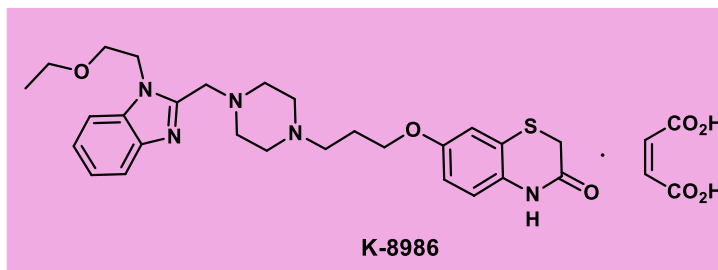
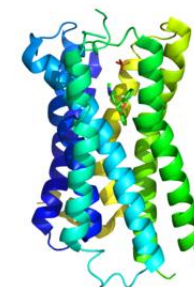
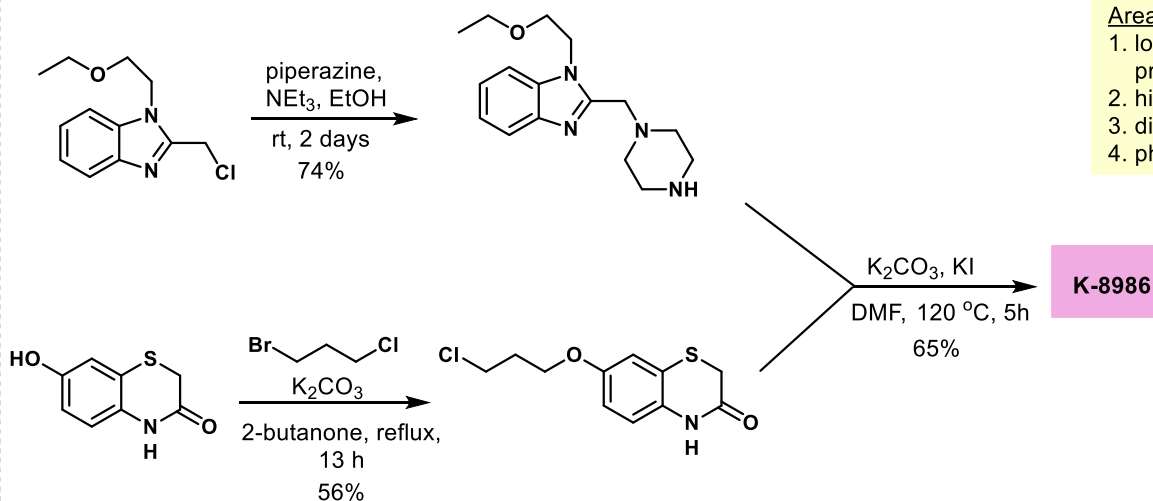


Reference: Fukuda, T. *et al.*, OPRD, 2019.

– potential therapeutic for treatment of allergic conjunctivitis (seasonal and perennial)
– H1-receptor antagonist



Discovery Route:

Areas for Improvement:

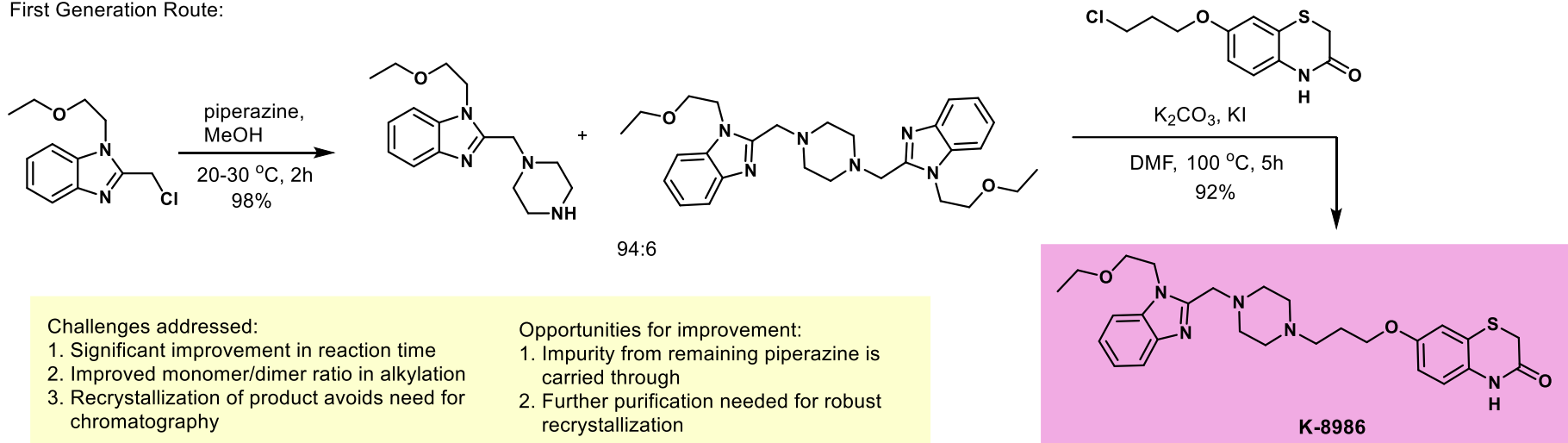
1. long reaction time (alkylation with piperazine) to suppress side products
2. high temperature and chromatographic purification of last step
3. difficult quality control of O-alkylated product
4. physicochemical properties of product (stability, solubility)

Physicochemical properties:

conditions	monomaleate	dimalate
thermal stability (80 °C, 1 week)	100.6%	98.9%
photostability (1.2 million lux h)	100.6%	94.3%
hygroscopicity (75% RH, 25 °C, 1 day)	- 0.1%	0.4%
hygroscopicity (93% RH, 25 °C, 1 day)	0.1%	11.0%
aqueous solubility (pH 5.5)	5.10 mg/mL	3.85 mg/mL
purity, HPLC area %	99.4%	97.2%

Fukuda, T. *et al.*, OPRD, 2019.

First Generation Route:



Second Generation Route:

