REMSPEC Application Note

00-02 The Michael Addition

Introduction

The Michael Addition involves the conjugate addition of a nucleophile to an α,β-unsaturated carbonyl compound. Protonation of the initially formed intermediate gives a chain-extended product, and the reaction is widely used in industrial synthetic chemistry. In an industrial process-development environment, it is sometimes necessary to take a strictly empirical approach to chemistry – reaction need to be optimized for yield and reaction times need to be minimized.

Real-time, in-situ monitoring of reaction progress is the ideal answer to questions about realistic reaction times. When the reactants, products or intermediates are infrared active and are present in adequate concentrations, the integrated Remspec Mid-IR Fiber-Optic Reaction Monitoring System provides the answer. With this system, any liquid-phase reaction can be monitored, even when a solid catalyst is present. The Remspec system uses an ATR (attenuated total reflectance) probe directly coupled to a fiber optic cable that is linked to the spectrometer. The use of the ATR technique largely eliminates the problem of signal absorption by the solvent, or of scattering by suspended solids. The sampling errors and delays associated with manual methods are avoided by in-situ measurement of the spectrum. Both room temperature and refluxing reactions can readily be monitored using the Remspec probe, allowing the chemist to know the status of a reaction in real-time. An added advantage is the slim design of the Remspec probe which allows it to be used with standard laboratory glassware – no special fittings are needed. The result is enhanced yields, higher-purity end products, and improved productivity.

Figure 1: Mid-IR Spectrum at start (blue) and after 60 minutes (red)

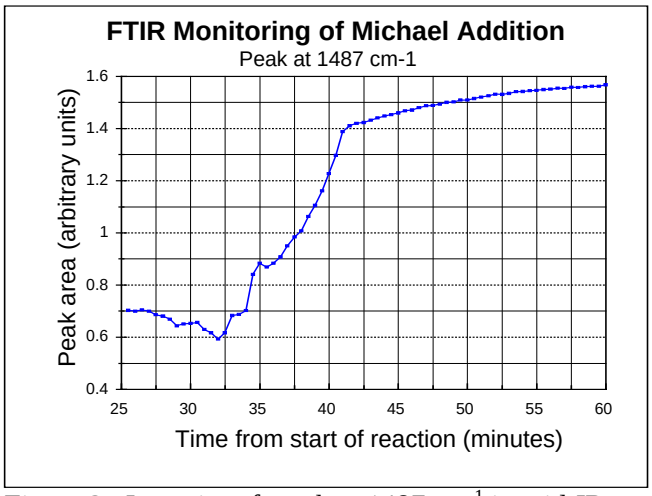

Figure 2. Intensity of peak at 1487 cm^{-1} in mid-IR spectrum of reaction mixture over time

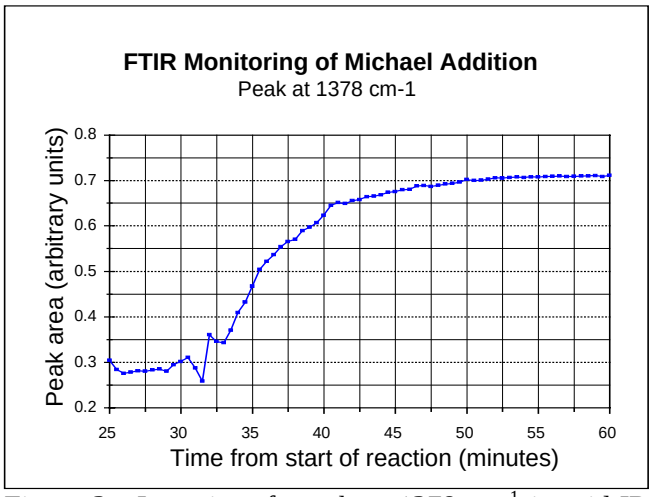

Figure 3. Intensity of peak at 1378 cm^{-1} in mid-IR spectrum of reaction mixture over time

Experimental

In the example described here, a Michael reaction was carried out in an industrial lab. so that real-time data could be collected for reaction optimization. Full details of the materials being used, and of the required product, were not available for proprietary reasons. The Remspec mid-IR probe, with a zinc selenide ATR crystal at its end, was inserted into the lab. reactor and the fiber optic cable was connected to an FTIR spectrometer. The spectrum of the reaction mixture was collected every 30 seconds.. Thirty-three minutes after beginning preparation of the nucleophile, an ester containing a C=C double bond was added to the room-temperature reaction mixture. Acqusition of mid-IR spectra continued for a further twenty-seven minutes to give a final total of 120 spectra spanning a period of one hour. Figure 1 shows the first and last spectra of the series in the region between 3200 and 1100 cm^{-1}.

After all the spectra had been collected, an automated peak-fitting program (Rempeak) was used to generate graphs of peak area versus time as the reaction progressed; two of these is shown in Figures 2 and 3. The peak at 1487 cm^{-1} increases rapidly in intensity after addition of the unsaturated ester, then the rate of increase levels off after about 41 minutes. The peak at 1378 cm^{-1} shows a similar trend, suggesting that both peaks may arise from the same product of the reaction. Interestingly, both graphs show some discontinuity in the slope immediately after the addition of the ester. This was associated with stirring problems in the reactor and illustrates the sensitivity of this technique to reaction conditions and progress. A real-time display of this type of profile, which is available using Rempeak, gives a true spectroscopic window into a reaction as it progresses.

Commentary

This reaction is typical of a class of chain-extending reactions that are routinely performed in chemical laboratories every day. By performing a series of peak-fitting calculations, it was possible to identify a peak whose evolution tracked the course of the reaction. For routine use, or for industrial process monitoring, automatic, real-time display of peak area/time curves for either reactants or products can be programmed using the spectrometer control software and, as this example illustrates, the approach can be used even in cases where the identity of the reactants is not fully known.

The use of the Remspec Mid-IR Fiber-Optic Immersion Probe gives the scientist or engineer the ability to follow the course of any reaction, organic or inorganic, rapid or slow, and in any liquid medium desired -- aqueous or non-aqueous -- for improved analytical and synthetic productivity.

For more information contact:
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