A categorical approach to synthetic chemistry

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Outline

Retrosynthetic analysis

(1) Start with the target molecule(s)

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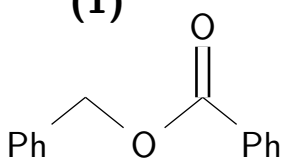

Retrosynthetic analysis

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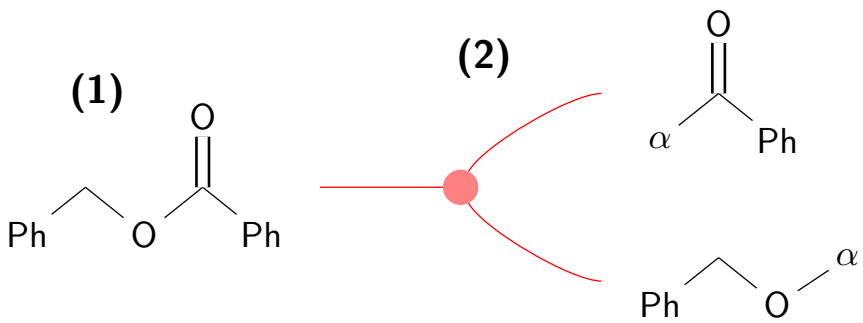
(2) Cut the target along some bond, creating *synthons*



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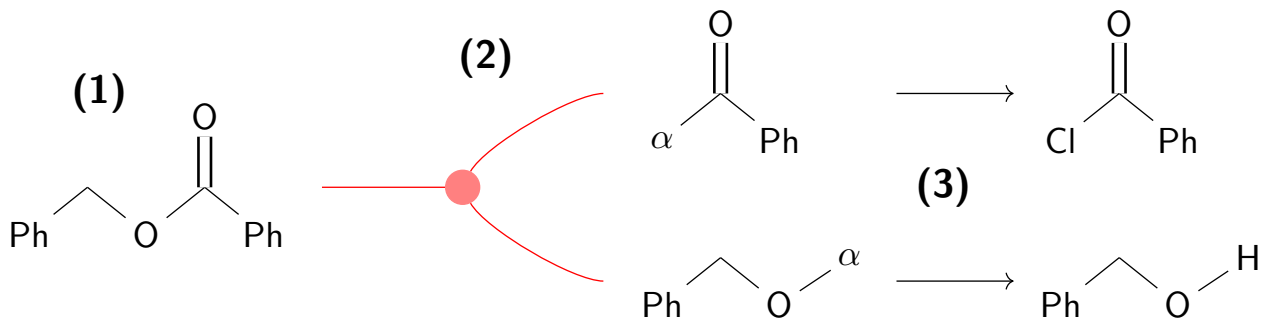

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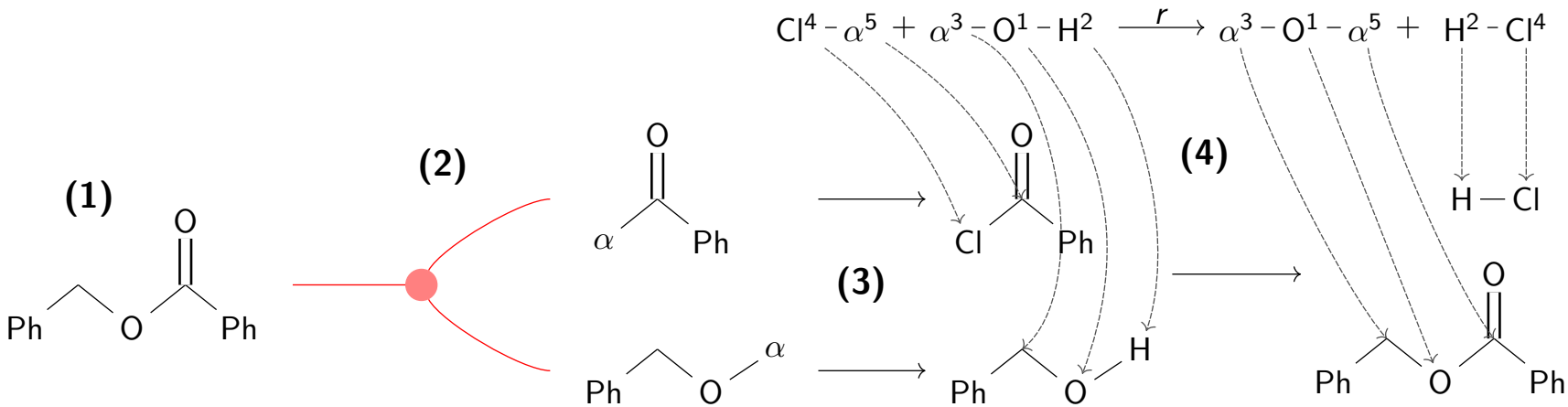

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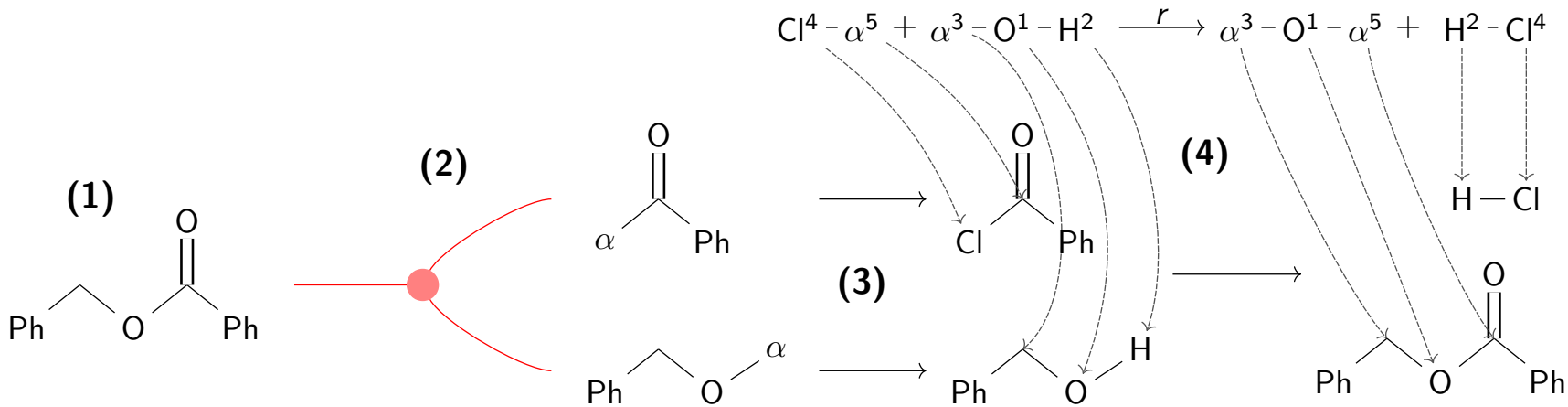
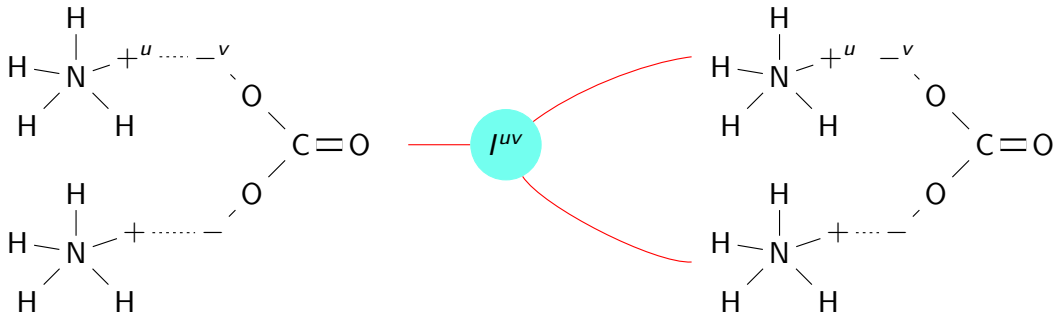
(5) Check whether the synthetic equivalents are known molecules: if yes, terminate, if no, return to **(1)** taking them as the target



Disconnection rules

Motto: Chemical reactions are movements of electrons



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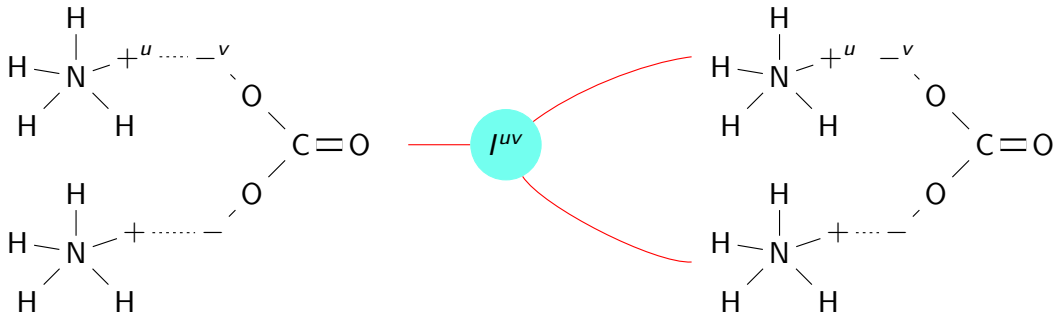

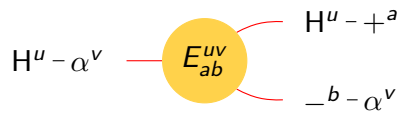

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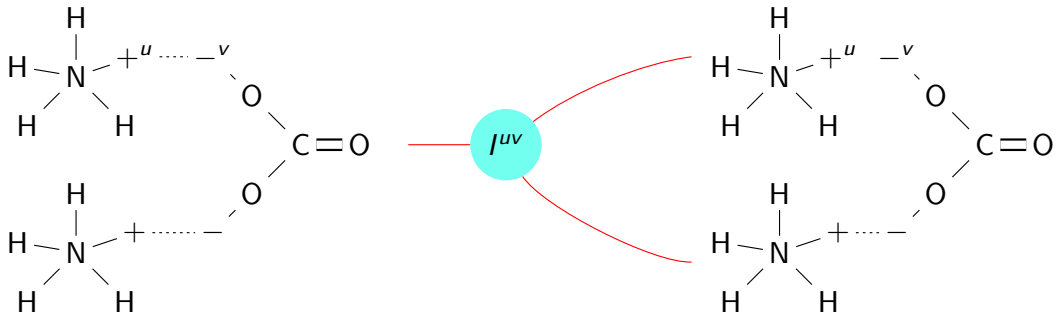

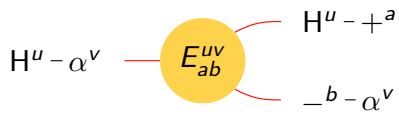

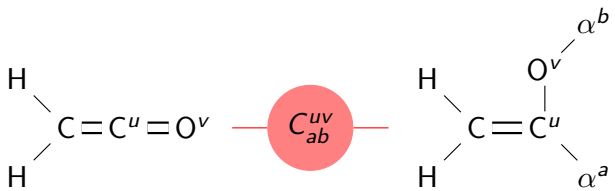

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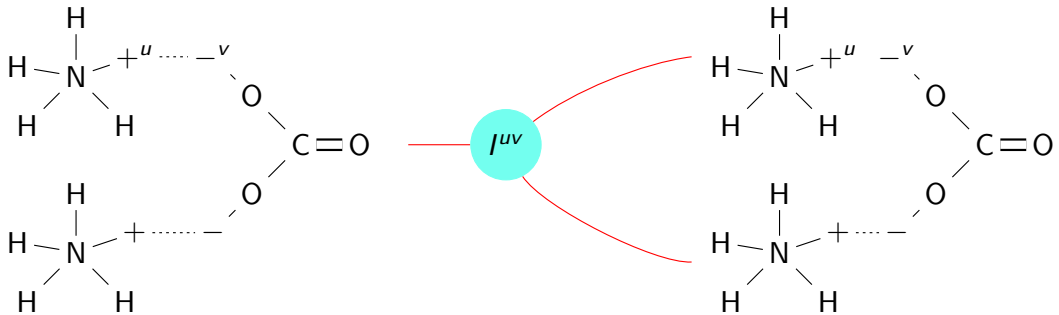

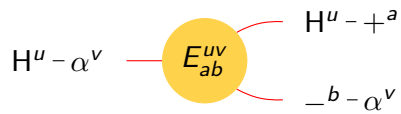

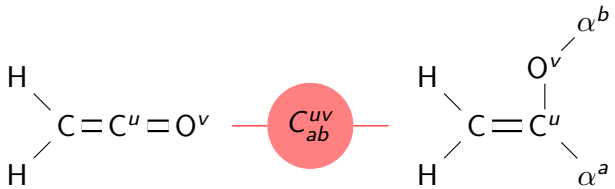

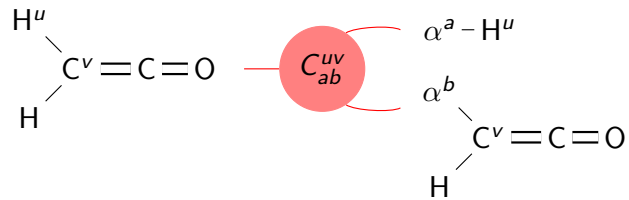

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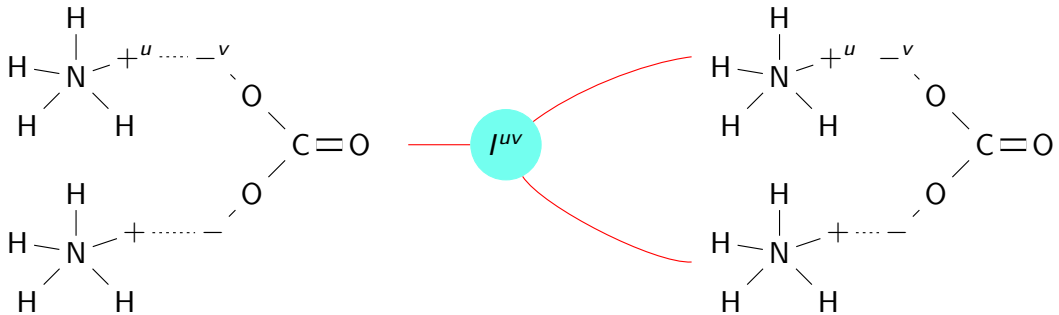
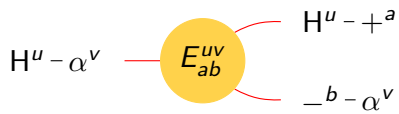
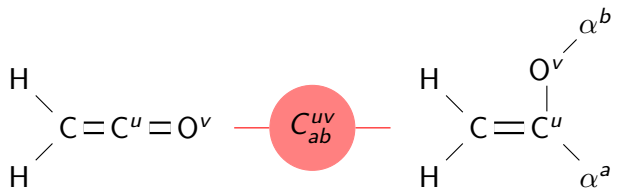
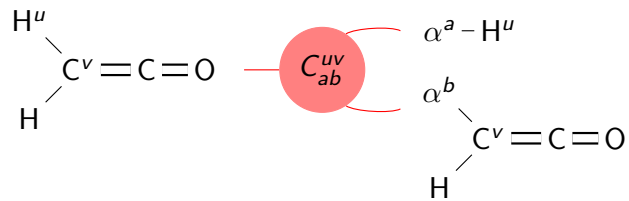
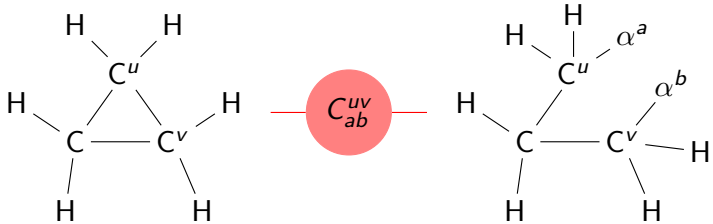




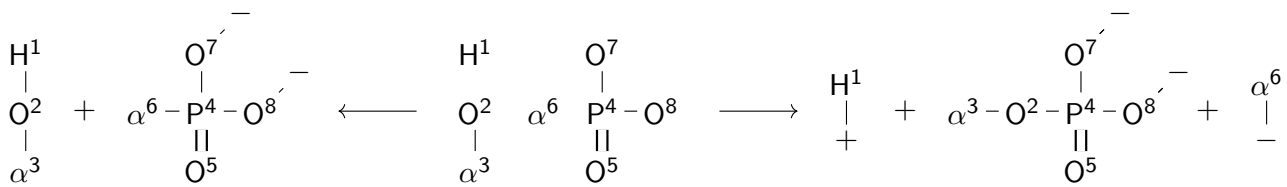






Reactions

Reactions are graph rewrites generated using *reaction schemes*:



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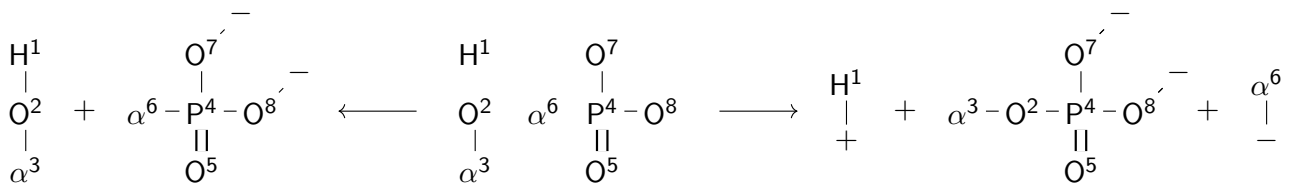
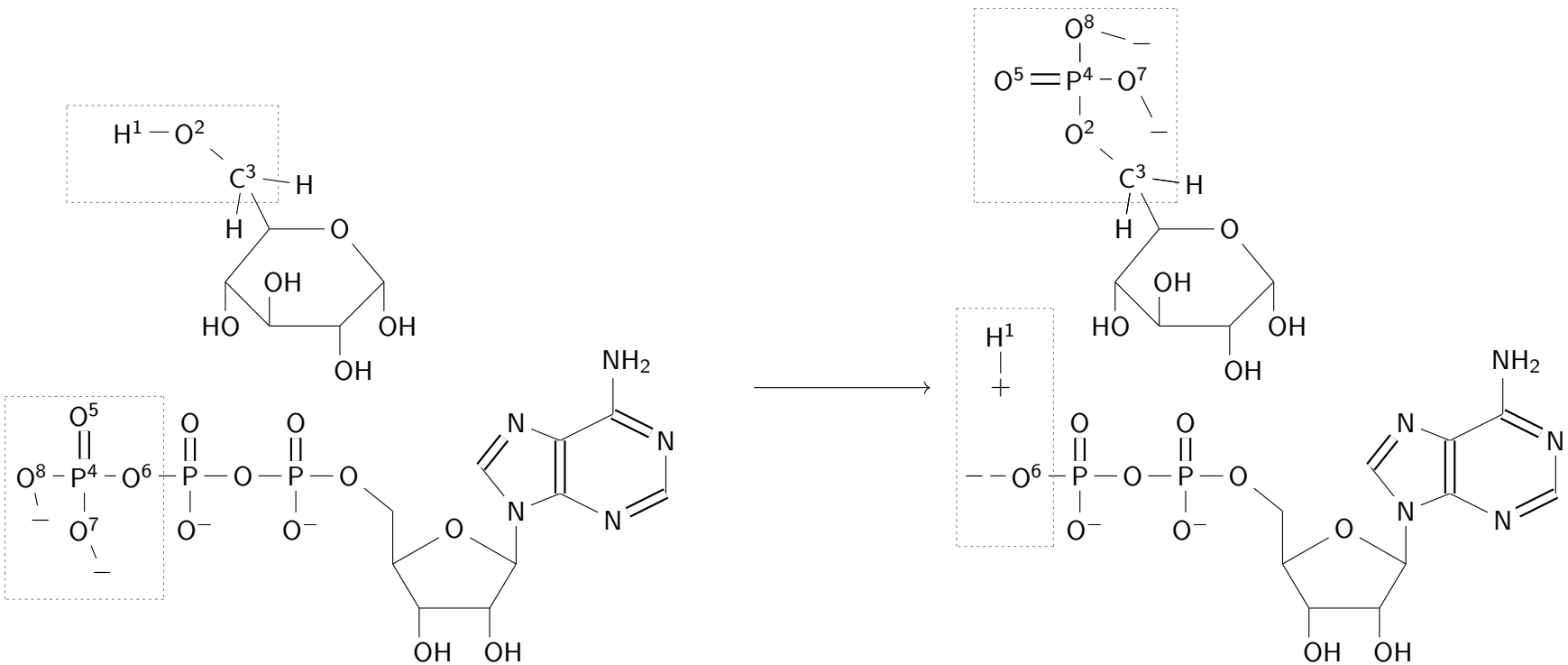
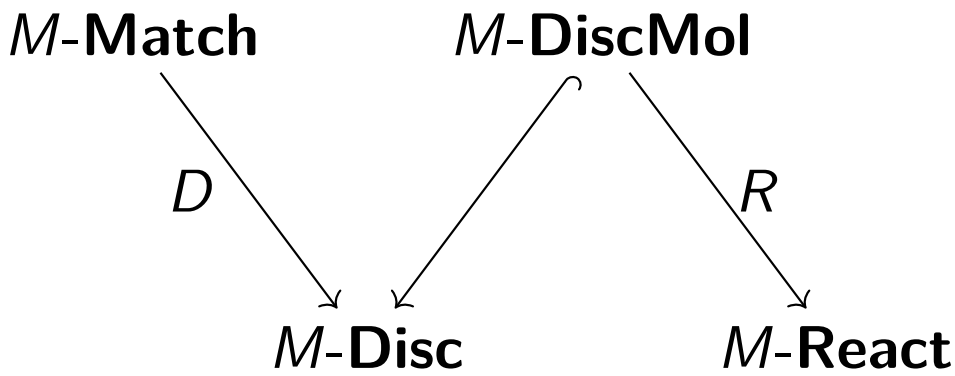


by finding a *matching* for the left-hand side in a larger entity:



Retrosynthesis, formalised

There are the following functors:



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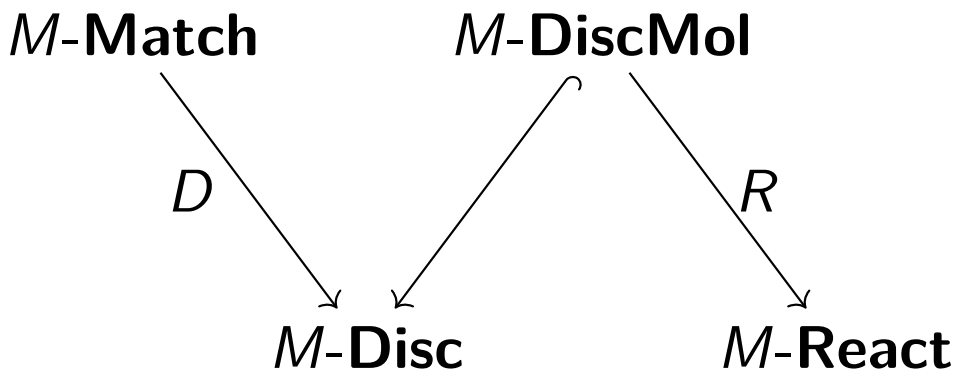
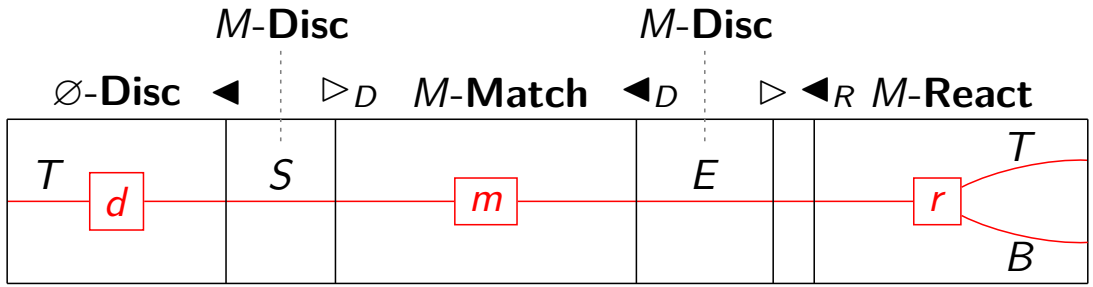


between categories of matchings, disconnection rules and reactions, all parameterised by the environmental molecules (solvent, catalyst, reagent). This is represented by a finite set of molecules M.

Retrosynthesis, formalised

This allows for the following definition of a retrosynthetic step:



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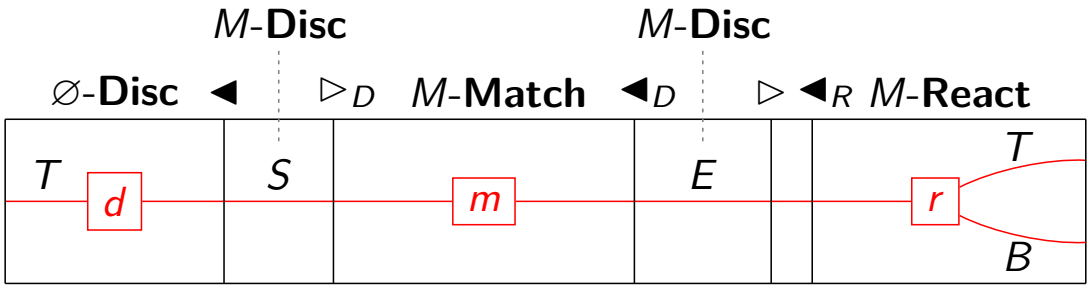
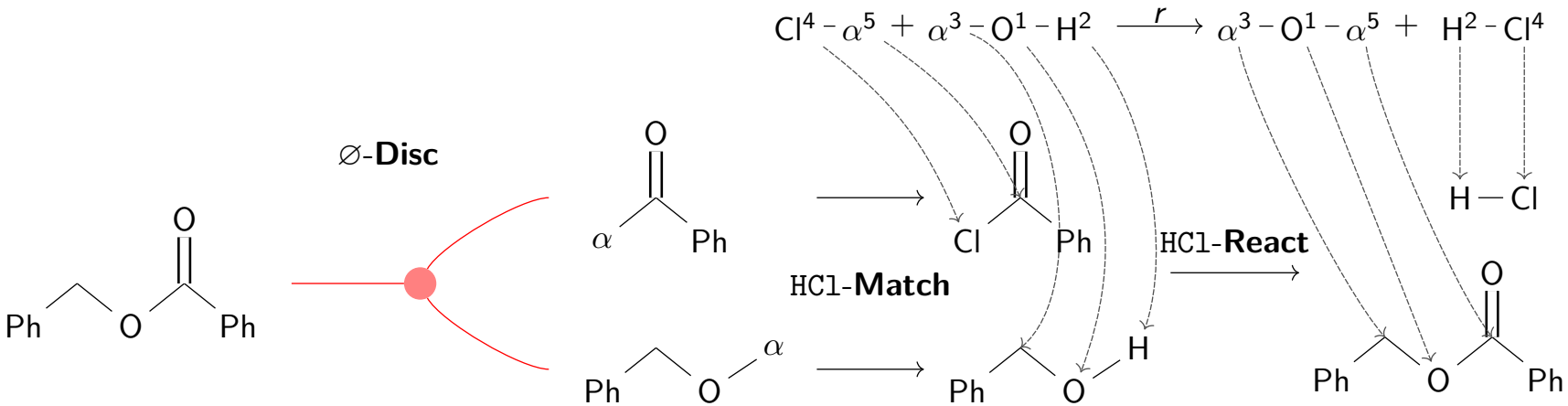
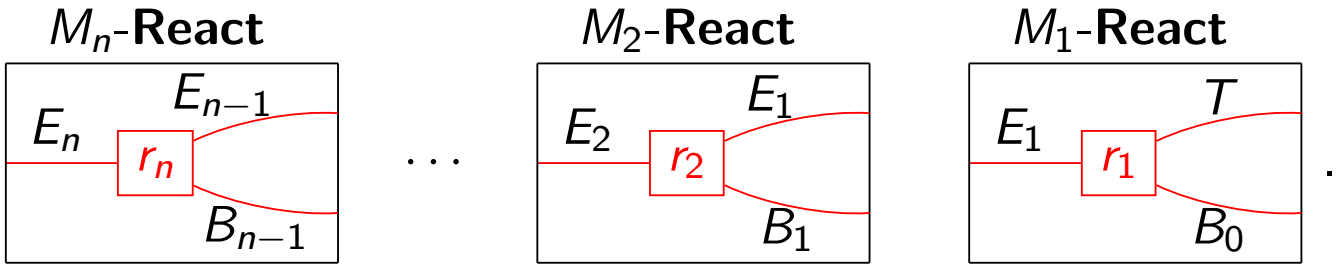




Retrosynthesis, formalised

Definition (Retrosynthetic sequence)

A *retrosynthetic sequence* for a target molecular entity T is a sequence of morphisms $r_1 \in M_1\text{-}\mathbf{React}(E_1, T + B_0)$, $r_2 \in M_2\text{-}\mathbf{React}(E_2, E_1 + B_1)$, $\ldots$, $r_n \in M_1\text{-}\mathbf{React}(E_n, E_{n-1} + B_{n-1})$ such that the domain of r_i is a connected subgraph of the codomain of r_{i+1}:



Retrosynthesis, formalised

Let T be some fixed molecular entity. We initialise by setting $i = 0$ and $E_0 := T$.

1. Choose a subset $\mathcal{D}$ of disconnection rules,
2. Provide at least one of the following:
   (a) a finite set of reaction schemes $\mathcal{S}$,
   (b) a function $\mathfrak{F}$ from molecular graphs to finite sets of molecular graphs,
3. Search for a retrosynthetic step with $d \in \varnothing\text{-}\mathbf{Disc}(E_i, S)$, $m \in M\text{-}\mathbf{Match}(S, E)$, and $r \in M\text{-}\mathbf{React}(E, E_i + B_i)$ such that all disconnection rules in d and $D(m)$ are in $\mathcal{D}$, and we have at least one of the following:
   (a) there is an $s \in \mathcal{S}$ such that the reaction r is an instance of s,
   (b) $E_i + B_i \in \mathfrak{F}(E)$;

   if successful, set $E_{i+1} := E$, $M_{i+1} := M$, $r_{i+1} := r$ and proceed to Step 4; if unsuccessful, stop,
4. Check if the molecular entities in E_{i+1} are known (commercially available): if yes, terminate; if no, increment $i \mapsto i + 1$ and return to Step 1.

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- Encode existing retrosynthesis algorithms within framework
- Suggest features for new algorithms: e.g. chirality, reaction environment, protection-deprotection steps

References

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- Clayden, Greeves, Warren. *Organic chemistry*. Oxford University Press. 2012.
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- Sun, Sahinidis. *Computer-aided retrosynthetic design: fundamentals, tools, and outlook*. Current Opinion in Chemical Engineering. 2022.
- Warren, Wyatt. *Organic synthesis: the disconnection approach*. Wiley. 2008.

Thank you for your attention!

Layers of abstraction

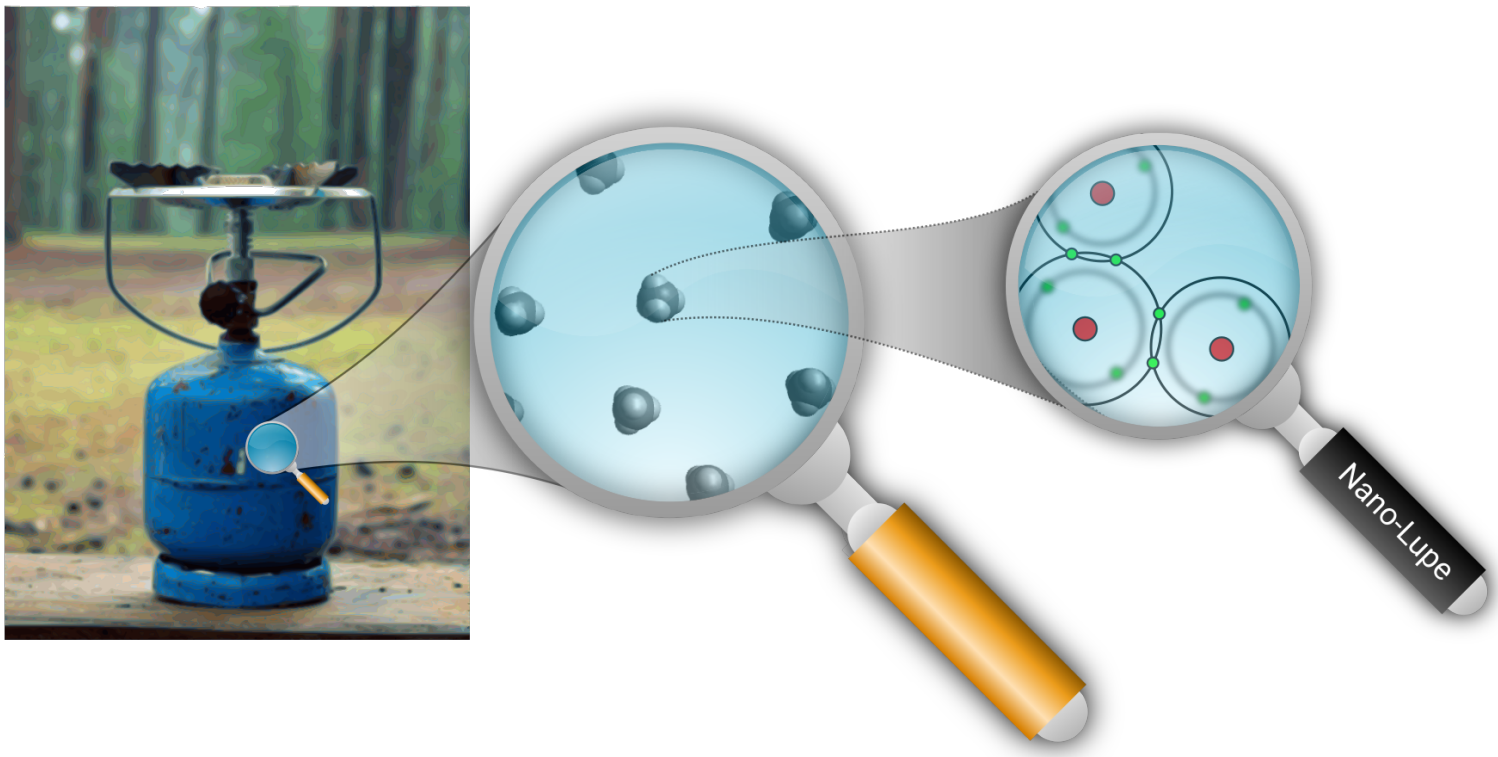

Image source: Openclipart

Layered props

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Layered props: 1-cells

$$\frac{\omega \le \tau \quad \alpha \in \Omega(\omega) \quad \Omega(\omega \le \tau) = f}{\omega \;\; \alpha \;\; f\alpha \;\; \tau : (\omega, \alpha \mid \tau, f\alpha)}$$

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$$\frac{\alpha, \beta \in \Omega(\omega) \quad \sigma : \alpha \to \beta}{\omega \;\; \alpha \;\; \sigma \;\; \beta \;\; \omega : (\omega, \alpha \mid \omega, \beta)}$$

$$\frac{\alpha \in \Omega(\omega) \quad \beta \in \Omega(\tau)}{\omega \;\; \alpha \;\; \beta \;\; \tau \;\; \tau \;\; \beta \;\; \alpha \;\; \omega : (\omega, \alpha; \tau, \beta \mid \tau, \beta; \omega, \alpha)}$$

$$\frac{}{: (\varepsilon \mid \varepsilon)}$$

$$\frac{}{\varepsilon \;\; \varepsilon \;\; \omega : (\varepsilon \mid \omega, I_\omega)}$$

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$$\frac{\alpha, \beta \in \Omega(\omega)}{\omega \;\; \alpha \;\; \omega \;\; \beta \;\; \alpha \;\; \beta \;\; \omega : (\omega, \alpha; \omega, \beta \mid \omega, \alpha \otimes_\omega \beta)}$$

$$\frac{\alpha, \beta \in \Omega(\omega)}{\omega \;\; \alpha \;\; \beta \;\; \alpha \;\; \omega \;\; \beta \;\; \omega : (\omega, \alpha \otimes_\omega \beta \mid \omega, \alpha; \omega, \beta)}$$

$$\frac{x : (t \mid s) \quad y : (s \mid u)}{x ; y : (t, u)}$$

$$\frac{x : (t \mid s) \quad y : (u \mid w)}{x \otimes y : (t; u \mid s; w)}$$

Layered props: 2-cells

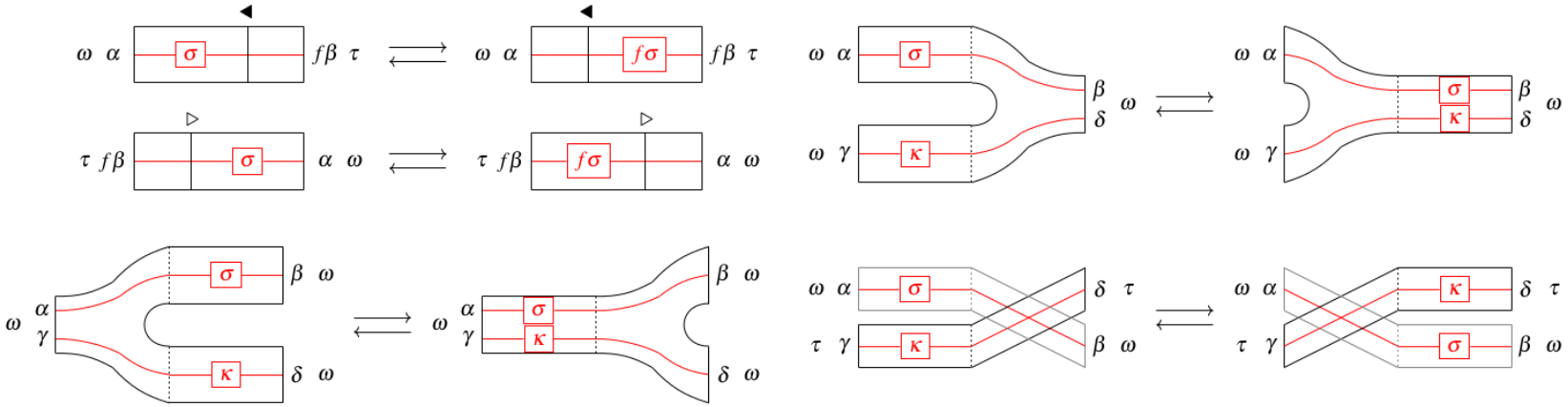

Figure 2: 2-cells of a layered prop expressing functoriality of refinement, coarsening, pants and copants.

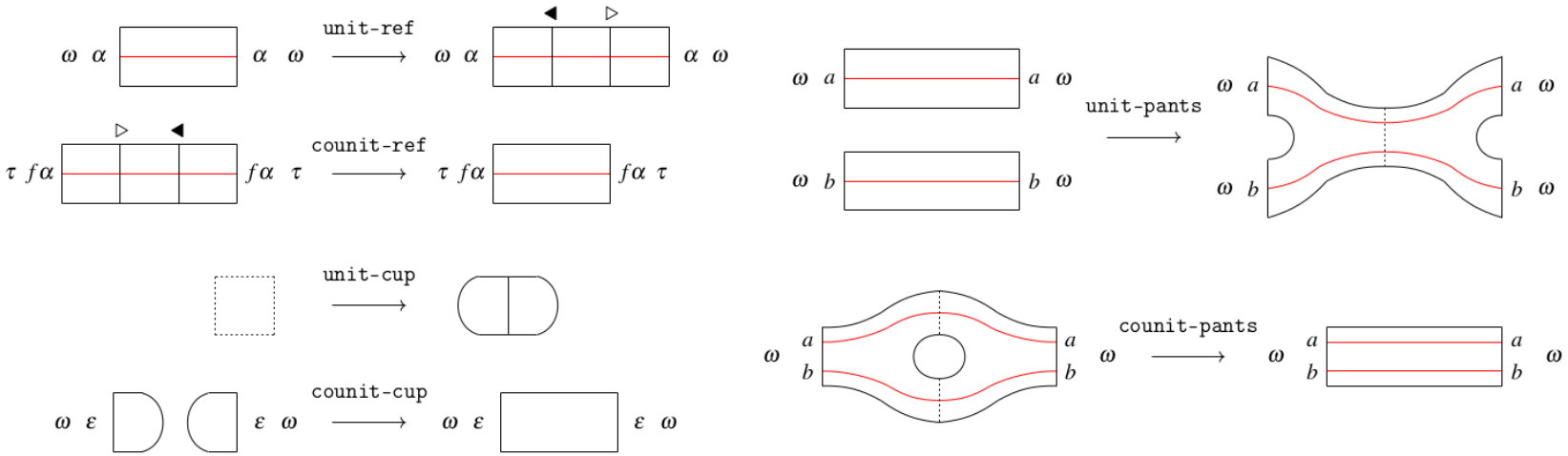

Figure 3: 2-cells of a layered prop that exhibit pants-copants and refinement-coarsening as two adjoint pairs.

Layered props: 2-cells

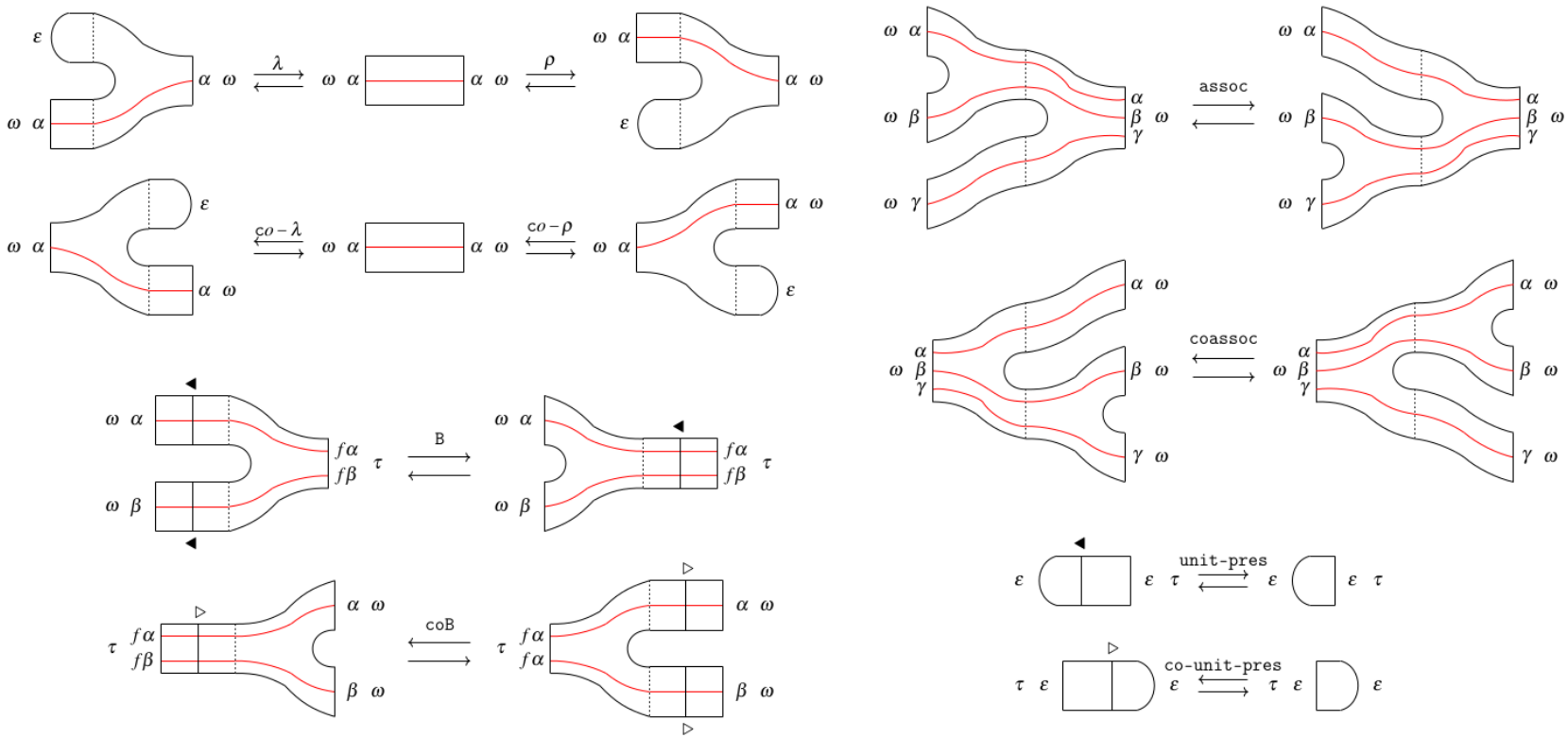

Figure 4: 2-cells of a layered prop that are motivated by monoidal categories and functors.