

# 2-MeTHF for greener processes

Dr Bogdan Comanita of Penn Specialty Chemicals shows how 2-MeTHF offers greener and more cost-effective processes than standard alternatives

2-methyltetrahydrofuran (2-MeTHF) can often replace tetrahydrofuran (THF) and diethyl ether (DEE) in organometallic reactions; the reaction yields are often superior, the stability of solvent to acid and base is increased and the work-up is simplified.<sup>1</sup> A previous article detailed the advantages provided by 2-MeTHF by comparison with THF.<sup>2</sup>

These included, but were not limited to, three key factors: easy product isolation (2-MeTHF is not water-miscible, whilst THF is); simple solvent recovery and drying (2-MeTHF forms a water-rich azeotrope at atmospheric pressure); and, improved extraction yields (2-MeTHF reduces costs by reducing the number of extraction steps).<sup>3</sup>

Anastas and Warner have developed the 12 principles of green chemistry,<sup>4</sup> which help to explain the critical decision criteria in designing green chemical processes. In this context, 2-MeTHF can make a very compelling case against THF on at least three of the 12 principles: renewable feedstocks, waste prevention and energy efficiency.

This article is intended to show that 2-MeTHF is a green, cost-effective alternative to THF, based on a detailed discussion of these three principles. Since the other nine principles of green chemistry are less relevant to the comparison between the two solvents, they are not included here.

## Renewable feedstock

2-MeTHF is derived from 2-furaldehyde (also known as furfural), which is produced from naturally occurring pentoses in agricultural waste like corncobs or bagasse (sugar cane),<sup>5</sup> in a two-step hydrogenation process via 2-methylfuran (Figure 1). Its raw material costs are therefore decoupled from the ever increasing cost of chemicals derived from oil.

By contrast, THF is currently made from 1,4-butanediol (BDO) by intramolecular cyclisation under acidic conditions. BDO, in turn, is a petroleum-derived product that uses acetylene as a key intermediate.<sup>6</sup>

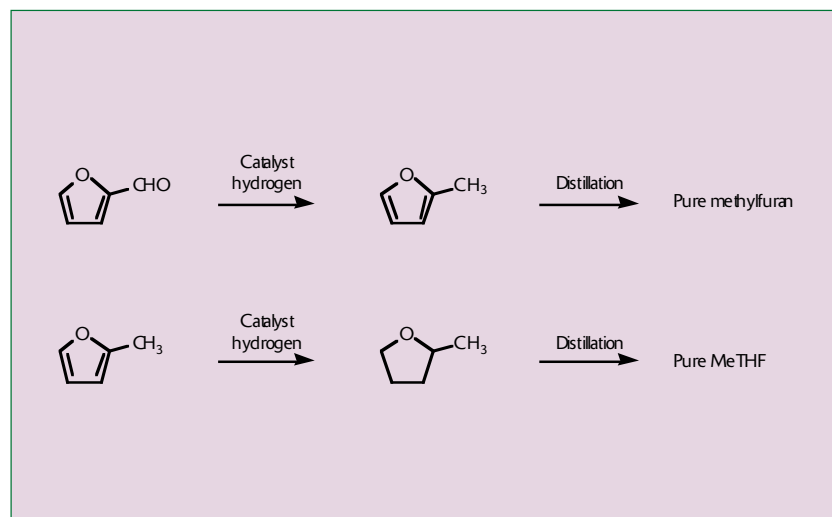


Figure 1 - 2-MeTHF Production Process from furfural

Table 1 - THF/toluene v. 2-MeTHF

	MeTHF	THF-Toluene	
API used kg	0.2	0.2	
Reaction solvent kg	1	1	0
Work up solvent kg	0.5	0	1.5
API recovered %	80%	56%	
API recovered kg	0.16	0.112	

## Waste prevention

THF reactions often call for the addition of a co-solvent, such as toluene, as a means to achieve phase separation. Otherwise, the water-miscible THF, together with reactants, will often form a persistent emulsion, making product isolation impossible. This practice is most common in small and medium-sized industrial production.

It was expected that 2-MeTHF would be a better extraction solvent than toluene, based on its higher polarity. The limited solubility of water in 2-MeTHF should enhance the extraction capability, particularly for polar compounds. This latter factor was invoked as a plausible explanation for the high reaction rates seen in the biphasic reactions where dichloromethane (DCM) had been replaced with 2-MeTHF.<sup>7</sup>

The vast superiority of 2-MeTHF as an extraction solvent is illustrated by the comparative back-to-back isopropanol (IPA) extractions illustrated in Table 1. IPA was used as a mimic compound for a valuable API or intermediate.

An 80% yield in extracted IPA is achieved using 1.5 parts of 2-MeTHF, 0.2 parts IPA and one part water. By using 1.5 part toluene, 0.2 parts IPA, 1 part water and 1 part THF, the extraction yield drops to 56%, a difference of 24%.

In all, the total volume of solvent used for this extraction is reduced by 40% (1.5 parts of 2-MeTHF versus 2.5 parts=1.5 parts toluene and 1 part THF) while the yield of this one-step extraction is improved by 24%.

Going to a second extraction step with 1.5 part toluene, one recovers the product in 68% combined yield for the two steps. A second extraction step with another 1.5 parts of 2-MeTHF recovers the product in 97% yield. The extraction yield difference increases from 24% to 29% while the total solvent volume used in the two steps falls by 25%.

This example shows the dramatic effect that the switch from THF to 2-MeTHF can have on the reduction of the total solvent volume used in extractions. At the same time, the extraction yield of the valuable (and often highly toxic) API is greatly improved. This is particularly true for hard-to-extract polar compounds, such as valuable amino acids, polyols and carboxylic acids.

(However, it should be noted that the beneficial yield difference is reduced if less polar compounds are used; for example, moving to 2-butanol, a less polar compound than

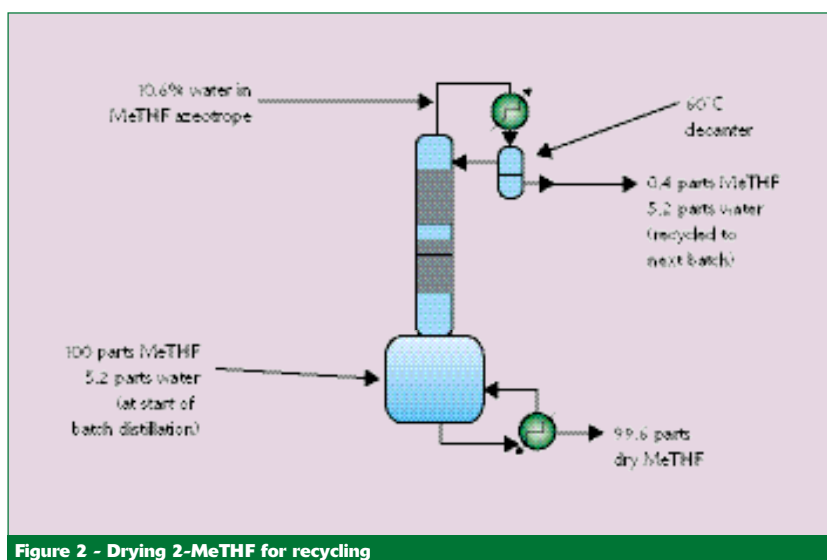


Figure 2 - Drying 2-MeTHF for recycling

IPA, the yield difference falls to 9% - there is 95% extraction for 2-MeTHF and 86% for toluene/THF, though 40% less solvent is still used.)

2-MeTHF is a very versatile reaction solvent and a wide range of chemistries can be carried out in it. Unlike THF, 2-MeTHF is much more stable to acidic and basic conditions. The extensive ring-opening reactions associated with THF will diminish considerably.<sup>8</sup> This is why a wide combination of consecutive reaction can be carried out successively in the same solution without the accumulation of impurities from solvent degradation.

Product isolation is not necessary after aqueous work-up; the next reaction step is carried out simply by adding the chemical reagent to the 2-MeTHF solution. Thus, by carrying out two consecutive reactions in the same solvent, the overall volume is reduced by 50% for two steps or 66% for three steps. As an added bonus, the 2-MeTHF-rich water azeotrope will help to dry the solution for the next step if it requires anhydrous conditions (Figure 2).

A collateral effect of using a co-solvent in the THF reaction work-up is the generation of a mixture of solvents that cannot be recycled economically for small and medium-sized industrial-scale reactions. For example, toluene/THF mixtures are relatively difficult to fractionate and solvent recovery often does not happen. The only solution is therefore to incinerate the solvent on site, thus increasing CO<sub>2</sub> emissions.

(The alternative is to pay for incineration; this also lowers CO<sub>2</sub> emissions on site, but third party incineration burdens the value chain with considerable costs: a personal survey showed that the incineration of wet THF mixtures costs €0.60-1.50/kg, depending on the water content and the location.)

Obviously, the higher boiling point of 2-MeTHF (80°C) compared to THF (64°C) will decrease the amount of solvent released into the air, reducing VOC emissions as well. As opposed to the THF/co-solvent mixtures, 2-MeTHF is recov-

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ered from the reaction as a relatively pure solvent by simple distillation. No special equipment of up-front investment is required. This makes recycling the solvent or recovery for other uses much more attractive than incineration.

### Energy efficiency

Medium-sized and large industrial-scale THF-based technologies are often carried out in dedicated plants. Some of these facilities have special equipment capable of recycling hundreds of tonnes/year.

For these large-scale consumers, recycling 2-MeTHF is much less energy-intensive than recycling THF, which has to be dried in a rather complicated manner called 'swing distillation', in which two columns are operated in tandem at different pressures.

As shown in Figure 2, by operating the decanter at 60°C, two phases separate easily and the 2-MeTHF solution is dried. In a short time, all the water is removed from the system and one can start collecting the dry 2-MeTHF. No special equipment is needed and the process is very simple and robust.

Likewise, Table 2 shows that the energy consumption related to the operation of a swing distillation system is much higher than the requirement for a simple distillation needed by 2-MeTHF. It is quite clear that the energy savings potential for recycling and drying 2-MeTHF versus THF varies by around 70%.

### Conclusions

Switching processes from THF-based to 2-MeTHF-based technologies provides a great opportunity to move innovative companies to greener technologies. A switch of solvent supply to renewable resources is particularly relevant in the present historical and political context.

For small and medium-sized consumers, solvent volume reductions are correlated to reduced CO<sub>2</sub> emissions. For large-scale users, 2-MeTHF recycling units can save around 70% of the energy consumption of THF recycling. Last but not at least, the higher boiling point of 2-MeTHF will reduce VOCs in all applications.

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Table 2 - Energy savings from drying & recovery of 2-MeTHF & THF at different water content

	% Water in Stream from Process							
	50%		25%		10%		6%	
	MeTHF	THF	MeTHF	THF	MeTHF	THF	MeTHF	THF
Weighted Total BTU's/ lb of material reclaimed	966	3,167	817	3,073	771	3,041	753	2,186
Energy Savings from Recovery/Drying	69%		73%		75%		66%	