A safe and simple synthesis of 1,4-bis(trimethylsilyl)buta-1,3-diyne[†]

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[†] Dedicated to Professor Graham Chandler on the occasion of his 80th Birthday and in celebration of his contributions to Chemistry.

Abstract

The buta-1,3-diynyl synthon 1,4-bis(trimethylsilyl)buta-1,3-diyne (**1**) is an important building block for the introduction of butadiyne motifs into organic and organometallic structures. Although **1** is commonly prepared from the Hay homo-coupling of trimethylsilylacetylene (catalytic CuI/tetramethylethylenediamine, O₂, acetone), the report of a significant explosion during this preparation, likely arising from a static discharge during addition of the catalyst solution to the alkyne/ acetone/O₂ rich atmosphere, prompts consideration of alternative procedures. Here we report the use of the robust Navale catalyst system (CuI/N,N-dimethylaminopyridine, O₂, NCMe) in the multigram-scale preparation of **1** through a procedure that entails minimal manipulation of all-glass apparatus, greatly simplifying the procedure and minimising risks associated with the preparation of this useful compound.

Substituted derivatives of buta-1,3-diyne are an important sub-class of conjugated organic molecules, offering rod-like physical structures with extensively delocalized electronic structures extending along the length of the carbon-chain. The parent compound, HC≡CC≡CH, is a condensable gas at atmospheric pressure, which readily polymerises, is extremely flammable and potentially highly explosive.^[1, 2] Symmetrically and asymmetrically di-substituted derivatives exhibit far greater thermal stability and through the application of suitably large groups, linearly conjugated oligoynes of remarkable length can be isolated.^[3-5] Substituted buta-1,3-diyne and conjugated polyynes have found application as structural elements and ‘wire-like’ conduits linking various fragments in organic compounds^[6-8] and organometallic complexes,^[9-12] and have been debated as models for the linear carbon

allotrope carbyne.^[5, 13] Conjugated diynes also serve as useful precursors for hetero- and metalla-cycles, and are found in many natural products and bio-active compounds^[14, 15] with potentially useful anti-inflammatory, anti-fungal, anti-viral and other therapeutic properties.^[16] The rod-like structure of di- and oligo-ynes makes them suitable for use in the construction of rotaxanes and the host of carbon-rich architectures.^[17-27]

Symmetrically substituted buta-1,3-diynes are commonly accessed through a variety of Cu-mediated or catalysed oxidative homo-coupling reactions of terminal alkynes, such as the Glaser-, Hay-, or Eglinton-coupling reactions (Scheme 1a).^[28] Asymmetrically substituted buta-1,3-diynes can be prepared through Pd(0)- and/ or Cu(I)-catalysed cross-coupling reactions of 1-halo-alkynes with a terminal alkyne, e.g. the Cadiot–Chodkiewicz-coupling (Scheme 1b). However, the synthesis of 1-halo-alkynes can be challenging or not possible due to the incompatibility of functional groups with the halogenation conditions. Alternatively, selective mono-deprotection of a symmetrically protected buta-1,3-diyne and subsequent reactions can be used to access a variety of 1,3-diyne derivatives.^[29-35]

Scheme 1 General reaction schemes for the formation of: (a) symmetrically substituted buta-1,3-diynes; (b) asymmetrically substituted buta-1,3-diynes.

As a stable, solid state and non-explosive buta-1,3-diyne synthon, 1,4-bis(trimethylsilyl)buta-1,3-diyne (**1**) is an important entry to buta-1,3-diyne containing organic and organometallic structures. The most convenient preparation of **1** involves the Hay-style oxidative coupling of trimethylsilylacetylene (TMSA) developed and described by Jones, Kendrick and Holmes (Scheme 2).^[36, 37] The Hay catalyst is prepared from copper(I) iodide (CuI) and tetramethylethylenediamine (TMEDA) in acetone. This catalyst solution is added portion-wise to a stirred solution of TMSA in acetone under a constant oxygen purge. As the homo-coupling reaction is exothermic, the temperature of the reaction mixture increases,

necessitating the use of a dry ice condenser to prevent loss of the highly volatile TMSA. The literature describes the need to add the catalyst portion-wise at a rate sufficient to contain the temperature below 35 °C, but also at a rate sufficient to maintain the catalyst in its active state. The active catalyst is rather poorly characterised,^[38, 39] but the catalytic cycle is dependent on the use of oxygen to complete the Cu-based redox cycle that is associated with alkyne oxidative homo-coupling. If the oxygen concentration in solution is insufficient, the catalyst is over-reduced, leading to the precipitation of elemental copper. If the oxygen concentration is too high over prolonged periods, the active copper(I) catalyst is subject to over-oxidation leading to the precipitation of copper(II) oxide. Therefore, the rate of oxygen bubbling through the solution has to be adjusted to maintain the copper(I)-TMEDA catalyst in solution and tune the reaction rate. This is adjudged by eye from the colour of the reaction solution, and necessitates considerable skill and experience in the reaction on the part of the experimentalist. The operator therefore has to constantly monitor the temperature of the reaction mixture, the rate of condensation of TMSA on the dry-ice-condenser and the colour of the reaction mixture and accordingly adjust the rate of addition of the catalyst solution, the oxygen flow and external cooling. Furthermore, the TMEDA leads to the enolisation of the acetone solvent, and subsequent aldol-style polymerisation of the solvent.

Further to these challenges, there has been a report of an explosion during the course of the reaction, causing injury.^[40] It was believed that static discharge between a metallic thermometer probe inside the reaction flask and the syringe needle used to add the catalyst solution caused ignition of the flammable vapours in the oxygen-rich atmosphere leading to the accident. Clearly an improved protocol that improves both the practicality and safety of the reaction is highly desired.

Scheme 2 General reaction scheme of the copper(I)-catalysed oxidative homo-coupling of TMSA

A recent study of copper-catalysed oxidative couplings of various terminal alkynes by Navale *et al.* explored different catalyst systems and solvents for the homo-coupling of various alkynes, with a 5 % CuI – 10 % 4-dimethylaminopyridine (DMAP) catalyst system used in a one-pot reaction in acetonitrile solution in air determined as most effective.^[41] The Navale method, although only reported on a 100 mg scale, appeared to offer significant potential to address safety concerns present in the existing Hay-based protocol. Attention was therefore turned to scale-up and optimisation of the synthesis of 1,4-bis(trimethylsilyl)buta-1,3-diyne using the Navale catalyst.

The Navale catalyst was prepared in the reaction flask by stirring CuI and DMAP in acetonitrile, giving a brown-green coloured solution. The reaction vessel was fitted with a dry ice condenser to avoid loss of the volatile TMSA during the reaction, which was carried out under an oxygen atmosphere. At the beginning of the reaction an external water bath at room temperature was applied for mild cooling. This proved sufficient to maintain the reaction temperature below 35 °C (monitored by a glass thermometer). Once the catalyst solution was prepared and the atmosphere enriched with oxygen, the alkyne was added in one single portion through a glass funnel to eliminate the risk of static discharge. This caused the colour of the reaction mixture to change to a teal blue within 5 minutes. Over the course of the reaction the colour of the reaction mixture returned to the brown-green colour of the initial catalyst solution. Upon completion of the reaction (ca. 8 hours) the reaction mixture was a black suspension with the catalyst completely oxidised to copper(II) oxide. Adjustment of the oxygen flow was unnecessary during the course of the reaction. During multiple reaction attempts, no over reduction of the catalyst was observed. Additionally, although a pure oxygen atmosphere was present, no over-oxidation was observed before the reaction was completed. Workup was performed simply, by removing the solvent followed by extraction of the residue with hexanes and filtration of the extracts through a silica plug. Removal of the solvent gave the desired compound **1**, the purity of which was determined to be 99.5 % by quantitative ¹H-NMR spectroscopy using 1,3,5-tri(methoxy)benzene as internal standard.

The yield of 1,4-bis(trimethylsilyl)buta-1,3-diyne (**1**) from the Hay-coupling of TMSA is reported to be 68-76 % on a 50 g scale.^[36, 37] The new procedure described here gave a slightly lower yield of 58 – 59 % on a 15-gram-scale and 52 % on a 50-gram-scale. Despite

the lower yields, the new method offers advantages in terms of experimental expedience, with a simple water bath used to maintain the reaction temperature below 35 °C to reduce the loss of alkyne; no manipulation of oxygen flow is necessary during the course of the reaction. The use of an all-glass setup further eliminates spark hazards. Unfortunately, the use of a pure oxygen atmosphere proved absolutely necessary. Carrying out the reaction in air, lead to the formation of copious amounts of red-brown precipitate which can be explained by the formation of elemental copper. By analogy with the Hay reaction, this is assumed due to over-reduction of the catalyst due to insufficient oxygen concentrations in solution when performed in air. Although this issue of handling terminal alkynes in an oxygen rich atmosphere remains due to the chemical nature of the reaction, the revised procedure reduces and manages risks and allows access to significant amounts of 1,4-bis(trimethylsilyl)buta-1,3-diyne at low cost in a reliable and safe manner.

Experimental

General comments:

Oxygen of industrial grade supplied by BOC was used. All other solvents and chemicals were of at least laboratory grade and used as received. No special precautions to exclude air or moisture were taken during work-up and isolation.

Preparation of 1,4-bis(trimethylsilyl)buta-1,3-diyne (1)

A 250-ml, three necked, round bottom flask was equipped with a dry ice condenser, thermometer and a 2.5-cm Teflon-coated, egg-shaped magnetic stirrer bar. The top of the dry ice condenser was connected by rubber tube to a glass T-piece which was connected to an oxygen cylinder and a bubbler. The three necked flask was charged with acetonitrile (100 ml),

copper (I) iodide (1.44 g, 7.6 mmol, 0.05 eq) and N,N-(dimethylamino)pyridine (1.86 g, 15.3 mmol, 0.1 eq) giving a green-brown solution (Figure S1).

After flushing the system while stirring with oxygen for 5 minutes, the three-necked flask was closed with a rubber septum. An external water bath at ambient temperature was applied to cool the three-necked flask, the dry ice condenser was charged with an acetone-dry ice cooling mixture and the oxygen flow regulated to a constant flow of approximately one bubble per second. (Figure S2). During the reaction a high stirring speed was applied to ensure a good gas intake into the solution through creation of a vortex.

Trimethylsilylacetylene (15 g, 152.7 mmol, 1 eq) was added to the green-brown catalyst solution via funnel through the free side neck. The internal temperature slowly rose up to a maximum of 32 °C and the colour changed to a blue-green in within 5 minutes (Figure S3). After 10 minutes, the internal temperature stabilised at 27 °C. After 15 minutes the mixture presented as a dark green solution with light-coloured precipitate. After 2 hours the colour of the mixture changed back to the green-brown colour of the initial catalyst solution with a light-coloured precipitate and the temperature equilibrated at ambient temperature. For the first two hours the dry-ice condenser was refilled with dry ice every 15 minutes.

The reaction mixture was stirred for another 6 hours during which the mixture darkened to black and the temperature dropped to ambient temperature indicating the completion of the reaction. The black thick slurry was poured into a 1-l single necked, round bottom flask. The three-necked flask with a thick oily black residue remaining on the walls of the flask was washed with CH₂Cl₂ (2 x 50 ml) and hexanes (2 x 50 ml) to help transferring the remaining black solids to the 1-l, single necked, round bottom flask, leaving only a partial copper-mirror left in the three necked flask. The solvent of the black mixture was removed by rotary evaporation. During the removal of the solvent higher temperatures and very low pressures were avoided as the product sublimes under such conditions. The oily black residue thus obtained was suspended in hexanes (4 x 25 ml) by sonication for 1 minute and filtered through a silica plug (silica, approx. 10 cm x 4.5 cm Ø) and eluted with hexanes (900 ml).

After removing the solvent on a rotary evaporator, the product was obtained as white crystalline solid. The product was dried under vacuum at ambient temperature (5 mbar for 40 minutes, 1 mbar for 1 minute). Yield: 8.7 – 8.8 g (58.5 - 59.3 %). ^1H NMR (300 MHz, CDCl_3 , ref. 7.26 ppm) δ / ppm: 0.18 (s, 18H). ^{13}C NMR (75 MHz, CDCl_3 , ref. 77.16 ppm) δ / ppm: 0.26, 86.08, 88.09. IR (ATR) $\bar{\nu}_{\text{max}}$: 2066 (m), 1263(m), 1250 (s) cm^{-1} . mp: 104-106 °C (lit. 106-108 °C,^[42] 107-108 °C^[43]). The purity of the sample was determined to be 99.5 % by quantitative NMR in CDCl_3 with 1,3,5-trimethoxybenzene as internal standard and estimated to be 100 % by standard GC-MS analysis.

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Conflict of Interest statement

The authors declare no conflicts of interest

References

- [1] P. G. Urben, *Bretherick's Handbook of Reactive Chemical Hazards (Seventh Edition)*, Vol. 1, Academic Press, Oxford, **2007**.
- [2] L. Brandsma, *Preparative Acetylenic Chemistry*, 2nd ed., Elsevier, Amsterdam, **1988**.
- [3] M. Krempe, R. Lippert, F. Hampel, I. Ivanović-Burmazović, N. Jux, R. R. Tykwinski, *Angew. Chem. Int. Ed.* **2016**, *55*, 14802-14806.
- [4] M. Tommasini, A. Milani, D. Fazzi, A. Lucotti, C. Castiglioni, J. A. Januszewski, D. Wendinger, R. R. Tykwinski, *J. Phys. Chem. C* **2014**, *118*, 26415-26425.
- [5] R. R. Tykwinski, *Chem. Rec.* **2015**, *15*, 1060-1074.

- [6] L.-O. Pålsson, C. Wang, A. S. Batsanov, S. M. King, A. Beeby, A. P. Monkman, M. R. Bryce, *Chem. Eur. J.* **2010**, *16*, 1470-1479.
- [7] D. C. Milan, O. A. Al-Owaedi, M.-C. Oerthel, S. Marqués-González, R. J. Brooke, M. R. Bryce, P. Cea, J. Ferrer, S. J. Higgins, C. J. Lambert, P. J. Low, D. Z. Manrique, S. Martin, R. J. Nichols, W. Schwarzacher, V. M. García-Suárez, *J. Phys. Chem. C* **2016**, *120*, 15666-15674.
- [8] P. Moreno-García, M. Gulcur, D. Z. Manrique, T. Pope, W. Hong, V. Kaliginedi, C. Huang, A. S. Batsanov, M. R. Bryce, C. Lambert, T. Wandlowski, *J. Am. Chem. Soc.* **2013**, *135*, 12228-12240.
- [9] M. I. Bruce, P. J. Low, A. Werth, B. W. Skelton, A. H. White, *J. Chem. Soc. Dalton Trans.* **1996**, 1551-1566.
- [10] W. Weng, T. Bartik, M. Brady, B. Bartik, J. A. Ramsden, A. M. Arif, J. A. Gladysz, *J. Am. Chem. Soc.* **1995**, *117*, 11922-11931.
- [11] S. Bock, S. G. Eaves, M. Parthey, M. Kaupp, B. Le Guennic, J.-F. Halet, D. S. Yufit, J. A. K. Howard, P. J. Low, *Dalton Trans.* **2013**, *42*, 4240-4243.
- [12] S. Szafert, F. Paul, W. E. Meyer, J. A. Gladysz, C. Lapinte, *C. R. Chim.* **2008**, *11*, 693-701.
- [13] P. Tarakeshwar, P. R. Buseck, H. W. Kroto, *J. Phys. Chem. Lett.* **2016**, *7*, 1675-1681.
- [14] A. L. K. Shi Shun, R. R. Tykwinski, *Angew. Chem. Int. Ed.* **2006**, *45*, 1034-1057.
- [15] F. Ungeheuer, A. Fürstner, *Chem. Eur. J.* **2015**, *21*, 11387-11392.
- [16] K. Yin, C. Li, J. Li, X. Jia, *Green Chem.* **2011**, *13*, 591-593.
- [17] L. D. Movsisyan, M. Franz, F. Hampel, A. L. Thompson, R. R. Tykwinski, H. L. Anderson, *J. Am. Chem. Soc.* **2016**, *138*, 1366-1376.
- [18] D. C. Milan, M. Krempe, A. K. Ismael, L. D. Movsisyan, M. Franz, I. Grace, R. J. Brooke, W. Schwarzacher, S. J. Higgins, H. L. Anderson, C. J. Lambert, R. R. Tykwinski, R. J. Nichols, *Nanoscale* **2017**, *9*, 355-361.
- [19] G.-L. Xu, C.-Y. Wang, Y.-H. Ni, T. G. Goodson, T. Ren, *Organometallics* **2005**, *24*, 3247-3254.
- [20] L. D. Movsisyan, D. V. Kondratuk, M. Franz, A. L. Thompson, R. R. Tykwinski, H. L. Anderson, *Org. Lett.* **2012**, *14*, 3424-3426.
- [21] H. Sahnoune, Z. Baranová, N. Bhuvanesh, J. A. Gladysz, J.-F. Halet, *Organometallics* **2013**, *32*, 6360-6367.
- [22] J. Stahl, J. C. Bohling, E. B. Bauer, T. B. Peters, W. Mohr, J. M. Martín-Alvarez, F. Hampel, J. A. Gladysz, *Angew. Chem. Int. Ed.* **2002**, *41*, 1871-1876.
- [23] J. Stahl, W. Mohr, L. de Quadras, T. B. Peters, J. C. Bohling, J. M. Martín-Alvarez, G. R. Owen, F. Hampel, J. A. Gladysz, *J. Am. Chem. Soc.* **2007**, *129*, 8282-8295.
- [24] L. de Quadras, E. B. Bauer, J. Stahl, F. Zhuravlev, F. Hampel, J. A. Gladysz, *New J. Chem.* **2007**, *31*, 1594-1604.
- [25] G. R. Owen, S. Gauthier, N. Weisbach, F. Hampel, N. Bhuvanesh, J. A. Gladysz, *Dalton Trans.* **2010**, *39*, 5260-5271.
- [26] L. de Quadras, E. B. Bauer, W. Mohr, J. C. Bohling, T. B. Peters, J. M. Martín-Alvarez, F. Hampel, J. A. Gladysz, *J. Am. Chem. Soc.* **2007**, *129*, 8296-8309.
- [27] G. R. Owen, J. Stahl, F. Hampel, J. A. Gladysz, *Organometallics* **2004**, *23*, 5889-5892.
- [28] G. Eglinton, W. McCrae, in *Recent Advances in Organic Chemistry, Vol. 4* (Eds.: R. A. Raphael, E. C. Taylor, H. Wynberg), Interscience, New York, **1963**, p. 225.
- [29] K. West, C. Wang, A. S. Batsanov, M. R. Bryce, *Org. Biomol. Chem.* **2008**, *6*, 1934-1937.
- [30] C. Wang, A. S. Batsanov, K. West, M. R. Bryce, *Org. Lett.* **2008**, *10*, 3069-3072.
- [31] K. West, L. N. Hayward, A. S. Batsanov, M. R. Bryce, *Eur. J. Org. Chem.* **2008**, *2008*, 5093-5098.

- [32] M. I. Bruce, M. Ke, P. J. Low, B. W. Skelton, A. H. White, *Organometallics* **1998**, *17*, 3539-3549.
- [33] K. West, C. Wang, A. S. Batsanov, M. R. Bryce, *J. Org. Chem.* **2006**, *71*, 8541-8544.
- [34] J. Lewis, B. Lin, P. R. Raithby, *Transition Metal Chemistry* **1995**, *20*, 569-573.
- [35] A. B. Holmes, C. L. D. Jennings-White, A. H. Schulthess, B. Akinde, D. R. M. Walton, *J. Chem. Soc. Chem. Commun.* **1979**, 840-842.
- [36] G. E. Jones, D. A. Kendrick, A. B. Holmes, *Org. Synth.* **1987**, *65*, 52-59.
- [37] G. E. Jones, D. A. Kendrick, A. B. Holmes, *Org. Synth. Coll. Vol. 8* **1993**, 63-70.
- [38] L. Fomina, B. Vazquez, E. Tkatchouk, S. Fomine, *Tetrahedron* **2002**, *58*, 6741-6747.
- [39] P. A. Schauer, P. J. Low, *Eur. J. Inorg. Chem.* **2012**, *2012*, 390-411.
- [40] D. F. Perepichka, S. Jeeva, *Chem. Eng. News* **2010**, *88*, 2.
- [41] B. S. Navale, R. G. Bhat, *RSC Advances* **2013**, *3*, 5220-5226.
- [42] F. V. Singh, M. F. Z. J. Amaral, H. A. Stefani, *Tetrahedron Lett.* **2009**, *50*, 2636-2639.
- [43] D. R. M. Walton, F. Waugh, *J. Organomet. Chem.* **1972**, *37*, 45-56.

Supporting Information

A safe and simple synthesis of 1,4-bis(trimethylsilyl)buta-1,3-diyne

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Figure S1: Green-brown colour of the catalyst solution prior to addition of trimethylsilylacetylene.

Figure S2: The reaction setup showing the three-neck flask, glass thermometer, dry-ice condenser and O₂ inlet.

Figure S3: The blue-green colour of the reaction solution obtained 5 minutes after the addition of trimethylsilylacetylene.

Spectroscopic characterisation of 1,4-bis(trimethylsilyl)buta-1,3-diyne (1)

Figure S4: ^1H -NMR spectrum of **1** (300 MHz, CDCl_3)

Figure S5: ^{13}C -NMR of **1** (75 MHz, CDCl_3)

Figure S6: IR(ATR)-spectrum of **1**

Standard GC-MS analysis of **1** was performed using a GC-MS was recorded on an Agilent 6890 GC connected to an Agilent 5973 mass-selective detector (Agilent Technologies, USA) using a BPX-5 column (5% phenyl polysilphenylene-siloxane, 30 m x 0.25 mm i.d. x 0.25 μm film thickness, SGE, Australia). Helium was used as the carrier gas with a constant flow rate of 1.0 mL/min. A scan range of m/z 45–400

and a solvent delay of 5 min were used with splitless injections of 1.0 μL for 1.0 min. The ion source was set to 230°C, and the transfer line temperature to 250°C. The oven temperature program was 40°C, held for 1 min, then ramped at 10°C /min to 250°C, and held for 10 min. The chromatogram only showed one peak in the chromatogram suggesting a 100% purity based on GC. In addition the mass spectrum of the peak present provided further confirmation of the identity of the compound with the molecular ion peak for M^+ at m/z 194 and the fragment peak for $[\text{M}-\text{CH}_3]^+$ at m/z 179 (Figure S7).

Figure S7: Gas chromatogram (top) and mass spectrum (bottom) of **1**

Quantitative NMR measurements of 1

1,3,5-trimethoxybenzene (99 %; Sigma-Aldrich) was used as internal standard. The purity of the sample was calculated from the following relationships.

$$\text{molar ratio} = \frac{\frac{I_{cpd}}{nH_{cpd}}}{\frac{I_{std}}{nH_{std}}}$$

$$\text{wt}\% = \frac{mg_{std} \times MW_{cpd} \times \text{molar ratio} \times P_{std}}{mg_{cpd} \times MW_{std}}$$

$$\text{wt}\% = \frac{mg_{std} \times MW_{cpd} \times I_{cpd} \times P_{std} \times nH_{std}}{mg_{cpd} \times MW_{std} \times I_{std} \times nH_{cpd}}$$

wt% ... purity of the compound (**1**)

I_{cpd} ... proton integral area of the compound (**1**)

I_{std} ... proton integral area of the internal standard

nH_{cpd} ... number of hydrogens associated with the compound (**1**) NMR resonance

nH_{std} ... number of hydrogens associated with the internal standard NMR resonance

mg_{cpd} ... mass of the compound (**1**) weighed out (in mg)

mg_{std} ... mass of the internal standard weighed out (in mg)

MW_{cpd} ... molecular weight of the compound (**1**) (194.42 g/mol)

MW_{std} ... molecular weight of the internal standard (168.19 g/mol)

P_{std} ... wt% purity of the internal standard (0.99)

All ^1H -NMR spectra were recorded on a Bruker Avance IIIHD 500MHz NMR spectrometer using a 30 degree pulse with an acquisition time of 5 seconds, 32 scans per spectrum and a relaxation delay of 30 seconds. The spectra were referenced against the protio solvent residue signal of CDCl_3 at 7.26 ppm. The methoxy resonance (3.60 – 3.94 ppm) of 1,3,5-trimethoxybenzene was used as the internal standard resonance representing 9 hydrogen atoms. The trimethylsilyl resonance of 1,4-bis(trimethylsilyl)buta-1,3-diyne was used as compound resonance (0.30 – 0.35 ppm) representing 18 hydrogen atoms. The purity was determined in triplicate (Table S1, Figure S8-S10). The average purity as determined from the 3 quantitative NMR measurements was 99.5%.

Run	I _{cpd}	I _{std}	nH _{cpd}	nH _{std}	MW _{cpd} / g/mol	MW _{std} / g/mol	mg _{cpd} / mg	mg _{std} / mg	P _{std}	wt%
1	18.2116	8.9942	18	9	194.42	168.19	17.54	14.96	0.99	98.82
2	18.8258	8.9913	18	9	194.42	168.19	18.47	15.34	0.99	99.50
3	11.9868	8.9859	18	9	194.42	168.19	19.64	25.8	0.99	100.27
Average										99.53

Figure S8: ^1H -NMR spectrum of run 1 of the quantitative NMR determination

Figure S9: ¹H-NMR spectrum of run 2 of the quantitative NMR determination

Figure S10: ¹H-NMR spectrum of run 3 of the quantitative NMR determination

Determination of the T₁ values for the internal standard and **1** were determined via an inversion recovery sequence on a Bruker Avance IIIHD 600MHz NMR spectrometer (Figure S11). After calibration of the 90° pulse using the automated routines in Topspin 3.5, the T₁ values were determined to be 2.0 s for the methoxy resonance of 1,3,5-trimethoxybenzene (as internal standard) and 3.0 s for the trimethylsilyl resonance of **1**. The relaxation time for quantitative NMR with a 90° pulse is recommended to be five times the longest T₁, thus requiring a 15s delay in the current system.^[1] In this case, using a 30° pulse and a relaxation delay of 30 seconds is extremely conservative and therefore fully ensures reliable quantitative results.

• T1 Analysis

Fitted function:	$f(t) = \ln * [1 - a * \exp(-t/T1)]$
Random error estimation of data:	RMS per spectrum (or trace/plane)
Systematic error estimation of data:	worst case per peak scenario
Fit parameter Error estimation method:	from fit using arbitrary uncertainties
Confidence level:	95%
Used peaks:	peaks from C:/Data/Low/SB6-57-T1/31/pdata/1/peaklist1D.xml
Used integrals:	area integral

Peak name	F2 [ppm]	T1 [s]	error
1	3.824	2.03	0.002588
2	0.249	2.99	0.06334

Figure S11: T1 analysis of 1,3,5-trimethoxybenzene and **1**

[1] S. K. Bharti, R. Roy, *Trends in Analytical Chemistry* **2012**, 35, 5-26.