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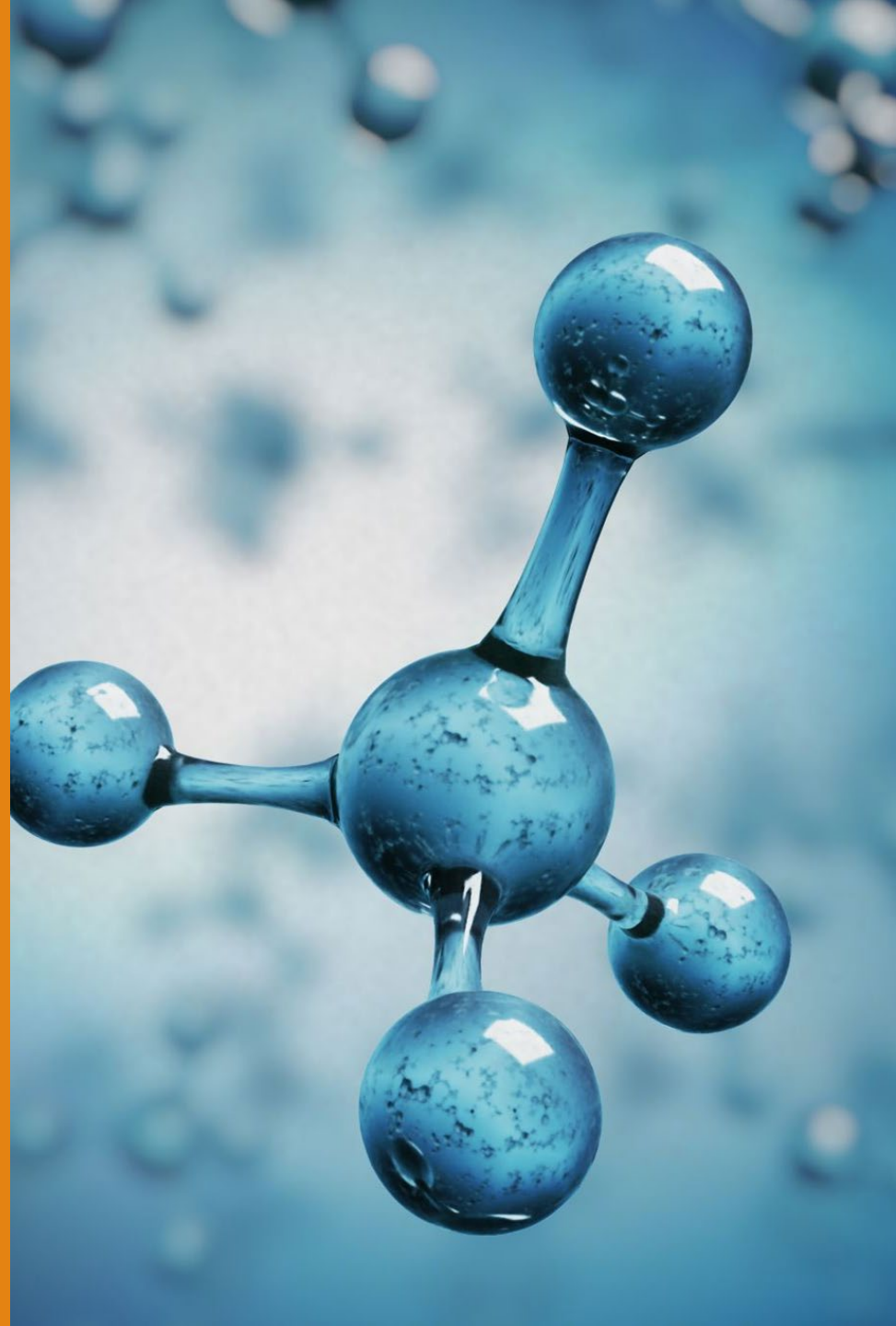

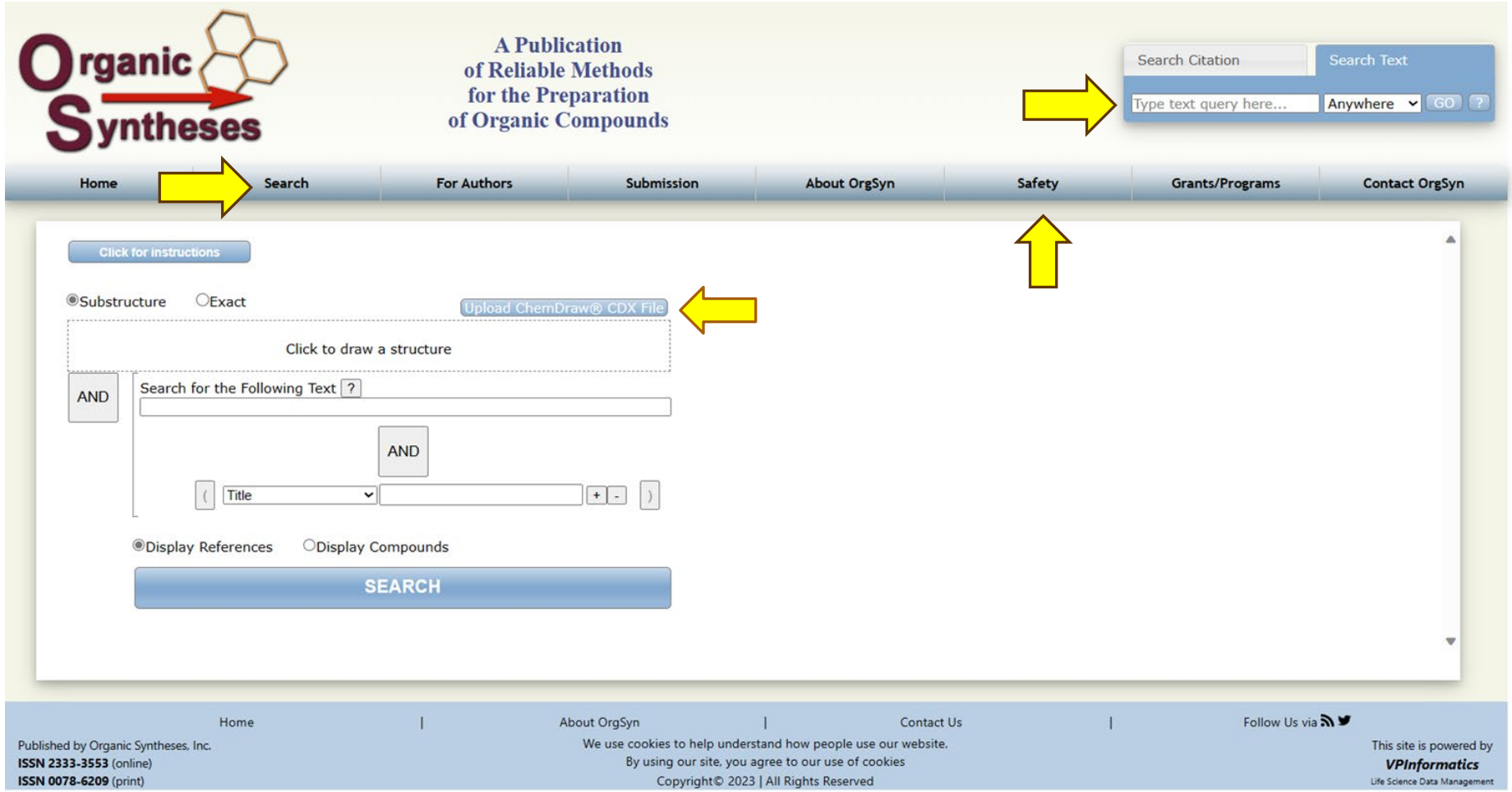

Organic Syntheses – Search & Safety

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Effective in August 2017, the first Note in every article is devoted to addressing the safety aspects of the procedures described in the article. The Article Template provides the required wording and format for Note 1, which reminds readers of the importance of carrying out risk assessments and hazard analyses prior to performing all experiments.

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Organic Syntheses - Safety

Organic Syntheses – Search Results for DMSO Anywhere in the Text

1

Preparation of MIDA Anhydride and Reaction with Boronic Acids

Peng-Jui Chen, Aidan M. Kelly, Daniel J. Blair, and Martin D. Burke

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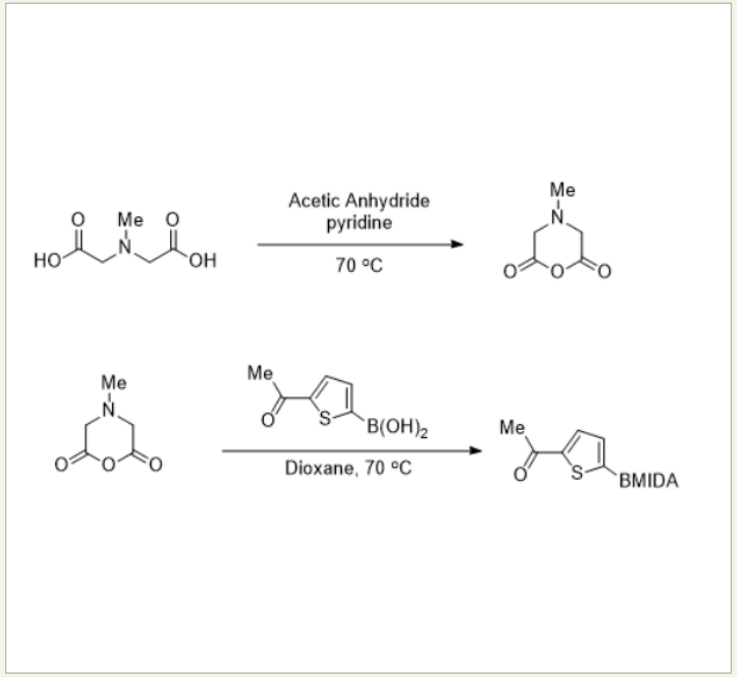
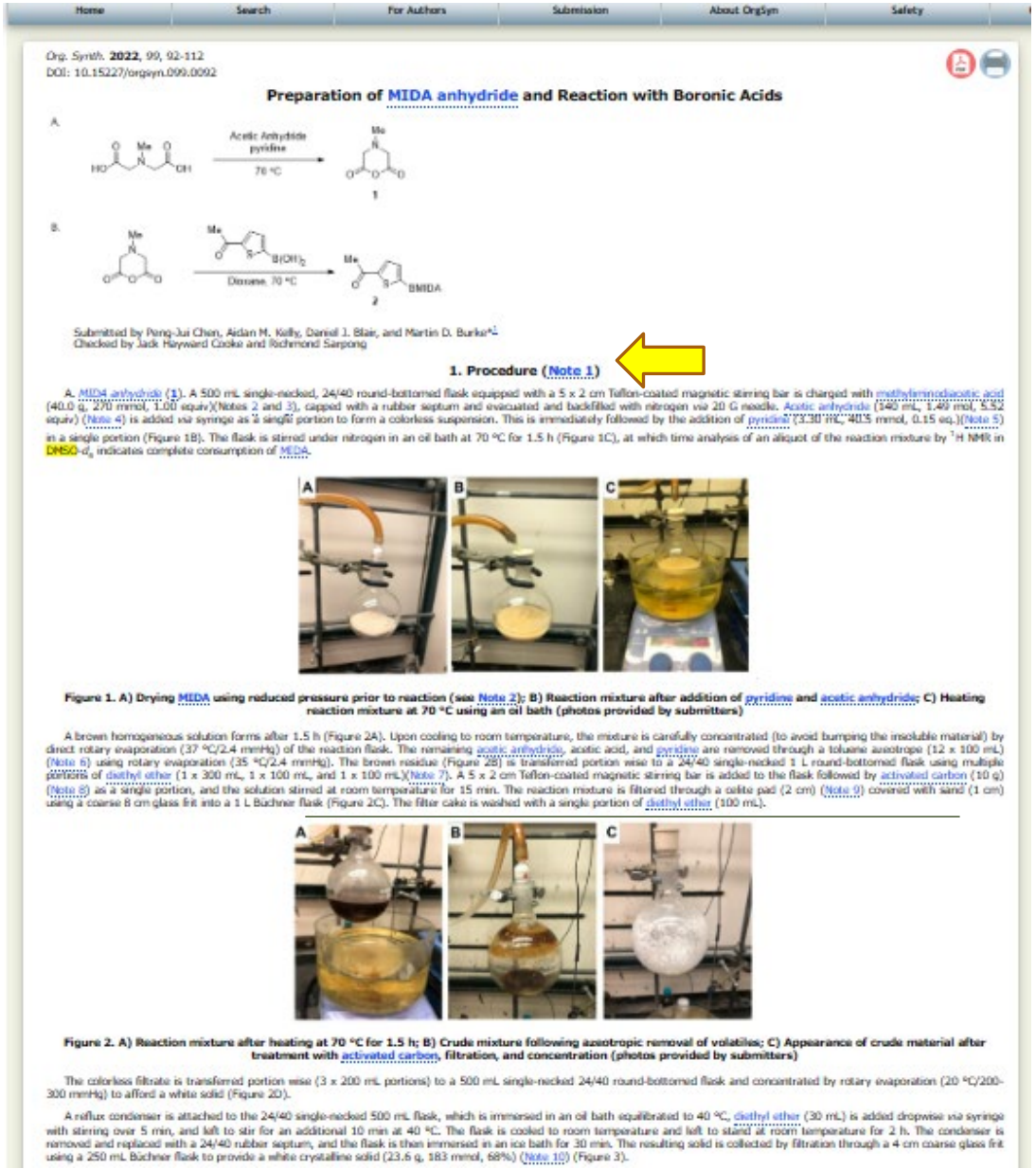


f an aliquot of the reaction mixture by 1H NMR in **dmso**-d6 indicates complete consumption of MIDA. Fig...23.3 g (67%) of 1. mp 42–44 °C; 1H NMR (500 MHz, **dmso**-d6) d: 2.31 (s, 3H), 3.60 (s, 4H); 13C NMR (126 MH....8 g (79%) of 2. mp 225–227 °C; 1H NMR (500 MHz, **dmso**-d6) δ: 2.53 (s, 3H), 2.64 (s, 3H) 4.17 (d, J = 17....



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Preparation of MIDA anhydride and Reaction with Boronic Acids

Submitted by Peng-Jui Chen, Aidan M. Kelly, Daniel J. Blair, and Martin D. Burke*
Checked by Jack Hayward Cooke and Richmond Sarpong

1. Procedure (Note 1)

A. MIDA anhydride (1). A 500 mL single-necked, 24/40 round-bottomed flask equipped with a 5 x 2 cm Teflon-coated magnetic stirring bar is charged with methyliminodiacetic acid (40.0 g, 270 mmol, 1.00 equiv)(Notes 2 and 3), capped with a rubber septum and evacuated and backfilled with nitrogen via 20 G needle. Acetic anhydride (140 mL, 1.49 mol, 5.52 equiv) (Note 4) is added via syringe as a single portion to form a colorless suspension. This is immediately followed by the addition of pyridine (3.30 mL, 40.5 mmol, 0.15 eq.)(Note 5) in a single portion (Figure 1B). The flask is stirred under nitrogen in an oil bath at 70 °C for 1.5 h (Figure 1C), at which time analysis of an aliquot of the reaction mixture by ^{1}H NMR in DMSO-d_6 indicates complete consumption of MIDA.

Figure 1. A) Drying MIDA using reduced pressure prior to reaction (see Note 2); B) Reaction mixture after addition of pyridine and acetic anhydride; C) Heating reaction mixture at 70 °C using an oil bath (photos provided by submitters)

A brown homogeneous solution forms after 1.5 h (Figure 2A). Upon cooling to room temperature, the mixture is carefully concentrated (to avoid bumping the insoluble material) by direct rotary evaporation (37 °C/2.4 mmHg) of the reaction flask. The remaining acetic anhydride, acetic acid, and pyridine are removed through a toluene azeotrope (12 x 100 mL) (Note 6) using rotary evaporation (35 °C/2.4 mmHg). The brown residue (Figure 2B) is transferred portion wise to a 24/40 single-necked 1 L round-bottomed flask using multiple portions of diethyl ether (1 x 300 mL, 1 x 100 mL, and 1 x 100 mL)(Note 7). A 5 x 2 cm Teflon-coated magnetic stirring bar is added to the flask followed by activated carbon (10 g) (Note 8) as a single portion, and the solution stirred at room temperature for 15 min. The reaction mixture is filtered through a celite pad (2 cm) (Note 9) covered with sand (1 cm) using a coarse 8 cm glass frit into a 1 L Büchner flask (Figure 2C). The filter cake is washed with a single portion of diethyl ether (100 mL).

Figure 2. A) Reaction mixture after heating at 70 °C for 1.5 h; B) Crude mixture following azeotropic removal of volatiles; C) Appearance of crude material after treatment with activated carbon, filtration, and concentration (photos provided by submitters)

The colorless filtrate is transferred portion wise (3 x 200 mL portions) to a 500 mL single-necked 24/40 round-bottomed flask and concentrated by rotary evaporation (20 °C/200-300 mmHg) to afford a white solid (Figure 2D).

A reflux condenser is attached to the 24/40 single-necked 500 mL flask, which is immersed in an oil bath equilibrated to 40 °C, diethyl ether (30 mL) is added dropwise via syringe with stirring over 5 min, and left to stir for an additional 10 min at 40 °C. The flask is cooled to room temperature and left to stand at room temperature for 2 h. The condenser is removed and replaced with a 24/40 rubber septum, and the flask is then immersed in an ice bath for 30 min. The resulting solid is collected by filtration through a 4 cm coarse glass frit using a 250 mL Büchner flask to provide a white crystalline solid (23.6 g, 183 mmol, 68%) (Note 10) (Figure 3).