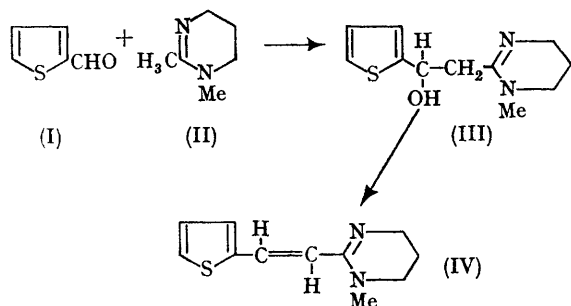


## Fluoride Catalysis of the Knoevenagel Reaction

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RAND *et al.*<sup>1</sup> report catalysis of the Knoevenagel reaction by alkali-metal fluorides. We have examined a wide range of metallic fluorides for catalytic effect on the condensation between thiophen-2-carboxaldehyde (I) and 1,2-dimethyl-1,4,5,6-tetrahydropyrimidine (II).



In this investigation, the rate of reaction was measured by the time taken for the rate of evolution of water, from a reaction mixture at reflux in

methylcyclohexane, to fall to a low level, and the extent of reaction by both the total water collected and the yield of isolated *trans*-1-methyl-2-(2-thienylvinyl)-1,4,5,6-tetrahydropyrimidine (IV). No activity is observed with lithium, potassium, caesium, iron(III), or nickel fluorides; some activity is noted for sodium, magnesium, calcium, zinc, barium, aluminium, cerium, and lead(II) fluorides, whereas considerable activity is shown by tin(II) fluoride. The activity of tin(II) fluoride is apparent with less than 0.013 atoms of fluorine per molecule of reactants, but does not increase significantly above 0.051 atoms per molecule.

By low-temperature reaction (30°) the intermediate secondary alcohol (III) can be isolated and dehydration carried out separately. The catalytic activity of tin(II) fluoride on each reaction was studied, leading us to the conclusion that the principal effect is at the dehydration stage, with only a doubling of the coupling rate. Clearly, the rate determining step in this synthesis is the dehydration stage which is considerably accelerated by addition of tin(II) fluoride.

We thank Pfizer Limited for permission to publish this work.

TABLE

Catalyst		Reaction time (hr.)	Water evolved (% of theory)	Yield (% stoich.)
Metallic Element	Atoms/mol. of (II)			
Uncatalysed		6	74.5	62.5
Lithium	0.052	5.25	100	55.9
Potassium	0.079	5.5	98.5	60.7
Caesium	0.053	5.0	100	55.6
Iron(III)	0.069	5.0	100	67.4
Nickel	0.053	5.25	100	66.7
Sodium	0.076	4.0	100	66.1
Magnesium	0.104	3.25	100	49.9
Calcium	0.082	3.75	100	55.1
Zinc	0.053	3.25	100	61.3
Barium	0.053	4.0	100	57.6
Aluminium	0.054	2.25	100	66.5
Cerium	0.255	4.0	100	54.2
Lead(II)	0.029	4.25	100	56.6
Tin(II)	0.093	1.0	100	60.5

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<sup>1</sup> L. Rand, J. V. Swisher, and C. J. Cronin, *J. Org. Chem.*, 1962, 27, 3505; L. Rand, D. Heidukewych, and R. J. Dollinski, *ibid.*, 1966, 31, 1272.