

Szerves kémiai szintézismódszerek

1. Bevezetés

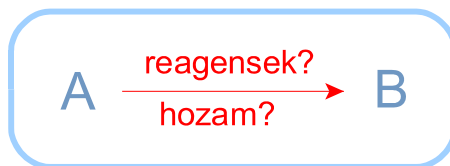
Kovács Lajos

Problémafelvetés

Egy szintézis akkor jó, ha...

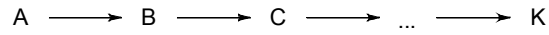
- a legjobb hozamban
- a legkevesebb lépésben
- a legszelektívebben
- a legolcsóbban
- a legflexibilisebben lehet megvalósítani

A szerves szintézisek célja a szerves kémia ismeretanyagának újratárgyalása egyetlen szempont alapján: hogyan lehet szerves vegyületeket előállítani?



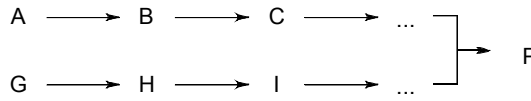
Szintézisfajták

Lineáris szintézisek



$$Y_K = \prod y_i$$

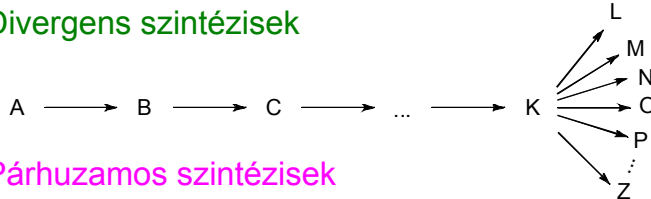
Konvergens szintézisek



$$Y_P = \prod y_i (y_m) y_n \dots$$

$l, m, n, \dots < i$

Divergens szintézisek



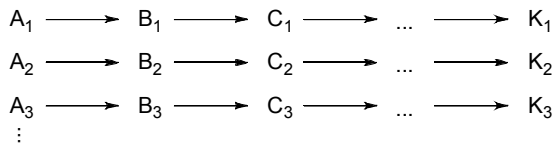
$$Y_L = \prod y_{i,L}$$

$$Y_M = \prod y_{i,M}$$

$$\vdots$$

$$Y_Z = \prod y_{i,Z}$$

Párhuzamos szintézisek

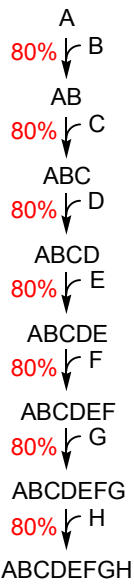


$$Y_{K_1} = \prod y_{i,K_1}$$

$$Y_{K_2} = \prod y_{i,K_2}$$

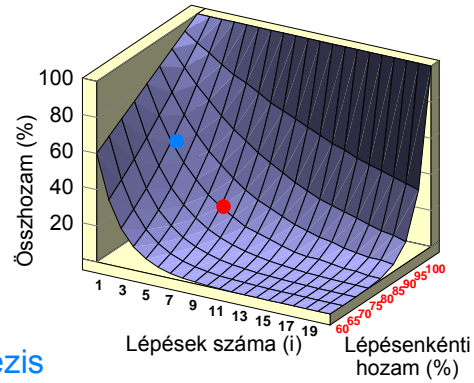
$$\vdots$$

Hozamok 1.

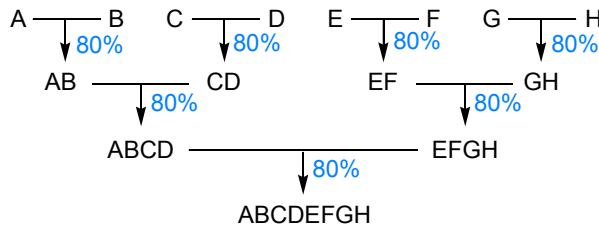


Lineáris szintézis

$$0.8^7 \times 100 = 21 \%$$



Konvergens szintézis



$$0.8^3 \times 100 = 51 \%$$

Hozamok 2.

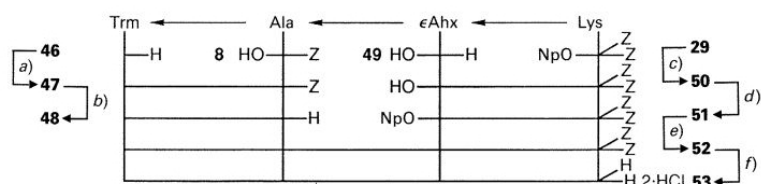


Készült cukor, növényi zsír, kakaópor, emulgeálószer (E-476, szójalecitin) és mesterséges aroma (vanília) felhasználásával. Tartalmazhat nyomokban egyéb olajos magvakat, tejszennyezőanyagot.
Kakao szárazanyag legalább 20%. Száraz, hűvös helyen tartandó!

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Hozamok 3.

- Ha lehet, kerüljük a lineáris szintézist
- Ha ez nem lehetséges, akkor
 - ♦ törekedjünk a legrövidebb szintézisútra
 - ♦ igyekezzünk a legjobb hozamú reakciókat alkalmazni
- A konvergens szintézis hatékonyabb, de nem mindig alkalmazható
- Szinte mindegyik szintézistípus tartalmaz lineáris elemeket



a) ClCO_2Et , Et_3N ; 69.0%. b) H_2 , Pd/C; 92.2%. c) N,N,N',N' -tetramethylguanidine; 52.6%. d) 4-nitrophenyl trifluoroacetate/py; 56.4%. e) 76.3%. f) H_2 , Pd/C, then HCl, 100%.

Termodinamikai fogalmak 1.

Szabadentalpia és reakcióhő

$$\Delta G = \Delta H - T\Delta S \quad (1)$$

$\Delta G < 0$ esetben a reakció végbemehet

$$\Delta G = -RT \ln K \quad (2)$$



$$\Delta G = + 101 \text{ kJ/mol}$$

$$K = 10^{-17} \text{ mol (25 }^\circ\text{C)}$$



$$\Delta H_f = + 2061 \text{ kJ/mol}$$

(átlagos kötési energiákból számítva);

+ 1985 kJ/mol (kísérleti érték)

A \rightleftharpoons B		(T=298 K)	
K	ΔG (kJ/mol)	B, %	A, %
1.00	0.00	50.00	50.00
1.22	-0.50	55.00	45.00
1.50	-1.00	60.00	40.00
1.86	-1.53	65.00	35.00
2.33	-2.10	70.00	30.00
3.00	-2.72	75.00	25.00
4.00	-3.43	80.00	20.00
5.67	-4.30	85.00	15.00
9.00	-5.44	90.00	10.00
19.00	-7.30	95.00	5.00
49.00	-9.64	98.00	2.00
99.00	-11.38	99.00	1.00
999.00	-17.11	99.90	0.10
9999.00	-22.82	99.99	0.01
99999.00	-28.52	99.9990	0.0010
999999.00	-34.23	99.9999	0.0001

Termodinamikai fogalmak 2.

Entrópia

$$S = S_{\text{trans}} + S_{\text{rot}} + S_{\text{vib}}$$

$$\text{CH}_4: S_{\text{trans}}^\circ = 144 \text{ J/mol}\cdot\text{K}; S_{\text{rot}}^\circ = 32 \text{ J/mol}\cdot\text{K}$$



$$\Delta H^\circ = + 167 \text{ kJ/mol}$$

$$T\Delta S (25^\circ\text{C}) = 35 \text{ kJ/mol}; \Delta S_{\text{trans}} = 117 \text{ J/mol}\cdot\text{K}, \Delta S_{\text{rot}}, \Delta S_{\text{vib}} \text{ kicsi}$$

$$T\Delta S (1000^\circ\text{C}) = 190 \text{ kJ/mol}; \Delta S_{\text{trans}} \sim 150 \text{ J/mol}\cdot\text{K}$$



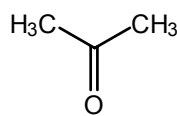
$$\Delta S_{\text{trans}} = - 4.6 \text{ J/mol}\cdot\text{K}, T\Delta S (25^\circ\text{C}) = 1.4 \text{ kJ/mol}$$

Termodinamikai fogalmak 3.

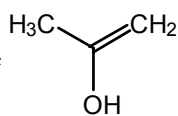
Entrópia

A \rightleftharpoons **B**

ΔS elhanyagolható



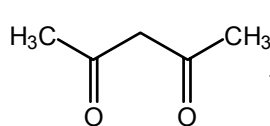
> 99 %



10⁻⁵ %

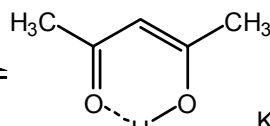
$$K = 10^{-7}$$

$$\Delta H (\Delta G) \sim 39.9 \text{ kJ/mol}$$



8 %

84 %



92 %

16 %

$$K = 11.5$$

$$\Delta H (\Delta G) \sim -6.6 \text{ kJ/mol}$$

$$\Delta H_{\text{H-kötés}} \sim 25 \text{ kJ/mol}$$

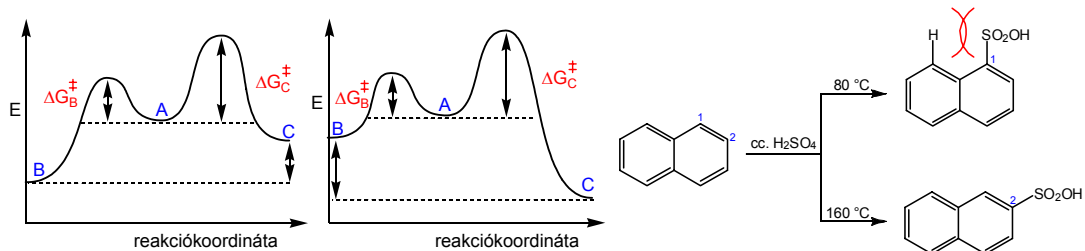
tisztán

$$K = 0.19$$

vizes oldatban

Termodinamikai fogalmak 4.

Kinetikus és termodinamikus kontroll



$$k_1 = 36 \text{ M}^{-1} \text{ s}^{-1}$$

$$k_2 = 0.73 \text{ M}^{-1} \text{ s}^{-1}$$

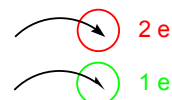
$$K_1 = \frac{k_{-1}}{k_1} = 2.14 \cdot 10^7$$

$$K_2 = \frac{k_{-2}}{k_2} = 7.6 \cdot 10^4$$

$$\Delta(\Delta G^\ddagger) = \Delta(\Delta G_2^\ddagger - \Delta G_1^\ddagger) = 9.6 \text{ kJ/mol}$$

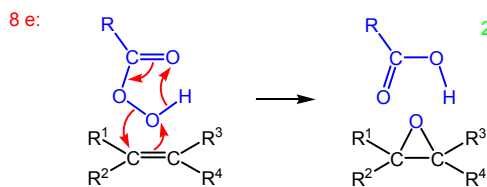
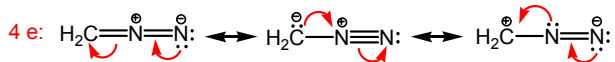
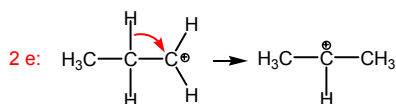
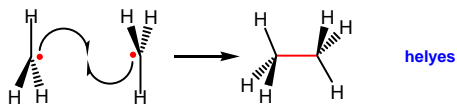
Elektronáramlások

Minden kémiai átalakulás a külső elektronok
(vegyértékelektronok és nemkötő elektronok)
átrendeződése az atomtörzsek között

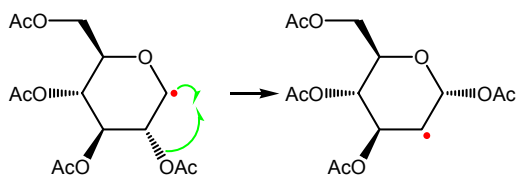


helyes

helytelen



2 x 1 e:

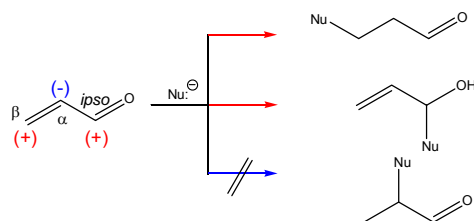
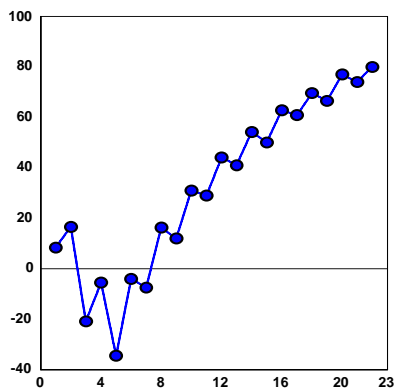


A kémiai reaktivitás értelmezése

A Lapworth-Evans modell: a molekulák, mint ionok aggregátumai

- Egyes fizikai tulajdonságok (op., fp., moláris térfogat, sűrűség, viszkozitás) a szénatomszám függvényében úgy változnak, hogy páros és páratlan sorozatok különíthetők el (Cuy, 1920)
- A kémiai reaktivásban is megfigyelhetők a páros és páratlan szénatomok közötti különbségek (Lapworth, 1920; Evans, 1971)

A n-karbonsavak olvadáspontja a szénatomszám függvényében

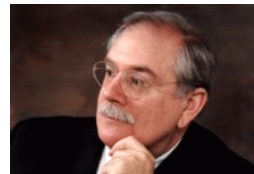
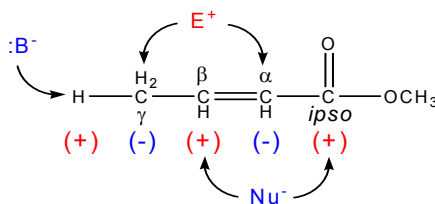


A Lapworth-Evans model 1.

Változó polaritások a szerves vegyületekben



Arthur Lapworth
(1872-1941)



David A. Evans (1941-)

A funkciós csoportok osztályozása Evans szerint (csak a heteroatom jelenti a funkciós csoportot):

E: az *ipso*-atomnak elektrofil jelleget biztosító csoportok

N (G): az *ipso*-atomnak nukleofil jelleget biztosító csoportok

A: az *ipso*-atomnak ambivalens jelleget biztosító csoportok

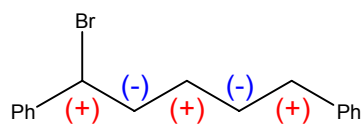
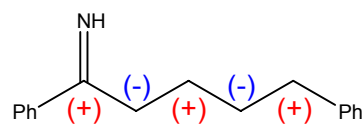
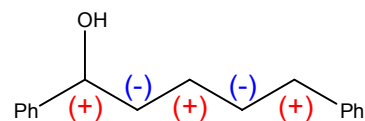
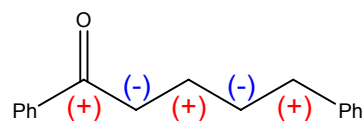
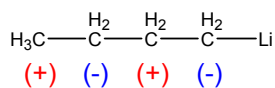
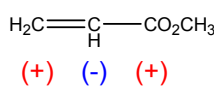
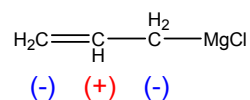
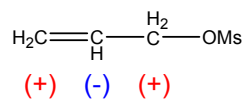
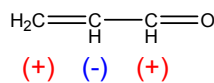
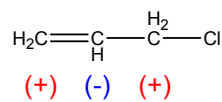
(+)
C-E
-OH, -OR
=O
-NR₂, =NR
-X

(-)
C-G
alkálifémek
alkáliföldfémek
-AlR₂, -SiR₃

(±)
C-A
-NO₂, =NOH, =NNHR, =N₂, ≡N, -N⁺R₃
-SR, -S(O)_xR, -S⁺R₂, -PR₂, -P(O)R₂, -P⁺R₃
-BR₂, =CR₂, ≡CR

A Lapworth-Evans model 2.

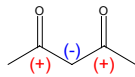
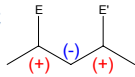
Példák



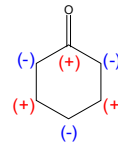
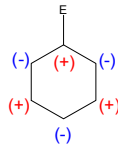
A Lapworth-Evans model 3.

Két funkciós csoport jelenléte: konszonáns (C) és disszonáns (D) viszonyok

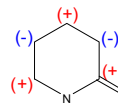
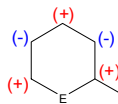
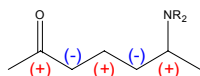
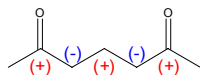
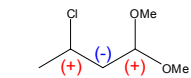
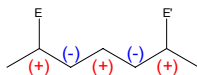
1,3-C



C-gyűrűk



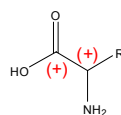
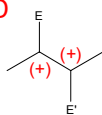
1,5-C



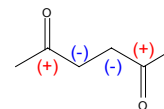
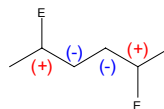
1,1-D



1,2-D



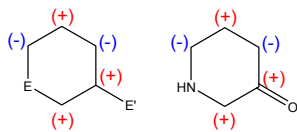
1,4-D



A Lapworth-Evans model 4.

Kétfunkciós csoportjelenléte: konszonáns (C) és disszonáns (D) viszonyok2.

1,2-D (1,4-D)



Általánosítva:

szerkezet	n páros	n páratlan
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$E-(C)_n E'$	D	C
--------------	---	---

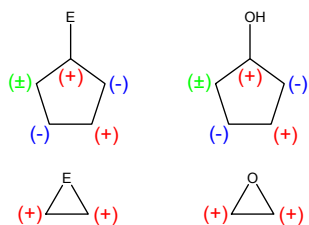
$G-(C)_n G'$	D	C
--------------	---	---

$E-(C)_n G$	C	D
-------------	---	---

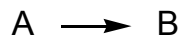
C_n	C	D
-------	---	---

C_n E E'	D	C
---------------	---	---

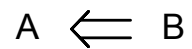
D-gyűrűk



Retroszintetikus elemzések 1.

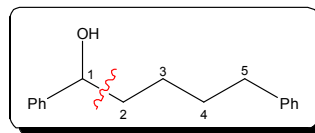


- szintézis
- reakciók

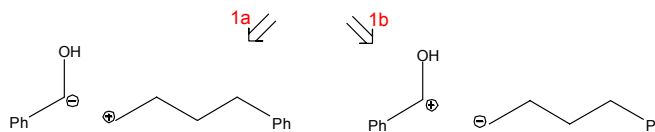


- retroszintézis
- szétkapcsolások (disconnections)

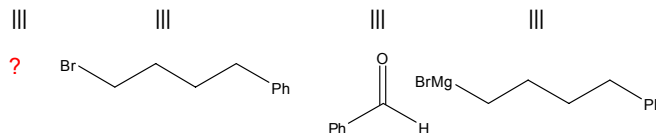
célvegyület:
1,5- difenil-pentán-1-ol



szintionok

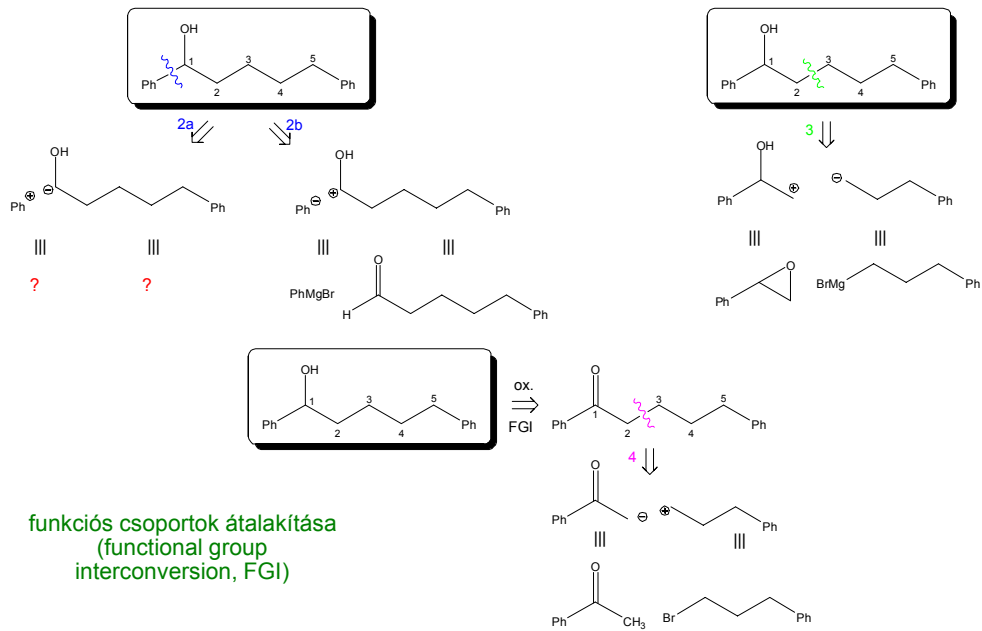


reagensek



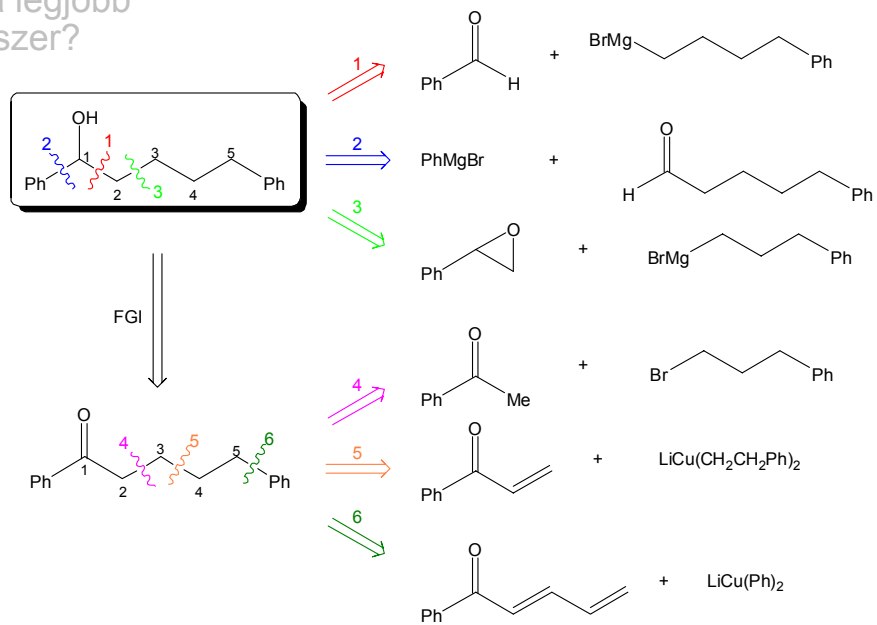
szinton = szintetikus ekvivalens

Retroszintetikus elemzések 2.



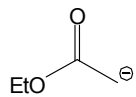
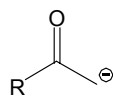
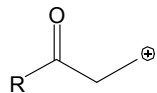
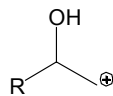
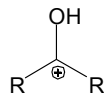
Retroszintetikus elemzések 4.

Melyik a legjobb módszer?



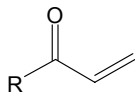
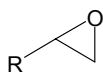
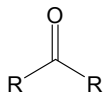
Néhány egyszerű szinton és a megfelelő reagensek

Szinton

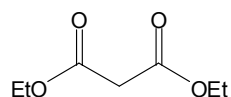
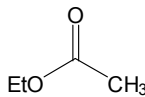
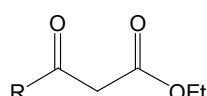
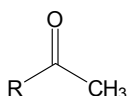


Reagens

RBr, RI, ROMs, ROTs (R = alkil, nem aril)



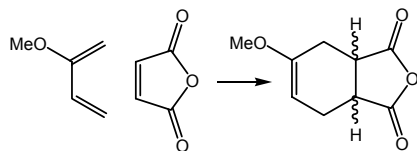
RMgBr, RLi, LiCuR₂



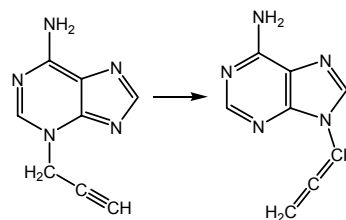
Feladatok 1.

Hogyan értelmezhetők elektronáramlások segítségével az alábbi reakciók?

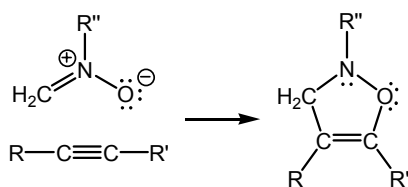
F1.1



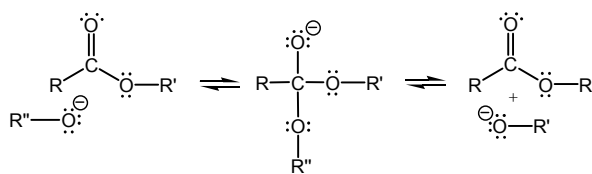
F1.2



F1.3



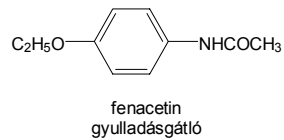
F1.4



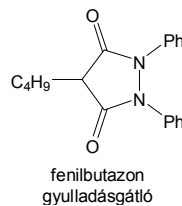
Feladatok 2.

Hogyan lehet előállítani az alábbi anyagokat?

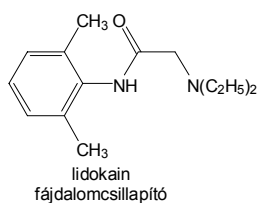
F1.5



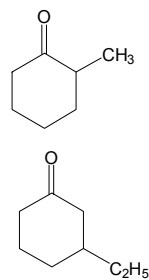
F1.6



F1.7



F1.8



Ajánlottolvasmányok

- J. R. Hanson (2002): Organic synthetic methods. Royal Society of Chemistry, Cambridge. 175 pages. pp. 1-9
- F. Serratosa (1990): Organic chemistry in action. The design of organic synthesis. (Studies in Organic Chemistry, 41.) Elsevier, Amsterdam. 395 pages. pp. 1-42.
- C. Willis, M. Wills (1995): Organic synthesis. (Series Ed: S. G. Davies. Oxford Chemistry Primers, 31.) Oxford University Press, Oxford. 92 pages. pp. 1-14.
- R. K. Mackie, D. M. Smith (1986): Szerves kémiai szintézisek ~~ú~~ Műzaki Könyvkiadó, Budapest. 357 o.
- R. O. C. Norman, J. M. Coxon (1993): Principles of organic synthesis. 3rd ed. Blackie Academic and Professional, London. 811 pages
- D. P. Weeks (1976): Electron movement. A guide for students of organic chemistry. W. B. Saunders, Philadelphia. 133 pages.