SYNFACTS

Highlights in Current
Synthetic Organic
Chemistry

REPRINT



Thieme

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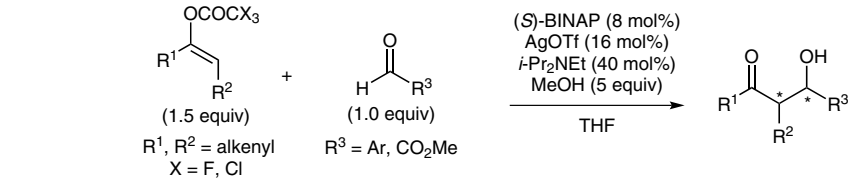
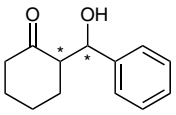
Asymmetric Aldol Reaction Catalyzed by a Chiral Phosphine–Silver Complex
*Eur. J. Org. Chem.* **2014**, 4248–4253.

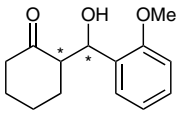
# Silver-Catalyzed Asymmetric Aldol Reaction Using Alkenyl Trihaloacetates



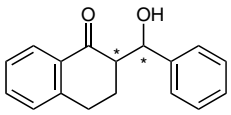

**Selected examples:**



(X = Cl)
92% yield, 94% ee
*anti*/*syn* = 86:14
–40 °C, 2 h

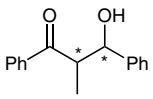


(X = Cl)
99% yield, 89% ee
*anti*/*syn* = 91:9
–40 °C, 12 h

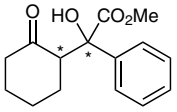


(X = F)
88% yield, 95% ee
*anti*/*syn* = 96:4
–78 °C, 3 h

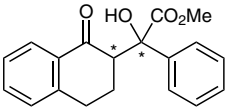
(X = Cl)
81% yield, 75% ee
*anti*/*syn* = 92:8
–40 °C, 20 h



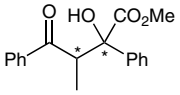
(X = F)
73% yield, 89% ee
*anti*/*syn* = 1:99
–78 °C, 24 h



(X = Cl)
>99% yield, 70% ee
dr = 57:43
–40 °C, 4 h

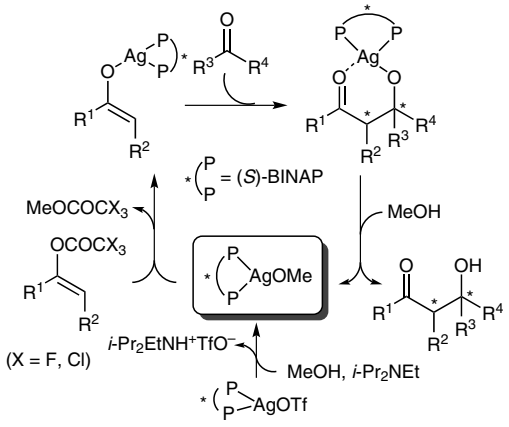


(X = F)
37% yield, 82% ee
dr = 89:11
–78 °C, 4 h

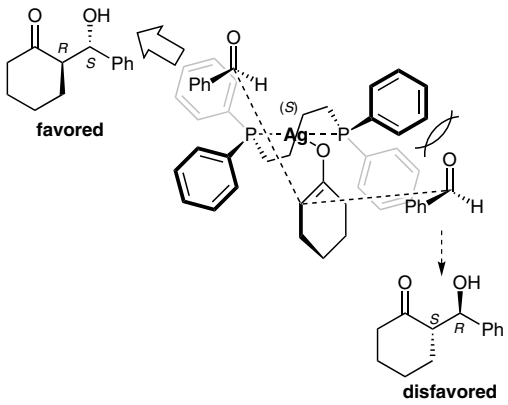


(X = F)
94% yield, 57% ee
dr > 99:1
–78 °C, 20 h

**Proposed mechanism:**




**Hypothesized transition state:**




**Significance:** The β-hydroxy carbonyl moiety is a key synthon for various natural products or bioactive compounds, and the aldol reaction is the most efficient way to synthesize that moiety. The authors reported a novel aldol reaction of an aldehyde with alkenyl trihaloacetate as source of an enolate equivalent.

**Comment:** The (*S*)-BINAP–AgOTf system affords the aldol product from alkenyl trihaloacetate in good to excellent yields with high enantioselectivity as well as good *anti*/*syn* selectivity. The reaction proceeds through the formation of chiral silver enolates from alkenyl trihaloacetates.

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