### **Supplementary Information**

#### E factor for the production of acetone from cumene

For calculating the E factor for the production of cumene a Monsanto patent<sup>1</sup> which uses a solid catalyst for a continuous liquid-phase process has been selected. There, an excess of benzene is used (propylene/benzene molar ratio is 0.12). The E factor is 7.6 but considering that the excess of benzene can be recovered, the specific E factor is 0.04.

For calculating the E factor for the synthesis of cumene hydroperoxide we have considered a Mitsubishi patent, where cumene is oxidized to cumene hydroperoxide in a liquid phase continuous process using an oxygen enriched air as oxidant agent.<sup>2</sup> According with this patent, if we consider the unreacted cumene as waste, we obtain an E factor of 2.03, but we have considered that unreacted cumene can be recovered and thus the E factor is 0.1

Finally, for the hydrolysis of cumene hydroperoxide to acetone plus phenol, we have considered a Texaco patent<sup>3</sup> where the hydrolysis is performed with a molar yield of 98 % in a continuous process using acidic clay as a catalyst. The E factor is 0.02. Thus, the global E factor in the production of acetone results 0.16.



 $E_{Tot} = 0.16$ 

## E factor for the synthesis of 4-methoxybenzaldehyde:

*Via i)* involves methylation of p-cresol giving p-methoxytoluene followed by catalytic oxidation with air. The methylation of p-cresol can be achieved with dimethyl sulphate in the presence of NaOH according to a BASF patent.<sup>4</sup> This process results in an E factor of 0.78. The subsequent oxidation of the p-methoxytoluene to p-methoxybenzaldehyde can be achieved by the vapour-phase air oxidation with a heterogeneous catalyst according to Ueshima et al.<sup>5</sup> and Kishimoto et al.<sup>6</sup> In both cases,

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higher conversions and selectivities to the aldehyde are obtained, and the E factor is 0.04. The total E factor for the synthesis of 4-methoxybenzaldehyde is 0.82.

*Via ii)* involves the formylation of anisole through a Vilsmeier reaction,<sup>7</sup> where the Vilsmeier salt is formed by reaction between phosgene and N,N-dimethyl formamide (in equimolar amounts), which is stabilised by adding AlCl<sub>3</sub> as Lewis acid. The reaction is performed using chloroform as solvent. If we accept that chloroform can be fully recovered by distillation, then the E factor of the reaction is 2.77.



#### E factors for the synthesis of 4-iodoanisole and methyl vinyl ketone

The synthesis of 4-iodoanisole can be carried out by different methodologies, we have selected for calculation of the E factor a green process recently reported by Earle et al.<sup>8</sup> There, the halogenation of anisole was carried out using an ionic liquid, and specifically when the iodation of anisole is performed with  $Bu_4NI$  in the presence of  $HNO_3$  (in an excess of 30 equivalents) the yield of iodoanisole was 99 %. Then, the E factor according to this process and considering that the ionic liquid can be fully recovered at the end of the reaction, is E=0.30.



The methyl vinyl ketone, is produced through the aldol condensation between acetone and formaldehyde. The process can be carried out either in gas-phase or in liquid phase. In liquid phase<sup>9</sup> the condensation is performed under mild reaction conditions and with

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high selectivity to MVK using as catalyst a halogen acid salt of a secondary amine and a nonsoluble solid oxide in an organic solvent such as dioxane. The E for this process, considering that acetone (3 equivalents) and the solvent are fully recovered, is E=0.99. However there is a gas-phase continuous process that uses fumed silica as solid catalyst<sup>10</sup> and a molar ratio acetone/formaldehyde= 23. In this case the calculated E factor is of 0.60, considering that the excess of acetone is fully recovered.

 $\begin{array}{c} E_2 = 0.60 \\ Funed silica \\ \hline gas-phase \end{array} \quad CH_2 = CHCOCH_3 + H_2O \end{array}$ 

# E factors in the preparation of 4-bromoanisole and methyl-3-hydroxy-2-methylene butyrate involved in the homogeneous Heck reaction

4-Bromoanisole, can be prepared with an ionic liquid (N-dodecil-Nmethylimidazolium bromide), as was previously done with 4-iodoanisole, in the presence of nitric acid<sup>8</sup> an E factor of 0.21 has been calculated for the production of 4bromoanisole.



On the other hand, the second reactant involved, methyl-3-hydroxy-2-methylene butyrate, is prepared through the Baylis-Hillman reaction between methylacrylate and acetaldehyde using DABCO (1,4-diazabiciclo[2.2.2]octane) as base catalyst in absence of solvent<sup>11</sup> with 90 % yield and with an E=0.77.

COOMe + CH<sub>3</sub>CHO 
$$\xrightarrow{\text{DABCO}}$$
  $E_2 = 0.77$  OH COOMe

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