

Hydration of Aromatic Alkynes Catalyzed by a Self-Assembled Hexameric Organic Capsule

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Reagents and Materials.

General

¹H NMR were recorded at 298 K, unless otherwise stated, on a Bruker AVANCE 300 spectrometer operating at 300.15 MHz. δ values in ppm are relative to SiMe₄. GC analysis were performed on HP SERIES II 5890 equipped with a HP5 column (30 m, I. D. 0.25 m, film 0.25 μm) using He as gas carrier and FID. GC-MS analyses were performed on a GC Trace GC 2000 equipped with a HP5-MS column (30 m, I.D. 0.25 mm, film 0.25 μm) using He gas carrier and coupled with a quadrupole MS Thermo Finnigan Trace MS with *Full Scan* method.

Solvents and reactants were used as received; otherwise they were purified as reported in the literature.¹ TLC analysis were performed on TLC Polygram [®] Sil G/UV254 of 0.25 mm thickness and flash-chromatography separations were performed on silica gel Merk 60, 230-400 mesh.²

Substrates and capsule

All aromatic alkynes phenylacetylene, 1-ethynyl-4-methylbenzene, 1-ethynyl-3-methylbenzene, 1-ethynyl-2-methylbenzene, 1-*tert*-butyl-4-ethynylbenzene, 1-ethynyl-4-pentylbenzene, 1-ethynyl-4-methoxybenzene, 1-ethynyl-4-methoxy-2-methylbenzene, 9-ethynylphenanthrene, 1-ethynyl-4-phenoxybenzene, prop-1-yn-1-ylbenzene, hex-1-yn-1-ylbenzene, tetrafluoroboric acid (48%), methanesulfonic acid, hydrochloric acid (37%), nitric acid (70%), tetraethyl ammonium tetrafluoroborate, resorcinol, 4-n-hexyl-resorcinol and acetic acid are all commercially available products (Aldrich) and were used as received without any further purification. Resorcin[4]arene³ was prepared as reported in the literature. All the hydration products were identified by GC-MS and ¹H-NMR analysis.

Catalytic Studies

Catalytic hydration of alkynes mediated by the hexameric capsule

In a 3 mL vial were introduced a water saturated chloroform solution of resorcin[4]arene (36 mM, 1.5 mL) followed by the proper terminal alkyne (10 eq. or 20 eq. with respect to resorcin[4]arene capsule, 60 mM or 120 mM) and the resulted mixture was stirred at 750 rpm until completely homogeneous. Subsequently the HBF₄ (0.5, 0.2 or 0.1 eq. with respect to the alkyne) was added, the vial sealed and thermostatted at room temperature or at 60°C. The reaction progress was followed by GC or ¹H-NMR analyses sampling the reaction mixture at different times and diluting the sample with water saturated chloroform. The hydration products were confirmed by GC-MS and ¹H NMR.

Experimental procedure as above reported was repeated adding tetraethyl ammonium tetrafluoroborate (10 equivalents with respect to the capsule, 132.6 mM) together with the substrates in order to carry out control tests of the catalytic activity of the activity within the capsule.

Catalytic hydration reaction of phenylacetylene with other acid

The procedure is the same but HCl, HNO₃ or methanesulfonic acid (0.5 or 0.2 equivalents) were added in place of HBF₄.

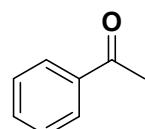
Control experiments for the catalytic hydration reactions of phenylacetylene

A series of control experiments were carried out in order to ascertain the real role of the capsule. In particular, tests were performed with the capsule in the presence of the competitive cationic guest **4** or with resorcinol, 4-n-hexyl-resorcinol or acetic acid as analogues of the capsule in terms of Brønsted acidity or H-bonding properties. Concentrations of the species were as in Table 1 of the manuscript following a procedure similar to that above reported for the capsule.

Internal Alkynes

In a 3 mL vial were introduced a water saturated chloroform solution of resorcin[4]arene (36 mM, 1.5 mL) followed by the proper internal alkyne (2 eq. with respect to resorcin[4]arene capsule, 12 mM) and the resulted mixture was stirred at 750 rpm until completely homogeneous. Subsequently the HBF₄ ~ 55 wt. % in H₂O (0.5 with respect to the alkyne) was added, the vial sealed and thermostatted at room temperature or at 60°C. The reaction was left under these condition overnight. The hydration products were confirmed by GC-MS and ¹H NMR. Experimental procedure as above reported was repeated adding tetraethyl ammonium trifluoromethanesulfonate (10 equivalents with respect to the capsule, 132.6 mM) together with the substrates in order to carry out control tests of the catalytic activity of the activity within the capsule.

Acetophenone



¹H NMR (300.15 MHz, CDCl₃): 7.98-7.3 (m, 4H), 2.60 (s, 3H). Corresponding to literature characterization.⁴

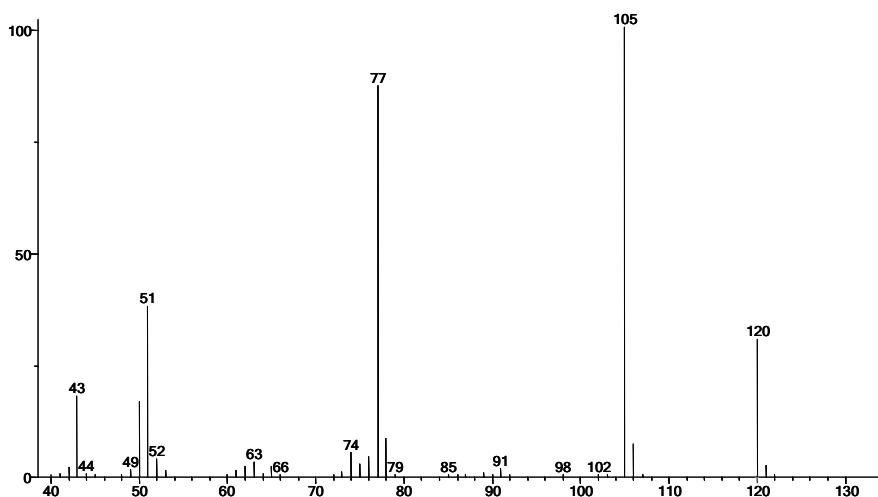
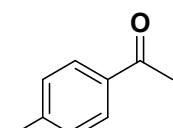


Figure 1. Mass spectrum of acetophenone

1-(p-tolyl)ethanone



¹H NMR (300.15 MHz, CDCl₃): 7.84 (d, J=8.2 Hz, 2H), 7.25 (d, J=8.1 Hz, 2H), 2.59 (s, 3H), 2.45 (s, 3H). Corresponding to literature characterization.⁵

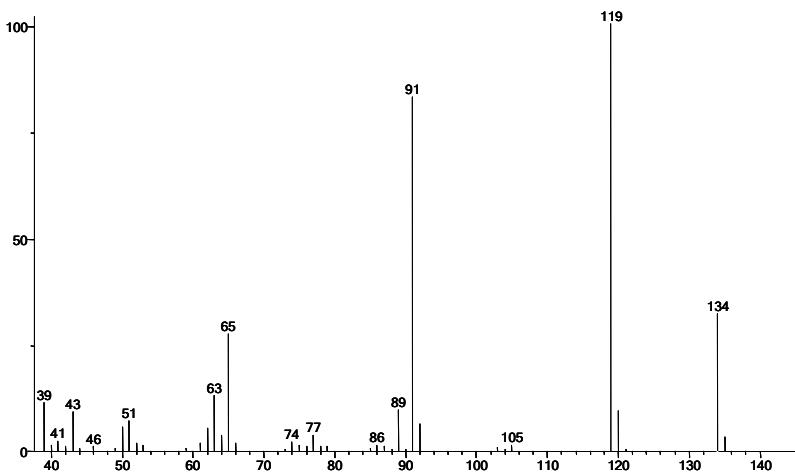
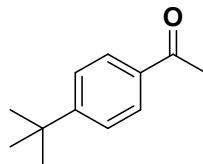


Figure 2. Mass spectrum of 1-(p-tolyl)ethanone

1-(4-(tert-butyl)phenyl)ethanone



^1H NMR (300.15 MHz, CDCl_3): 7.90 (d, $J=8.5$ Hz, 2H), 7.48 (d, $J=8.5$ Hz, 2H), 2.57 (s, 3H), 1.34 (s, 9H). Corresponding to literature characterization.⁶

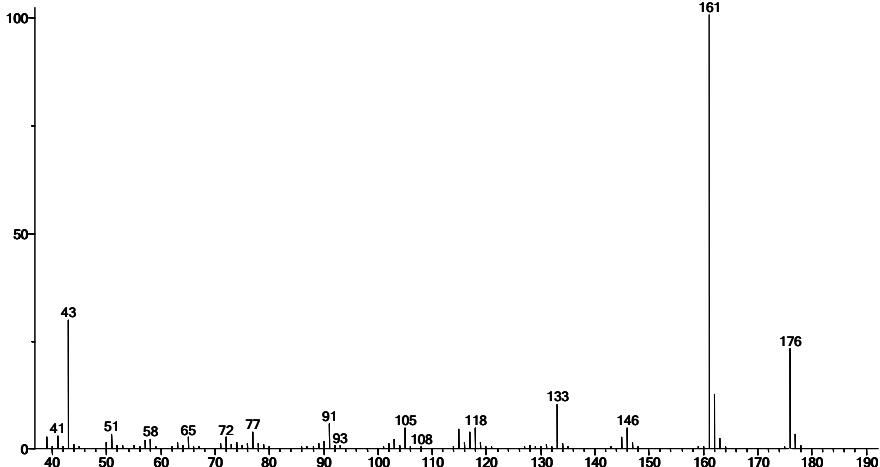
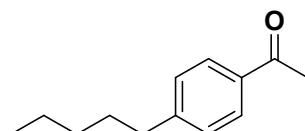


Figure 3. Mass spectrum of 1-(4-(tert-butyl)phenyl)ethanone

1-(4-pentylphenyl)ethanone



^1H NMR (300.15 MHz, CDCl_3): 7.90 (d, $J = 8.1$ Hz, 2H), 7.26 (d, $J = 8.1$ Hz, 2H), 2.68 (t, $J = 7.6$ Hz, 2H), 2.58 (s, 3H), 1.69-1.57 (m, 2H), 1.40-1.27 (m, 4H), 0.89 (t, $J = 6.8$ Hz, 3H). Corresponding to literature characterization.⁷

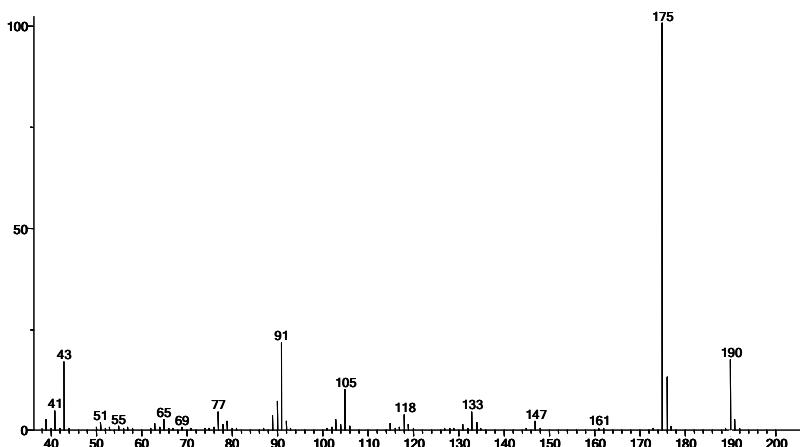
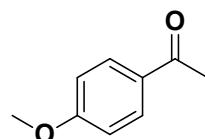


Figure 4. Mass spectrum of 1-(4-pentylphenyl)ethanone

1-(4-methoxyphenyl)ethanone



^1H NMR (300.15 MHz, CDCl_3): 7.91 (m, 2H), 6.91 (m, 2H), 3.83 (s, 3H), 2.53 (s, 3H). Corresponding to literature characterization.⁸

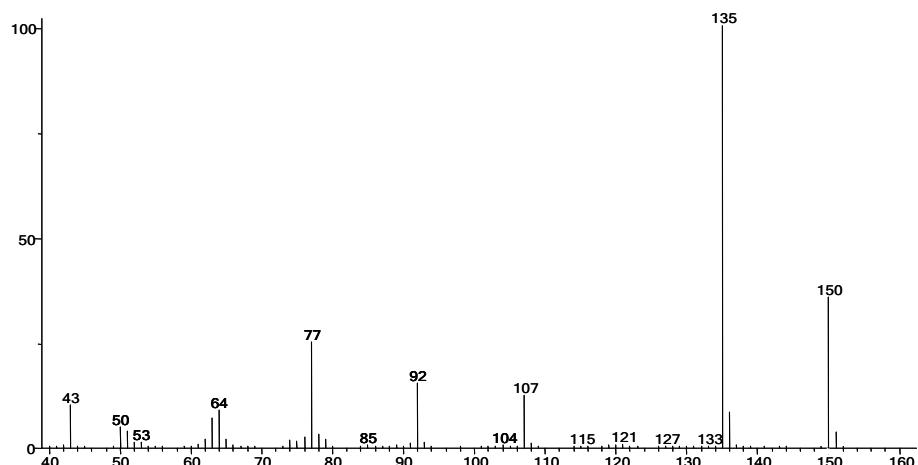
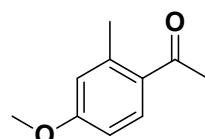


Figure 5. Mass spectrum of 1-(4-methoxyphenyl)ethanone

1-(4-methoxy-2-methylphenyl)ethanone



^1H NMR (300.15 MHz, CDCl_3): 8.15 (d, $J=8.5$, 2H), 7.15 (s, 1H), 6.91 (d, $J=8.5$, 2H), 3.85 (s, 3H), 2.56 (s, 3H), 2.45 (s, 3H). Corresponding to literature characterization.⁹

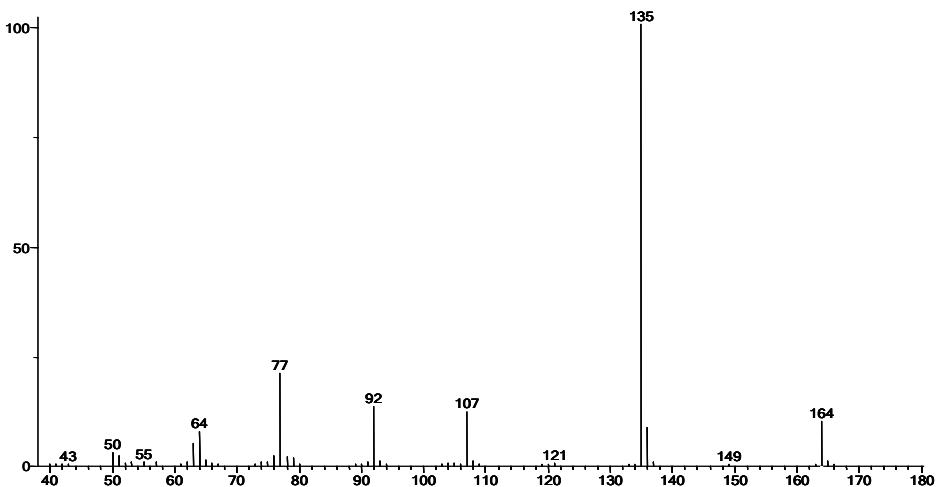
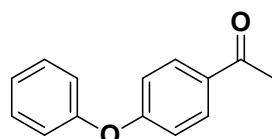


Figure 6. Mass spectrum of 1-(4-methoxy-2-methylphenyl)ethanone

1-(4-phenoxyphenyl)ethanone



^1H NMR (300.15 MHz, CDCl_3): 7.94 (d, $J=8.7$ Hz, 2H), 7.39 (t, $J=7.4$ Hz, 2H), 7.20 (t, $J=7.4$ Hz, 1H), 7.07 (d, $J=7.8$ Hz, 2H), 6.95 (d, $J=8.8$ Hz, 2H), 2.57 (s, 3H). Corresponding to literature characterization.¹⁰

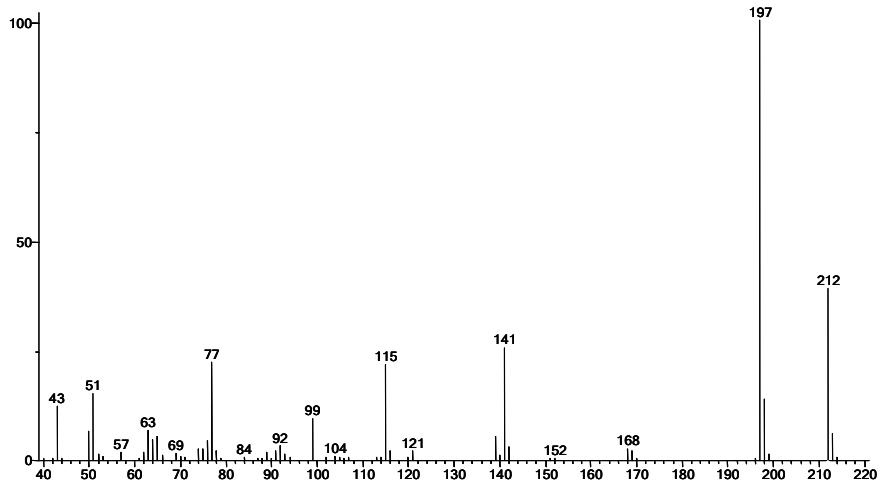
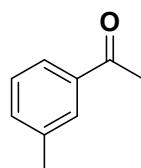


Figure 7. Mass spectrum of 1-(4-phenoxyphenyl)ethanone

1-(m-tolyl)ethanone



^1H NMR (300.15 MHz, CDCl_3): 7.79-7.71 (m, 2 H), 7.40-7.29 (m, 2 H), 2.59 (s, 3 H), 2.41 (s, 3 H). Corresponding to literature characterization.¹¹

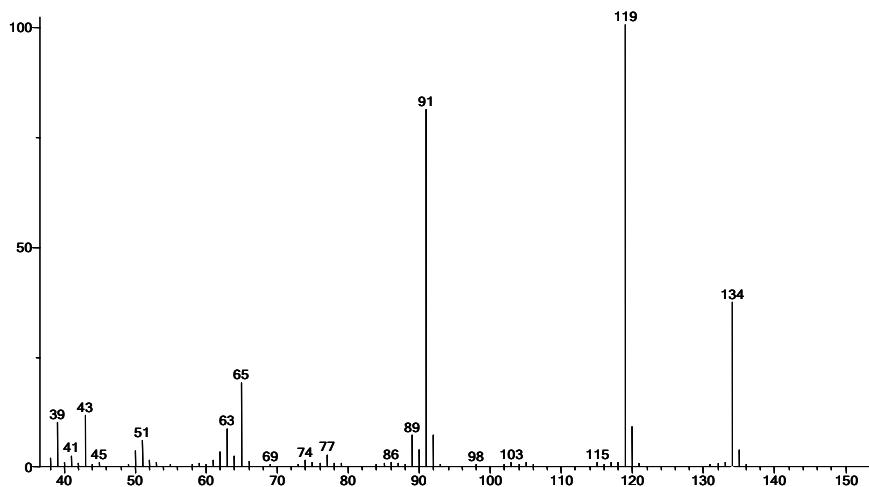
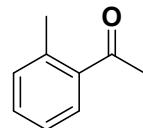


Figure 8. Mass spectrum of 1-(m-tolyl)ethanone

1-(o-tolyl)ethanone



^1H NMR (300.15 MHz, CDCl_3): 7.94 (d, $J = 7.4$ Hz, 2 H), 7.45-7.35 (m, 1 H), 7.30-7.24 (m, 2 H), 2.58 (s, 3 H), 2.53 (s, 3 H). Corresponding to literature characterization.¹²

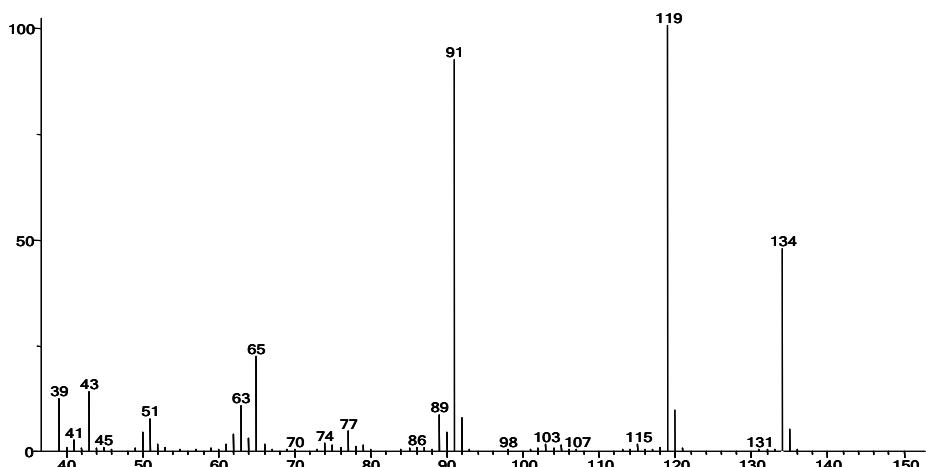
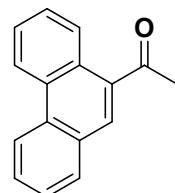


Figure 9. Mass spectrum of 1-(o-tolyl)ethanone

1-(phenanthren-9-yl)ethanone



^1H NMR (300.15 MHz, CDCl_3): 8.77-8.67 (m, 3H), 8.21 (s, 1 H), 8.00-7.95 (m, 1H), 7.80-7.63 (m, 4H), 2.84 (s, 3H). Corresponding to literature characterization.¹³

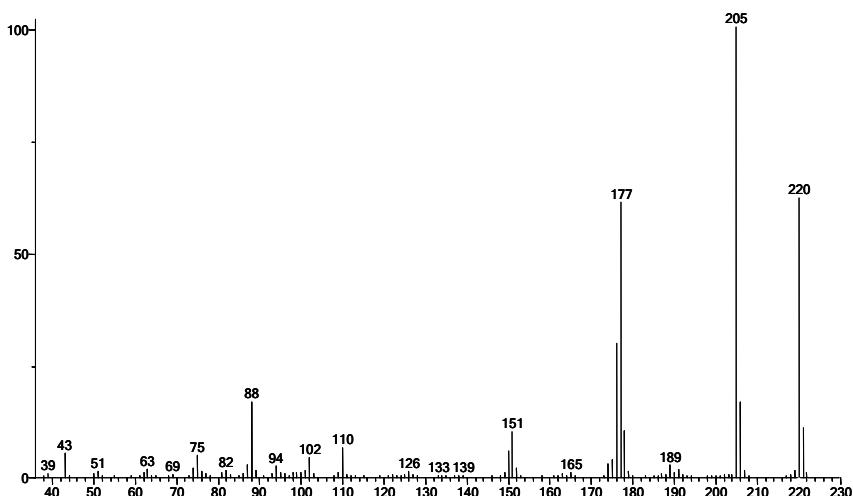
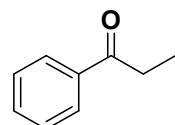


Figure 10. Mass spectrum of 1-(o-tolyl)ethanone

1-Phenyl-propan-1-one



^1H NMR (300.15 MHz, CDCl_3): δ 7.96-7.99 (m, 2H), 7.53-7.59 (m, 1H), 7.43-7.49 (m, 2H), 3.02 (q, J = 7.2 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H). Corresponding to literature characterization.⁸

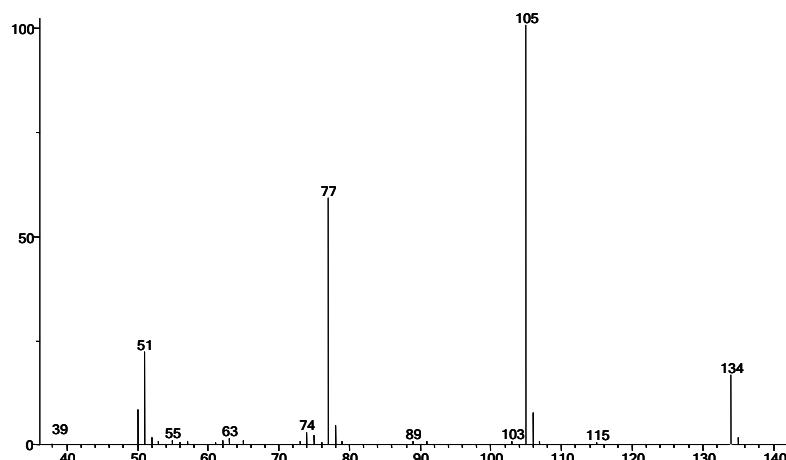
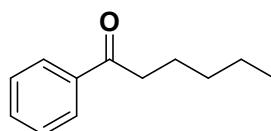


Figure 11. Mass spectrum of 1-Phenyl-propan-1-one

1-phenylhexan-1-one



^1H NMR (300.15 MHz, CDCl_3): δ 7.96 (dd, J = 8.3, 1.2 Hz, 2H), 7.55 (d, J = 7.3 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 2.99 – 2.92 (m, 2H), 1.74 (dq, J = 14.8, 7.4 Hz, 2H), 1.37 (td, J = 7.2, 3.6 Hz, 4H), 0.91 (t, J = 7.1 Hz, 3H). Corresponding to literature characterization.¹⁴

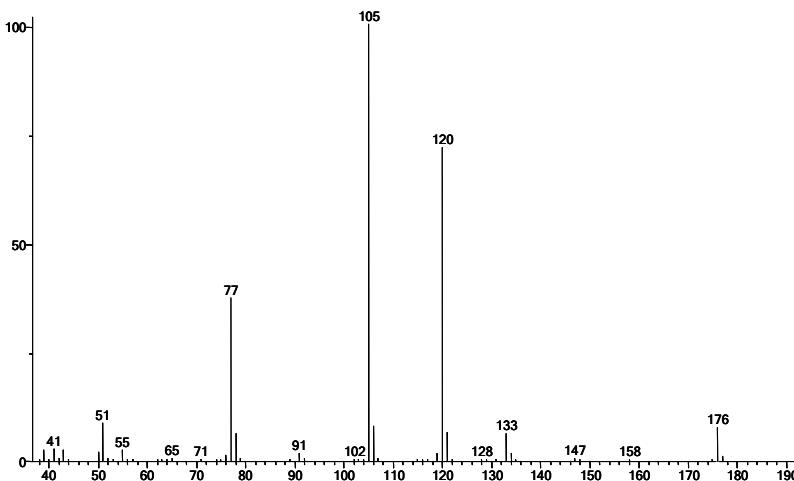


Figure 12. Mass spectrum of 1-phenylhexan-1-one

References

- 1 D.D. Perrin, W.L.F. Armarego, Purification of laboratory chemicals, 3rd edition, , Pergamon Press, 1993.
- 2 W. C. Still, M. Khan, A. Mitra *J. Org. Chem.* 1978, **43**, 2923.
- 3 Y. Aoyama, Y. Tanaka, S. Sugahara, *J. Am. Chem. Soc.* **1989**, *111*, 5397-5404.
- 4 Z. Hyder, J. Ruan, J. Xiao, *Chem. Eur. J.* **2008**, *14*, 5555 – 5566.
- 5 M.M. Hossain, W.-K. Huang, H.-J. Chen, P.-H. Wang, S.-G. Shyu, *Green Chem.* **2014** , *16*, 3013 – 3017.
- 6 X. Wang, M. Liu, L. Xu, Q. Wang, J. Chen, J. Ding, H. Wu, *J. Org. Chem.* **2013**, *78*, 5273 – 5281.
- 7 C. Xu, W. Du, Y. Zeng, B. Dai, H. Guo, *Org. Lett.* **2014**, *16*, 948 – 951.
- 8 C. Berini, O.H. Winkelmann, J. Otten, D.A. Vacic, O. Navarro, *Chem. Eur. J.* **2010**, *16*, 6857 – 6860.
- 9 R. Qiu, G. Zhang, Y. Zhu, X. Xu, L. Shao, Y. Li, D. An, S. Yin, *Chem. Eur. J.* **2009**, *15*, 6488 – 6494.
- 10 K. Popov, G. Ushchenko, *Russ. J. Org. Chem.* **2004** , *40*, 912 – 913.
- 11 M. Jereb, D. Vrazic, *Org. Biomol. Chem.* **2013**, *11*, 1978 – 1999.
- 12 S. Liang, G.B. Hammond, B. Xu, *Chem. Commun.* **2015** , *51*, 903 – 906.
- 13 M. Bassetti, S. Ciceri, F. Lancia, C. Pasquini, *Tetrahedron Lett.* **2014** , *55*, 1608 – 1612.
- 14 W. J. Ang, Y. Lam, *Org. Biomol. Chem.* **2015**,*13*, 1048-1052.