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A microcell for ReactIR™†

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Abstract

An adjustable-volume ReactIR™ microcell for monitoring reactions having total volumes as small as 50 μL is described.

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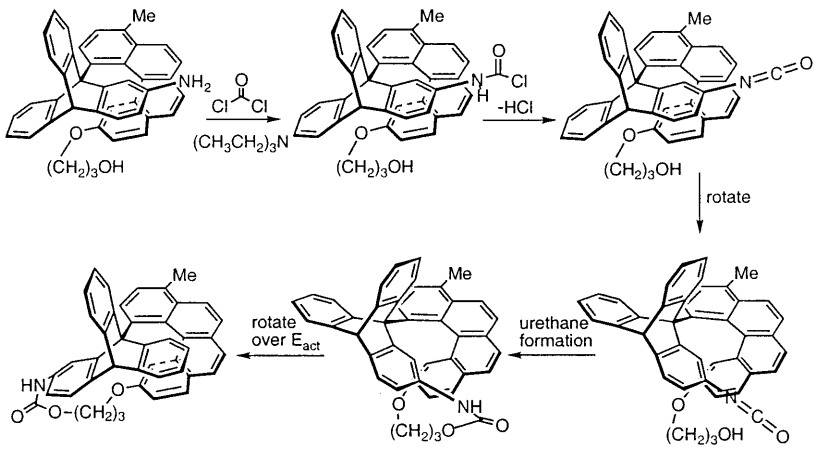
We recently described a prototype of the first rationally designed, chemically powered molecular motor.[1] During the course of that work it was necessary to examine the sequence of events in Scheme 1. In particular, we sought to determine which reactions were fast and which were slow, and which species accumulated during different stages of the transformation. ^{1}H



Scheme 1.

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† Dedicated to Professor Harry H. Wasserman in celebration of his 80th birthday.

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NMR spectroscopy was of some use, but was inadequate to rigorously distinguish among various possible species (^{13}C NMR was too insensitive to characterize the ebb and flow of small quantities of time-sensitive species). Given the cavalcade of IR-probeable functional groups, in principle ReactIR™ technology[2,3] offered a perfect solution, since it makes it possible to now use infrared spectroscopy to routinely monitor the progress of reactions in situ in real time. As

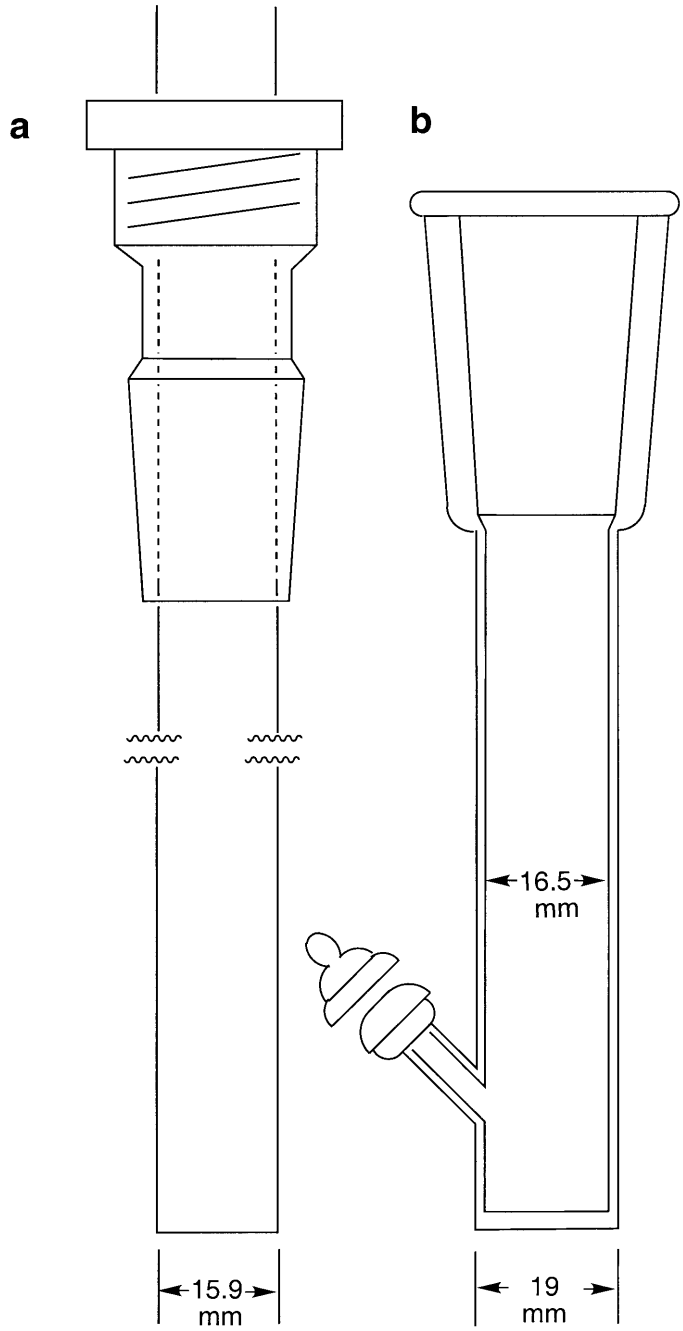


Figure 1. Full size depiction (a) of ReactIR™ probe; (b) of microcell

represented full-size in Fig. 1a, however, the ReactIR™ probe (which must be inserted directly into the reaction solution) has a diameter of 5/8 inch (15.9 mm) and is fitted with a 24/25 standard taper ground glass joint. First impressions based on the probe diameter and joint size might suggest that current ReactIR™ technology is limited to medium or large-scale reactions. Nonetheless, we now describe a microcell with an easily adjustable volume that permits reactions having total volumes as small as 50 μL to be monitored straightforwardly.

The apparatus is shown schematically in Fig. 1b. It was fabricated from standard Pyrex 19 mm outside diameter (standard wall) tubing (which has an inner diameter of 16.5 mm). The tubing was cut squarely with a carbide saw. Optical plate glass was fused to the tubing to form the bottom of the cell. This method of construction (rather than just sealing the tubing using a torch) creates a sharp 90° angle on the inside where the wall of the tubing meets the bottom, and allows one to insert the ReactIR™ probe all the way down to the bottom of the cell. Since the position of the 24/25 joint on the probe can be changed, thanks to the threaded fitting, the exact operating length of the probe is variable, which is equivalent to the cell volume being adjustable. The sidearm, which can be fitted with a septum, is short enough to permit standard 1 or 10 μL Hamilton syringe needles to reach the bottom of the cell (if the probe is temporarily withdrawn slightly). Depending simply on how deep the probe is inserted into the cell, reaction volumes of 50 μL to over 10 mL can be achieved without difficulty and reaction temperatures other than ambient are easily accommodated.[4]

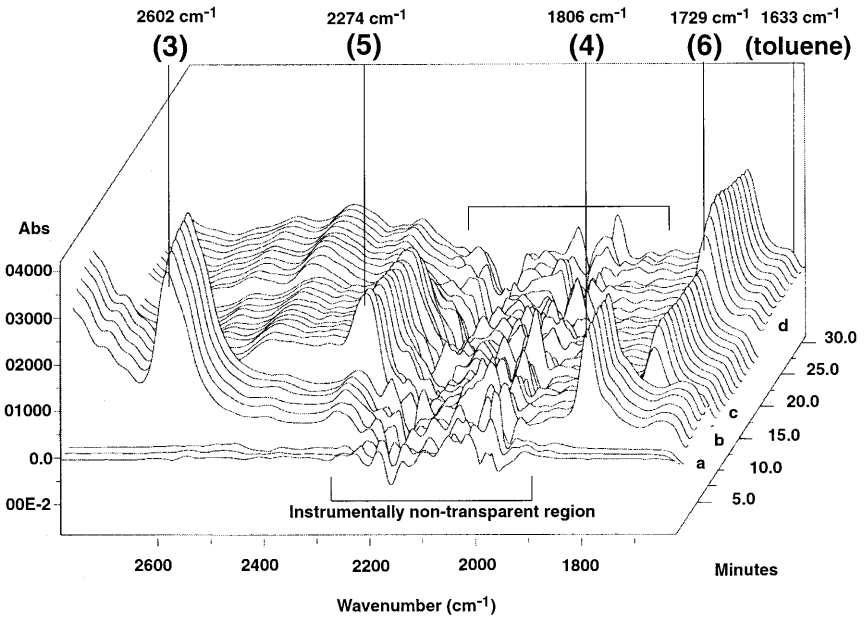
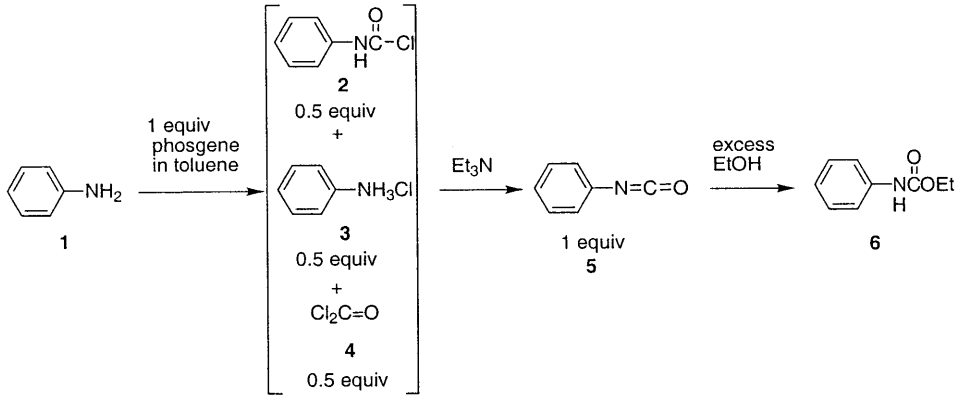


Figure 2. ReactIR™ monitoring of the sequence of reactions summarized in Scheme 2; bold numbers refer to compounds in Scheme 2. The reaction was carried out with 2.0 mg of aniline and the total reaction volume was 100 μL. (a) Solution of aniline in ethanol-free (amylenes-stabilized; Aldrich # 41,469-7) $CHCl_3$. (b) Add 1 equiv. $Cl_2C{=}O$ as a 20% solution in toluene. Spectrum shows major peaks for phosgene carbonyl (1806 cm^{-1}), 1° amine hydrochloride (2602 cm^{-1}) and toluene (1633 cm^{-1}). (c) Add 5 equiv. of Et_3N. Phosgene carbonyl peak replaced by isocyanate peak (2274 cm^{-1}); Et_3N neutralization of $PhNH_3Cl$ shown by disappearance of 2602 cm^{-1} peak. (d) Add ca. 20 equiv. CH_3CH_2OH. Isocyanate peak (2274 cm^{-1}) replaced by that of urethane (1729 cm^{-1})

Fig. 2 illustrates the operation of the present cell monitoring changes primarily in the carbonyl and isocyanate regions of the IR spectra for the sequence of reactions shown in Scheme 2. The reaction was carried out with 2.0 mg of aniline and the total reaction volume was 100 μL.



Scheme 2.

Given the synthetic chemist's chronic shortage of starting material, we believe that the reaction cell described herein substantially expands the utility of ReactIR™ technology.

Acknowledgements

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References

1. For reports from this laboratory where the microcell was utilized, see: Kelly, T. R.; De Silva, H.; Silva, R. A. *Nature* **1999** *401*, 150–152. Kelly, T. R.; Silva, R. A.; De Silva, H.; Jasmin, S.; Zhao, Y. *J. Am. Chem. Soc.* **2000** *122*, 6935–6949.
2. ASI Applied Systems, Millersville, MD 21109, USA.
3. For a bibliography of applications see www.asirxn.com.
4. We have avoided problems with trapping air bubbles next to the ATR element by tipping the probe and microcell when assembling them.