

## ®T3P Technology for Major Cost Reductions in API Synthesis

®T3P, a unique reagent for amide/peptide bond formations, increases yields and simplifies processes significantly and with good success probabilities. Total cost reductions of more than 30 % can be achieved. Archimica consults you and supports rapid realisation of such cost savings projects by transfer of its know-how.

### ®T3P – Adding Value by Reducing Cost

Innovative pharmaceutical companies as well as generics manufacturers today are facing enormous cost pressures.

®T3P can be a way to reduce manufacturing costs for API by up to 30 % and more (for examples see page 2).

Such cost savings are highest for reactions with expensive raw materials, for low-

yield processes and for reactions with poor cycle times and tedious workup.

The general success probabilities are good: According to statistics based on the feedback of our customers, ®T3P offers cost reduction potentials in approximately 65 % of the reactions mentioned above.

### Numerous Advantages for a Variety of Applications

®T3P (n-Propanephosphonic acid anhydride) is a high-yielding and very selective reagent for all kinds of condensation reactions. Its application typically results in very economic processes, because of simple mixing/hydrolysis/phase separation type processes with short cycle times.

Its advantages compared to other water-removing agents are

- very high yields (typically 86-96 %)
- very high product purities (high end-product purities; typically lowest extent of racemisation/epimerisation and other side reactions)
- easy development and upscaling
- improved overall process economics/costs by simplification of processes
- non-toxic
- available ex stock

The most important applications are

- amide- and peptide bond formations
- esterifications (including acrylic acid esters)
- conversion of acids, amides and oximes to nitriles
- conversion of formamides into isonitriles
- Moffatt oxidation of alcohols into aldehydes without DCC

**We are ready to support you for our common success!**

#### Step 1

Exchange of information under CDA

#### Step 2

Archimica does the necessary tests in-house (free application program) or transfers the know-how to you

#### Step 3

In case of success, Archimica supports your upscaling

## Calculation of Cost Reductions from a Switch to ®T3P

**Scenario I:** Base case, DCC/HOBt in a typical peptide bond formation.

**Scenario II:** ®T3P instead of DCC/HOBt. Unlikely scenario, almost always ®T3P yields are higher.

**Scenario III:** 20 % yield increase. Such yield improvements have been achieved quite often by switching to ®T3P. The result is a more than 21 % total cost reduction, significant both in terms of material cost savings and in liberating production capacity.

**Scenario IV** is a very likely scenario based on numerous development projects at Archimica and its customers. A 20 % higher yield and a 25 % higher volume efficiency is assumed. This results in a more than 23 % cost

Scenario	I	II	III	IV	V	VI
<b>Description</b>	DCC + HOBt	®T3P	®T3P	®T3P + 25 % higher concentration	DCC + HOBt	®T3P
<b>Yield</b>	75 %	75 %	95 %	95 %	75 %	95 %
<b>Raw material costs excl. coupling agent [€/kg]</b>	300	300	237	237	900	711
<b>Costs of coupling agent [€/kg]</b>	16	57	45	45	16	45
<b>Conversion costs [€/kg]</b>	82	41	32	24	82	32
<b>Total costs [€/kg]</b>	398	398	314	306	998	788
<b>Cost savings from ®T3P [€/kg]</b>	–	0	84	92	–	210
<b>Total savings [%]</b>	–	0	21	23	–	21
<b>Total annual savings [€]</b>	–	0	8,4 M	9,2 M	–	21 M

reduction. Again, both raw material spent is reduced significantly and plant capacity is increased massively.

**Scenarios V and VI** demonstrate the same comparison with higher raw material costs. Sourcing or manufacturing costs for all raw materials except the coupling agent is assumed to cause costs of 900 €/kg (75 % yield). If ®T3P offers 20 % yield increase, the annual savings can amount to more than 21 million € per year (improvements in cycle times/concentrations not considered).

Such impressive results have been achieved by several Archimica customers already, and numerous other projects are under development or already close to realisation. Based on our experiences, in the beginning

of a project, especially for the intended switch of a commercial and large-volume manufacturing product, a thorough technology transfer from Archimica or even a common development between a customer and the Archimica team has proven to save time and to avoid to give up on significant cost saving opportunities by seeing too low yields in the first few experiments. Amongst others, we offer free samples, technical application packages and frequent discussions with our technical experts.

®T3P has unique properties in terms of yield, throughput and cycle time optimisation by just slight modification of the reaction conditions – we are ready to support all your efforts for our common success!

### Assumptions used in the calculations above

- Reaction type: Amide bond formation or esterification
- Current process: DCC coupling with HOBt to suppress racemisation/epimerisation
- Utilisation of 1,0 equivalents of coupling reagent
- Molecular mass of coupling product 600 g/mol
- Costs of raw materials excluding coupling agent 300 €/kg at 75 % yield (scenarios I-IV) and 900 €/kg (scenarios V and VI).
- ®T3P costs: 40 €/kg (50 % w/w solution); DCC costs: 14 €/kg; HOBt costs: 32 €/kg.
- Conversion costs: 165 kg batch size, cost rate 280 €/hour.
- DCC reaction time: 2 h preparation, 10 h reaction, 36 h workup (urea elimination) = total 48 h.
- ®T3P reaction time: 2 h preparation, 10 h reaction, 12 h workup = total 24 h.
- Annual production 100 mtons/year

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