ solution. The mini-workup provided a clear visualization of the reaction mixture which avoids streaking due to the excess amine.

18. The saturated, aqueous $NaHCO_3$ was added dropwise to control a rapid exotherm that occurred upon the initial addition. Once the initial exotherm subsides, the saturated, aqueous $NaHCO_3$ solution can be slowly added by pouring the solution down the side of the flask. The pH was determined by testing with pH paper.
19. The pH of the mixture should not be higher than pH = 9 as this can sometimes result in the detrimental basic hydrolysis of the isocyanide to the formamide.
20. Care should be taken during the extraction; the separatory funnel should be gently shaken to avoid emulsions and the risk of a pressure build up from the evolution of CO_2.
21. Celite™ 545 (CAS # 68855-54-9) was purchased from Millipore Sigma and used as is.
22. Silica gel (SiliaFlash P60, 40 - 63 μm (230 - 400 mesh), 60 Å), was purchased from Silicycle and used as is.
23. 1H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.37 (td, *J* = 8.2, 7.6, 1.7 Hz, 1H), 6.98 (td, *J* = 7.6, 1.2 Hz, 1H), 6.93 (dd, *J* = 8.2, 1.2 Hz, 1H), 4.57 (s, 2H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.88 (t, N), 158.85 (*C*-O, *J* = 5 Hz), 134.7, 134.7, 130.9, 121.5, 118.8, 111.3, 56.0, 56.0, 42.9 (t, *C*-NC, *J* = 6 Hz); IR (ATR) 2940, 2838, 2137, 751 cm^{-1}, mp 25-27 °C. Asmic can be recrystallized from CCl_4 and pentane: Asmic (5.76 g) was dissolved in CCl_4 (8 mL) at rt and then was diluted with small volume of pentane and then cooled, initially to 0 °C and then to -20 °C. Additional pentane was added to initiate crystallization and the solution left at -20 °C for 3 days. The crystals were filtered, washed with three, 5 mL portions of CCl_4/pentane (1:5) and then dried under high vacuum at rt to afford 4.04 g (73%) of pure Asmic as a colorless crystalline solid. Concentration and recrystallization of the filtrate afforded an additional 0.93 g (17%) of pure Asmic for a total yield of 4.97 g (90%).

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

text can be accessed 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.

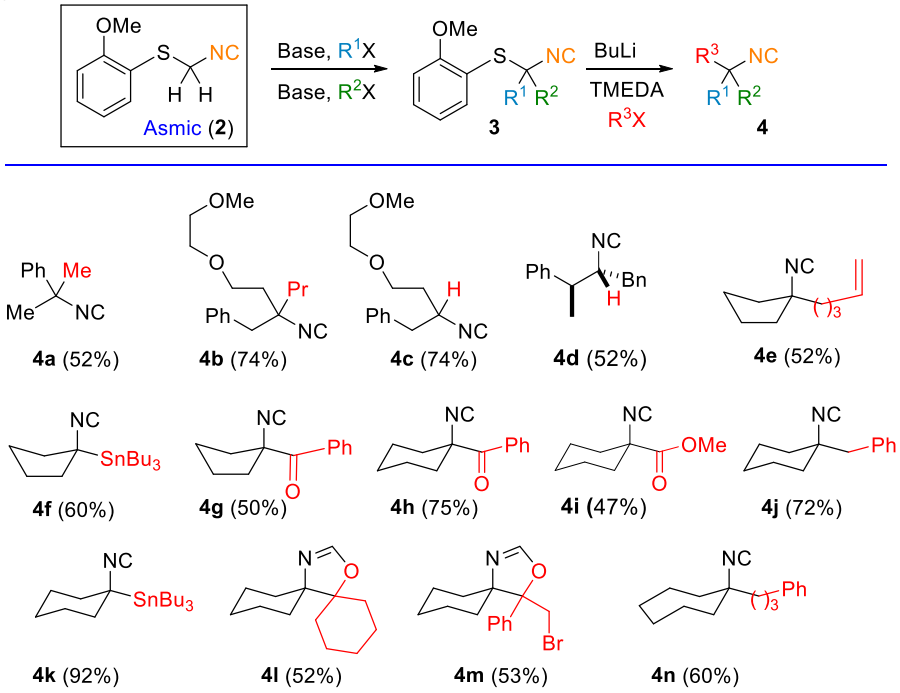
Discussion[1]

Isocyanides are extremely important precursors for a diverse suit of bond forming reactions: multi-component reactions,[2] transition metal insertions,[3] and radical reactions.[4] The promiscuous reactivity, driven by conversion of the terminal, divalent carbon to a more stable tetravalent state, obscures the limited availability of isocyanides; only *24* isocyanides are commercially available at prices less than $50/g of which almost half are derivatives of Tosmic.[5] Structurally complex isocyanides therefore require assembly from simpler precursors, most often via sequential formylation and dehydration of primary amines.[6]

Asmic (**2**), Anisylsulfanylmethylisocyanide,[7] fills the void by providing an efficient isocyanide building block that allows rapid access to structurally diverse substituted isocyanides[8] and heterocycles.[9] Formed by a sequential Mannich formylation-dehydration sequence, Asmic is a bench-stable, crystalline solid that stores well with minimal odor. Asmic is readily deprotonated by a variety of bases (NaH, LDA, BuLi) to afford a nucleophilic

organometallic that efficiently intercepts electrophiles (Scheme 1, **2** → **3**). The deprotonation-alkylation can be performed in separate steps or efficiently telescoped into a single synthetic operation to convert Asmic into dialkylAsmic **3**; the telescoped alkylation with α,ω-dihalides affords cyclic dialkylAsmic derivatives **3**.

Scheme 1. Asmic-Based Synthesis of Di- and Tri-Substituted Isocyanides

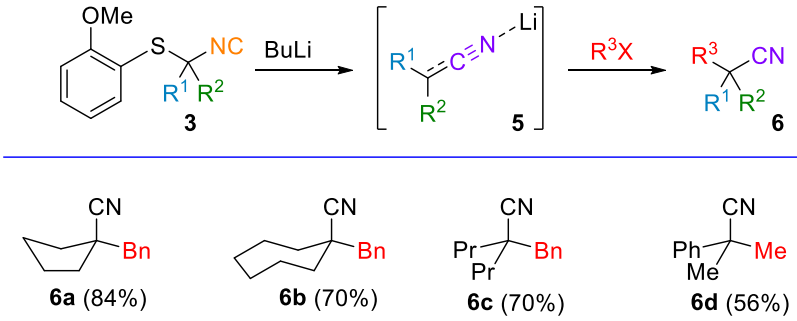


Treatment of dialkylAsmic **3** with BuLi triggers the rapid formation of a highly nucleophilic organolithium whose trapping with a variety of electrophiles efficiently generates tri-substituted isocyanides **4** (Scheme 1). The conversion of disubstituted Asmic derivatives **3** to reactive intermediates is extremely fast; the reaction with BuLi is essentially complete within 5 min at -78 °C. Subsequent trapping with an array of electrophiles ranging from alkyl halides to carbonyls to heteroatom species affords the corresponding trisubstituted isocyanide (Scheme 1 **4a – 4b**, **4e – 4k**, and **4n**, respectively); ketones react to afford oxazolines formed by attack of the intermediate alkoxide on the electrophilic isocyanide (Scheme 1, **4l** and **4m**). Disubstituted

isocyanides are accessed through two sequential alkylations of Asmic followed by the addition of BuLi and NH_4Cl (see **4c** and **4d**, Scheme 1). The Asmic-based syntheses allows an efficient route to substituted isocyanides with functionality that is otherwise difficult to access, such as the ketoisocyanides **4g** and **4h**.

DialkylAsmic derivatives **3** provide an efficient route to quaternary nitriles **6** (Scheme 2).[10] Omitting TMEDA during the addition of BuLi triggers a facile sulfur-lithium exchange-isomerization to afford the corresponding lithiated nitrile **5**, excellent nucleophiles that efficiently intercept a range of electrophiles.[11] Trapping the lithiated nitriles **5** with carbon electrophiles installs quaternary centers. The BuLi-initiated isocyanide-nitrile isomerization is equally efficient in forming cyclic nitriles (**6a** and **6b**) as for acyclic nitriles (**6c** and **6d**).

Scheme 2. Asmic-Based Synthesis of Quaternary Nitriles



Asmic is a versatile isocyanide building block whose sequential alkylations afford di- and tri-substituted isocyanides. The sequenced double alkylation, BuLi-exchange-alkylation provides a rapid route to isocyanides or nitriles that are otherwise difficult to access. The Asmic-based isocyanide synthesis is ideally suited to accessing homologous isocyanides for structure activity assays because the strategy is modular in nature and highly efficient.

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References

1. Contact information for the authors should be given in Reference 1, including email address and ORCID of the corresponding author. Use Palatino 10 pt font (Word Style "OS References"). This footnote should include acknowledgment of financial support.

Appendix
Chemical Abstracts Nomenclature (Registry Number)

N-((2-methoxyphenylthio)methyl)formamide: Formamide, *N*-[[(2-methoxyphenyl)thio]methyl]-; (118617-57-5)
Asmic, anisylsulfanylmethylisocyanide: Benzene, 1-[(isocyanomethyl)thio]-2-methoxy-; (1803329-89-6)

Fraser Fleming obtained a BS (Hons.) at Massey University, New Zealand, in 1986 and a Ph. D. in 1990 from the University of British Columbia, Canada under the direction of Edward Piers. He completed postdoctoral research with James D. White at Oregon State University before taking his first faculty position at Duquesne University, Pittsburgh in 1992. In 2013 he began a two-year appointment as a Program Director at the National Science Foundation working in the Synthesis and the Catalysis Programs. In 2015 he moved to Drexel University where his research is focused on the reactions of isocyanides and nitriles.

Embarek Alwedi received his B.S in 2001 and M.S in 2006 from Alfatah University, Libya. He remained at his alma mater for a further two years working as a lecturer before relocating to the US to pursue Ph.D with Prof. Paul Blakemore at Oregon State University. He completed his postdoctoral studies under the supervision of Prof. Fraser Fleming before moving to Merck, Rahway where he is working as research chemist in process R&D. His research interests lie in the development of new synthetic methodology and processes.

Bilal Altundas obtained his BS with honors in chemistry from Middle East Technical University in Ankara, Turkey in 2013 before moving to Miami University to pursue an MS in organic chemistry under the direction of Professor Hong Wang. Upon completing his MS in 2016, he started his Ph. D. under the guidance of Professor Fraser F. Fleming in the Department of Chemistry at Drexel University. His research interests are in synthetic methodology as applied to the reactions of ketenimines and in uncovering new reactions of metalated isocyanides.

Allen Chao obtained a B.S. in chemistry from the University of Pittsburgh in 2007 followed by industrial experience before embarking on a Ph. D. He began his graduate career at Duquesne University then moved with Prof. Fleming to complete his Ph. D. at Drexel University in 2018. He is currently working as a post-doctoral fellow in the Wistar Institute, Philadelphia. His research interests include development of PROTACs as therapeutic agents in treating cancer. He is invested in helping bridge the communication gap between the chemistry and biology disciplines.

Zachary L. Ziminsky began his undergraduate career at Drexel University. He worked on the large-scale synthesis of Asmic as a summer research student with Prof. Fleming.

Maanasa Natrajan completed her high school at Jnanodaya school, Bengaluru in India. In 2016, she started her undergraduate at Drexel University where she is currently a senior pursuing an individualized course of interdisciplinary study drawing upon neuroscience, chemistry, biophysics, and computation. She started research in organic chemistry with Prof. Fleming in her first year and then continued as a research assistant. She has performed systems biology research at Thomas Jefferson University, bioinformatics and phage biology at the Genome Institute of Singapore, and theoretical and computational neuroscience at Howard Hughes Medical Institute, Janelia. She plans to pursue a Ph. D. in neuroscience.