

Anti-obesity drugs

Tomáš Goněc

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Obesity

severe world-wide spread disease

increases DM II, cardiovascular risk, osteoporosis

Body mass index (BMI) = body weight [kg] / (body height [m])²

Obesity definition (WHO):

BMI 20-25	normal
BMI 25-30	overweight
BMI 30-40	obesity
BMI >40	severe obesity

Visceral obesity: waistline > 80cm (F) or > 94cm (M)



Anti-obesity therapy

- **low-energy diet**
- **aerobic exercise**
- **farmacotherapy**

Anti-obesity drugs

□ **Central (Anorectics)**

- inhibits centre of appetite in brain
- increase sympathetic tonus

□ **Peripheral**

- inhibits digestion and/or absorption of lipids and carbohydrates
- accelerates their metabolism



Central anorectics

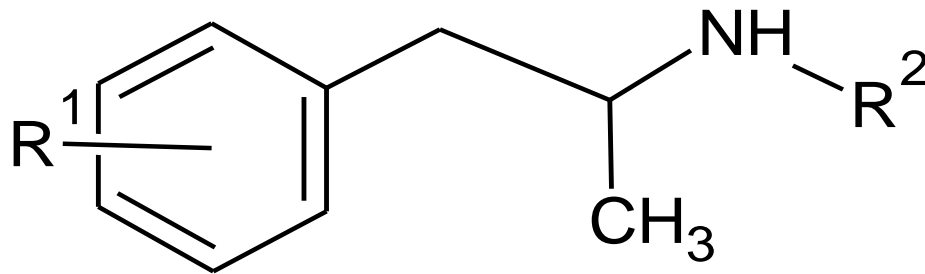
- decreases appetite
- causes feeling full
- increases lipolysis

Mechanism of action:

- indirect central adrenergic stimulants
- indirect 5-HT mimetics
- cannabinoid receptor 1 antagonists

Amphetamine derivatives

- increases catecholamine synaptic release



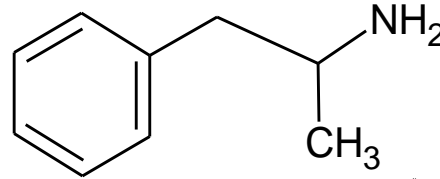
Structure-activity relationships:

R1: -H, -OH or 3,4- -OCH₂O-

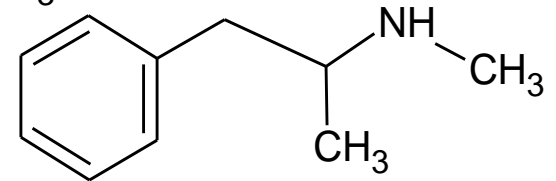
R2: methyl, ethyl

Amphetamine derivatives

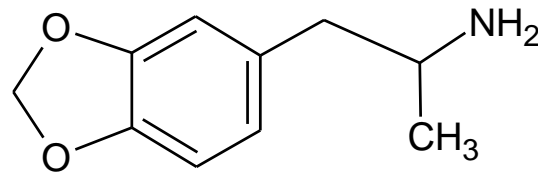
Amphetamine



Metamphetamine (Pervitine)

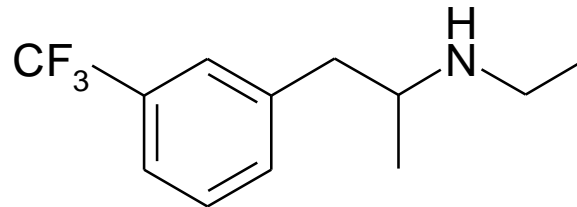


Tenamfetamine



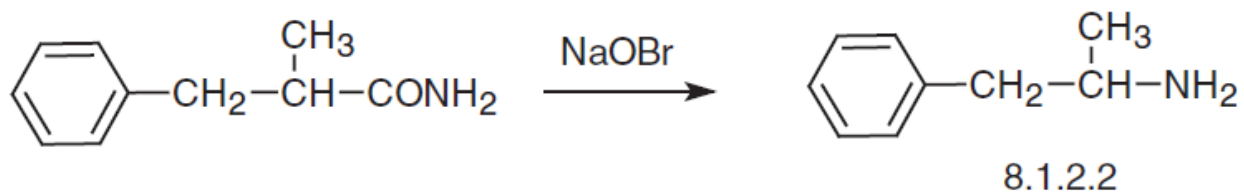
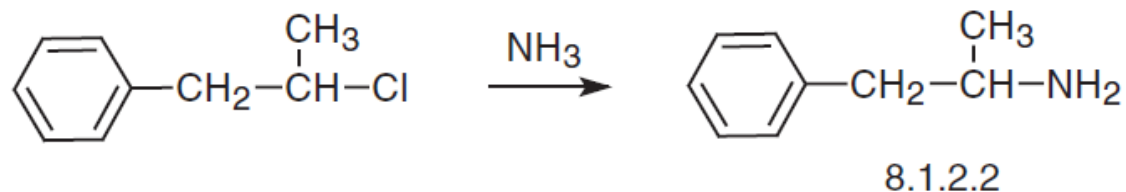
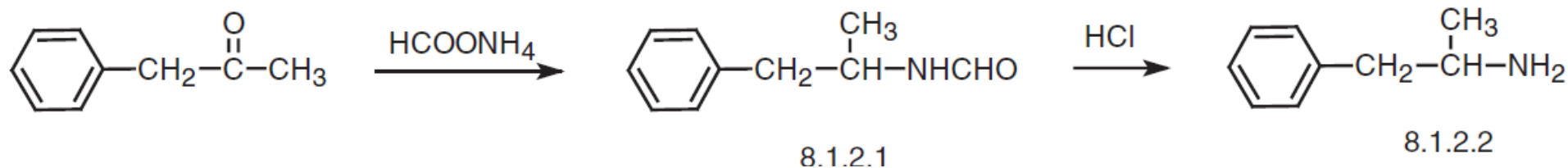
-withdrawed from market due to habit and toleration

Fenfluramine

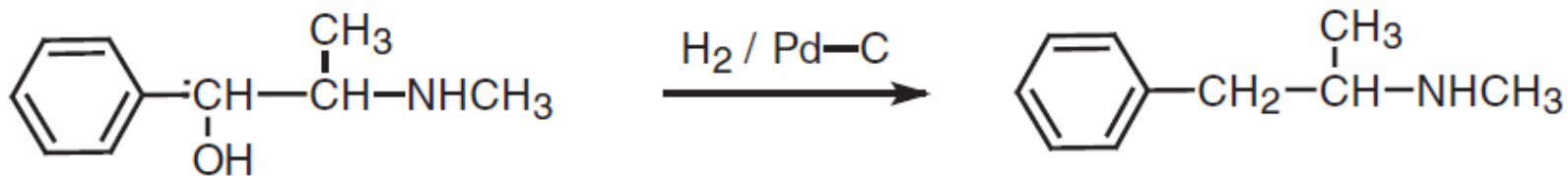


-withdrawed from market due to severe cardiovascular side-effects

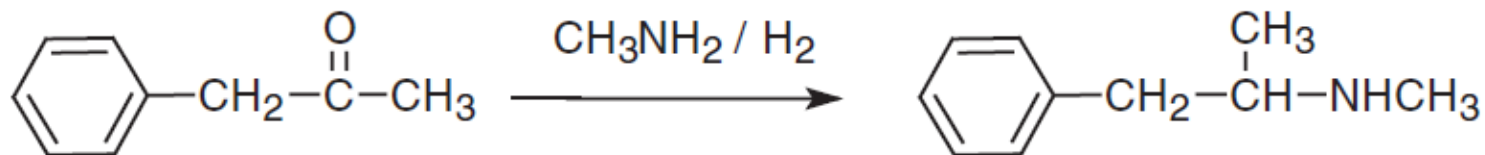
Amphetamine synthesis



Metamphetamine synthesis



8.1.2.3

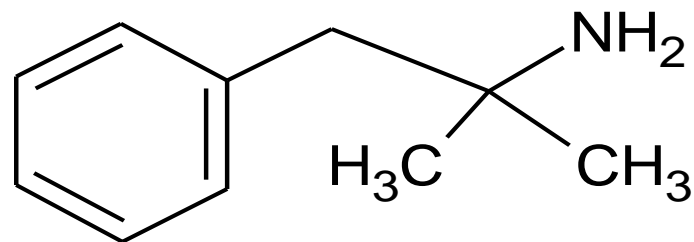


8.1.2.3

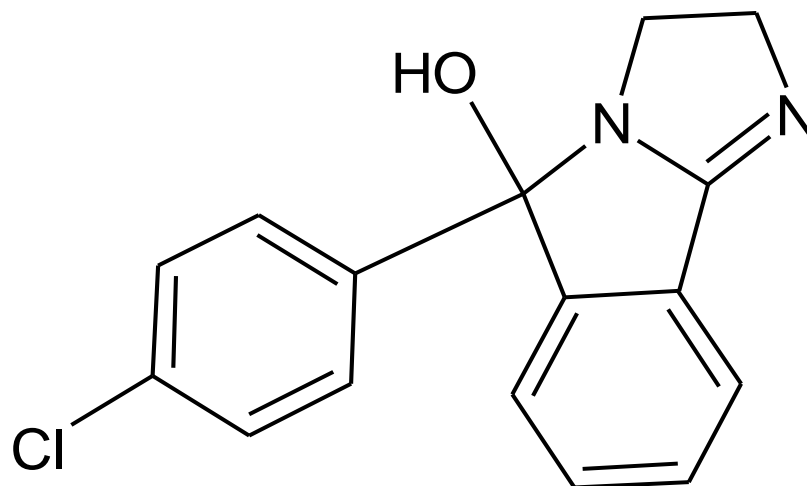
Amphetamine derivatives

Fentermine

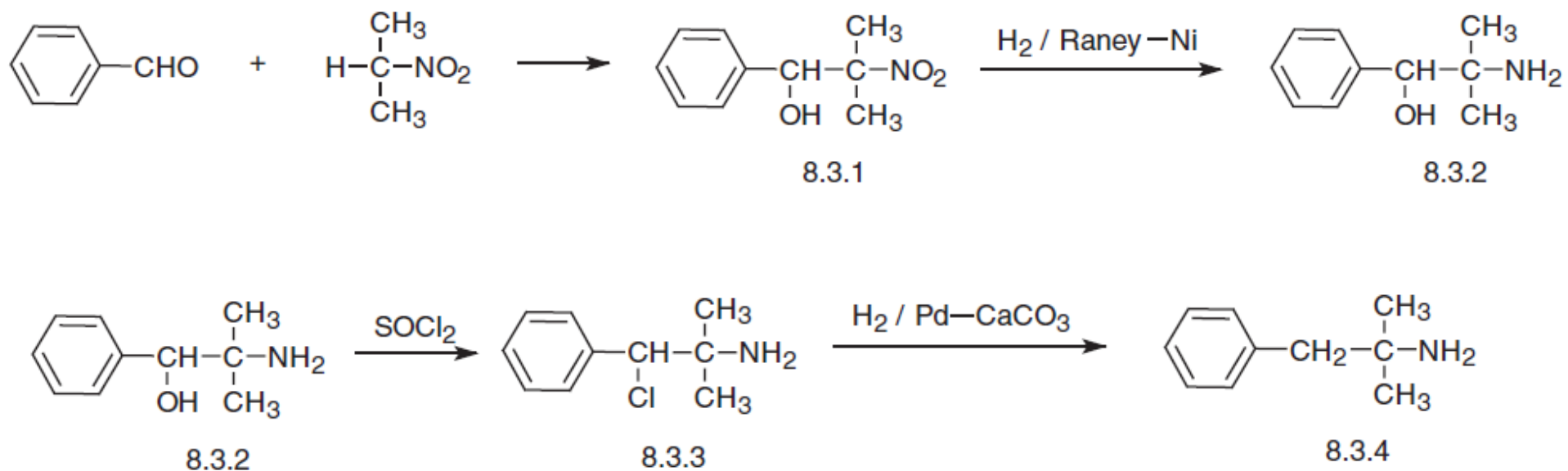
used as resinate
(complex with resine polymer)



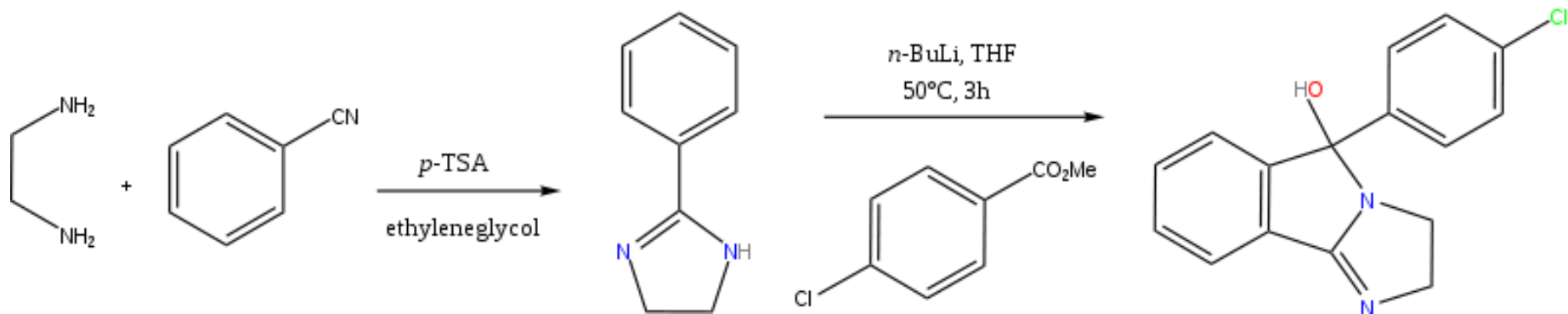
Mazindole



Fentermine synthesis

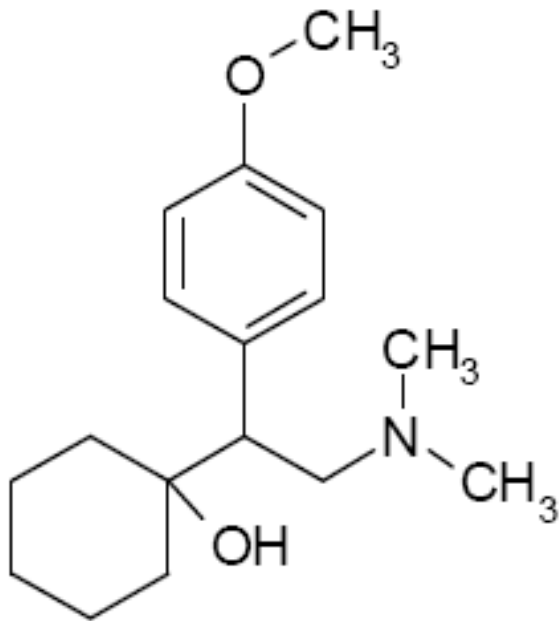


Mazindole synthesis

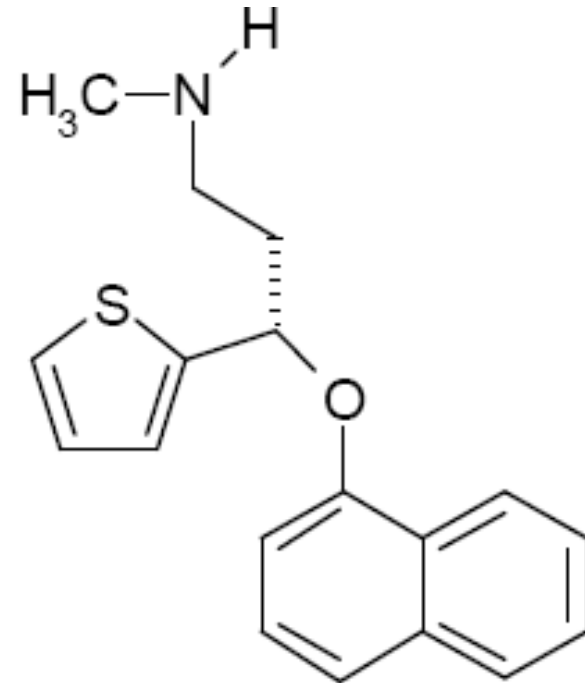


Serotonin-Noradrenaline Reuptake Inhibitors (SNRIs)

Antidepressants with anorectic activity

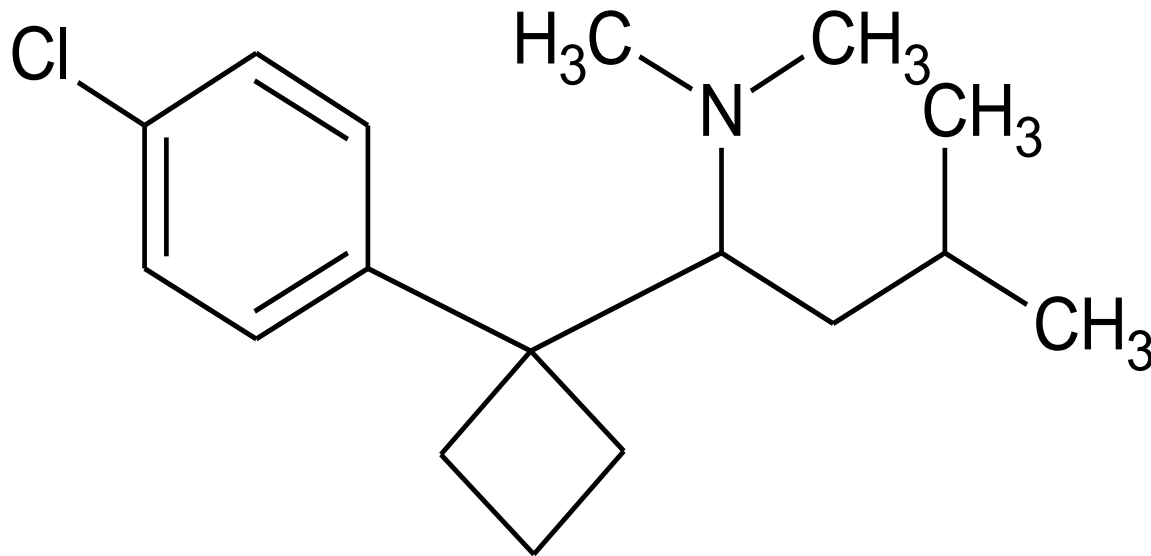


Venlafaxine



Duloxetine

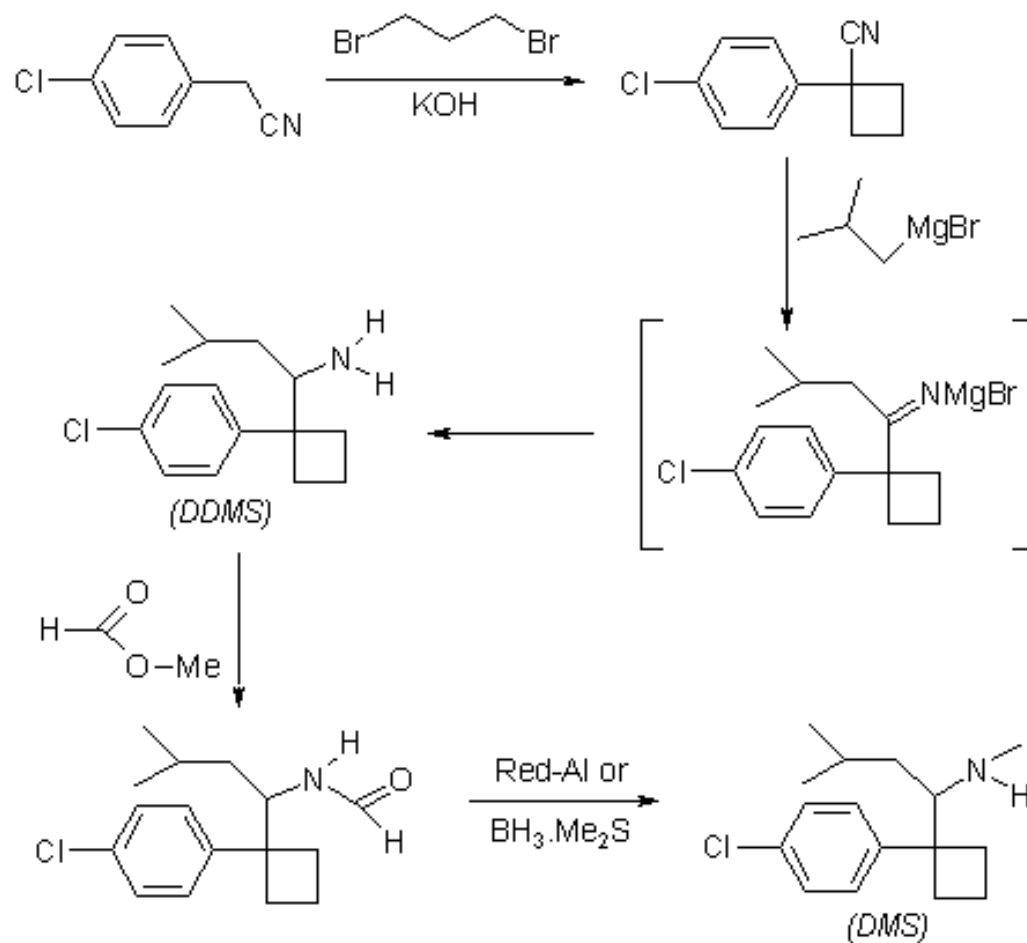
Serotonin-Noradrenaline Reuptake Inhibitors (SNRIs)



Sibutramine

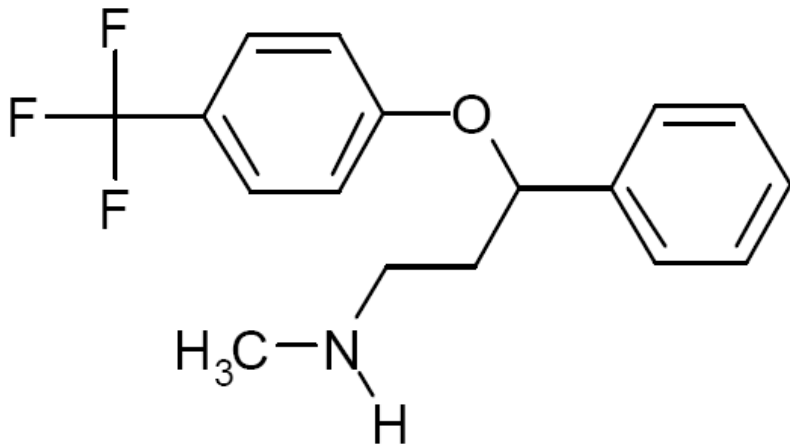
widely used in therapy, manifesting several cardiovascular side-effects

Sibutramine synthesis

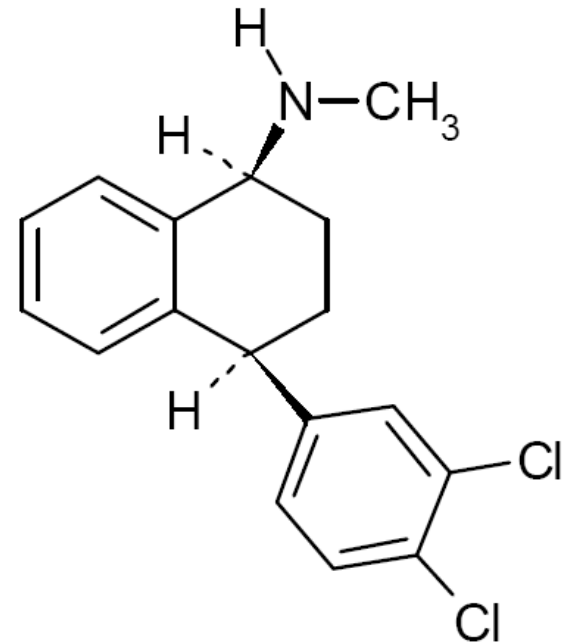


Selective Serotonin Reuptake Inhibitors (SSRIs)

Antidepressants with anorectic activity

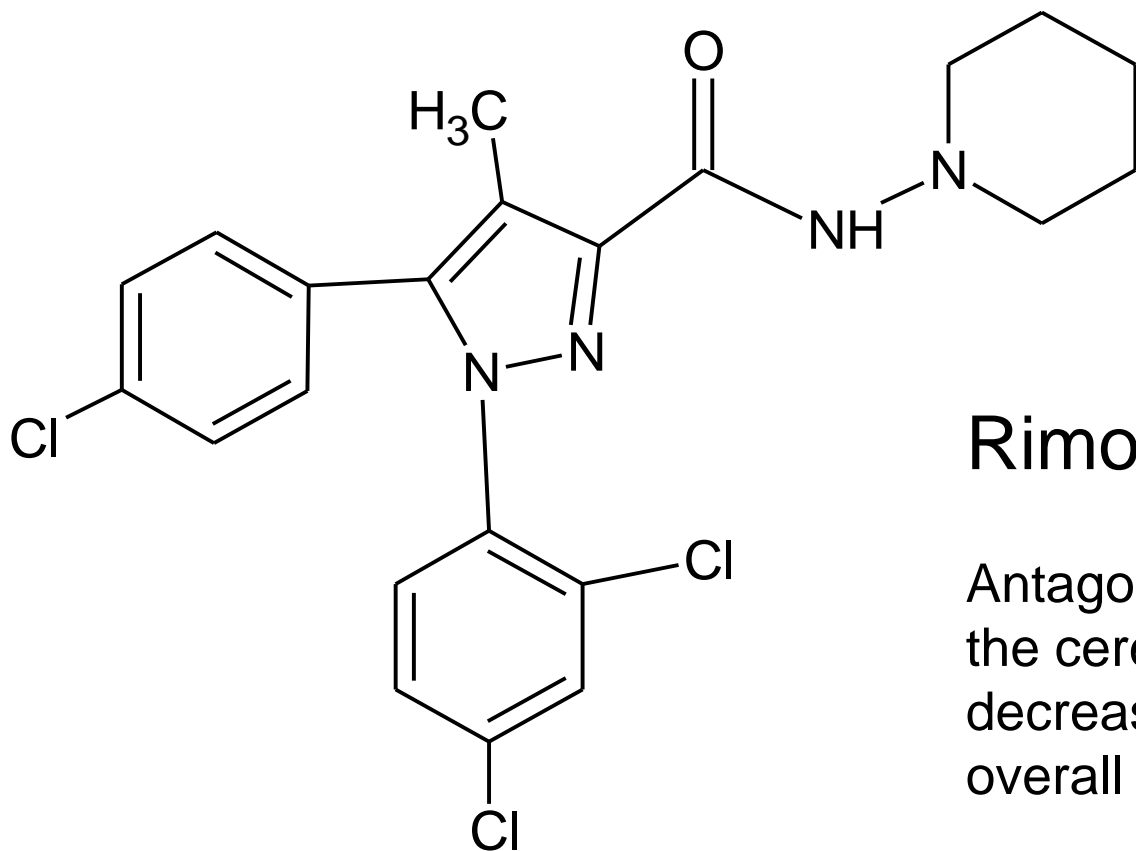


Fluoxetine



Sertraline

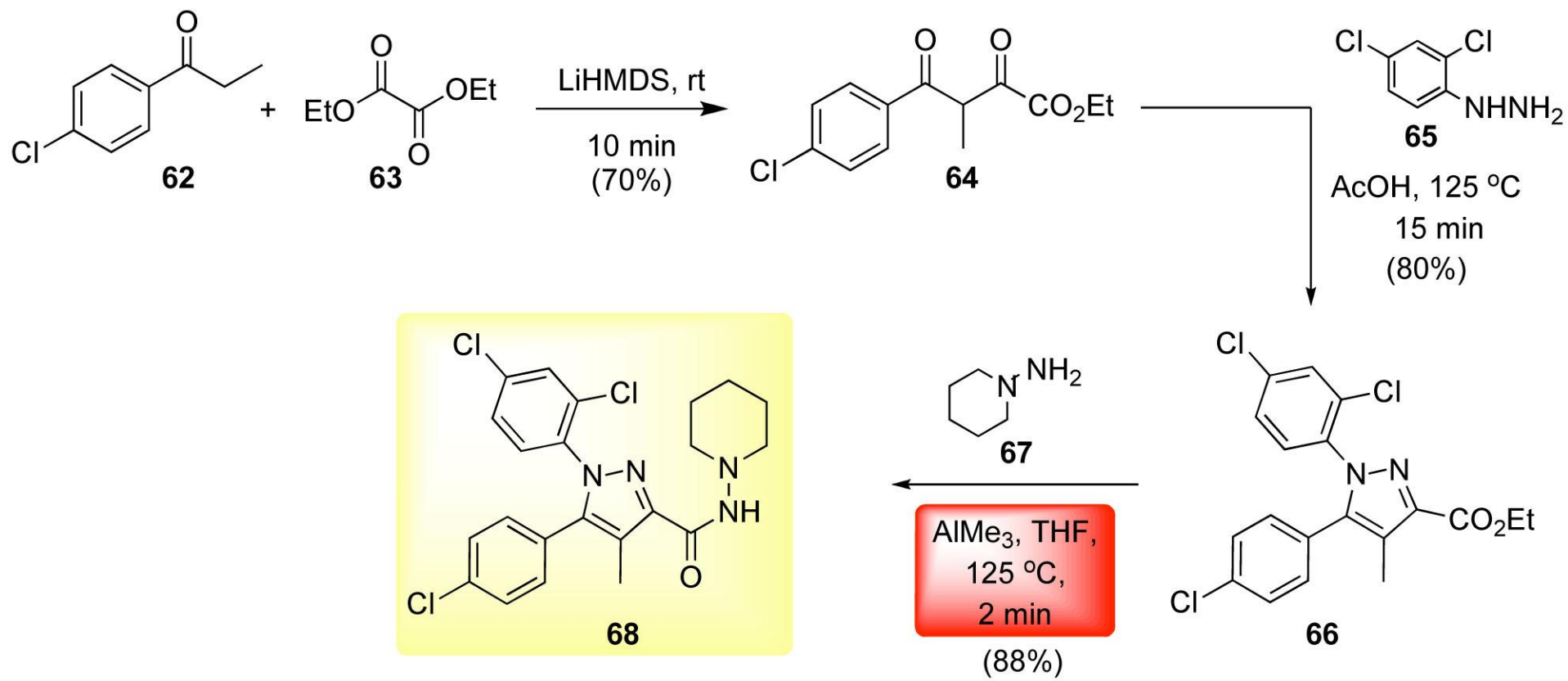
Cannabinoid receptor CB1 inhibitors



Rimonabant

Antagonism on
the cerebral CB1 receptors
decreases appetite and
overall food intake

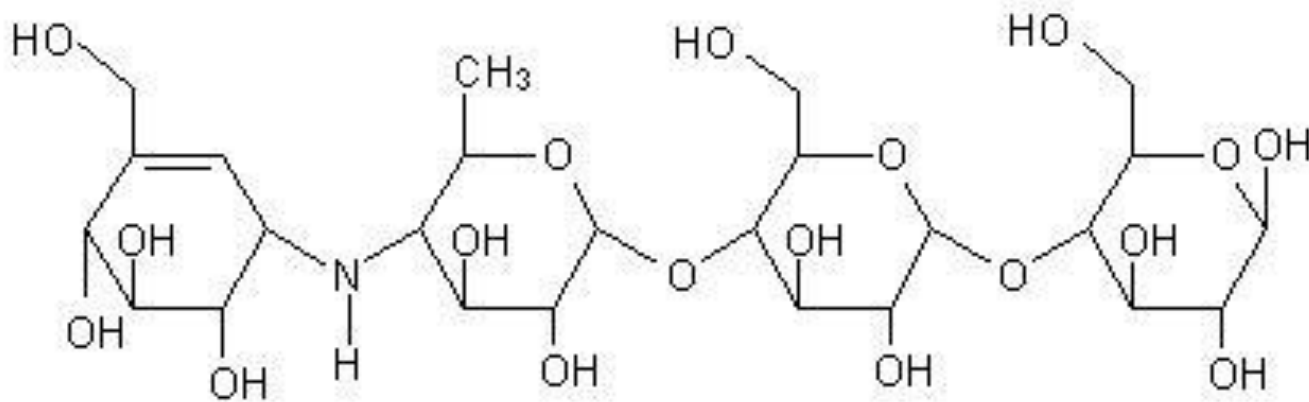
Rimonabant synthesis



Rimonabant®

0.4 g/h, 49% overall

Peripheral anti-obesity drugs

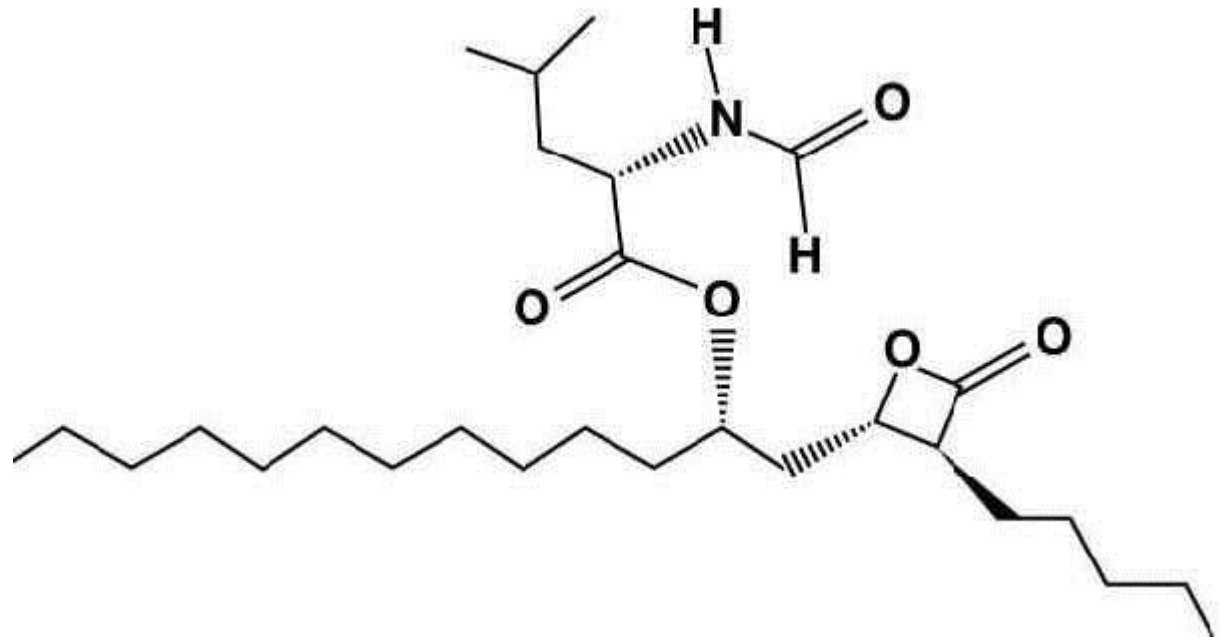


Acarbose

α -glucosidase inhibitor

– carbohydrates are not digested in the intestine

Peripheral anti-obesity drugs



Orlistat

both ventricular and pancreatic lipase inhibitor
- lipids are not digested in all digestive organs

Important side-effect:

undigested lipids causes diarrhoea