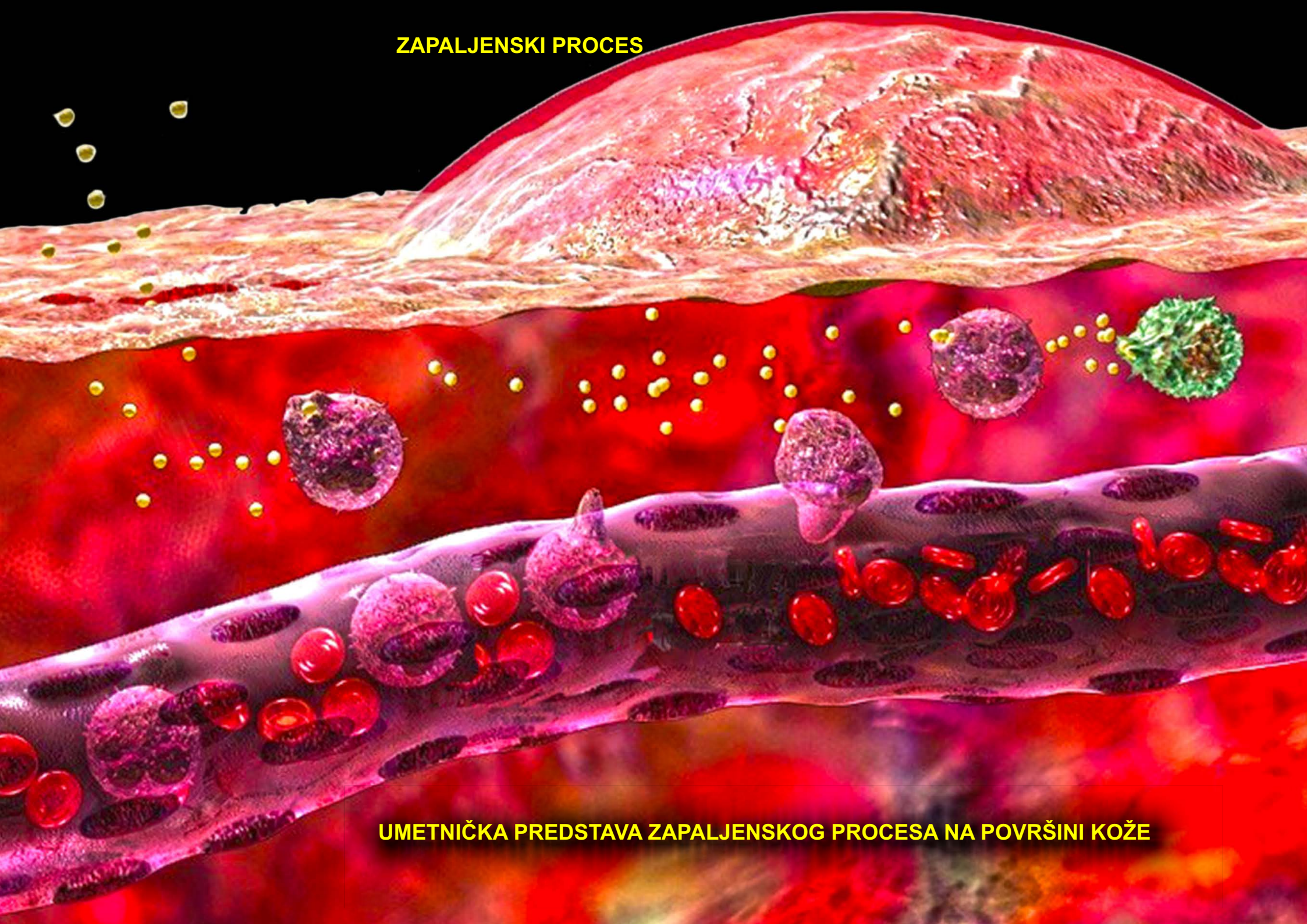
NSAID

NON-STEROID ANTI-INFLAMATORY DRUGS

NE-STEROIDNI LEKOVI PROTIV ZAPALJENSKIH PROCESA


ZAPALJENSKI PROCES
UMETNIČKA PREDSTAVA ZAPALJENSKOG PROCESA NA POVRŠINI KOŽE

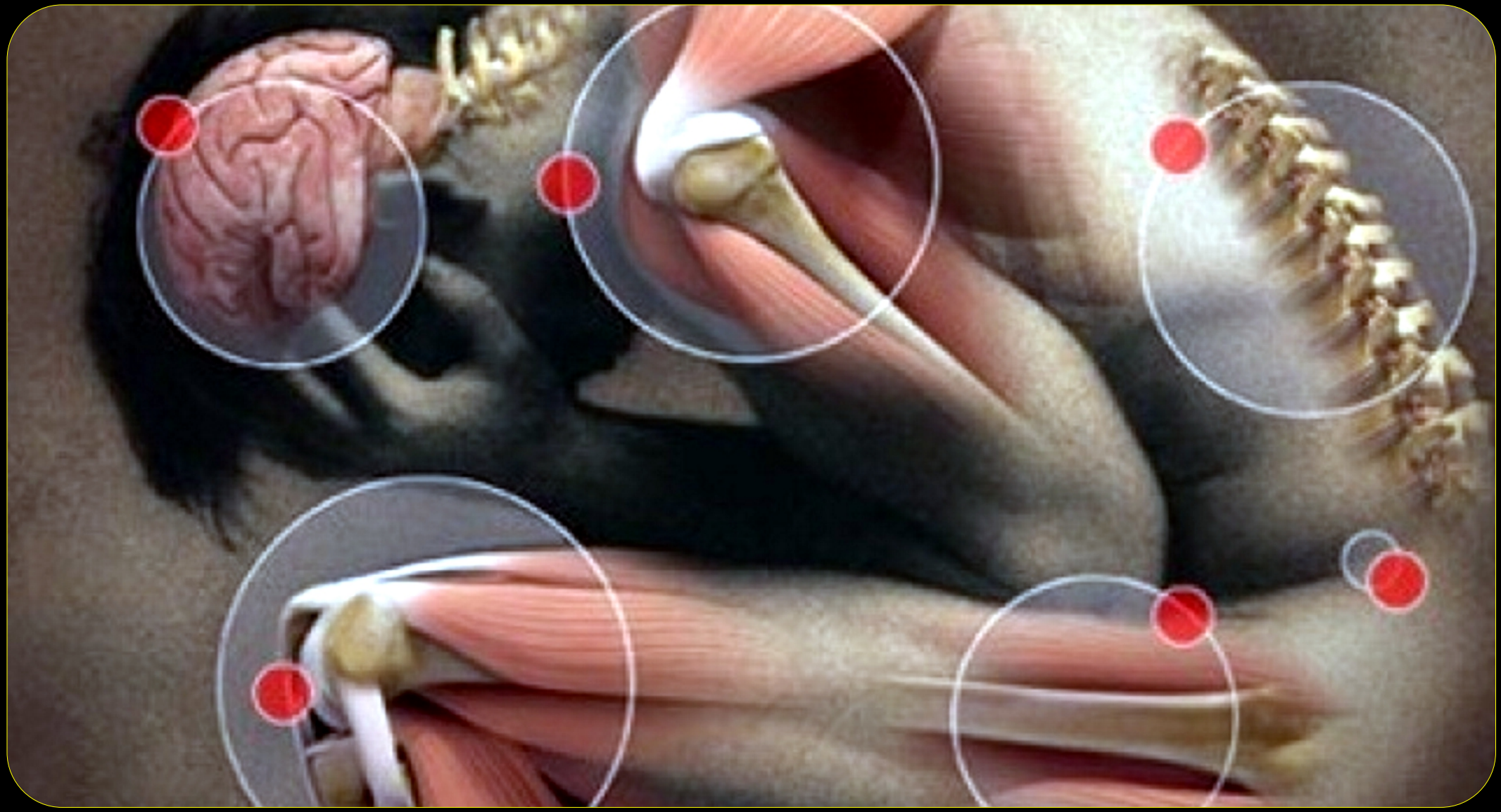
KADA U NEKOM DELU TELA DOĐE DO ZAPALJENSKOG PROCESA, TIPIČNO SE JAVLJAJU SLEDEĆI SIMPTOMI:

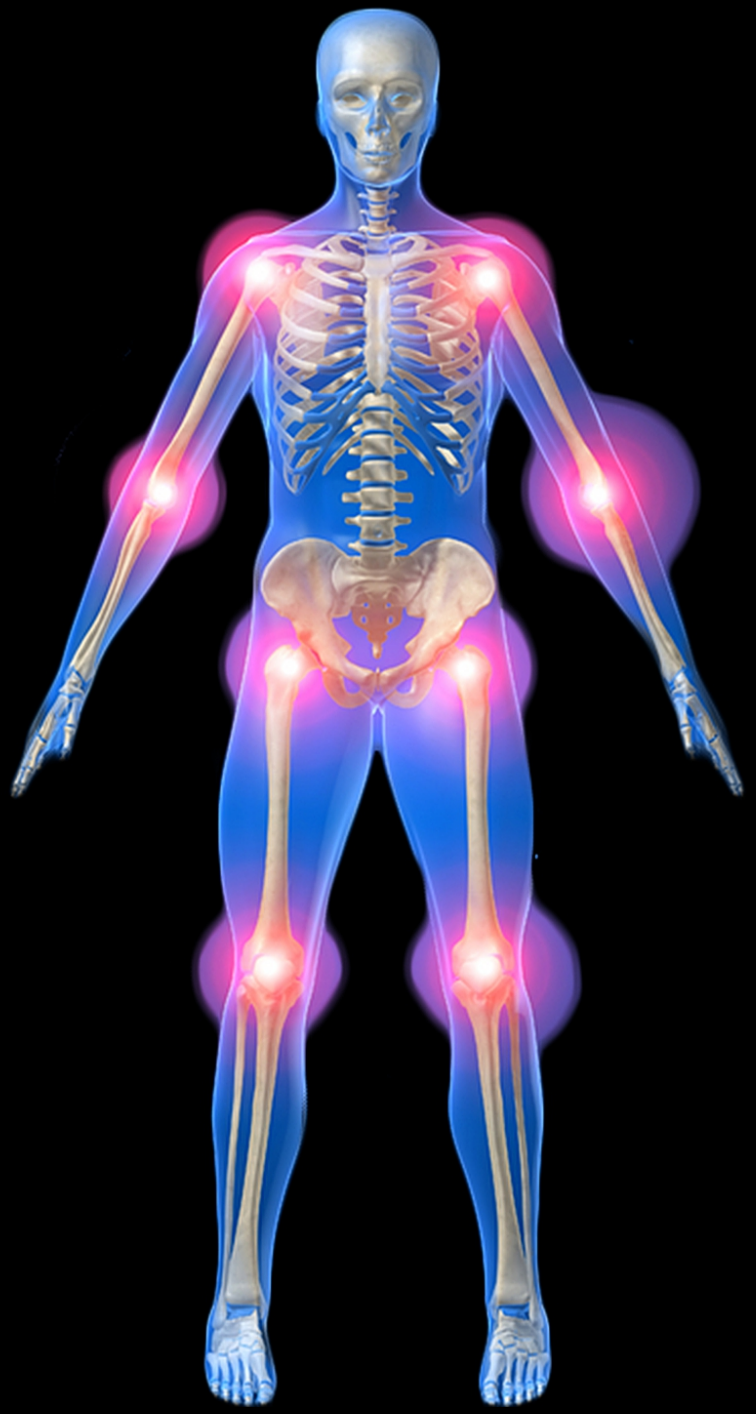
- CRVENILO TKIVA (KOŽE, SLUZOKOŽE I DR.)
- LOKALNO POVIŠENJE TEMPERATURE TKIVA
- OTOK
-BOL

ZAPALJENSKI PROCES UOBIČAJENO PREDSTAVLJA NORMALNU ODBRANU ORGANIZMA OD INFEKCIJE, MEHANIČKE POVREDE, TERMIČKOG ILI HEMIJSKOG OŠTEĆENJA TKIVA I DR.

- U IDEALNOM SLUČAJU, ZAPALJENSKI PROCES VODI REGENERACIJI OŠTEĆENOG TKIVA I OZDRAVLJENJU, PRI ČEMU SIMPTOMI ZAPALJENJA POSTEPENO NESTAJU.
- U MNOGIM SLUČAJEVIMA, ORGANIZAM NE MOŽE SAM DA SE ODBRANI NA OVAJ NAČIN (NPR. OD INFEKCIJE) I TADA SE PRIMENJUJU RAZLIČITI ANTI-BAKTERIJSKI I DRUGI PREPARATI
- TAKOĐE, ZAPALJENSKI PROCES MOŽE BITI ISUVIŠE IZRAŽEN I BOLAN I MORA SE SUZBIJATI ANTI-INFLAMATORNIM LEKOVIMA, DAKLE LEKOVIMA KOJI LOKALNO (NA MESTU ZAPALJENJA) UBLAŽAVAJU OTOK I BOL.
- POSEBNE SITUACIJE SE JAVLJAJU KOD RAZLIČITIH AUTO-IMUNIH OBOLJENJA, KAO ŠTO JE REUMATIZAM, KADA ORGANIZAM, "GREŠKOM" NAPADA SOPSTVENA, ZDRAVA TKIVA. SUZBIJANJE SIMPTOMA OVAKVIH OBOLJENJA (OTOK, BOL) ZAHTEVA PRODUŽENO UZIMANJE ANTI-INFLAMATORNIH LEKOVA, KOJI MOGU IZAZVATI OZBILJNE PA I FATALNE SPOREDNE EFEKTE.

ZAPALJENSKI PROCESI ČESTO SE JAVLJAJU I KOD NEKIH STANJA KAO ŠTO SU UPALE MIŠIĆA, POJEDINE VRSTE GLAVOBOLJA (NE MIGRENE) KAO I NEKIH HRONIČNIH, AUTO-IMUNIH OBOLJENJA, POSEBNO REUMATIZMA.



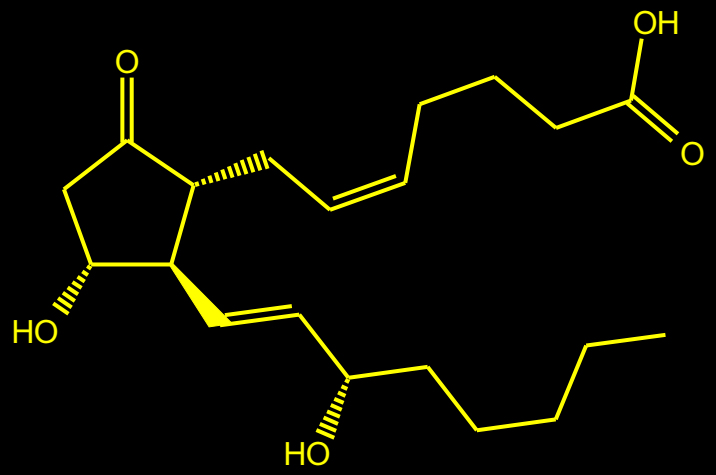


PROSTAGLANDINI - STRUKTURA, BIOSINTEZA I FIZIOLOŠKA ULOGA (KRAJNJE POJEDNOSTAVLJENO)

- POZNAT JE VEĆI BROJ PROSTAGLANDINA KOJI POSTAJU BIOSINTEZOM U ORGANIZMU. IMAJU SLIČNU STRUKTURU (PRIMER: PGE2).

-BIOSINTEZA:

ARAHIDONSKA KISELINA



PRIMER STRUKTURE PROSTAGLANDINA - PGE2

PROSTAGLANDINI - STRUKTURA, BIOSINTEZA I FIZIOLOŠKA ULOGA (KRAJNJE POJEDNOSTAVLJENO), nastavak

- FIZIOLOŠKA ULOGA PROSTAGLANDINA:

IMAJU BROJNE, ESENCIJALNE ULOGE U NORMALNOM FUNCIONISANJU ORGANIZMA, PORED OSTALOG I

-ODRŽAVANJU NORMALNOG STANJA SLUZOKOŽE U DIGESTIVNOM TRAKTU (SPREČAVAJU KRVARENJE)

-UČESTVUJU U NASTAJANJU ZAPALJENSKOG PROCESA, KAO NORMALNOG ODGOVORA ORGANIZMA NA INFEKCIJE I DR.

- ŠIRE KRVNE SUDOVE I SPREČAVAJU NASTAJANJE UGRUŠAKA (TJ. AGLOMERACIJU TROMBOCITA)

-I MNOGE DRUGE.....

MEĐUTIM, HIPER-PRODUKCIJA POJEDINIH PROSTAGLANDINA TOKOM ZAPALJENSKOG PROCESA, DOVODI DO PREVIŠE INTENZIVNOG ZAPALJENJA (BOLA, OTOKA, CRVENILA) I MORA SE SUZBIJATI LEKOVIMA.

NE-STEROIDNI ANTI-INFLAMATORNI LEKOVI

- UBLAŽAVAJU BOLOVE KOD RAZNIH ZAPALJENSKIH PROCESA I SNIŽAVAJU POVIŠENU TELESNU TEMPERATURU

-POSTOJI VELIKI BROJ LEKOVA SA OVAKVIM FARMAKOLOŠKIM DEJSTVOM.

-ZA RAZLIKU OD CENTRALNIH (NARKOTIČKIH, OPIOIDNIH) ANALGETIKA, NE DELUJU NA CNS, NE UTIČU NA STANJE SVESTI, NE IZAZIVAJU RESPIRATORNU DEPRESIJU (”USPAVLJIVANJE CENTRA ZA DISANJE”) NITI STVARAJU BILO KAKVU NAVIKU, TOLERANCIJU I/ILI ZAVISNOST. NJIHOVO DEJSTVO SE OZNAČAVA KAO LOKALNO.

MEHANIZAM DEJSTVA: INHIBIRAJU ENZIME CIKLOOKSIGENAZE (COX-1 I/ILI COX-2), SNIŽAVAJU PRODUKCIJU PROSTAGLANDINA I TIME PRIVREMENO UBLAŽAVAJU SIMPOTOME ZAPALJENJA.

PRIMENA: UBLAŽAVANJE SLABIJEG DO UMERENOG BOLA UGLAVNOM ZAPALJENSKOG POREKLA (ZUBOBOLJE, UPALE MIŠIĆA ILI ZGLOBOVA KAO POSLEDICE REUMATIČNIH OBOLJENJA, POVREDA, INFEKCIJA I DR.)

NE-STEROIDNI ANTI-INFLAMATORNI LEKOVI (nastavak)

-NEKI OD OVIH PREPARATA I SNIŽAVAJU POVIŠENU TELESNU TEMPERATURI KOD AKUTNIH OBOLJENJA KAO ŠTO JE GRIP, TEŽI NAZEBI I DR (IZRAZITO POVIŠENA TEMPERATURA SE MORA SNIŽAVATI JER PREDSTAVLJA AKUTNU OPASNOST PO ORGANIZAM -SLABI I VITALNE FUNKCIJE, MOŽE DOVESTI DO PRIVREMENOG OTKAZIVANJA FUNKCIJA POJEDINIH ORGANA A TAKOĐE I DO NJIHOVOG TRAJNOG OŠTEĆENJA)

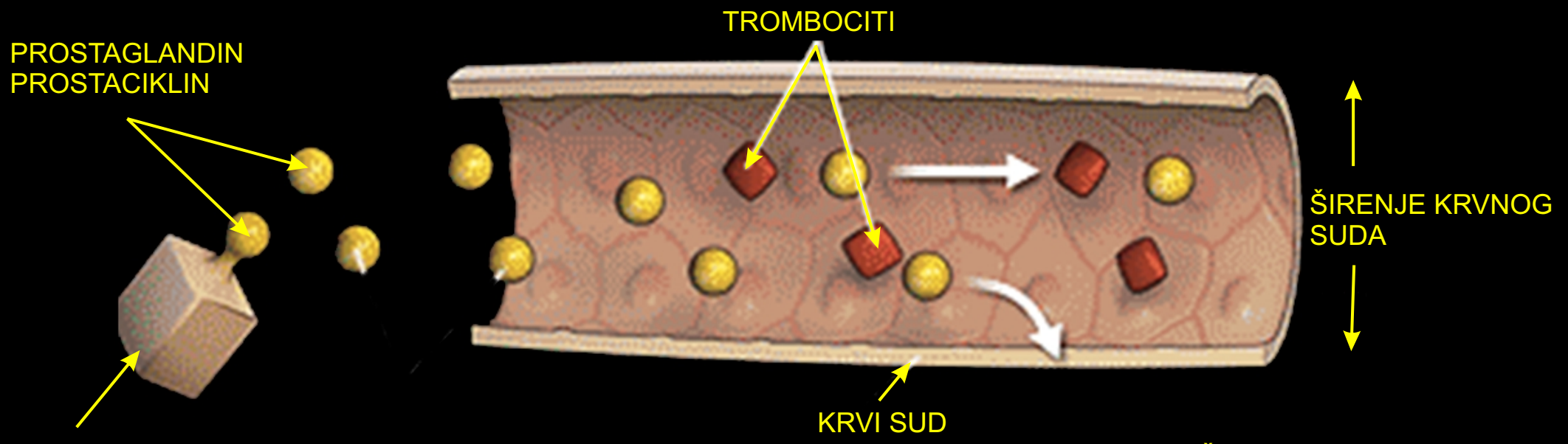
NESELEKTIVNI: INHIBIRAJU OBE CIKLOOKSIGENAZE (COX-1 I COX-2), PRIMER: ASPIRIN

NAŽALOST, ČESTO DOLAZI DO SPOREDNIH EFEKATA, KAO ŠTO SU MUČNINA, STOMAČNI BOLOVI I KRVARENJE IZ SLUZOKOŽE DIGESTIVNOG TRAKTA. OVO JE POSEBNO KARAKTERISTIČNO ZA ASPIRIN I MOŽE BITI OPASNO.

SELEKTIVNI: INHIBIRAJU SAMO CIKLOOKSIGENAZU-2 (COX-2), PRIMER: Celecoxib

DALEKO MANJE NADRAŽAJU DIGESTIVNI TRAKT. MEĐUTIM POŠTO BLOKIRAJU BIOSINTEZU ONIH PROSTAGLANDINA KOJI ŠIRE KRVNE SUDOVE I SPREČAVAJU NASTAJANJE UGRUŠAKA, ZNAČAJNO POVEĆAVAJU RIZIK OD INFARKTA I MOŽDANOG UDARA. POSEBNO SU OPASNI KOD HRONIČNE PRIMENE (REUMATSKI BOLOVI I DR.)

SPOREDNI EFEKTI SELEKTIVNIH COX-2 INHIBITORA:

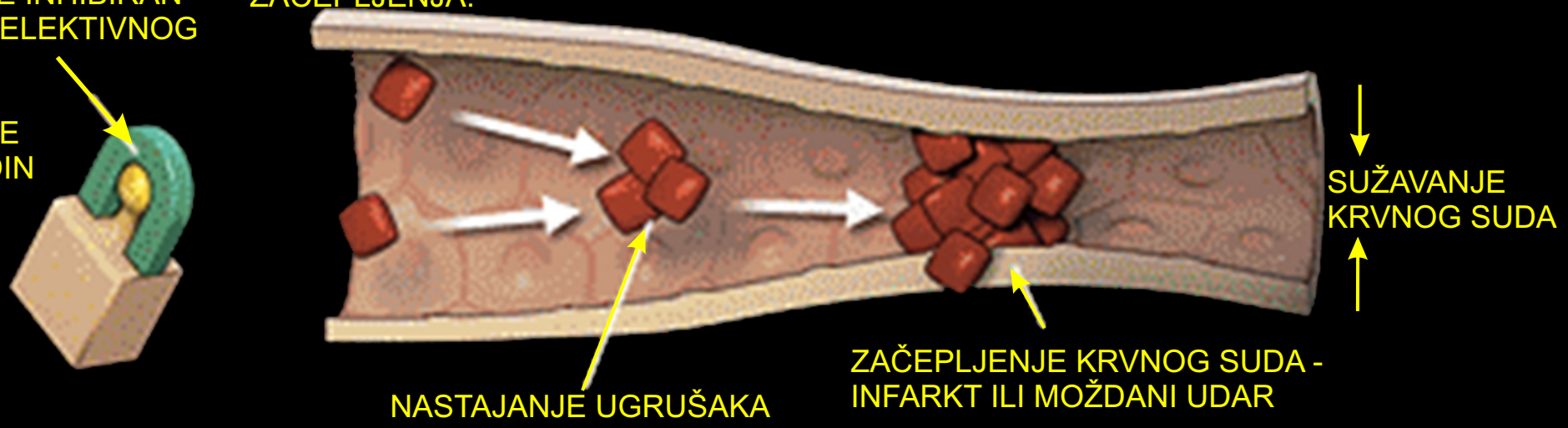


ENZIM COX-2 SINTETIZUJE PROSTAGLANDIN PROSTACIKLIN KOJI ŠIRI KRVNE SUDOVE I OTEŽAVA NASTAJANJE UGRUŠAKA (TJ. AGLOMERACIJU TROMBOCITA)

ENZIM COX-2 JE INHIBIRAN MOLEKULOM SELEKTIVNOG INHIBITORA;

NE SINTETIZUJE PROSTAGLANDIN PROSTACIKLIN

POSLEDICA: KRVNI SUD SE SUŽAVA, UGRUŠAK NASTAJE LAKŠE I DOLAZI DO ZAČEPLJENJA.



ZA ISTRAŽIVANJE BIOLOŠKE ULOGE PROSTAGLANDINA, A POSEBNO ZA OTKRIĆE INHIBITORNOG DEJSTVA LEKOVA KAO ŠTO JE ASPIRIN NA BIOSINTEZU PROSTAGLANDINA, BIOHEMIČARI SUNE K. BERGSTRÖM, BENGT I. SAMUELSSON I JOHN R. VANE ZAJEDNIČKI SU DOBILI NOBELOVU NAGRADU ZA MEDICINU I FIZIOLOGIJU 1982.

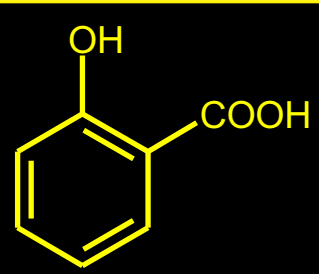
Bengt Ingemar Samuelsson
(21. V. 1934-)

Karl Sune Detlof Bergström
(10 I 1916 – 15 VIII 2004.)

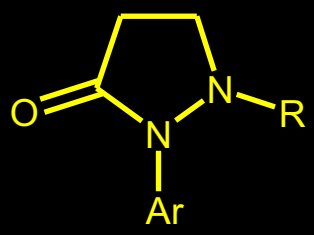
John R. Vane
(29 III 1927 - 19 XI 2004.)

PODELA NE-STEROIDNIH ANTI-INFLAMATORNIH LEKOVA PREMA HEMIJSKOJ STRUKTURI

NSAID

1. 

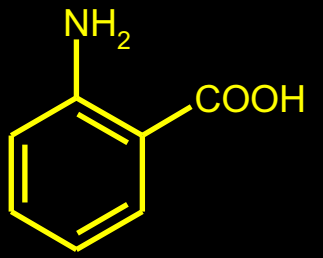
DERIVATI SALICILNE KISELINE

2. 

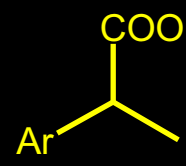
DERIVATI PIRAZOLONA

3. 

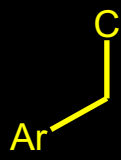
DERIVATI p-AMINO-FENOLA

4. 

DERIVATI ANTRANILNE KISELINE

5. 

DERIVATI 2-ARIL PROPIONSKE KISELINE

6. 

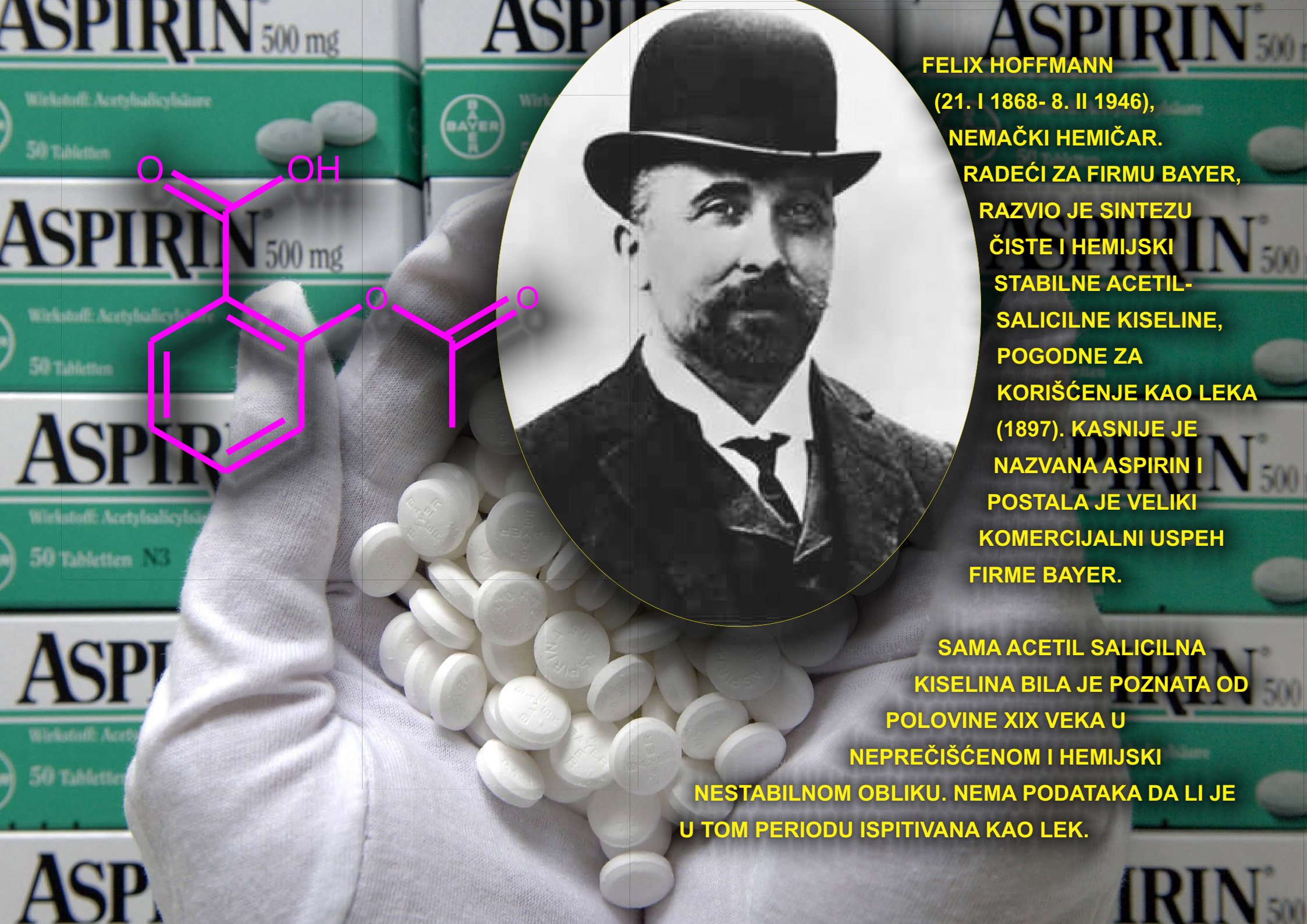
DERIVATI - ARIL SIRĆETNE KISELINE

7. 

DERIVATI OKSIKAMA

SALICILNA KISELINA JE BIOGENOG POREKLA. U ZNATNOJ KONCENTRACIJI SREĆE SE U KORI BELE VRBE, . EKSTRAKT KORE JE OD ANTIČKIH VREMENA KORIŠĆEN ZA SNIŽENJE TELESNE TEMPERATURE I UBLAŽAVANJE BOLOVA IZAZVANIH ZAPALJENJIMA.

Bela vrba (*Salix alba*)

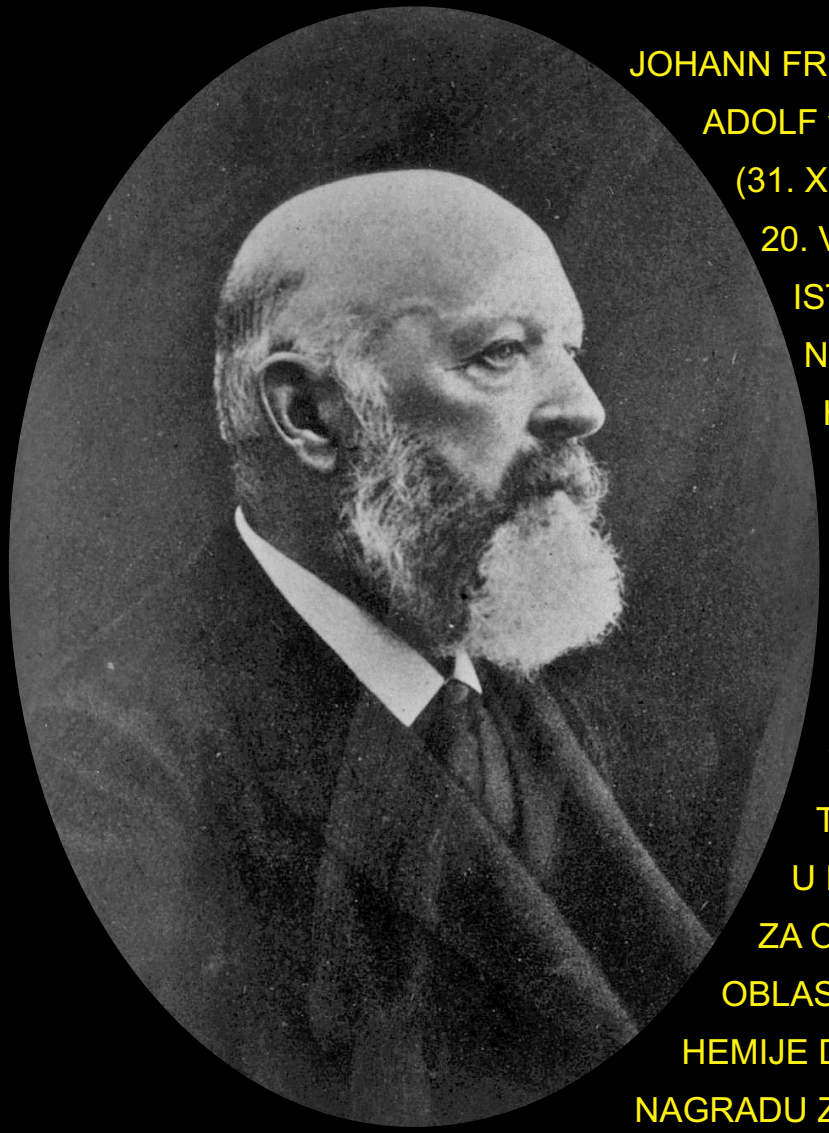


FELIX HOFFMANN (21. I 1868- 8. II 1946), NEMAČKI HEMIČAR. RADEĆI ZA FIRMU BAYER, RAZVIO JE SINTEZU ČISTE I HEMIJSKI STABILNE ACETIL-SALICILNE KISELINE, POGODNE ZA KORIŠĆENJE KAO LEKA (1897). KASNIJE JE NAZVANA ASPIRIN I POSTALA JE VELIKI KOMERCIJALNI USPEH FIRME BAYER.

SAMA ACETIL SALICILNA KISELINA BILA JE POZNATA OD POLOVINE XIX VEKA U NEPREČIŠĆENOM I HEMIJSKI NESTABILNOM OBLIKU. NEMA PODATAKA DA LI JE U TOM PERIODU ISPITIVANA KAO LEK.

FRIEDRICH BAYER (6 VI 1825 - 6. V 1880)
OSINIVAČ FIRME ZA PROIZVODNJU BOJA KOJA
JE KASNIJE PO NJEMU DOBILA IME BAYER.
NIJE BIO HEMIČAR I NIJE IMAO VEZE SA SINTEZOM
ASPIRINA (UMRO JE GOTOVO 20 GODINA RANIJE).

http://www.news.bayer.com/baynews/baynews.nsf/pic/8FEA76BF06514872C1257AD700414EA6?Open&ccm=000&l=EN



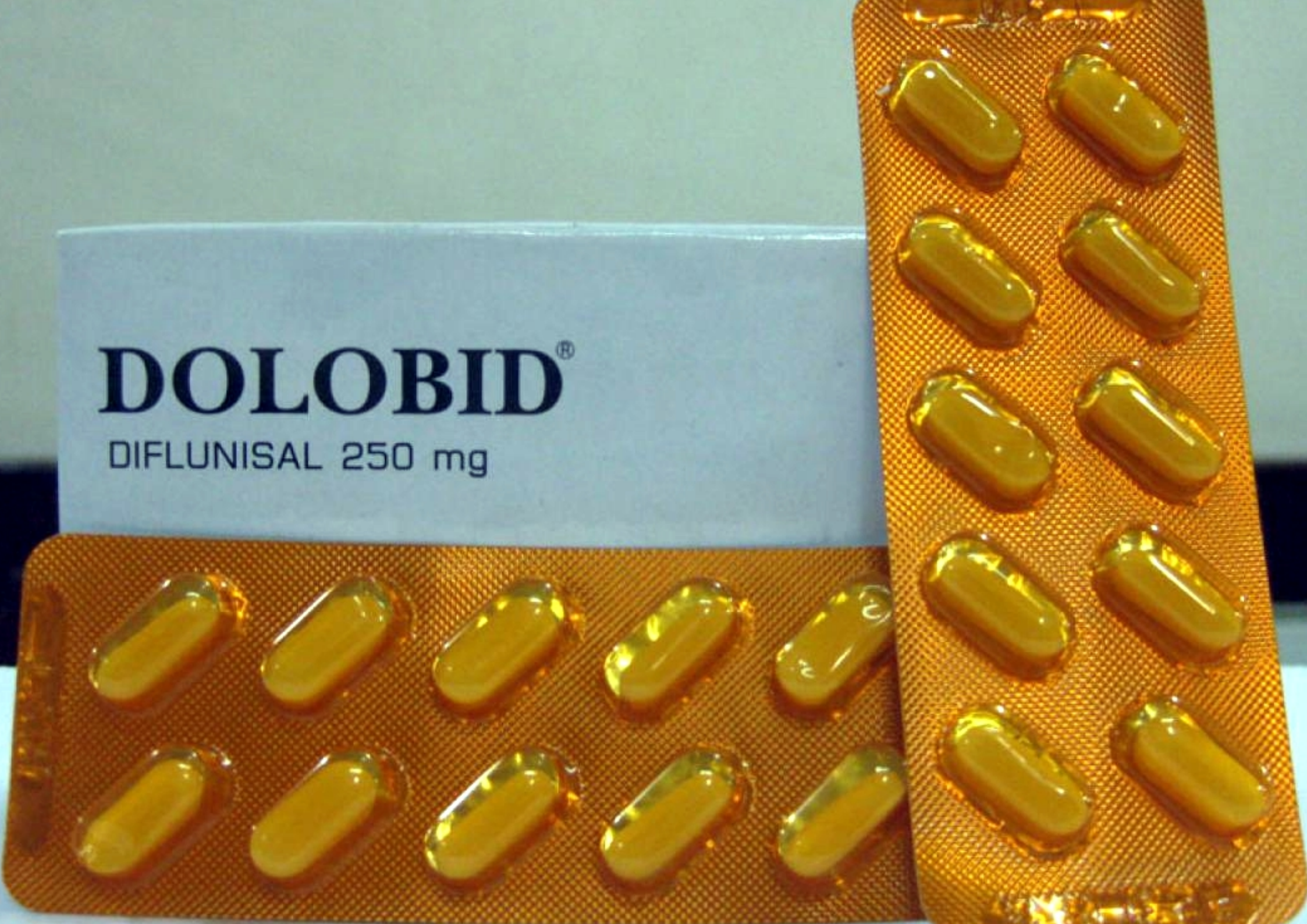
JOHANN FRIEDRICH WILHELM
ADOLF von BAEYER.
(31. X 1835 -
20. VIII 1917.)
ISTAKNUTI
NEMAČKI
HEMIČAR.
BAVIO SE
HEMIJOM
HETEROCIKLIČNIH
I AROMATIČNIH
JEDINJENJA.
TAKOĐE RAZVIO I
TEORIJU NAPONA
U PRSTENOVIMA.
ZA OTKRIĆA U
OBLASTI ORGANSKE
HEMIJE DOBIO NOBELOVU
NAGRADU ZA HEMIJU 1905.

NEMA PODATAKA DA JE IMAO BILO KAKVU
SARADNJU SA FRIEDRICH BAYER-om NITI FIRMOM
BAYER.
TAKOĐE, NIJE IMAO VEZE SA SINTEZOM ASPIRINA.

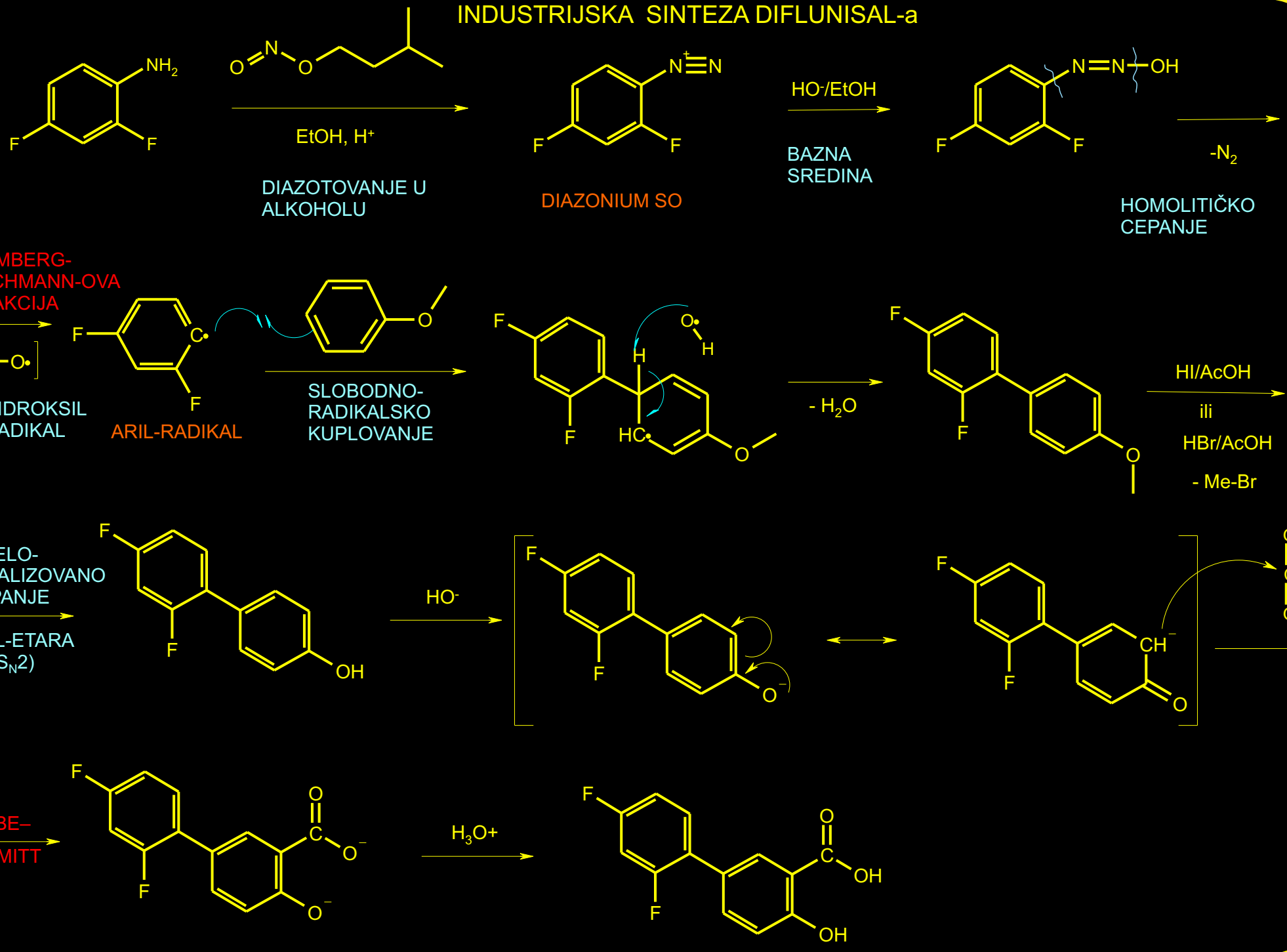
NE-STEROIDNI ANALGETICI - PODELA PREMA HEMIJSKOJ STRUKTURI

1. DERIVATI SALICILNE KISELINE **PRIMERI:** ASPIRIN, DIFLUNISAL

DIFLUSINAL

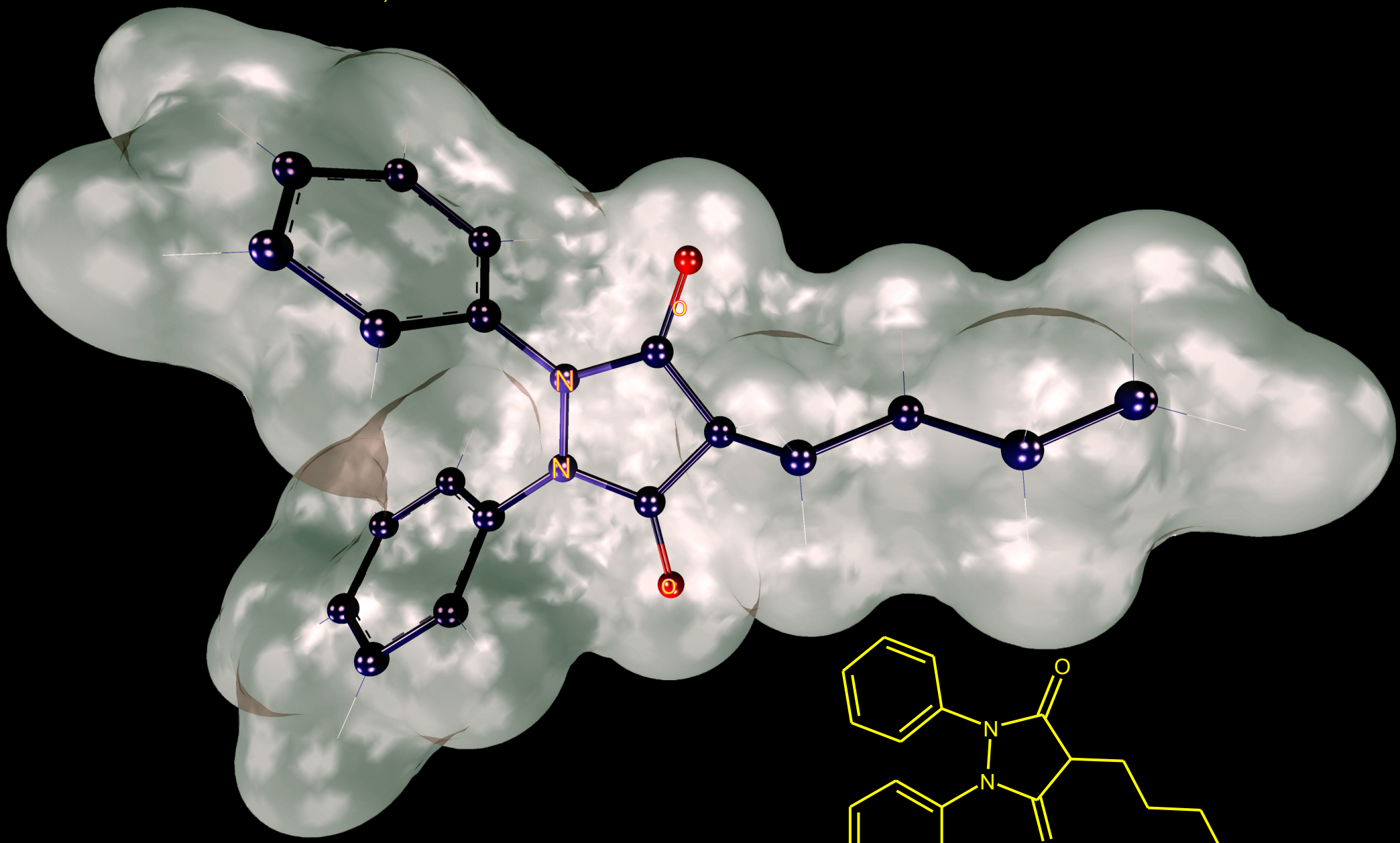

DOLOBID®
DIFLUNISAL 250 mg

INDUSTRIJSKA SINTEZA DIFLUNISAL-a



NE-STEROIDNI ANALGETICI 2. PIRAZOLONI (PYRAZOLONE)

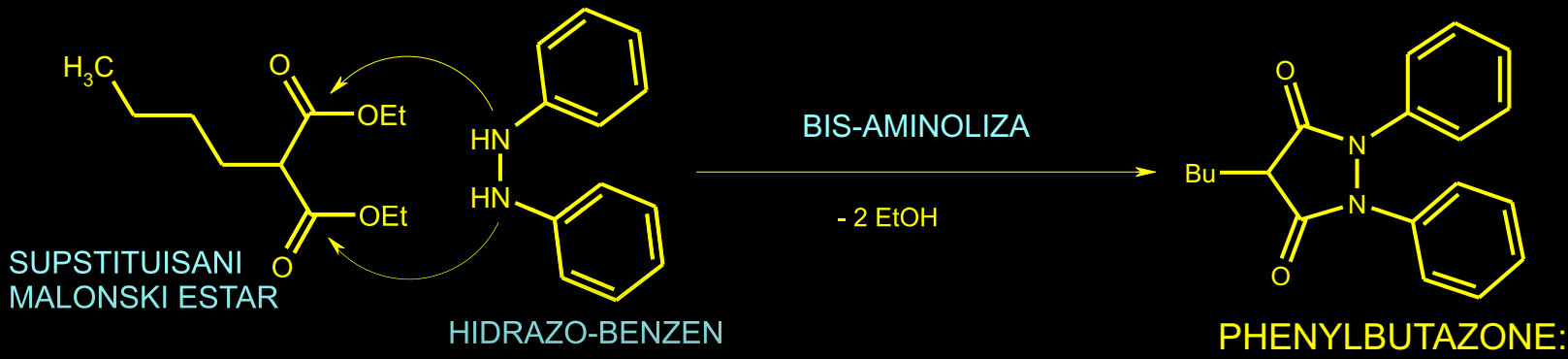
PRIMERI: PHENYLBUTAZONE, METAMIZOL



NE-STEROIDNI ANALGETICI 2. PIRAZOLONI (PYRAZOLONE)

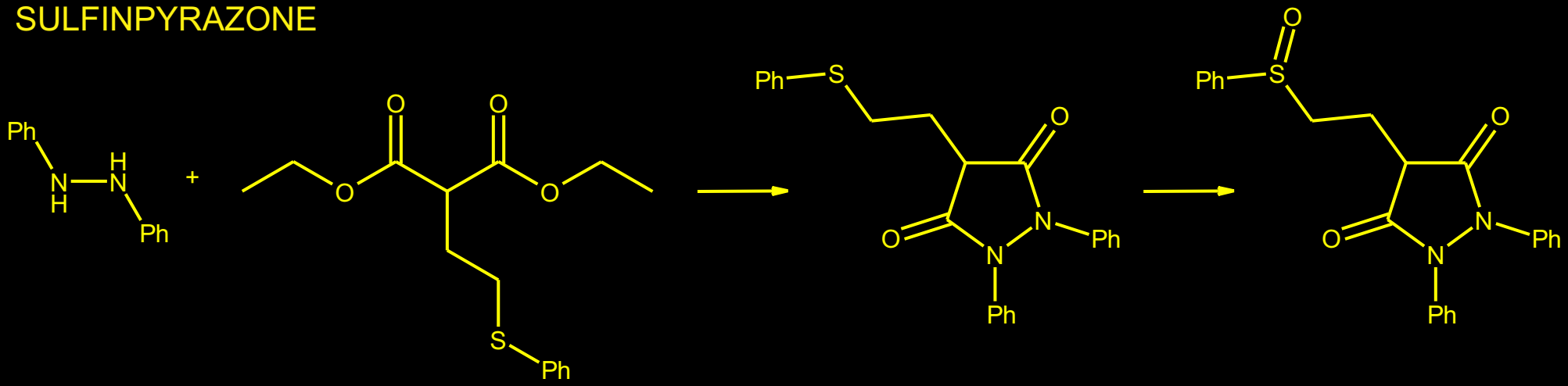
INDIKACIJE - PRETEŽNO U VETERINI (REUMATSKA OBOLJENJA ITD.)

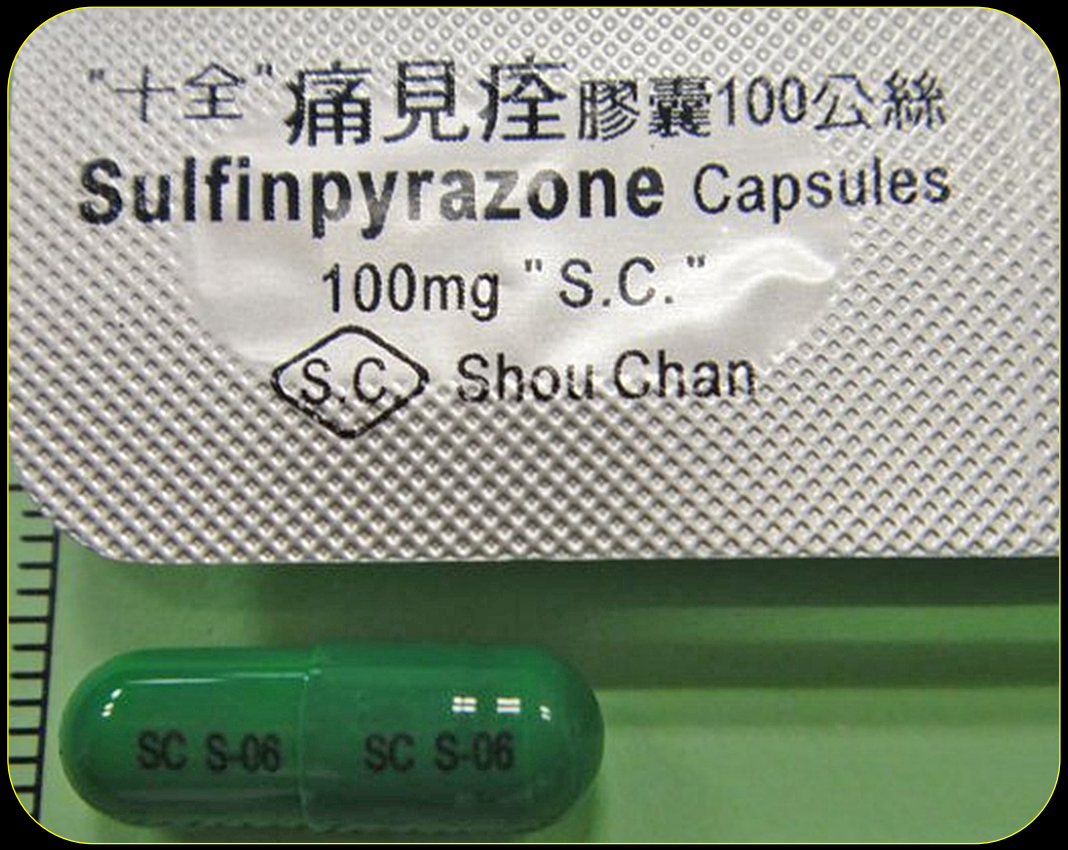
PHENYLBUTAZONE:



2. PIRAZOLONI (PYRAZOLONE) -nastavak

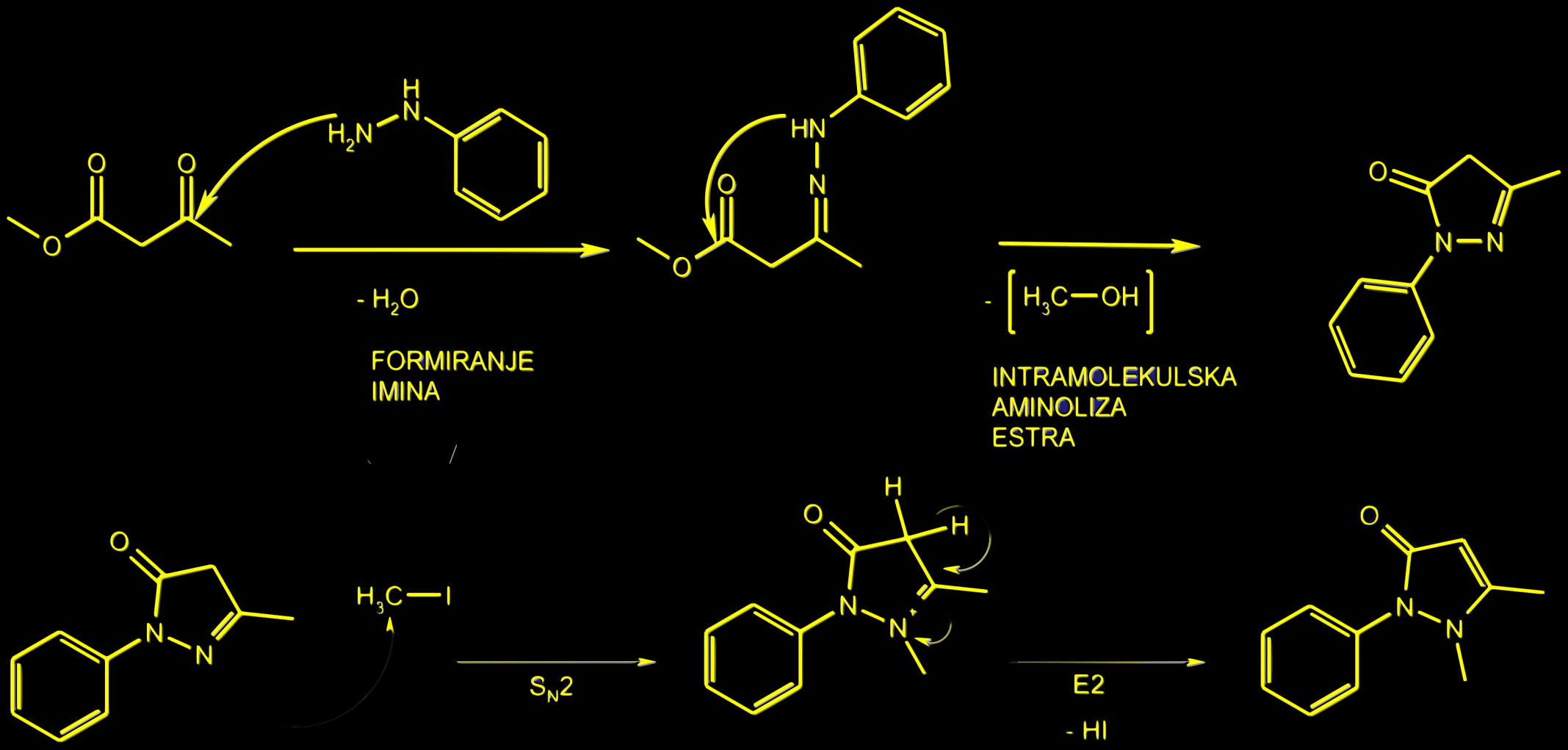
SULFINPYRAZONE



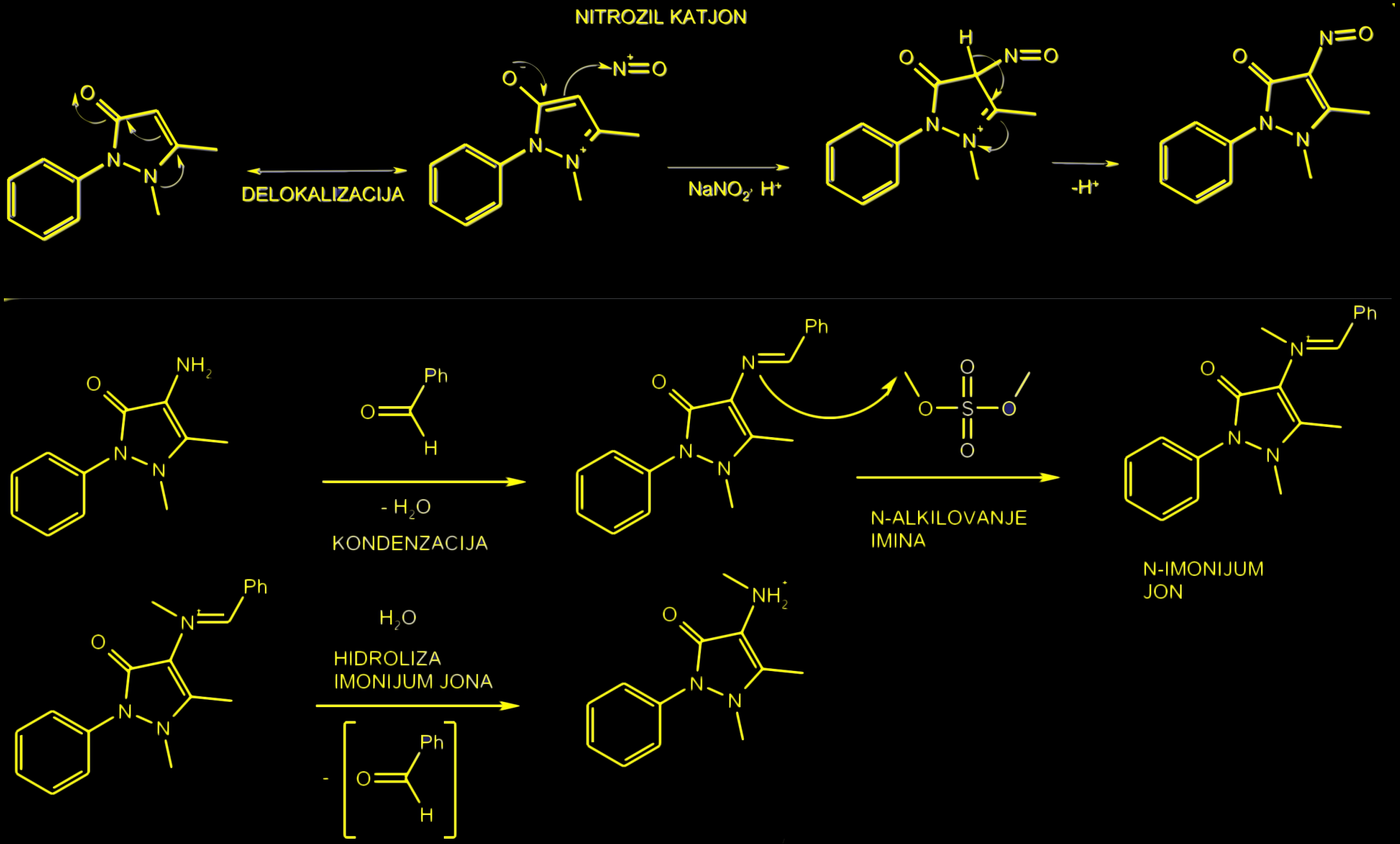


2. PIRAZOLONI (PYRAZOLONE) -nastavak SINTEZA ANALGINA (Metamizole)

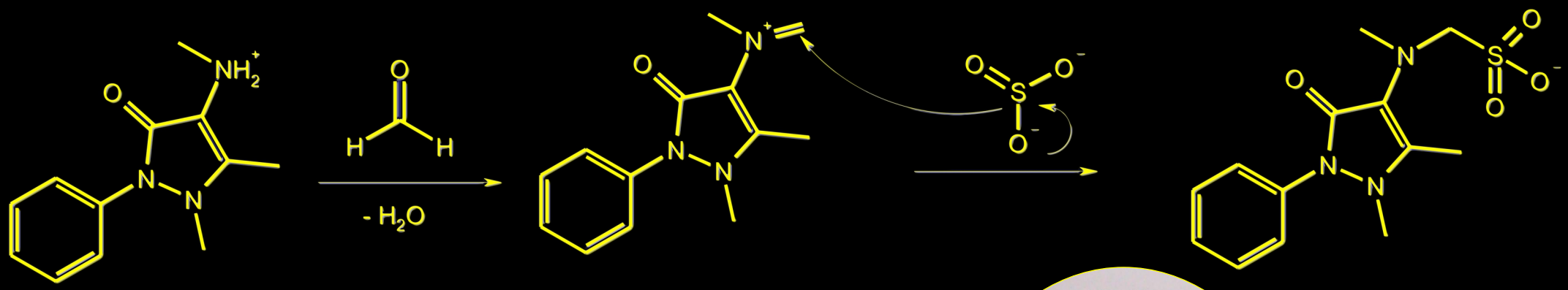
BIO JE ŠIROKO KORIŠĆEN ZA UBLAŽAVANJE ZAPELJENSKIH BOLOVA I SNIŽENJE POVIŠENE TEMPERATURE. OD SEDAMDESETIH GODINA XX VEKA MANJE SE KORISTI JER, U VRLO RETKIM SLUČAJEVIMA MOŽE IZAZVATI FATALNI POREMEĆAJ KRVI (AGRANULOCITOZU).

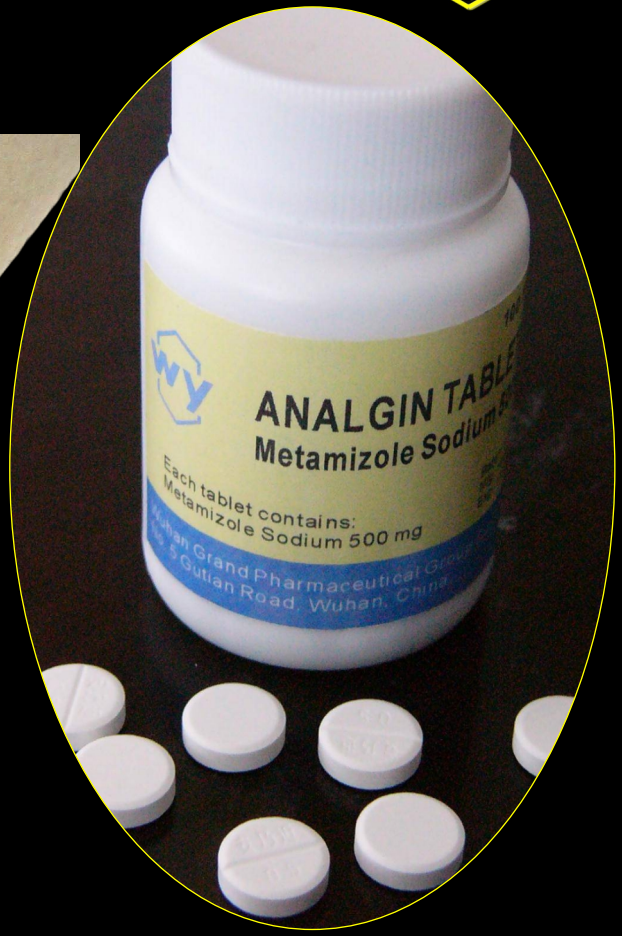


2. PIRAZOLONI (PYRAZOLONE) SINTEZA ANALGINA -nastavak

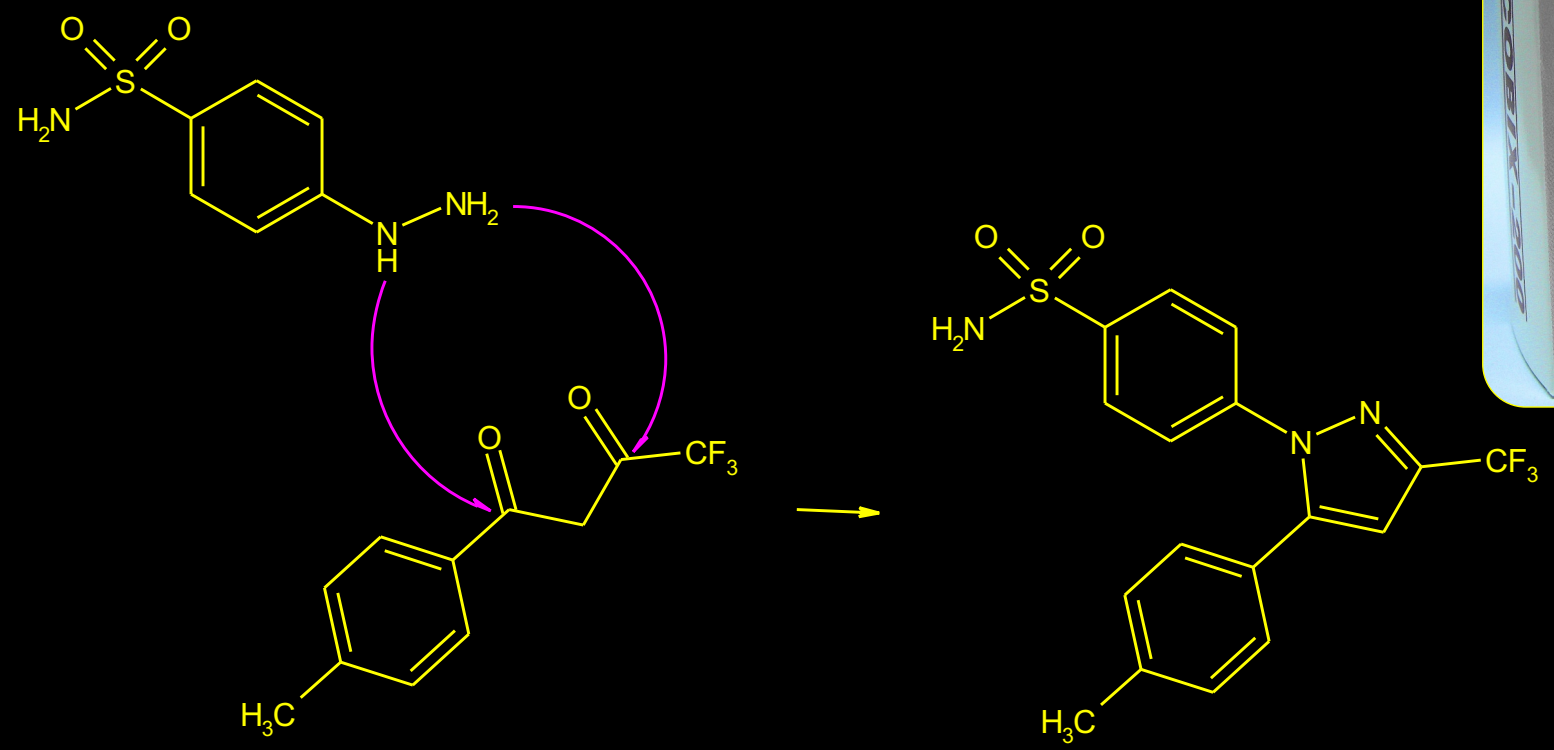


2. PIRAZOLONI (PYRAZOLONE) SINTEZA ANALGINA -nastavak



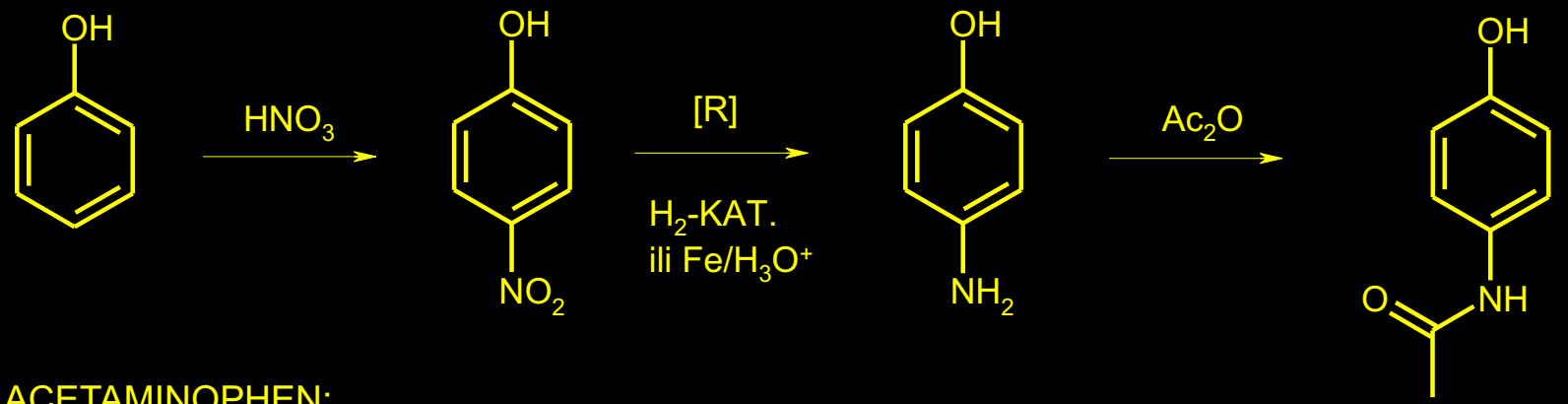


2. PIRAZOLONI (PYRAZOLONE) SINTEZA ANALGINA -nastavak



Monograph Number: 1968
Title: Celecoxib
CAS Registry Number: 169590-42-5
CAS Name: 4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
Manufacturers' Codes: SC-58635; YM-177
Trademarks: Celebrex (Searle)
Molecular Formula: C17H14F3N3O2S
Molecular Weight: 381.38.
Percent Composition: C 53.54%, H 3.70%, F 14.94%, N 11.02%, O 8.39%, S 8.41%
Literature References: Selective cyclooxygenase-2 (COX-2) inhibitor. Prepn: J. J. Talley et al., WO 95 15316; eidem, US 5466823 (both 1995 to Searle); T. D. Penning et al., J. Med. Chem. 40, 1347 (1997). Clinical pharmacology: P. E. Lipsky, P. C. Isakson, J. Rheumatol. 24, Suppl. 49, 9 (1997). Clinical trials in arthritis: L. S. Simon et al., Arthritis Rheum. 41, 1591 (1998). Evaluation of risk of gastrointestinal toxicity in patients with arthritis: F. E. Silverstein et al., J. Am. Med. Assoc. 284, 1247 (2000).
Properties: Pale yellow solid, mp 157-159°.
Melting point: mp 157-159°
Therap-Cat: Anti-inflammatory.

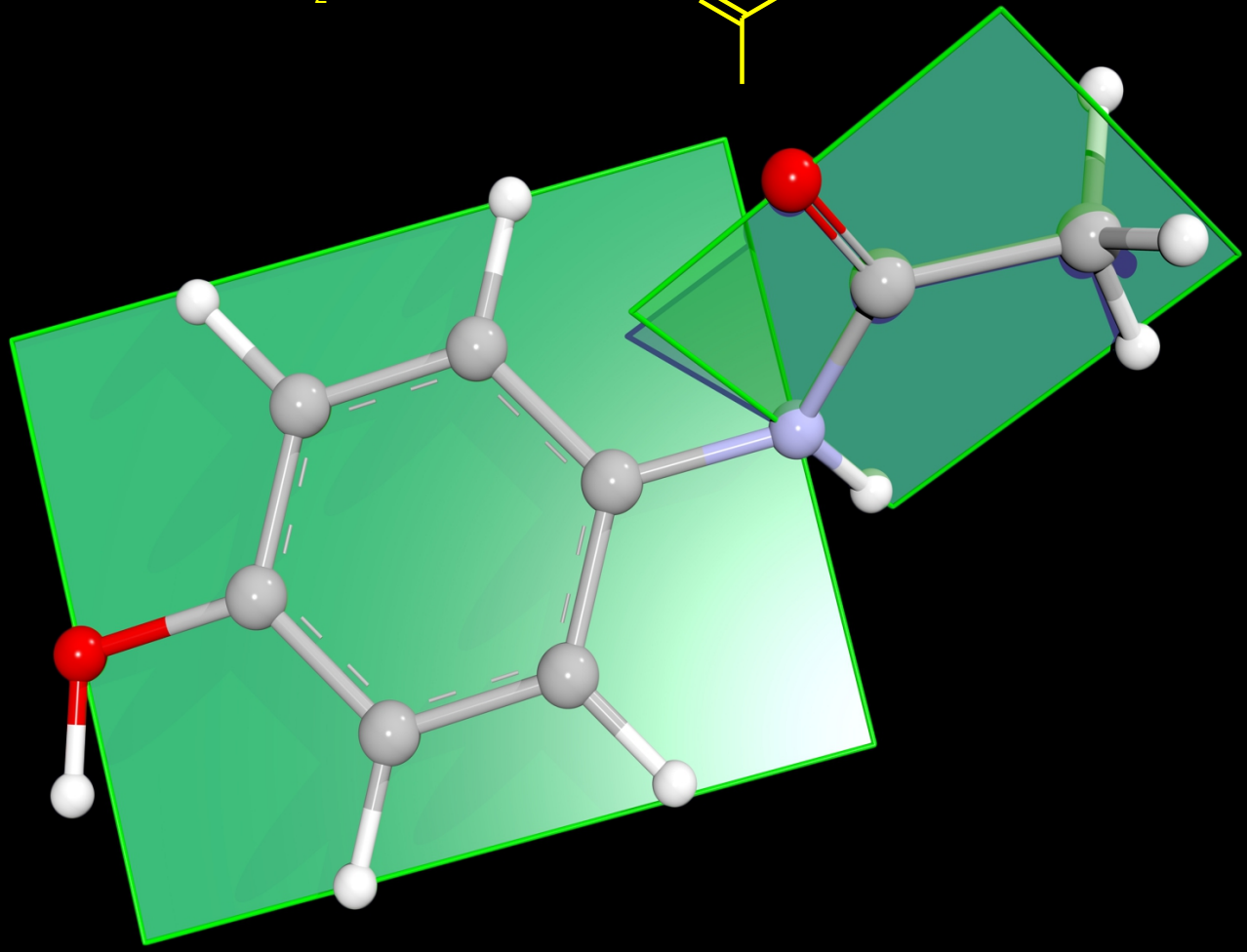
NE-STEROIDNI ANALGETICI 3. DERIVATI p-AMINO-FENOLA



ACETAMINOPHEN: ,

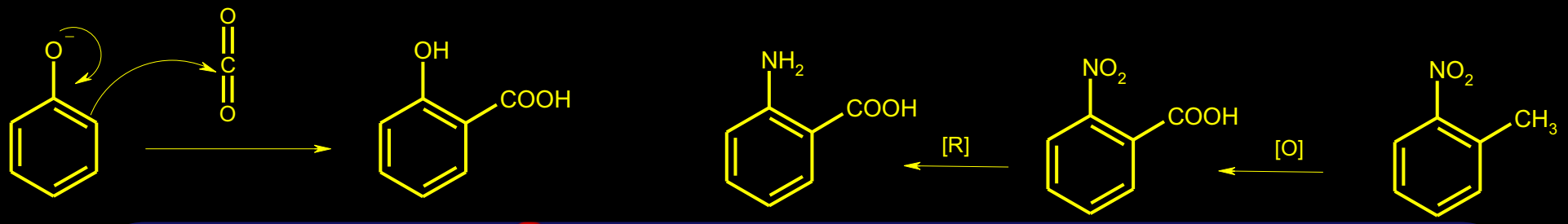
p-ACETAMINOPHENOL

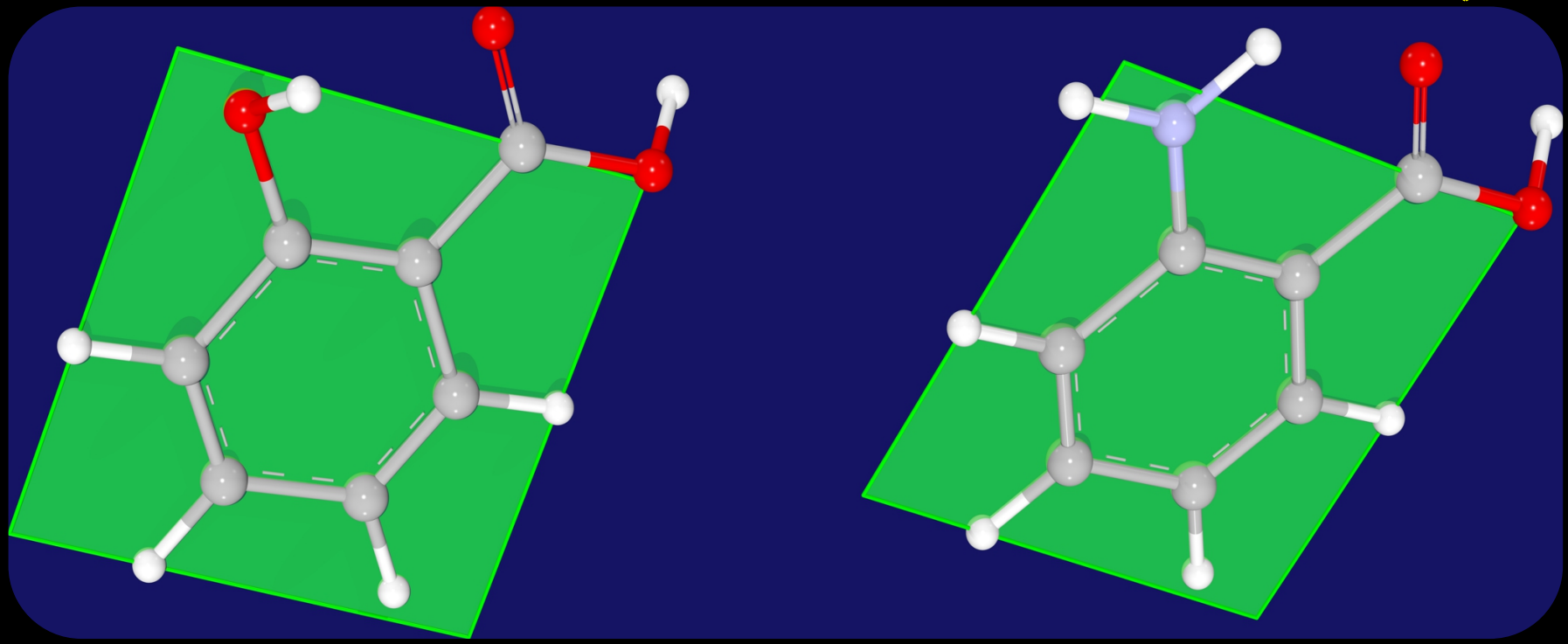
(PARACETAMOL, TYLENOL)



NE-STEROIDNI ANALGETICI - 4. DERIVATI ANTRANILNE KISELINE (Anthranylic acid)

ANTRANILNA KISELINA STRUKTURNO JE ANALOGNA SALICILNOJ KISELINI.



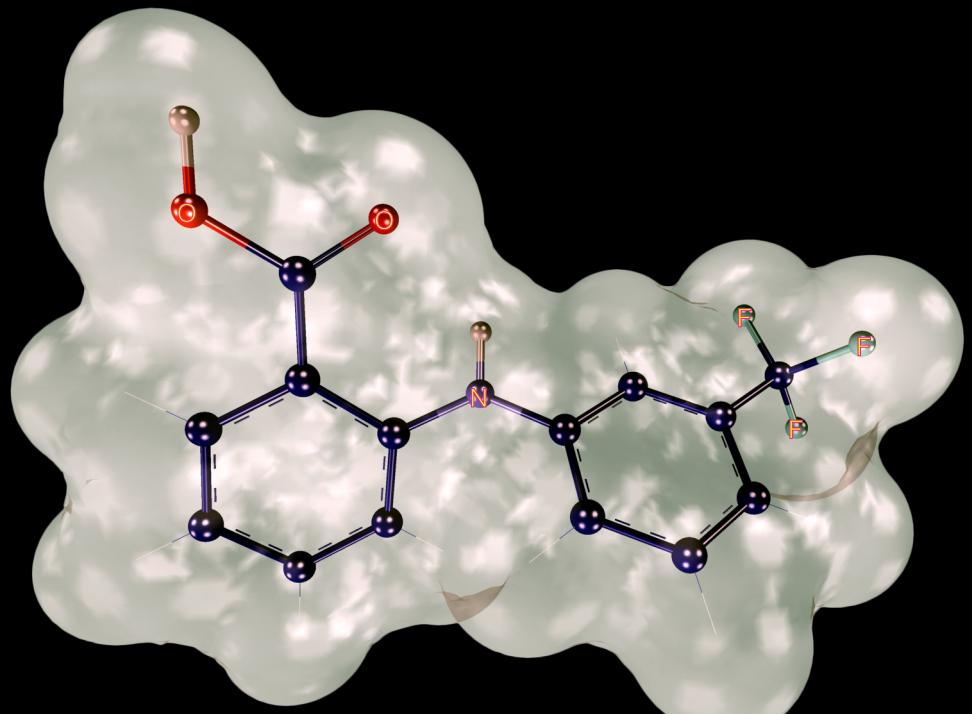


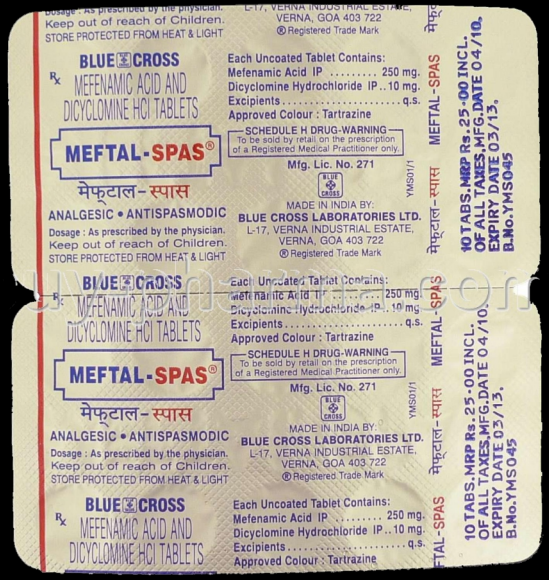
- FARMAKOLLOŠKE OSOBINE - ANALGETICI, ANTI-INFLAMATORNI LEKOVI,
  TAKOĐE SNIŽAVAJU POVIŠENU TELESNU TEMPERATURU KOD GROZNICE

ZNAČAJNIJI PREDSTAVNICI: FLUFENAMIC ACID, MEFENAMIC ACID, MECLOFENAMIC ACID, NIFLUMIC ACID
INDIKACIJE - GLAVOBOLJE, REUMATSKA OBOLJENJA ITD.

NE-STEROIDNI ANALGETICI 4. DERIVATI ANTRANILNE (ANTHRANYLIC) KISELINE

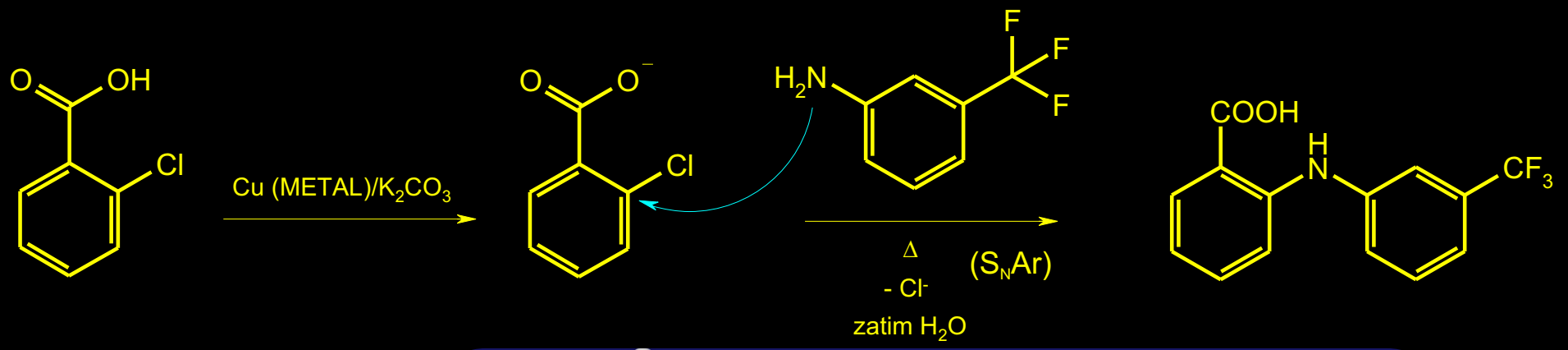
PRIMERI: FLUFENAMIC ACID, MEPHENAMIC ACID, MECLOPHENAMIC ACID



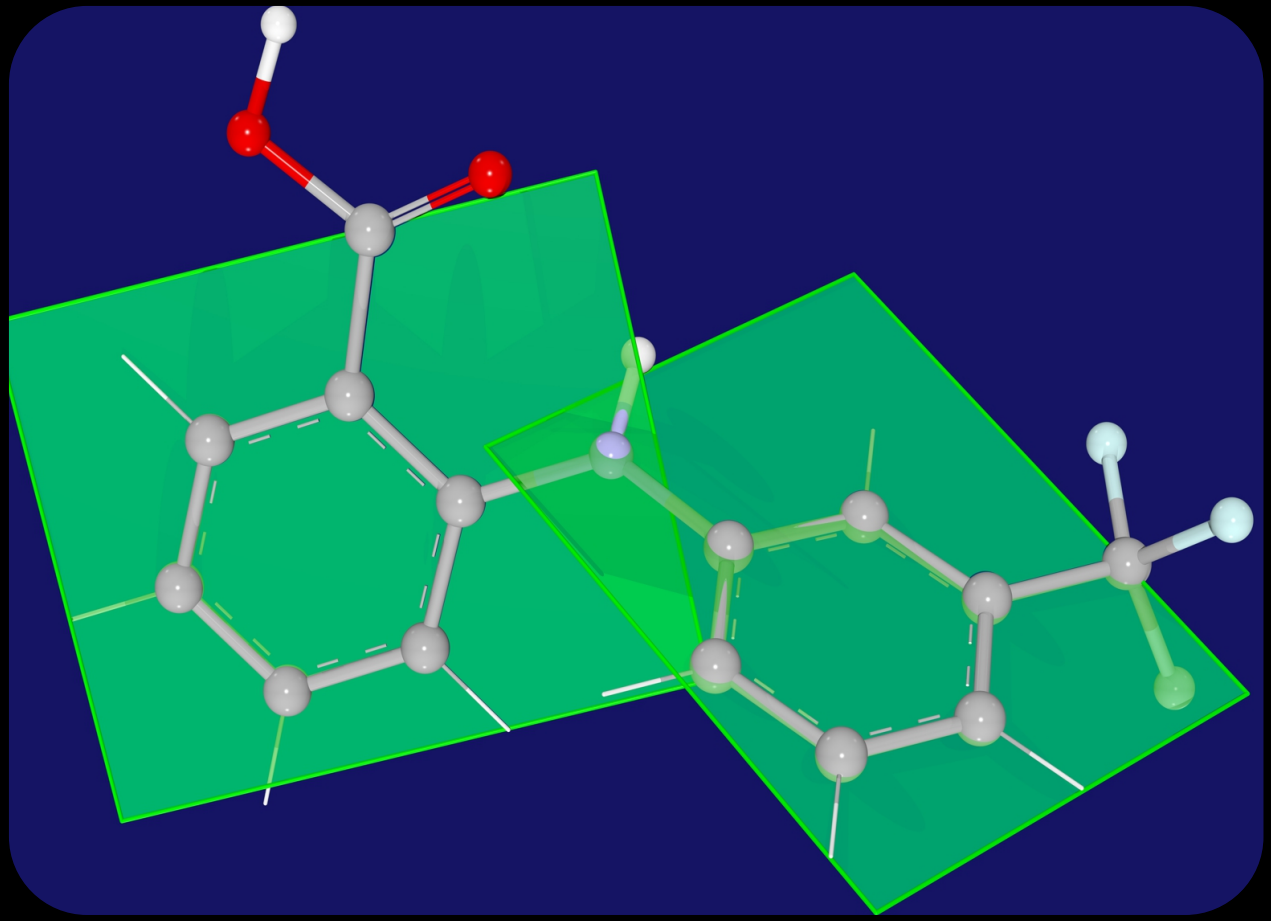


NE-STEROIDNI ANALGETICI 4. DERIVATI ANTRANILNE KISELINE - NASTAVAK

FLUFENAMINSKA KISELINA (Flufenamic acid):

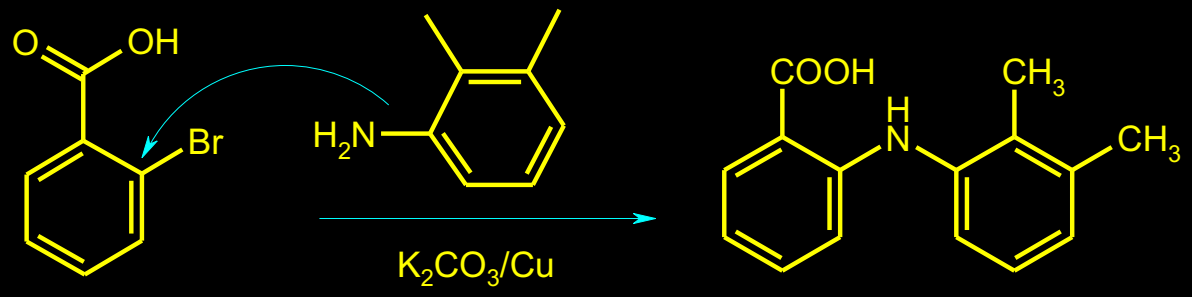


SINTEZA SUPSTITUISANIH DIFENIL AMINA (ANALOGNO SINTEZI AROMATIČNIH ETARA PO ULLMANN-u)

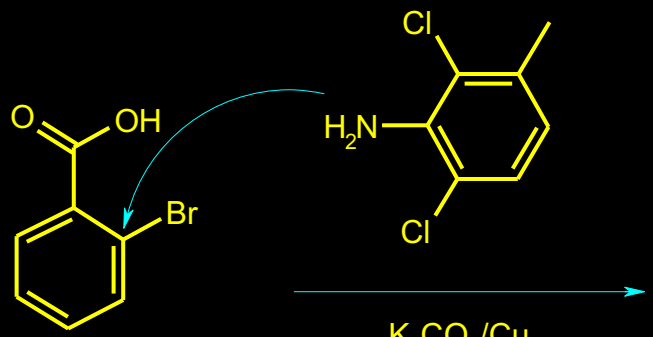


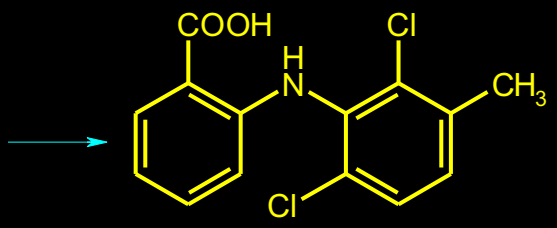
NE-STEROIDNI ANALGETICI 4. DERIVATI ANTRANILNE KISELINE - NASTAVAK

MEFENAMINSKA KIS. (Mefenamic acid):

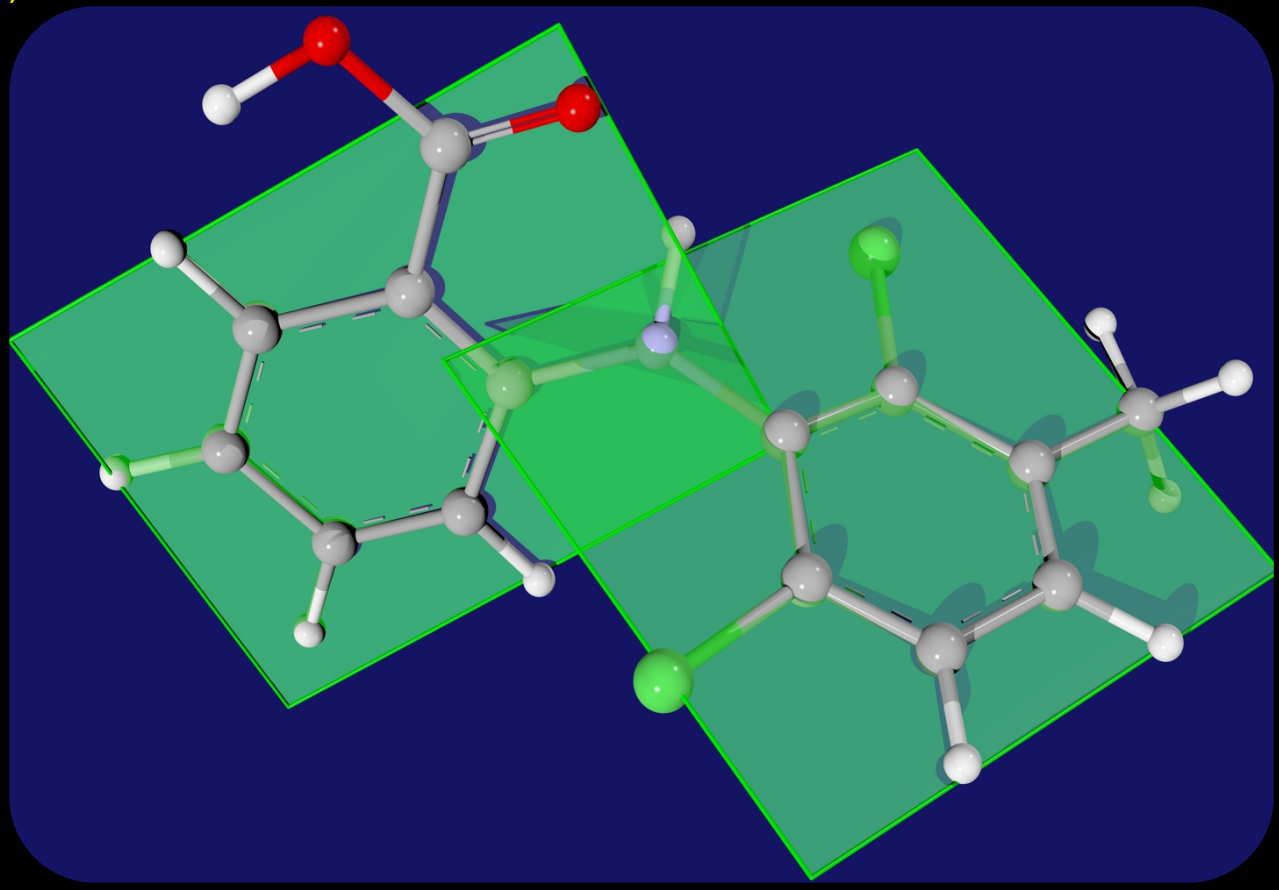


MEKLOFENAMINSKA KIS.(Meclofenamic acid) :



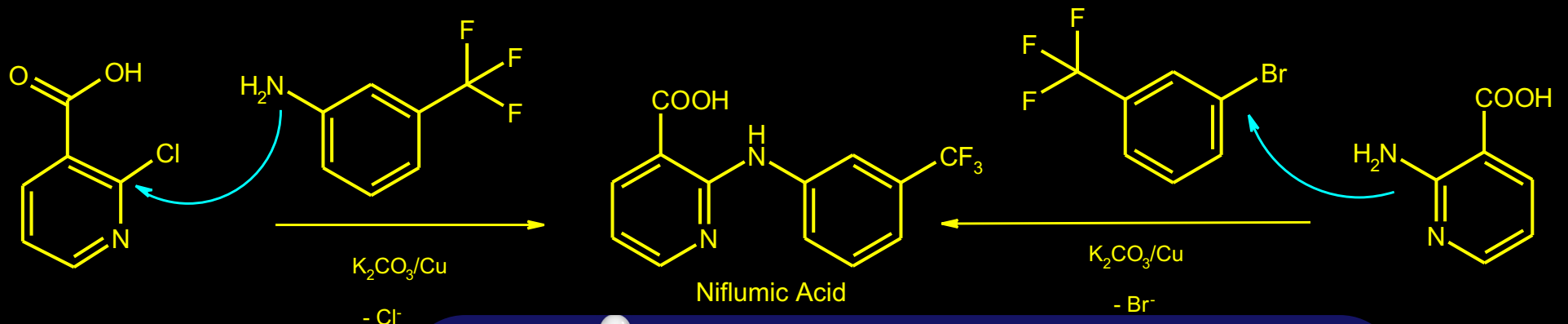


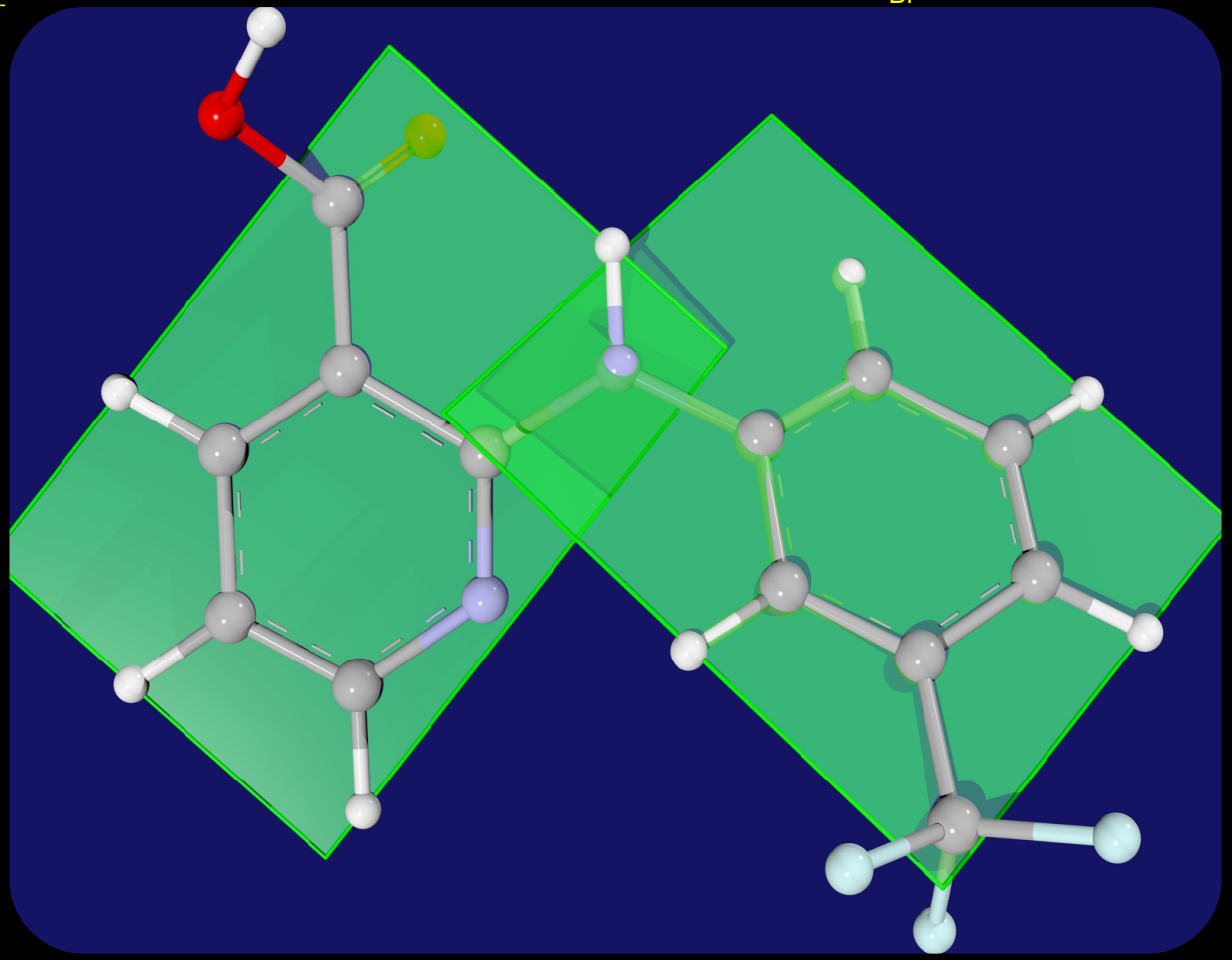
Meclofenamic Acid



NE-STEROIDNI ANALGETICI **4.** DERIVATI ANTRANILNE KISELINE - NASTAVAK

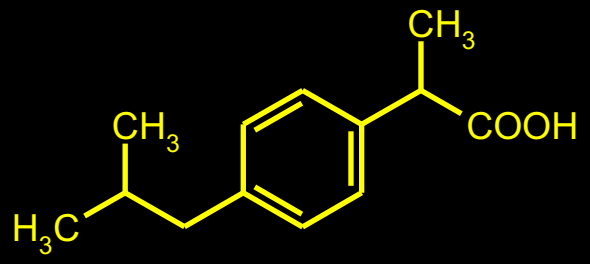
NIFLUMINSKA KISELINA (Niflumic acid):

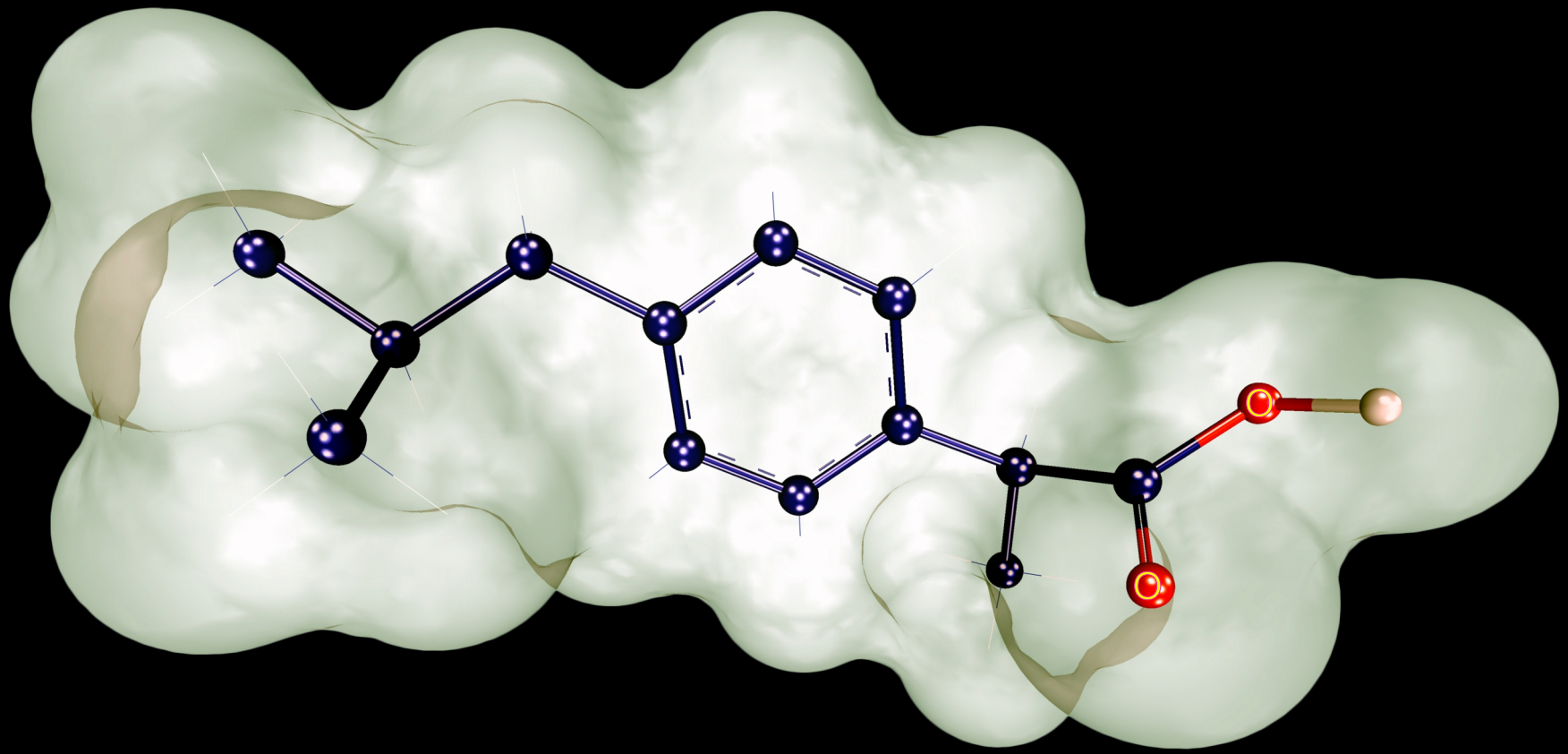




NE-STEROIDNI ANALGETICI 5. **DERIVATI** DERIVATI 2-ARIL-PROPIONSKE KISELINE

PRIMERI: IBUPROFEN, KETOPROFEN, NAPROXENE, FENPROFEN



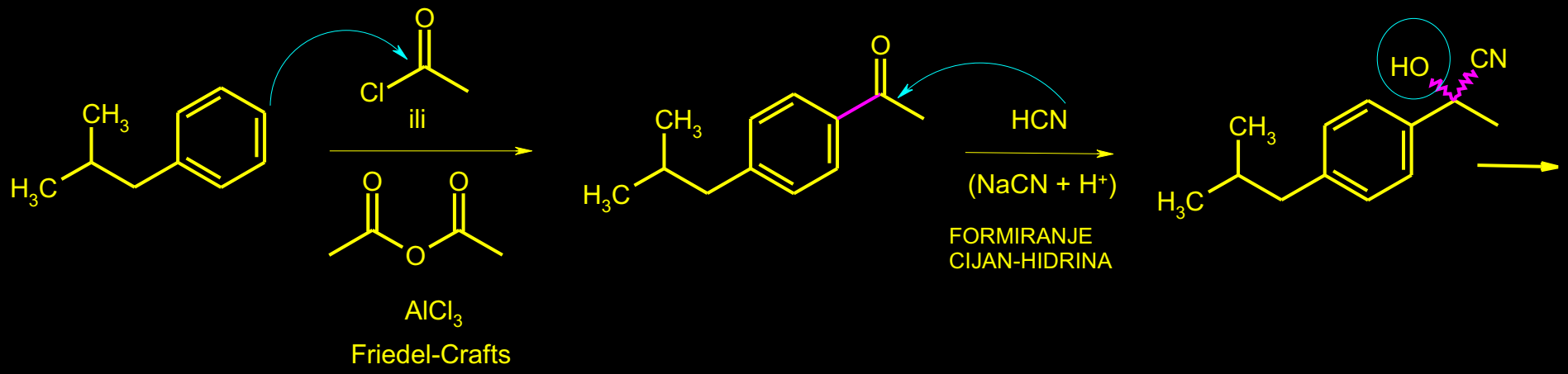


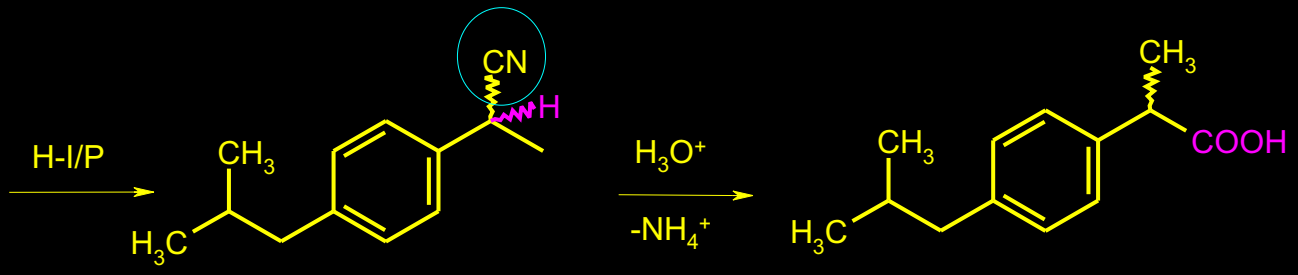
NE-STEROIDNI ANALGETICI 5. DERIVATI 2-ARIL-PROPIONSKE KISELINE

- FARMAKOLLOŠKE OSOBINE - ANALGETICI, ANTI-INFLAMATORNI LEKOVI, TAKOĐE SNIŽAVAJU POVIŠENU TELESNU TEMPERATURU KOD GROZNICE

ZNAČAJNIJI PREDSTAVNICI: IBUPROFEN, NAPROXENE, KETOPROFEN, FENPROFEN INDIKACIJE - GLAVOBOLJE, REUMATSKA OBOLJENJA ITD.

IBUPROFEN (BRUFEN):



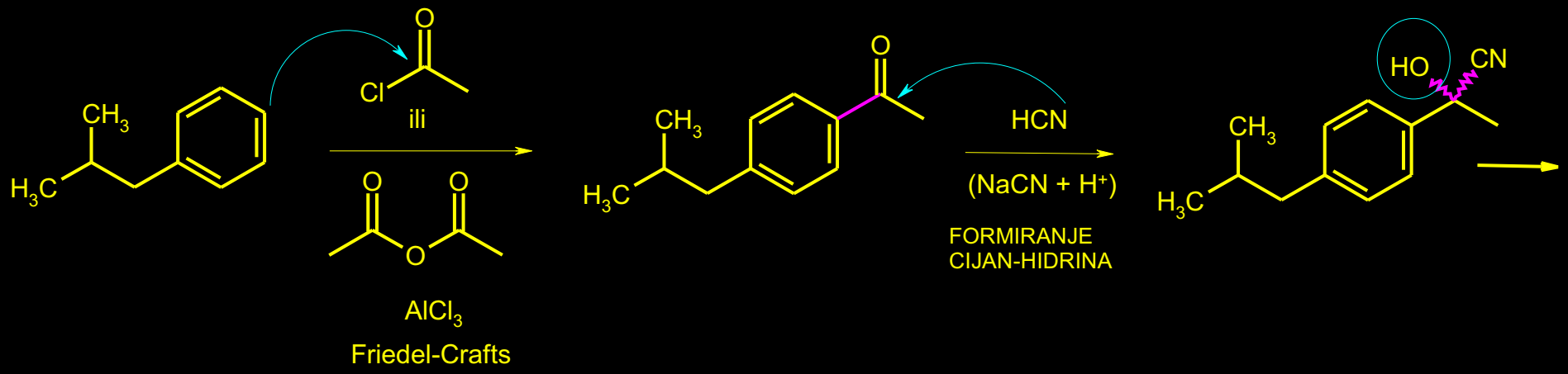


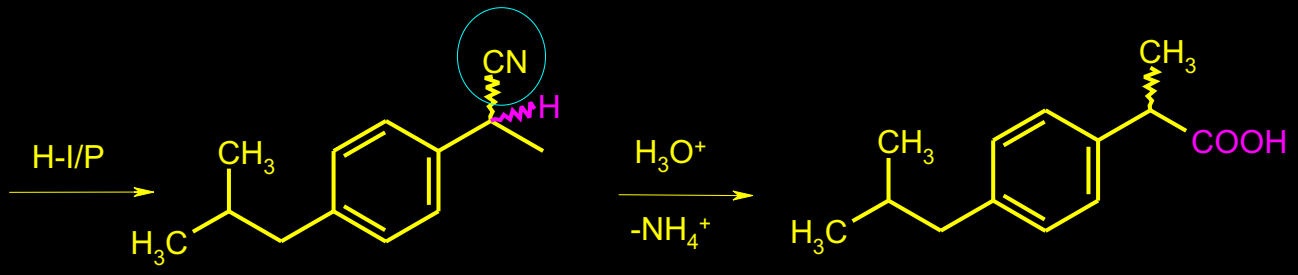
NE-STEROIDNI ANALGETICI 5. DERIVATI 2-ARIL-PROPIONSKE KISELINE

- FARMAKOLLOŠKE OSOBINE - ANALGETICI, ANTI-INFLAMATORNI LEKOVI, TAKOĐE SNIŽAVAJU POVIŠENU TELESNU TEMPERATURU KOD GROZNICE

ZNAČAJNIJI PREDSTAVNICI: IBUPROFEN, NAPROXENE, KETOPROFEN, FENPROFEN INDIKACIJE - GLAVOBOLJE, REUMATSKA OBOLJENJA ITD.

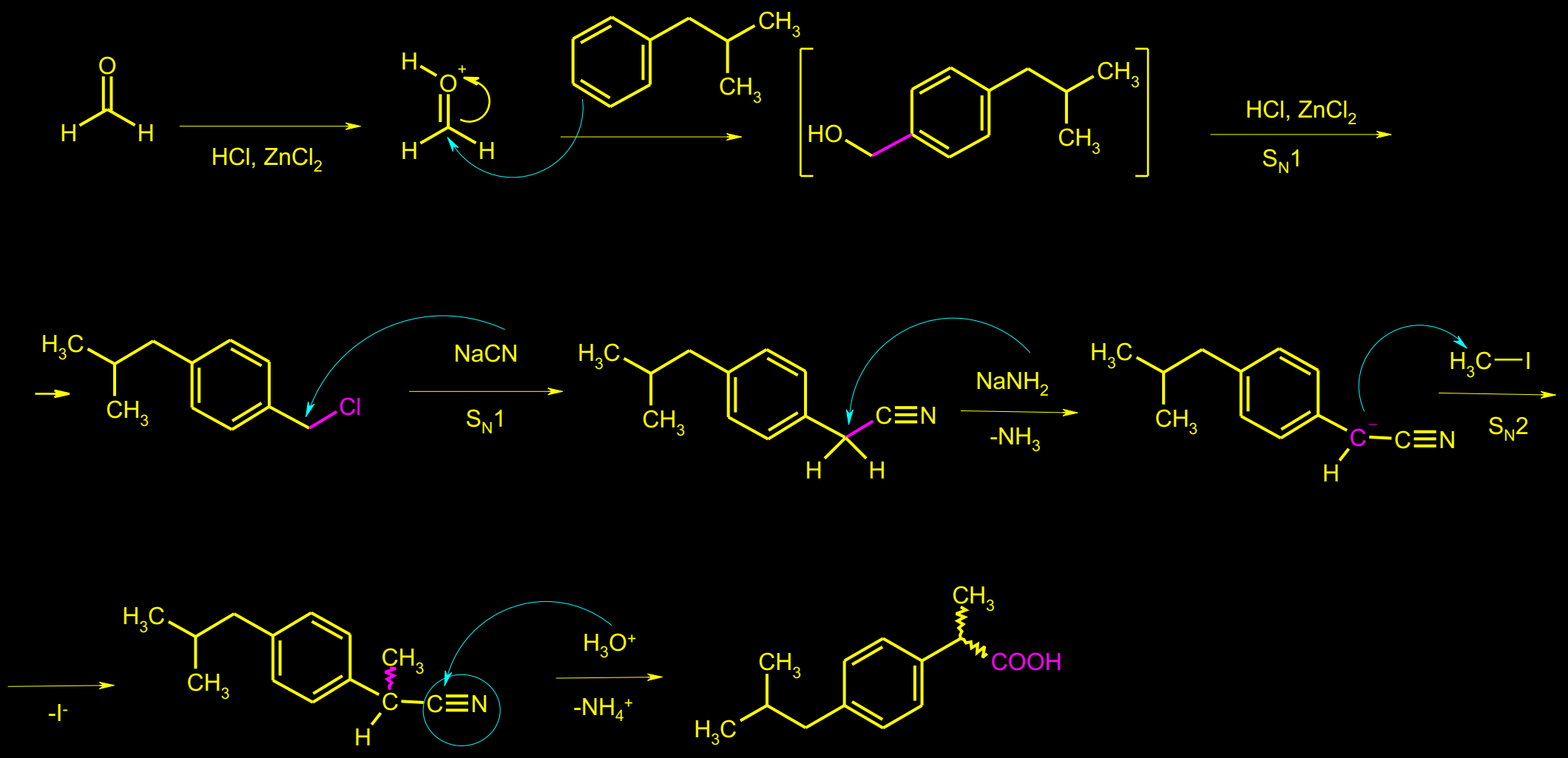
IBUPROFEN (BRUFEN):





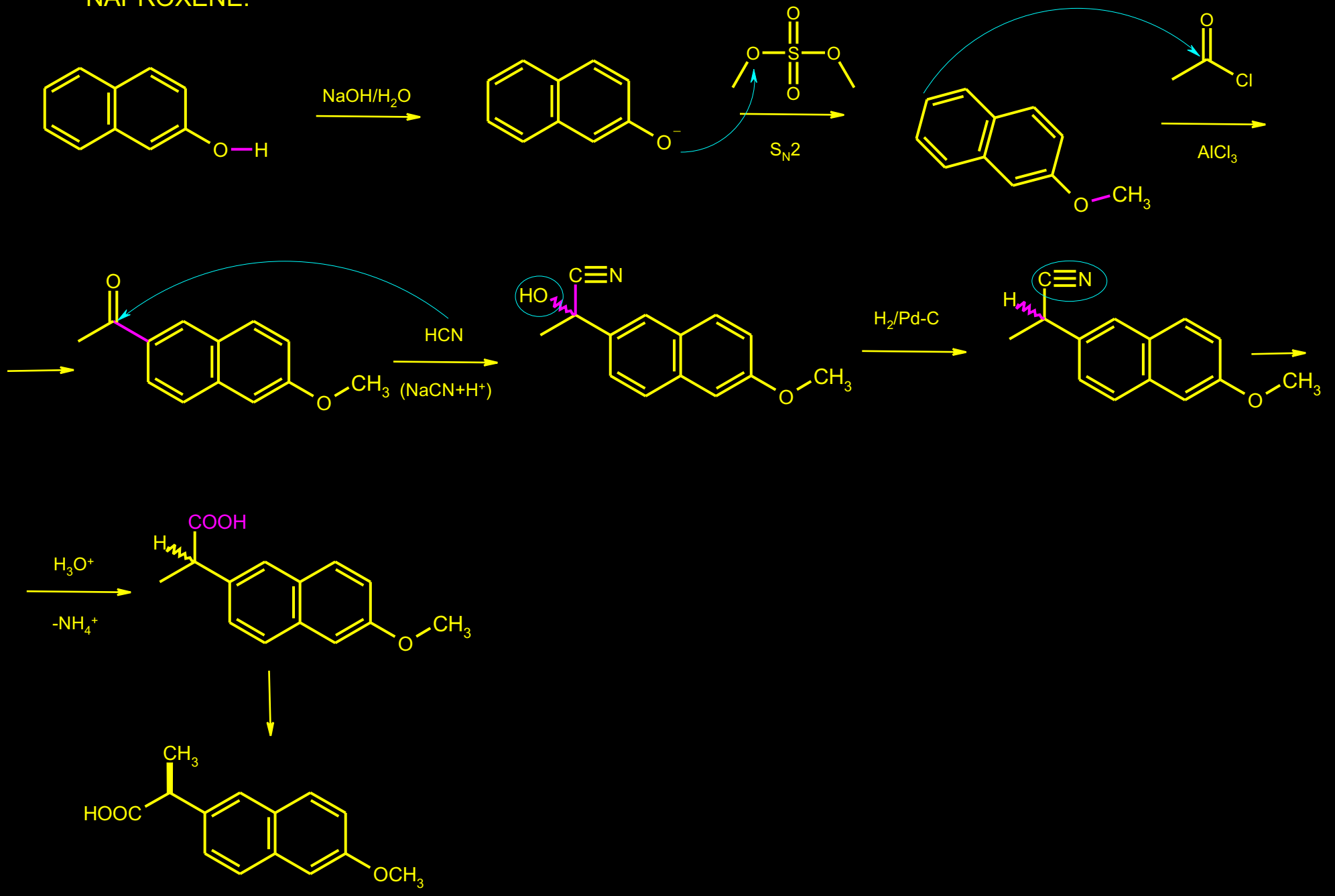
NE-STEROIDNI ANALGETICI 5. DERIVATI 2-ARIL-PROPIONSKE KISELINE -NASTAVAK

IBUPROFEN - ALTERNATIVNA SINTEZA:



NE-STEROIDNI ANALGETICI 5. DERIVATI 2-ARIL-PROPIONSKE KISELINE - NASTAVAK

NAPROXENE:



Monograph Number: 6443
Title: Naproxen
CAS Registry Number: 22204-53-1
CAS Name: (αS)-6-Methoxy-α-methyl-2-naphthaleneacetic acid
Additional Names: d-2-(6-methoxy-2-naphthyl)propionic acid; MNPA
Manufacturers' Codes: RS-3540
Trademarks: Bonyl (Erco); Dysmenalgit (Krewel); Equiproxen (Syntex); Floginax (Lifepharma); Laraflex (Lagap); Laser (Tosi); Malexin (BASF); Naixan (Tanabe); Napren (Nycomed); Naprius (Magis); Naprosyn (Syntex); Naprosyne (Syntex); Naprux (Andromaco); Naxen (Syntex); Nycopren (Nycomed); Pranoxen (Napp); Prexan (LaFare); Proxen (Syntex); Proxine (Del Saz & Filippini); Veradol (Schering AG); Xenar (Alfa)
Molecular Formula: C14H14O3
Molecular Weight: 230.26.
Percent Composition: C 73.03%, H 6.13%, O 20.85%
Literature References: Nonsteroidal anti-inflammatory. Prepn: J. H. Fried, I. T. Harrison, ZA 67 07597; eidem, US 3904682; eidem, US 4009197 (1968, 1975, 1977 all to Syntex); I. T. Harrison et al., J. Med. Chem. 13, 203 (1970). Pharmacology: Roszkowski et al., J. Pharmacol. Exp. Ther. 179, 114 (1971). Activity may be due to the ability to inhibit prostaglandin biosynthesis. Mode of action studies: Tomlinson et al., Biochem. Biophys. Res. Commun. 46, 552 (1972). Metabolism: Runkel et al., J. Pharm. Sci. 61, 703 (1972). HPLC determn in plasma and serum: P. J. Streete, J. Chromatog. 495, 179 (1989). Stereoselective synthesis: K. T. Wan, M. E. Davis, Nature 370, 449 (1994). Clinical studies: Katona et al., Clin. Trials J. 8, 3 (1972); Runkel, Chem. Pharm. Bull. 20, 1457 (1972). Review: Arzneimittel-Forsch. 25, 278-332 (1975). Review of pharmacology and therapeutic efficacy: R. N. Brogden et al., Drugs 18, 241-277 (1979). Comprehensive description: F. J. Al-Shammary et al., Anal. Profiles Drug Subs. Excip. 21, 345-373 (1992).

Properties: Crystals from acetone-hexane, mp 152-154°. [□]D +66° (in chloroform). Sol in 25 parts ethanol (96%), 20 parts methanol, 15 parts chloroform, 40 parts ether. Practically insol in water. LD50 in mice (mg/kg): 435 i.v.; 1234 orally; in rats (mg/kg): 575 i.p.; 534 orally (Roszkowski).
Melting point: mp 152-154°
Optical Rotation: [□]D +66° (in chloroform)
Toxicity data: LD50 in mice (mg/kg): 435 i.v.; 1234 orally; in rats (mg/kg): 575 i.p.; 534 orally (Roszkowski)

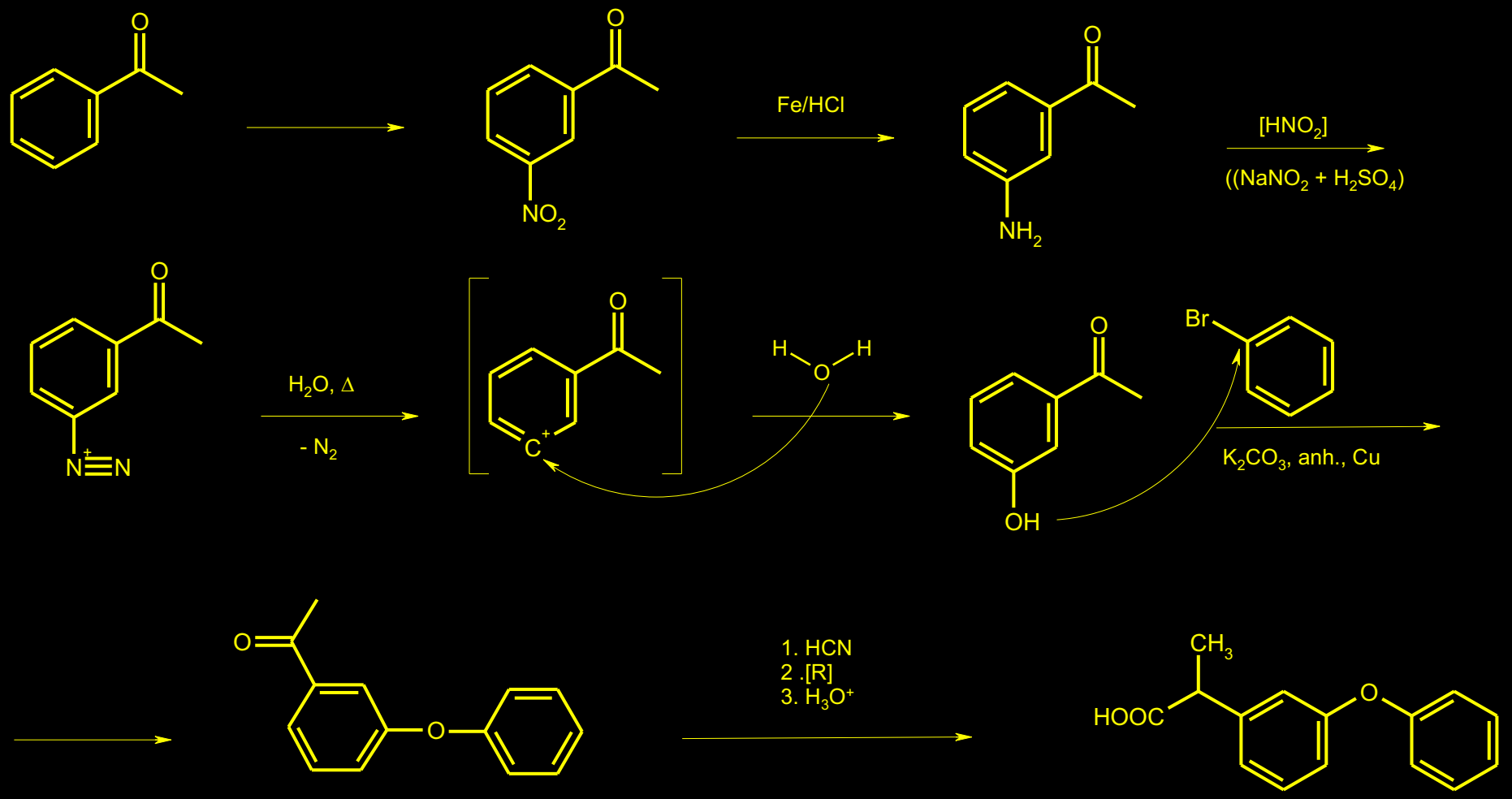
Derivative Type: Piperazine salt
CAS Registry Number: 70981-66-7
Additional Names: Piproxen
Trademarks: Numidan (Coop. Farm.)
Molecular Formula: (C14H14O3)2.C4H10N2
Molecular Weight: 546.65.
Percent Composition: C 70.31%, H 7.01%, O 17.56%, N 5.12%

Derivative Type: Sodium salt
CAS Registry Number: 26159-34-2
Manufacturers' Codes: RS-3650
Trademarks: Aleve (Procter & Gamble); Anaprox (Syntex); Antalgin (Syntex); Apranax (Syntex); Axer Alfa (Alfa); Flanax (Syntex); Gynestrel (Recordati); Miranax (Syntex); Naprelan (Wyeth-Ayerst); Primeral (Master); Synflex (Recordati)
Molecular Formula: C14H13NaO3
Molecular Weight: 252.24.
Percent Composition: C 66.66%, H 5.19%, Na 9.11%, O 19.03%
Properties: Crystals from acetone, mp 244-246°. [□]D -11° (in methanol).
Melting point: mp 244-246°
Optical Rotation: [□]D -11° (in methanol)

Therap-Cat: Anti-inflammatory; analgesic; antipyretic.

NE-STEROIDNI ANALGETICI 5. DERIVATI 2-ARIL-PROPIONSKE KISELINE- NASTAVAK

Fenoprofen:



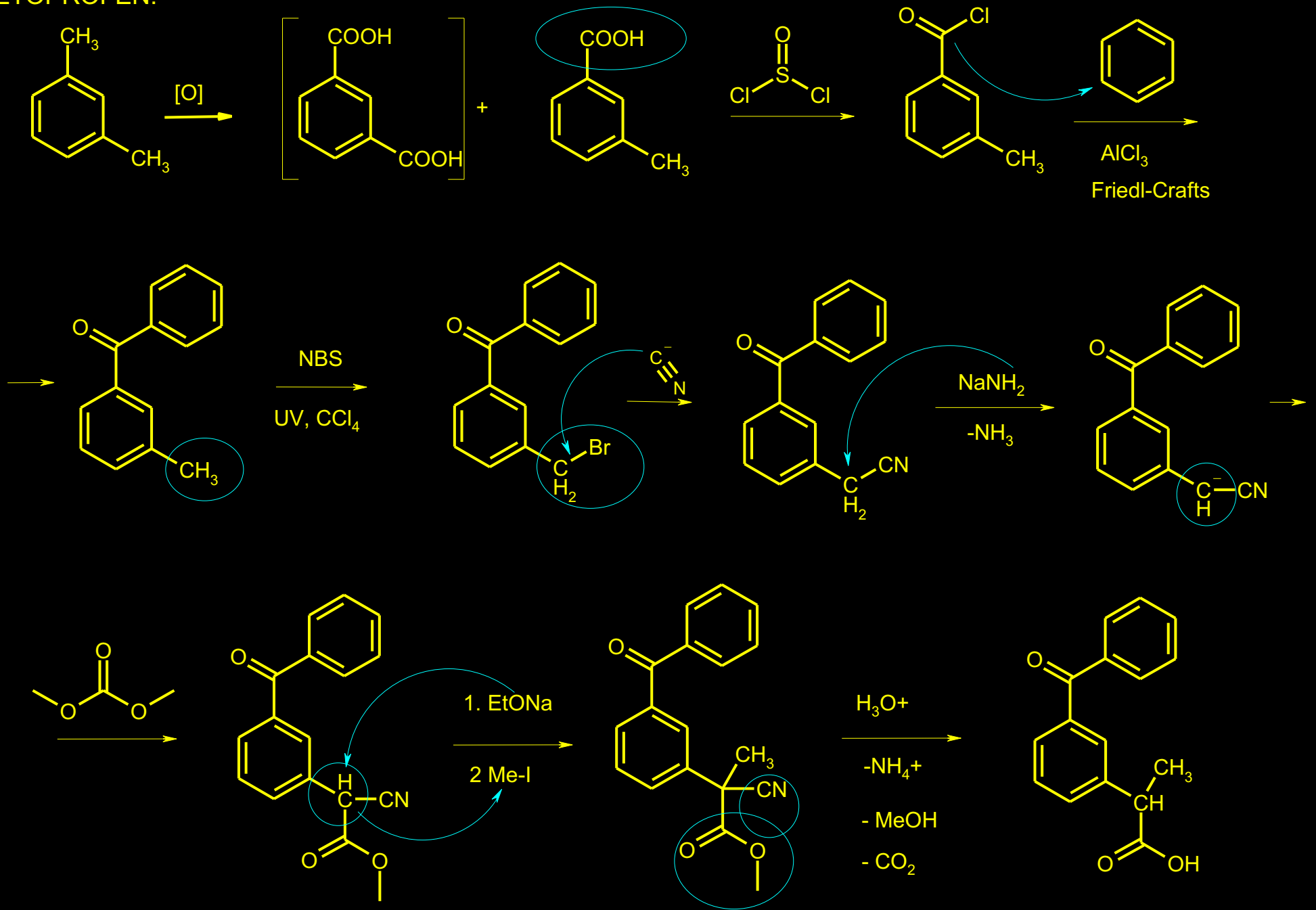
Monograph Number: 4007
Title: Fenoprofen
CAS Registry Number: 31879-05-7
CAS Name: α-Methyl-3-phenoxybenzeneacetic acid
Additional Names: (±)-m-phenoxyhydratropic acid; α-dl-2-(3-phenoxyphenyl)propionic acid
Manufacturers' Codes: Lilly 53838
Molecular Formula: C15H14O3
Molecular Weight: 242.27.
Percent Composition: C 74.36%, H 5.82%, O 19.81%
Literature References: Prepn: Marshall, FR 2015718 corresp to US 3600437 (1970, 1971 to Lilly). Pharmacology: Rubin et al., J. Pharm. Sci. 60, 1797 (1971); 61, 800 (1972); Herrmann, Proc. Soc. Exp. Biol. Med. 139, 548 (1972). Metabolism: Rubin et al., J. Pharmacol. Exp. Ther. 183, 449 (1972). Toxicology: J. L. Emmerson et al., Toxicol. Appl. Pharmacol. 25, 444 (1973). Comprehensive description: C. K. Ward, R. E. Schirmer, Anal. Profiles Drug Subs. 6, 161-182 (1977). Review: R. N. Brogden et al., Drugs 13, 241-265 (1977); R. Nickander et al., in Pharmacological and Biochemical Properties of Drug Substances vol. 1, M. E. Goldberg, Ed. (Am. Pharm. Assoc., Washington, DC, 1977) pp 183-213.
Properties: Viscous oil, bp0.11 168-171°. nD25 1.5742. pKa 7.3.
Boiling point: bp0.11 168-171°
pKa: pKa 7.3
Index of refraction: nD25 1.5742

Derivative Type: Calcium salt dihydrate
CAS Registry Number: 53746-45-5
Manufacturers' Codes: Lilly 69323
Trademarks: Fenopron (Dista); Fepron (Lilly); Feprona (Lilly); Nalfon (Lilly); Nalgesic (Lilly); Progesic (Lilly)
Molecular Formula: C30H26CaO6.2H2O
Molecular Weight: 558.64.
Percent Composition: C 64.50%, H 5.41%, Ca 7.17%, O 22.91%
Properties: White crystalline powder. Soly in mg/ml at 37°: n-hexanol 11; methanol 8; water 2.5; chloroform 0.01. pKa 4.5. Aq solns sensitive to intense uv light. LD50 orally in mice: 800 mg/kg (Emmerson).
pKa: pKa 4.5
Toxicity data: LD50 orally in mice: 800 mg/kg (Emmerson)

Therap-Cat: Anti-inflammatory; analgesic.

NE-STEROIDNI ANALGETICI 5. DERIVATI 2-ARIL-PROPIONSKE KISELINE- NASTAVAK

KETOPROFEN:



Monograph Number: 5322
Title: Ketoprofen
CAS Registry Number: 22071-15-4
CAS Name: 3-Benzoyl-α-methylbenzeneacetic acid
Additional Names: m-benzoylhydratropic acid; 2-(3-benzoylphenyl)propionic acid
Manufacturers' Codes: RP-19583
Trademarks: Alreumat (Bayer); Alrheumun (Bayer); Capisten (Kissei); Epatec (Nissan); Fastum (Menarini); Iso-K (San Carlo); Ketofen (Fort Dodge); Ketopron (Alcon); Menamin (RPR); Meprofen (Agips); Orudis (RPR); Oruvail (RPR); Profenid (RPR); Toprec (RPR); Toprek (RPR)
Molecular Formula: C16H14O3
Molecular Weight: 254.28.
Percent Composition: C 75.57%, H 5.55%, O 18.88%
Literature References: Prepn: D. Farge et al., ZA 68 00524; eidem, US 3641127 (1968, 1972 both to Rhône-Poulenc); G. A. Pinna et al., Farmaco Ed. Sci. 35, 684 (1980). Resolution of isomers: S. Rendic et al., Chimia 29, 170 (1975). Enantioselective synthesis and absolute configuration of (+)-form: G. Comisso et al., Gazz. Chim. Ital. 110, 123 (1980). Pharmacology of enantiomers: P. J. Hayball et al., Chirality 4, 484 (1992). HPLC determn in plasma: R. Lovlin et al., J. Chromatog B 679, 196 (1996). Toxicity data: K. Ueno et al., J. Med. Chem. 19, 941 (1976). Comprehensive description: G. G. Liversidge, Anal. Profiles Drug Subs. 10, 443-471 (1981). Review of pharmacokinetics: F. Jamali, D. R. Brocks, Clin. Pharmacokinet. 19, 197-217 (1990); of clinical experience: E. M. Veys, Scand. J. Rheumatol. Suppl. 90, 3-44 (1991).
Properties: Crystals from 6:20 benzene-petr ether, mp 94°. uv max (methanol): 255 nm (log ε 4.33). Sol in ether, alc, acetone, chloroform, DMF, ethyl acetate. Slightly sol in water.
LD50 orally in rats: 101 mg/kg (Ueno).
Melting point: mp 94°
Absorption maximum: uv max (methanol): 255 nm (log ε 4.33)
Toxicity data: LD50 orally in rats: 101 mg/kg (Ueno)

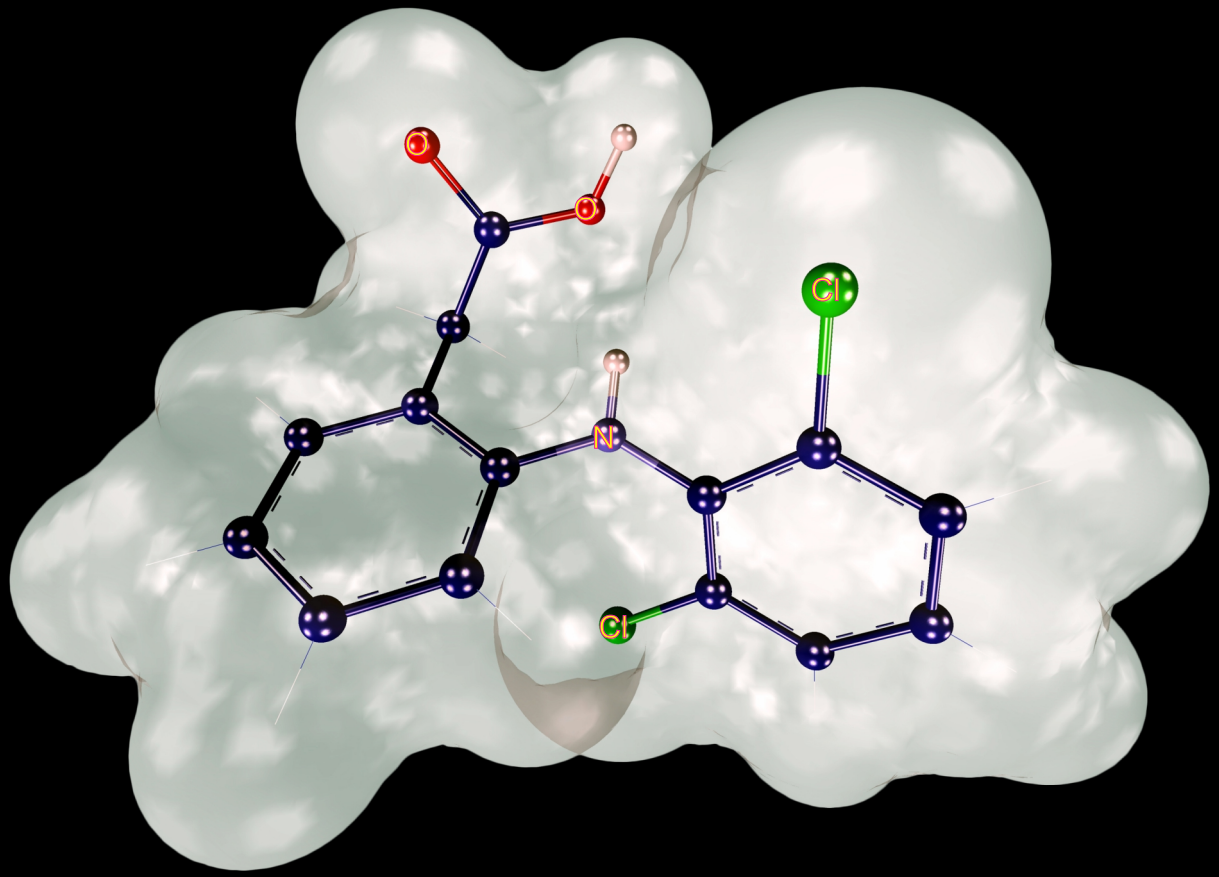
Derivative Type: Lysine salt
CAS Registry Number: 57469-78-0
Trademarks: Artrosilene (Dompé)
Molecular Formula: C16H14O3.C6H14N2O2
Molecular Weight: 400.47.
Percent Composition: C 65.98%, H 7.05%, O 19.98%, N 7.00%

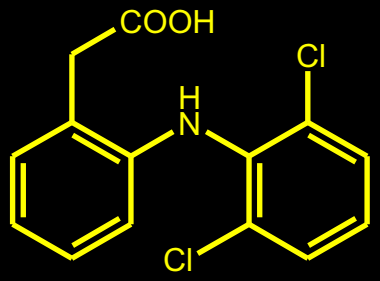
Derivative Type: (S)-(+)-Form tromethamine salt
CAS Registry Number: 156604-79-4
Additional Names: Dexketoprofen trometamol
Trademarks: Enantyum (Menarini); Keral (Menarini)
Molecular Formula: C16H14O3.C4H11NO3
Molecular Weight: 375.41.
Percent Composition: C 63.99%, H 6.71%, O 25.57%, N 3.73%
Literature References: Prepn: G. Carganico et al., WO 94 11332 (1994 to Menarini). Clinical trial: C. Gay et al., Clin. Drug Invest. 11, 320 (1996).
Properties: White crystalline solid from ethanol-ethyl acetate, mp 104.8-105.1°. [α]D20 -5.2° (c = 1.47 in methanol).
Melting point: mp 104.8-105.1°
Optical Rotation: [α]D20 -5.2° (c = 1.47 in methanol)

Therap-Cat: Anti-inflammatory; analgesic.

NE-STEROIDNI ANALGETICI 6. DERIVATI ARIL-SIRĆETNIH KISELINA

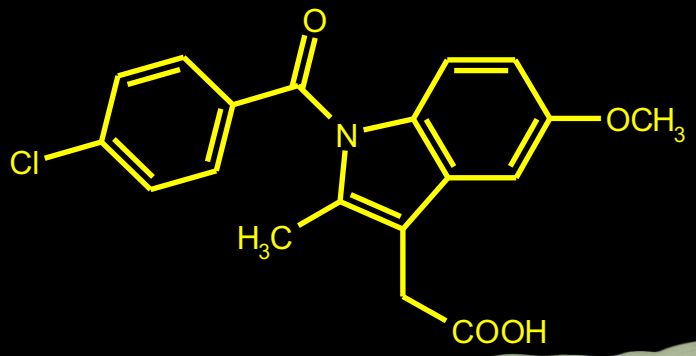
PRIMERI: DICLOFENAC, PHENCLOFENAK

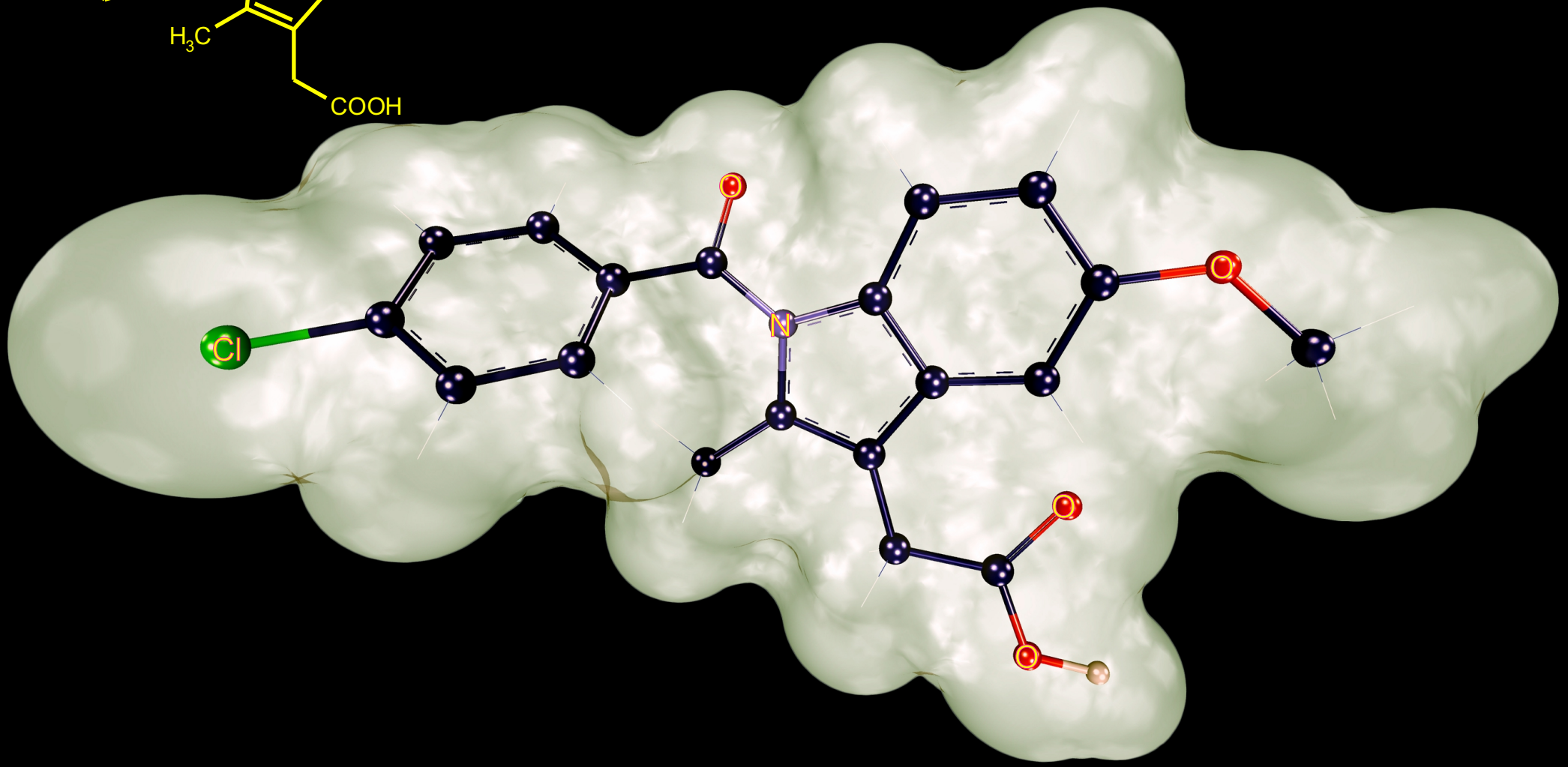




NE-STEROIDNI ANALGETICI 6. **DERIVATI ARIL-SIRĆETNE KISELINE (INDOLYL- SIRĆETNIH KISELINA).**

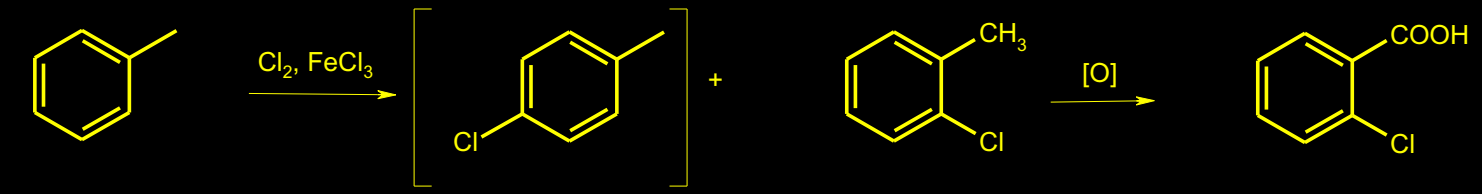
PRIMERI: INDOMETHACIN, SULINDAC

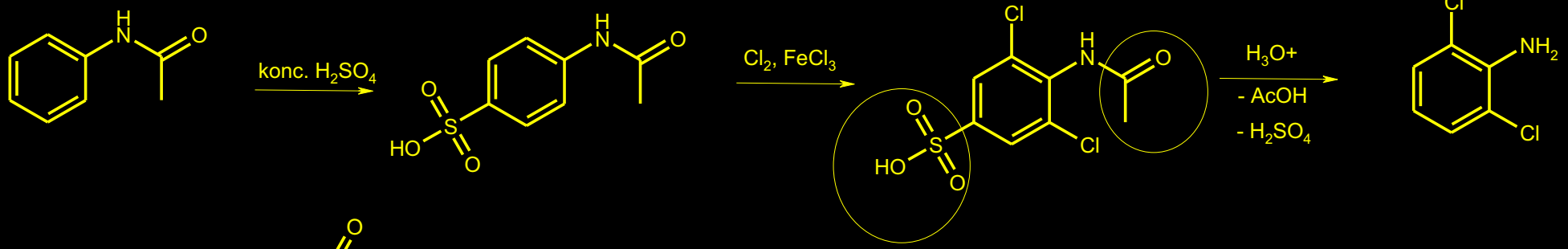


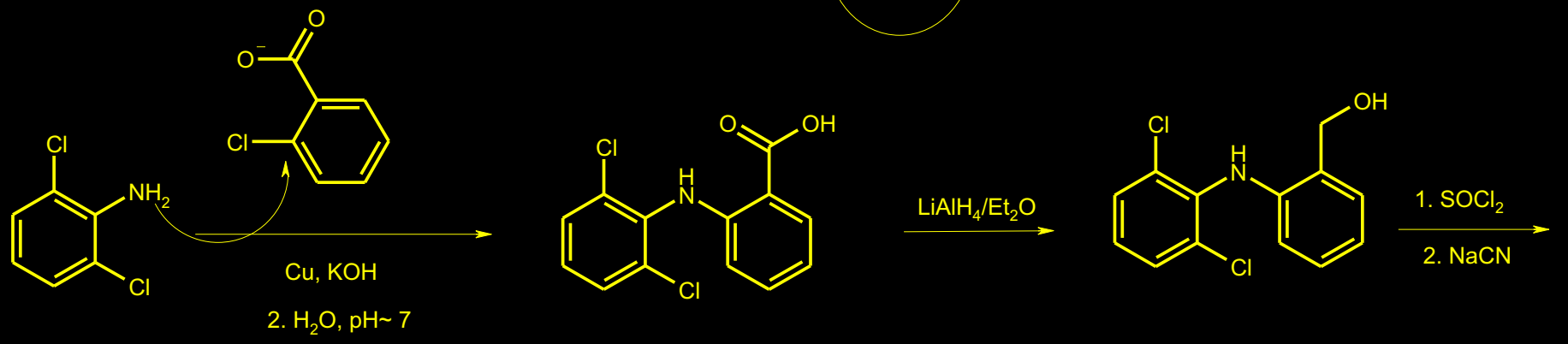


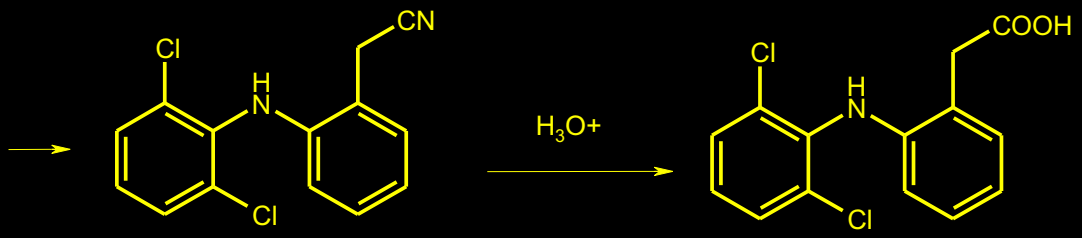
NE-STEROIDNI ANALGETICI 6. DERIVATI ARIL-SIRĆETNE KISELINE

DICLOFENAC







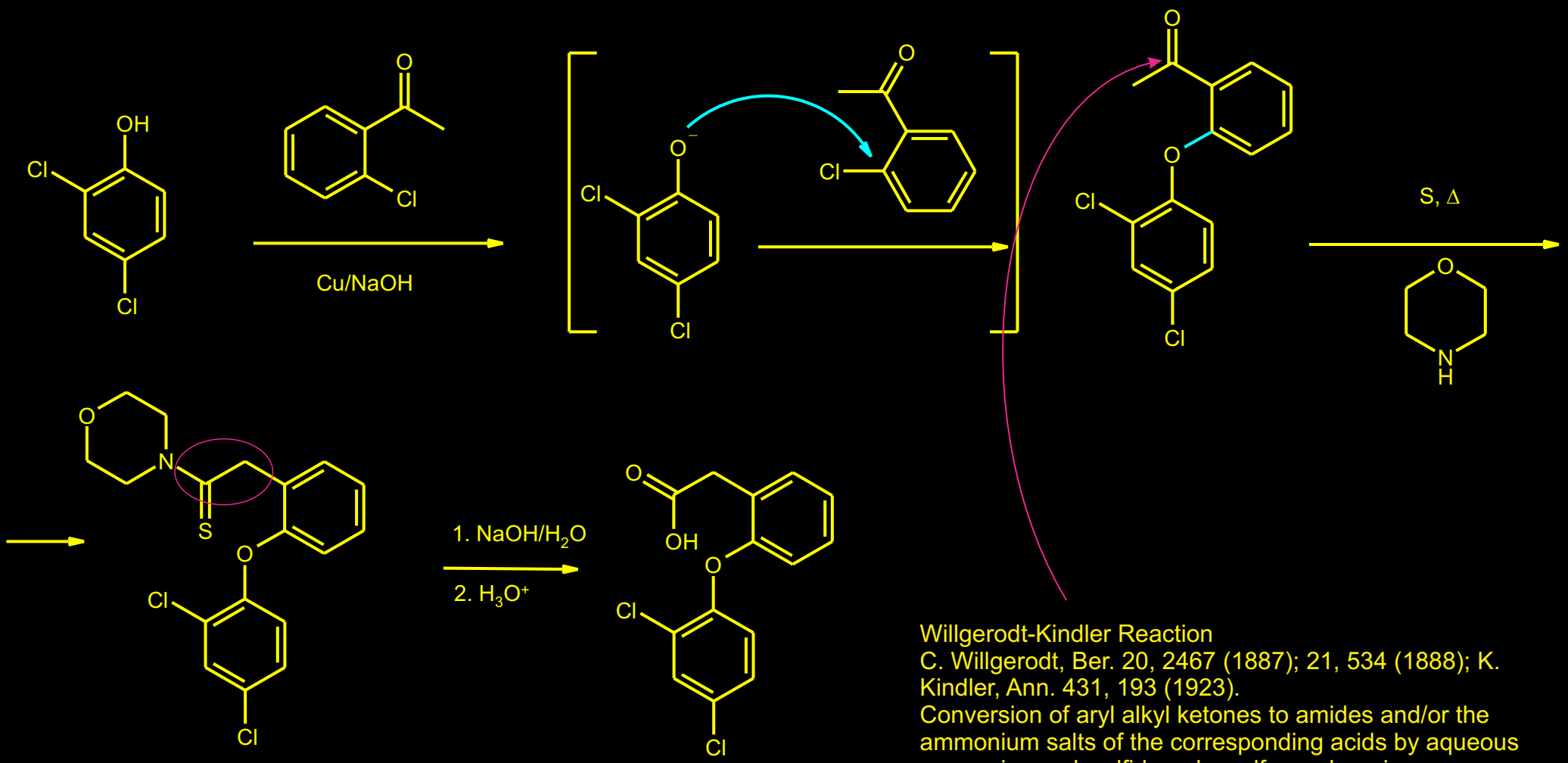


Monograph Number: 3108
Title: Diclofenac
CAS Registry Number: 15307-86-5
CAS Name: 2-[(2,6-Dichlorophenyl)amino]benzeneacetic acid
Additional Names: [o-(2,6-dichloroanilino)phenyl]acetic acid
Trademarks: Voltarol (Novartis)
Molecular Formula: C14H11Cl2NO2
Molecular Weight: 296.15.
Percent Composition: C 56.78%, H 3.74%, Cl 23.94%, N 4.73%, O 10.80%
Literature References: Prepn: NL 6604752; A. Sallmann, R. Pfister, US 3558690 (1966, 1971 both to Geigy).
Pharmacology: Renaud, Lecompte, Thromb. Diath. Haemorrh. 24, 577 (1970), C.A. 74, 86215m (1971); Krupp et al., Experientia 29, 450 (1973). HPLC determn in plasma and urine: J. Godbillon et al., J. Chromatog. 338, 151 (1985). Symposium on pharmacology and clinical experience: Semin. Arthritis Rheum. 15, Suppl. 1, 57-110 (1985); on pharmacology, efficacy and safety: Am. J. Med. 80, Suppl. 4B, 1-87 (1986). Comprehensive description: C. M. Adeyeye, P-K. Li, Anal. Profiles Drug Subs. 19, 123-144 (1990). Review of clinical trials in actinic keratosis: D. C. Peters, R. H. Foster, Drugs Aging 14, 313-319 (1999).
Properties: Crystals from ether-petr ether, mp 156-158°.
Melting point: mp 156-158°
Derivative Type: Sodium salt
CAS Registry Number: 15307-79-6
Manufacturers' Codes: GP-45840
Trademarks: Allvoran (TAD); Benfofen (Sanofi-Synthelabo); Dealgic (Searle); Deflamat (Sankyo); Delphinac (Lederle); Diclomax (Parke-Davis); Diclometin (Pharmacia & Upjohn); Diclophlogont (Azupharma); Diclo-Puren (Isis); Dicloreum (Alfa); Diclo-Spondyril (Orion); Dolobasan (BASF); Duravolten (Durachemie); Ecofenac (Ecosol); Effekton (Am. Home); Lexobene (Merckle); Motifene (Sankyo); Neriodin (Teikoku Kagaku); Novapirina (Novartis); Primofenac (Streuli); Prophenatin (Hishiyama); Rewodina (Asta); Rhumalgan (Lagap); Trabona (Leiras); Tsudohmin (Toho); Valetan (Tobishi); Voldal (Novartis); Voltaren (Novartis); Xenid (Biogalenique)
Molecular Formula: C14H10Cl2NNaO2
Molecular Weight: 318.14.
Percent Composition: C 52.86%, H 3.17%, Cl 22.29%, N 4.40%, Na 7.23%, O 10.06%
Properties: Crystals from water, mp 283-285°. uv max (methanol) 283 nm (1.05 105); (phosphate buffer, pH 7.2) 276 nm (1.01 105). Soly at 25°C (mg/ml): deionized water (pH 5.2) >9; methanol >24; acetone 6; acetonitrile <1; cyclohexane <1; HCl (pH 1.1) <1; phosphate buffer (pH 7.2) 6. pKa 4. Partition coefficient (N-octanol/aq. buffer): 13.4. LD50 in mice, rats (mg/kg): ~390, 150 orally (Krupp).
Melting point: mp 283-285°
pKa: pKa 4
Log P: Partition coefficient (N-octanol/aq. buffer): 13.4
Absorption maximum: uv max (methanol) 283 nm (1.05 105); (phosphate buffer, pH 7.2) 276 nm (1.01 105)
Toxicity data: LD50 in mice, rats (mg/kg): ~390, 150 orally (Krupp)
Derivative Type: Potassium salt
CAS Registry Number: 15307-81-0
Manufacturers' Codes: CGP-45840B
Trademarks: Cataflam (Novartis)
Molecular Formula: C14H10Cl2KNO2
Molecular Weight: 334.24.
Percent Composition: C 50.31%, H 3.02%, Cl 21.21%, K 11.70%, N 4.19%, O 9.57%

Therap-Cat: Anti-inflammatory.

NE-STEROIDNI ANALGETICI 6. DERIVATI ARIL-SIRĆETNE KISELINE

Fenclofenac:

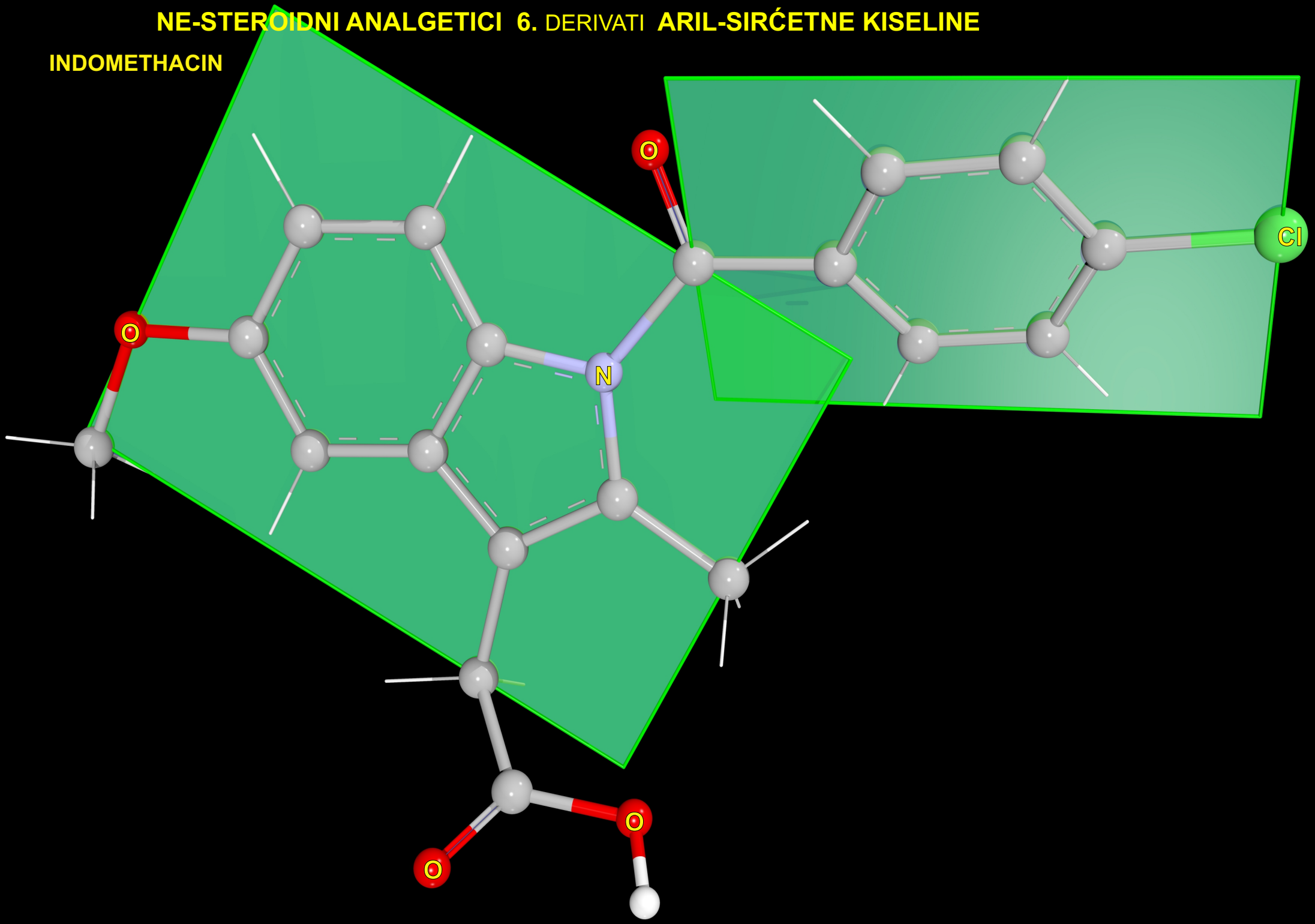


Willgerodt-Kindler Reaction
C. Willgerodt, Ber. 20, 2467 (1887); 21, 534 (1888); K. Kindler, Ann. 431, 193 (1923).
Conversion of aryl alkyl ketones to amides and/or the ammonium salts of the corresponding acids by aqueous ammonium polysulfide or by sulfur and a primary or secondary amine:

$$ArCO(CH_2)_nCH_3 \xrightarrow[H_2O]{(NH_4)_2S_x} Ar(CH_2)_{n+1}\text{—}CONH_2 + Ar(CH_2)_{n+1}\text{—}COO^- \; NH_4^+$$

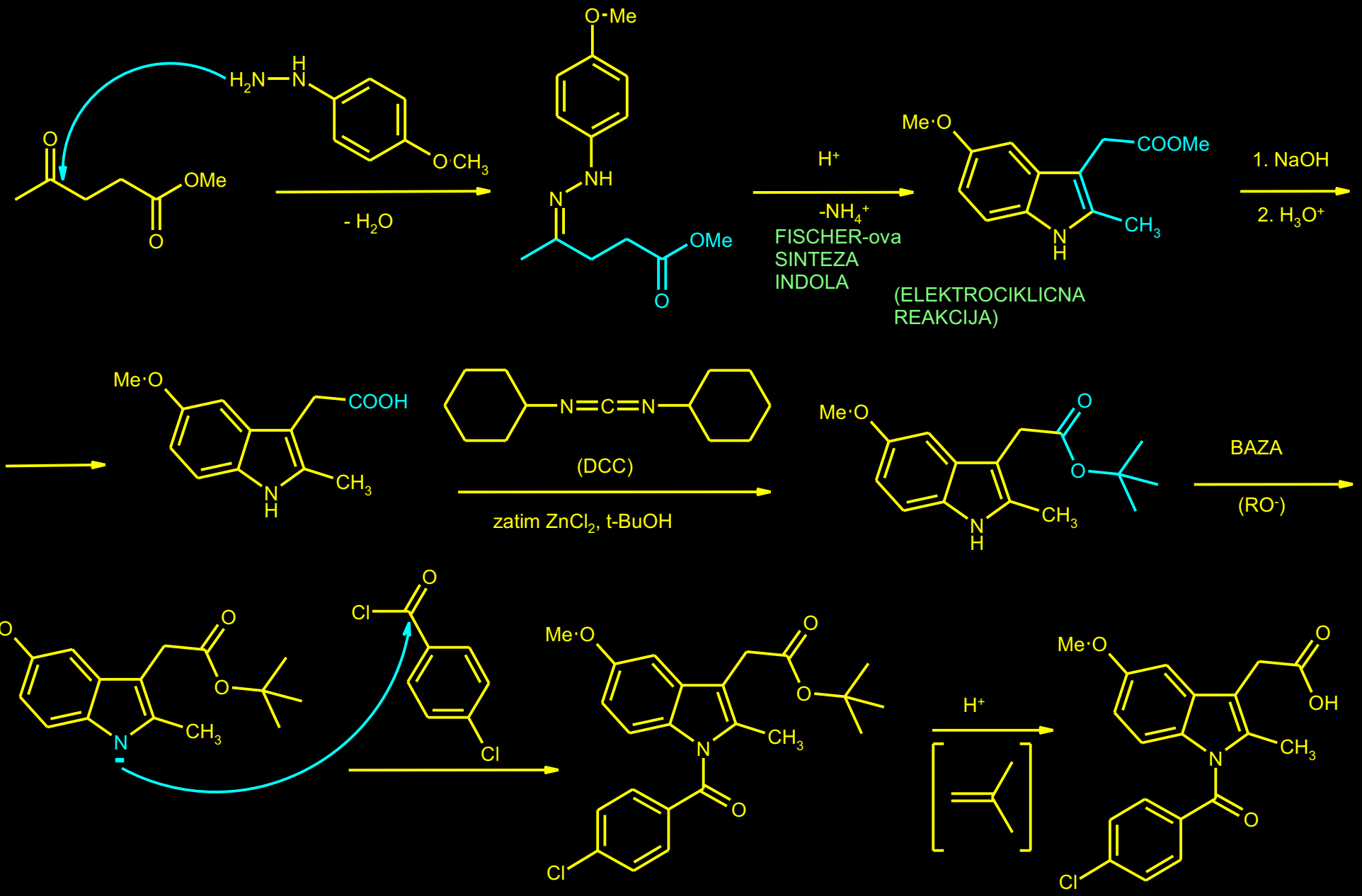
NE-STEROIDNI ANALGETICI 6. DERIVATI ARIL-SIRĆETNE KISELINE

INDOMETHACIN



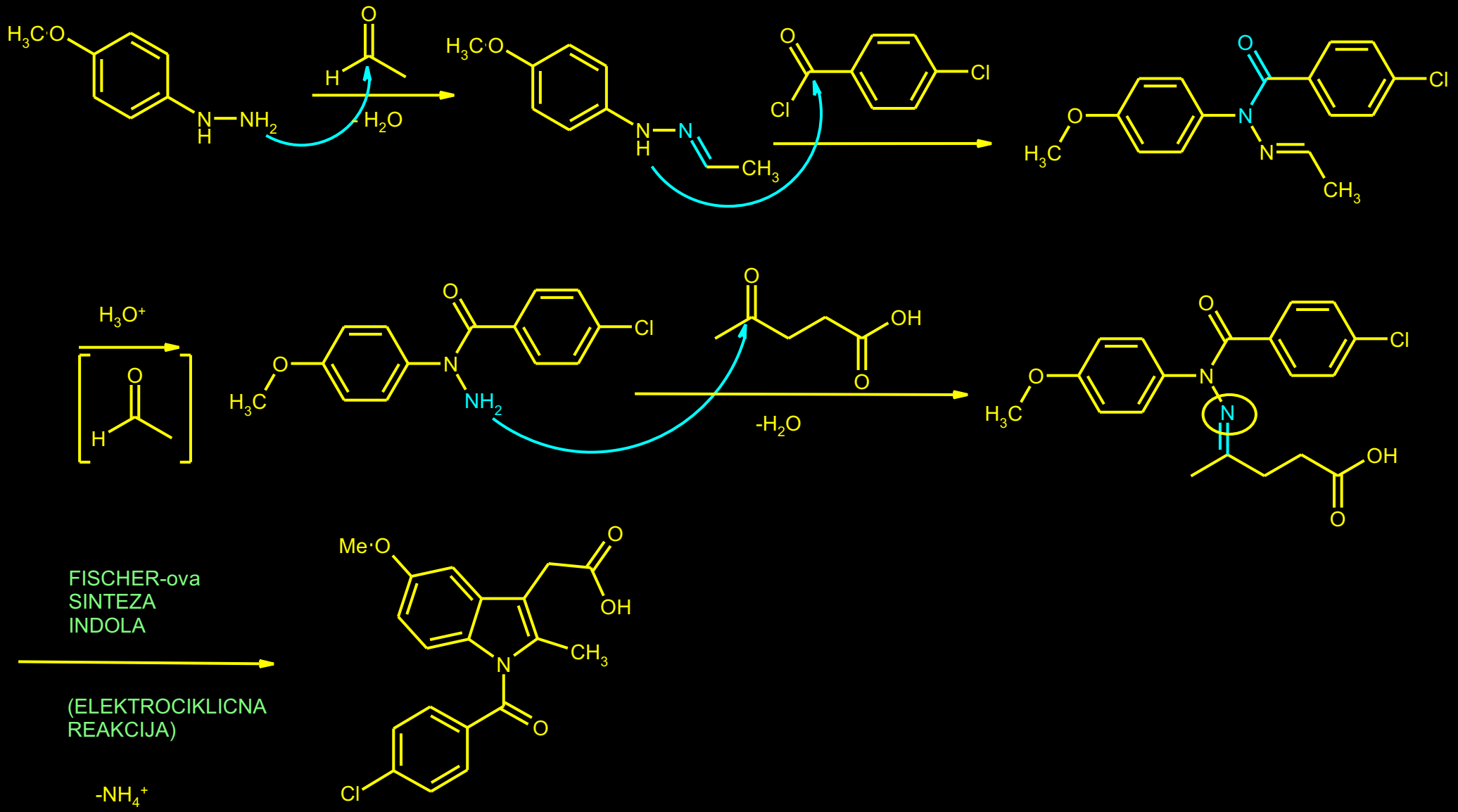
NE-STEROIDNI ANALGETICI 6. DERIVATI ARIL-SIRĆETNE KISELINE

INDOMETHACIN



NE-STEROIDNI ANALGETICI 6. DERIVATI ARIL-SIRĆETNE KISELINE

INDOMETHACIN - ALTERNATIVNA SINTEZA



Monograph Number: 4990
Title: Indomethacin
CAS Registry Number: 53-86-1
CAS Name: 1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetic acid
Additional Names: 1-(p-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetic acid
Trademarks: Amuno (Merck & Co.); Argun (Merckle); Artracin (DDSA); Artrinovo (Llorns, Spain); Bonidon (Mepha); Catlep (Sumitomo); Chibro-Amuno (Chibret); Chrono-Indocid (Merck & Co.); Confortid (Dumex); Dolcidium (Galephar); Durametacin (Durachemie); Elmetacin (Luitpold); Idomethine (Kowa); Imbrilon (Berk); Inacid (Merck & Co.); Indacin (Merck & Co.); Indocid (Merck & Co.); Indocin (Merck & Co.); Indomed (Merck & Co.); Indomee (Merck & Co.); Indomethine (Teika Seiyaku); Indomod (Benzon); Indo-Phlogont (Azupharma); Indoptic (Merck & Co.); Indoptol (Merck & Co.); Indorektal (Sanorania); Indo-Tablinen (Sanorania); Indoxen (Sigma-Tau); Inflazon (Taisho); Infrocin (Frosst); Inteban (Sumitomo); Lausit (Showa Yakuhin); Mezolin (Meiji); Mikametan (Mikasa); Mobilan (Galen); Rheumacin LA (CP Pharm.); Serastar (Yamanouchi); Tannex (Duncan, Flockhart); Vonum (Lichtenstein)
Molecular Formula: C19H16ClNO4
Molecular Weight: 357.79.
Percent Composition: C 63.78%, H 4.51%, Cl 9.91%, N 3.91%, O 17.89%
Literature References: Prepn: T. Y. Shen et al., J. Am. Chem. Soc. 85, 488 (1963); T. Y. Shen, US 3161654 (1964 to Merck & Co.). Alternate process: BE 679678 (1966 to Sumitomo). Pharmacology: Winter et al., J. Pharmacol. Exp. Ther. 141, 369 (1963). Metabolic studies: Yesair et al., Biochem. Pharmacol. 19, 1579 (1970). Indomethacin blocks prostaglandin biosynthesis: see Prostaglandin Synthetase Inhibitors Their Effects on Physiological Functions and Pathological States, H. J. Robinson, J. R. Vane, Eds. (Raven Press, New York, 1974) 395 pp. Toxicity: C. D. Klaassen, Toxicol. Appl. Pharmacol. 38, 127 (1976). Review: T. Y. Shen, C. A. Winter in Advances in Drug Research vol. 12, A. B. Simmons, Ed. (Academic Press, New York, 1977) pp 89-245; Semin. Arthritis Rheum. 12, Suppl. 1, 77-151 (1982).
Properties: Crystals exhibiting polymorphism, mp for one form ~155°, for the other ~162°. uv max (ethanol): 230, 260, 319 nm (20800, 16200, 6290). pKa 4.5. Sol in ethanol, ether, acetone, castor oil. Practically insol in water. Stable in neutral or slightly acidic media; dec by strong alkali. LD50 i.p. in rats: 13 mg/kg (Klaassen).
Melting point: mp for one form ~155°, for the other ~162°
pKa: pKa 4.5
Absorption maximum: uv max (ethanol): 230, 260, 319 nm (20800, 16200, 6290)
Toxicity data: LD50 i.p. in rats: 13 mg/kg (Klaassen)

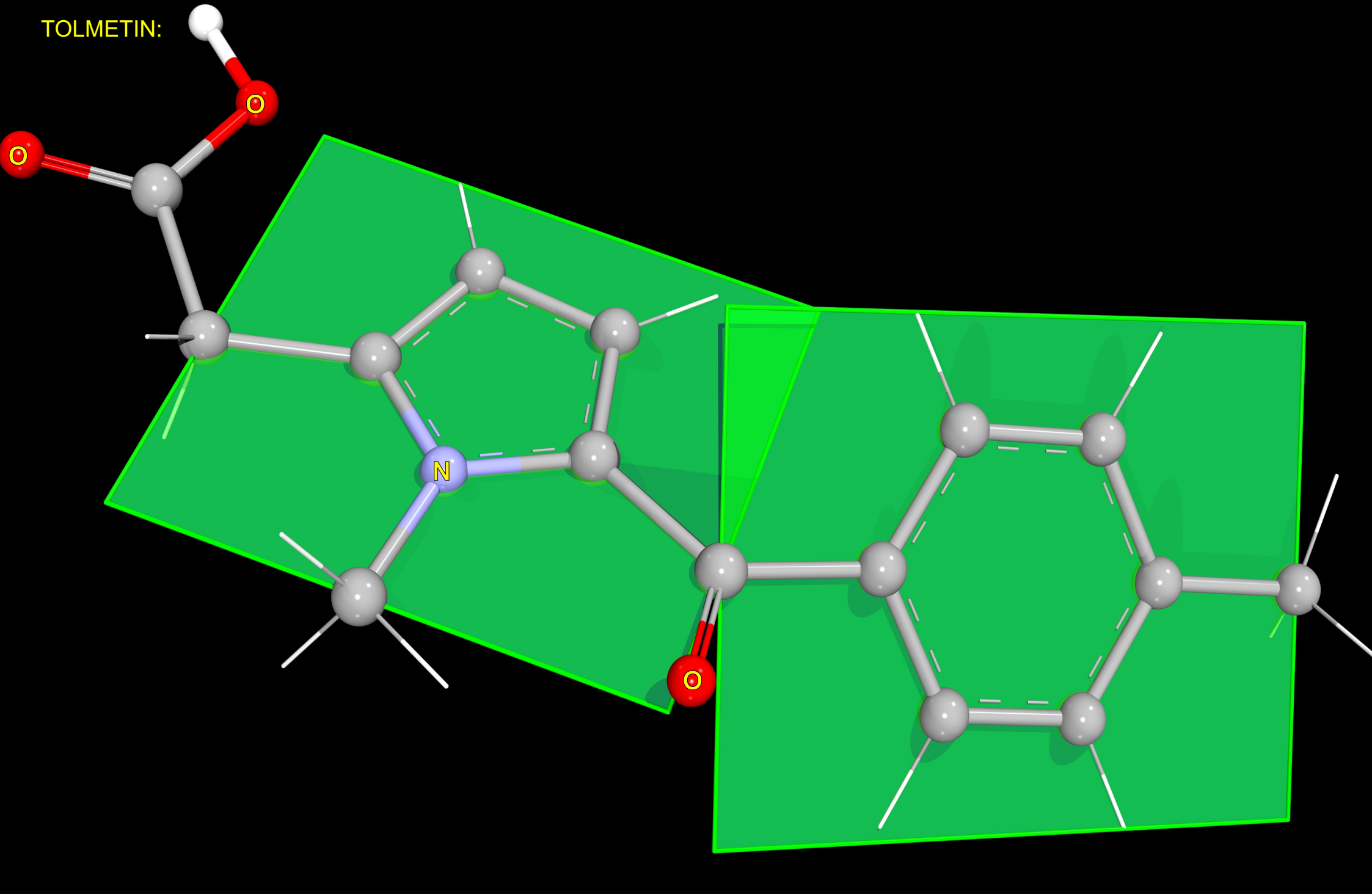
Derivative Type: Sodium salt trihydrate
CAS Registry Number: 74252-25-8
Molecular Formula: C19H15ClNNaO4.3H2O
Molecular Weight: 433.82.
Percent Composition: C 52.60%, H 4.88%, Cl 8.17%, N 3.23%, Na 5.30%, O 25.82%
Properties: Pale yellow crystalline powder. pH of 1% soln: 8.4. Very sol in methanol; sol in water, ethanol. Very slightly sol in chloroform, acetone.

Derivative Type: Meglumine salt
Trademarks: Liometacen (Chiesi)

Therap-Cat: Anti-inflammatory, antipyretic, analgesic.

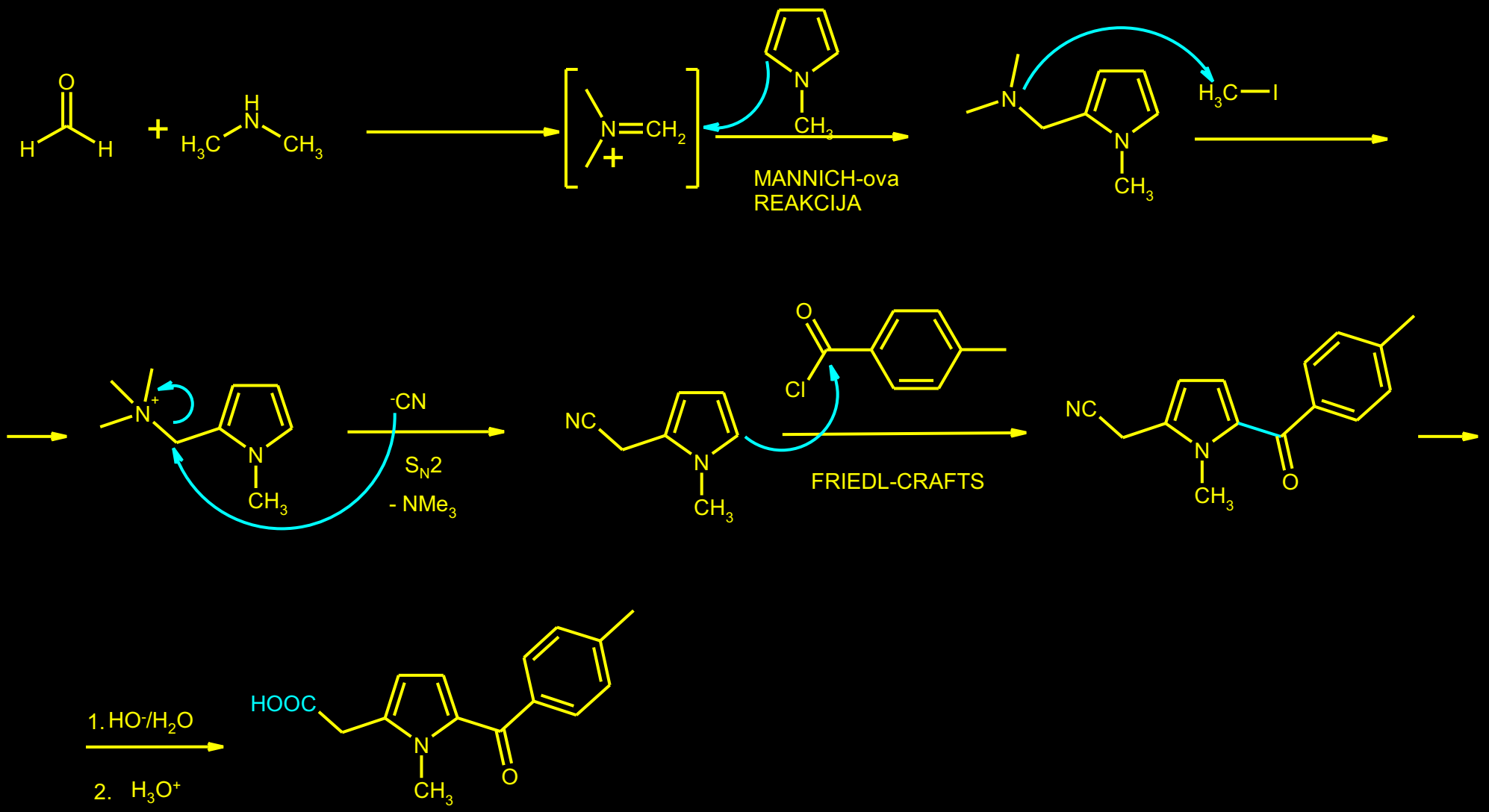
NE-STEROIDNI ANALGETICI 6. DERIVATI ARIL-SIRĆETNE KISELINE

TOLMETIN:



NE-STEROIDNI ANALGETICI 6. DERIVATI ARIL-SIRĆETNE KISELINE

TOLMETIN:



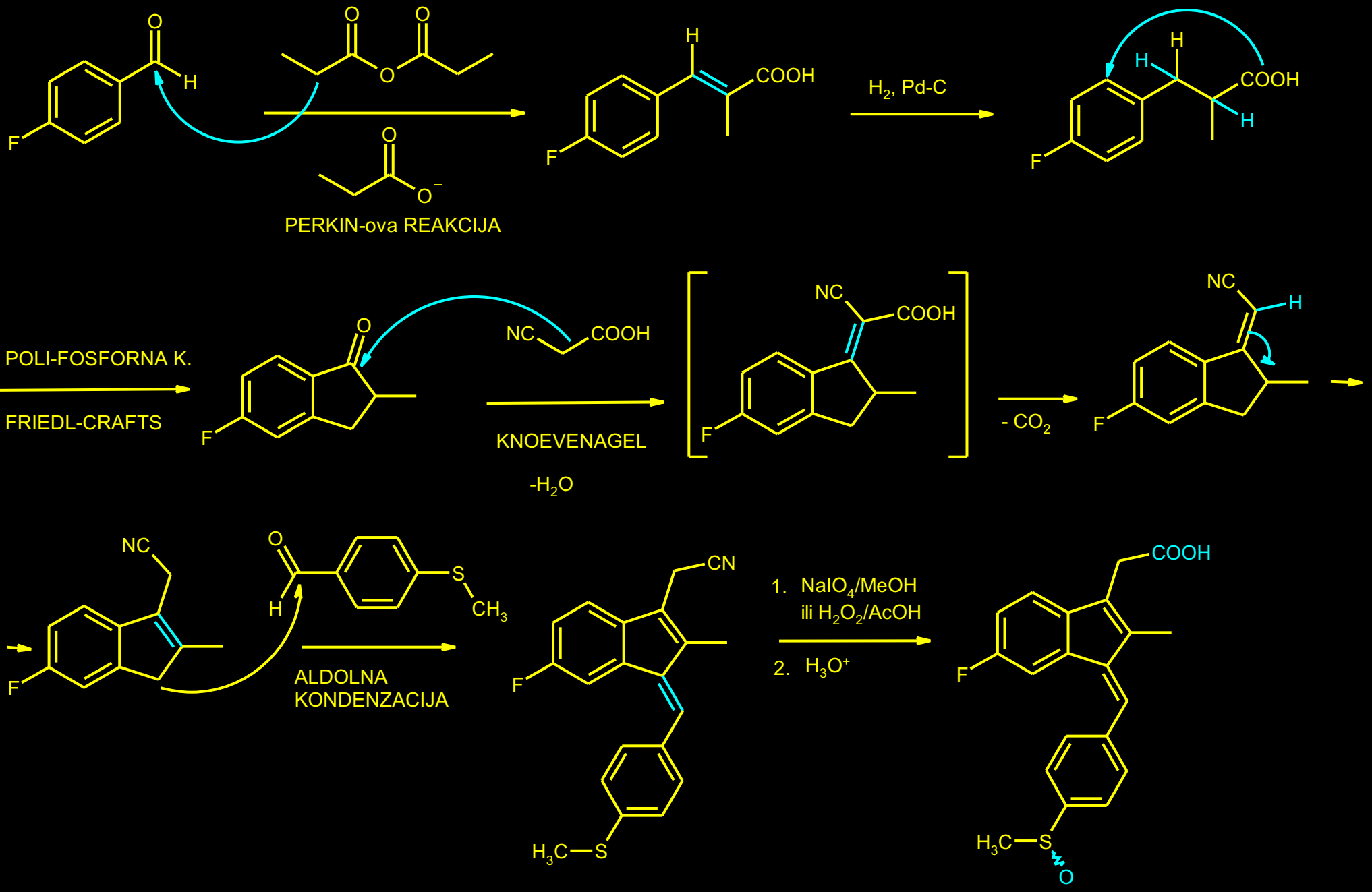
Monograph Number: 9595
Title: Tolmetin
CAS Registry Number: 26171-23-3
CAS Name: 1-Methyl-5-(4-methylbenzoyl)-1H-pyrrole-2-acetic acid
Additional Names: 1-methyl-5-p-toluoylpyrrole-2-acetic acid; 5-(p-toluoyl)-1-methylpyrrole-2-acetic acid
Manufacturers' Codes: McN-2559
Molecular Formula: C15H15NO3
Molecular Weight: 257.28.
Percent Composition: C 70.03%, H 5.88%, N 5.44%, O 18.66%
Literature References: Prepn: Carson, FR 1574570 (1969 to McNeil Labs.), C.A. 72, 100498y (1969). Pharmacology: Carson et al., J. Med. Chem. 14, 646 (1971); S. Wong et al., J. Pharmacol. Exp. Ther. 185, 127 (1973). Review: S. Wong in Pharmacological and Biochemical Properties of Drug Substances vol. 1, M. E. Goldberg, Ed. (Am. Pharm. Assoc., Washington, DC, 1977) pp 233-255. Review of pharmacology and therapeutic efficacy: R. N. Brogden et al., Drugs 15, 429-450 (1978).
Properties: Crystals from acetonitrile, mp 155-157° (dec).
Melting point: mp 155-157° (dec)

Derivative Type: Sodium salt dihydrate
CAS Registry Number: 64490-92-2
Manufacturers' Codes: McN-2559-21-98
Trademarks: Reutol (Errekappa); Tolectin (McNeil); Tolmene (Sigma-Tau)
Molecular Formula: C15H14NNaO3.2H2O
Molecular Weight: 315.30.
Percent Composition: C 57.14%, H 5.75%, N 4.44%, Na 7.29%, O 25.37%

Therap-Cat: Anti-inflammatory.

NE-STEROIDNI ANALGETICI 6. DERIVATI ARIL-SIRĆETNE KISELINE

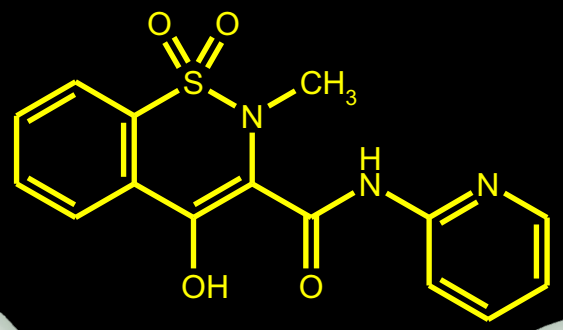
SULINDAC:



Monograph Number: 9072
Title: Sulindac
CAS Registry Number: 38194-50-2
CAS Name: (1Z)-5-Fluoro-2-methyl-1-[[4-(methylsulfinyl)phenyl]methylene]-1H-indene-3-acetic acid
Additional Names: cis-5-fluoro-2-methyl-1-[p-(methylsulfinyl)benzylidene]indene-3-acetic acid
Manufacturers' Codes: MK-231
Trademarks: Aflodac (Janus); Algocetil (Francia); Arthrocine (Merck & Co.); Artribid (Merck & Co.); Citireuma (CT); Clinoril (Merck & Co.); Clisundac (Lagap); Reumofil (Ausonia); Reumyl (Lenza); Sudac (Errekappa); Sulinol (ICT); Sulreuma (Von Boch)
Molecular Formula: C20H17FO3S
Molecular Weight: 356.42.
Percent Composition: C 67.40%, H 4.81%, F 5.33%, O 13.47%, S 9.00%
Literature References: Non-steroidal anti-inflammatory drug. Prepn: T.-Y. Shen et al., DE 2039426; eidem, US 3654349 (1971, 1972 both to Merck & Co.). Stereospecific synthesis: R. F. Shuman et al., J. Org. Chem. 42, 1914 (1977); enantioselective synthesis: A. R. Maguire et al., Synlett 2001, 41. 13C-NMR study: A. W. Douglas, Can. J. Chem. 56, 2129 (1978). Metabolism and disposition: H. B. Hucker et al., Drug Metab. Dispos. 1, 721 (1973). HPLC determn in biological fluids: D. G. Musson et al., J. Pharm. Sci. 73, 1270 (1984). Book: Current Concepts on Anti-inflammatory Drugs, K. Miehlke, Ed. (Biomedical Information Corp., New York, 1980) 240 pp. Review of pharmacology and efficacy in rheumatic disease: R. N. Brogden et al., Drugs 16, 97-114 (1978); in treatment of colorectal polyps: F. Tonelli et al., Dig. Dis. 12, 259-264 (1994). Review of clinical pharmacokinetics: N. M. Davies, M. S. Watson, Clin. Pharmcokinet. 32, 437-459 (1997).
Properties: Yellow odorless crystals from ethyl acetate, mp 182-185° (dec). uv max (methanolic 0.1N HCl): 327, 285, 256, 226 nm (E1%1cm 375, 420, 410, 540). pKa (25°) 4.7.
Sparingly sol in methanol, U.S.P. alcohol; slightly sol in ethyl acetate. Practically insol in water at pH <4.5. Soly increases with rising pH to ~3.0 mg/ml at pH 7. Stable in aq acid and base. Solid stable for at least three days in air at 100°.
Melting point: mp 182-185° (dec)
pKa: pKa (25°) 4.7
Absorption maximum: uv max (methanolic 0.1N HCl): 327, 285, 256, 226 nm (E1%1cm 375, 420, 410, 540)
Therap-Cat: Anti-inflammatory.

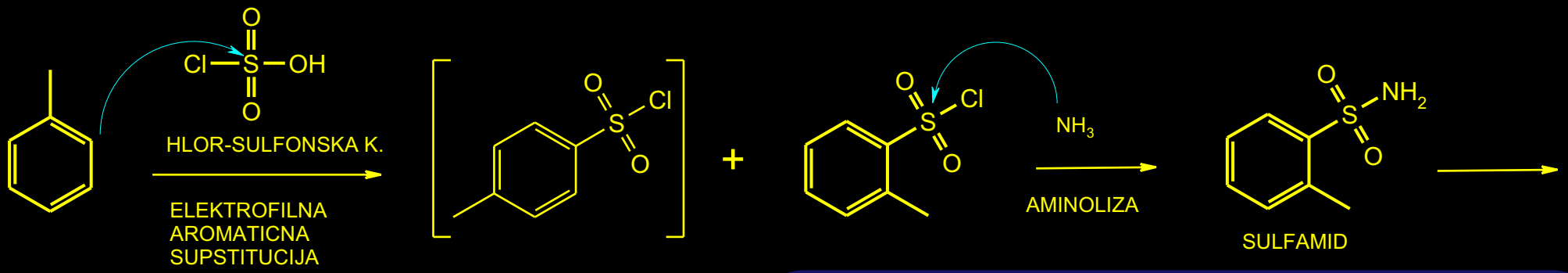
NE-STEROIDNI ANALGETICI 7. OKSIKAMI (OXICAME)

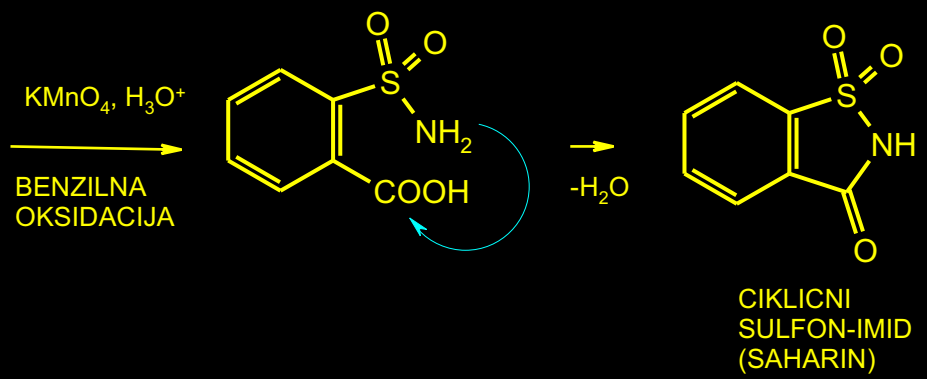
PRIMERI: PYROXICAM, ISOXYCAM

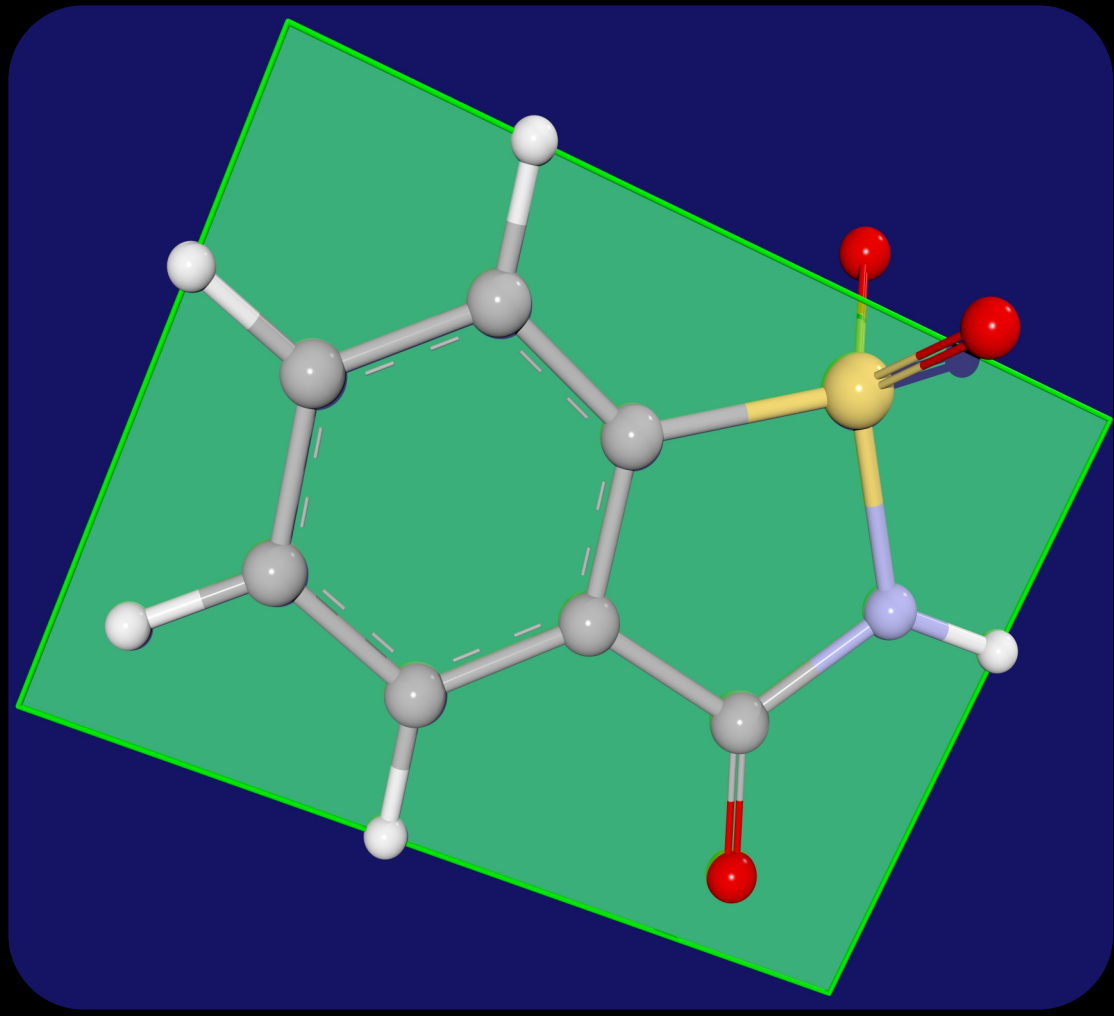


NE-STEROIDNI ANALGETICI 7. OKSIKAMI - DERIVATI SAHARINA

SINTEZA SAHARINA (METODA I)

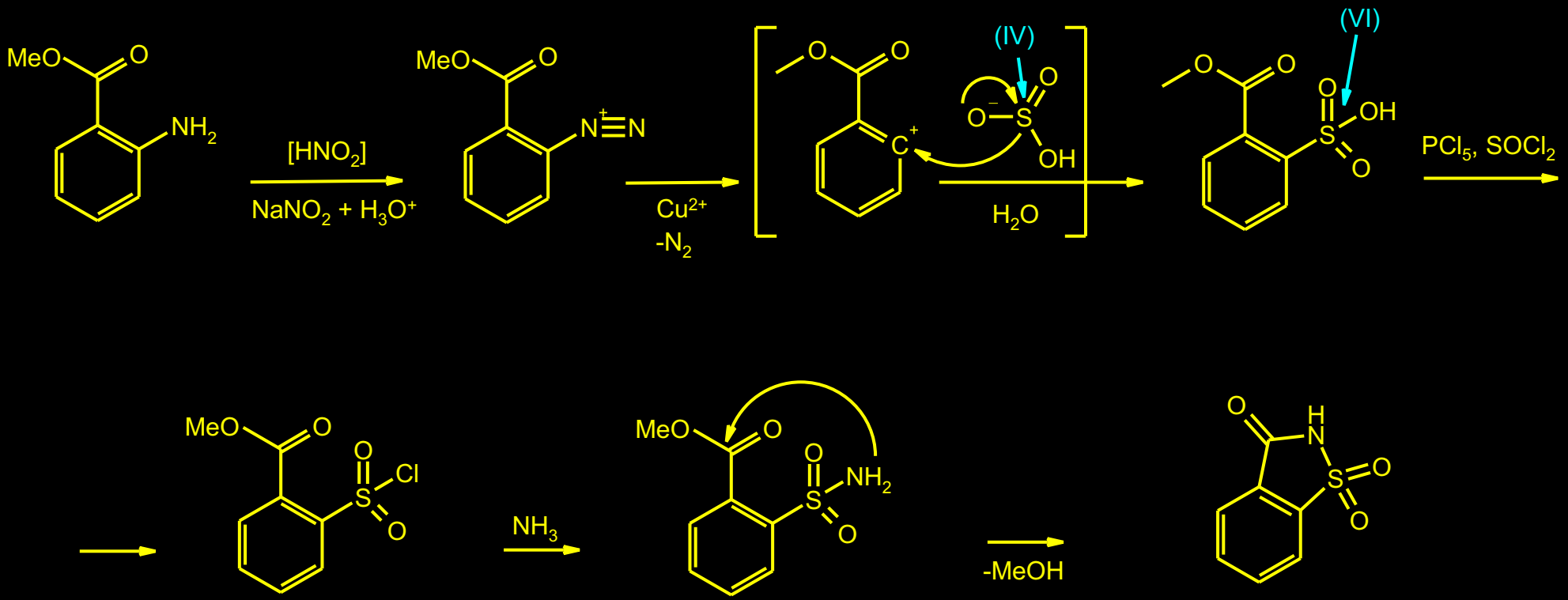






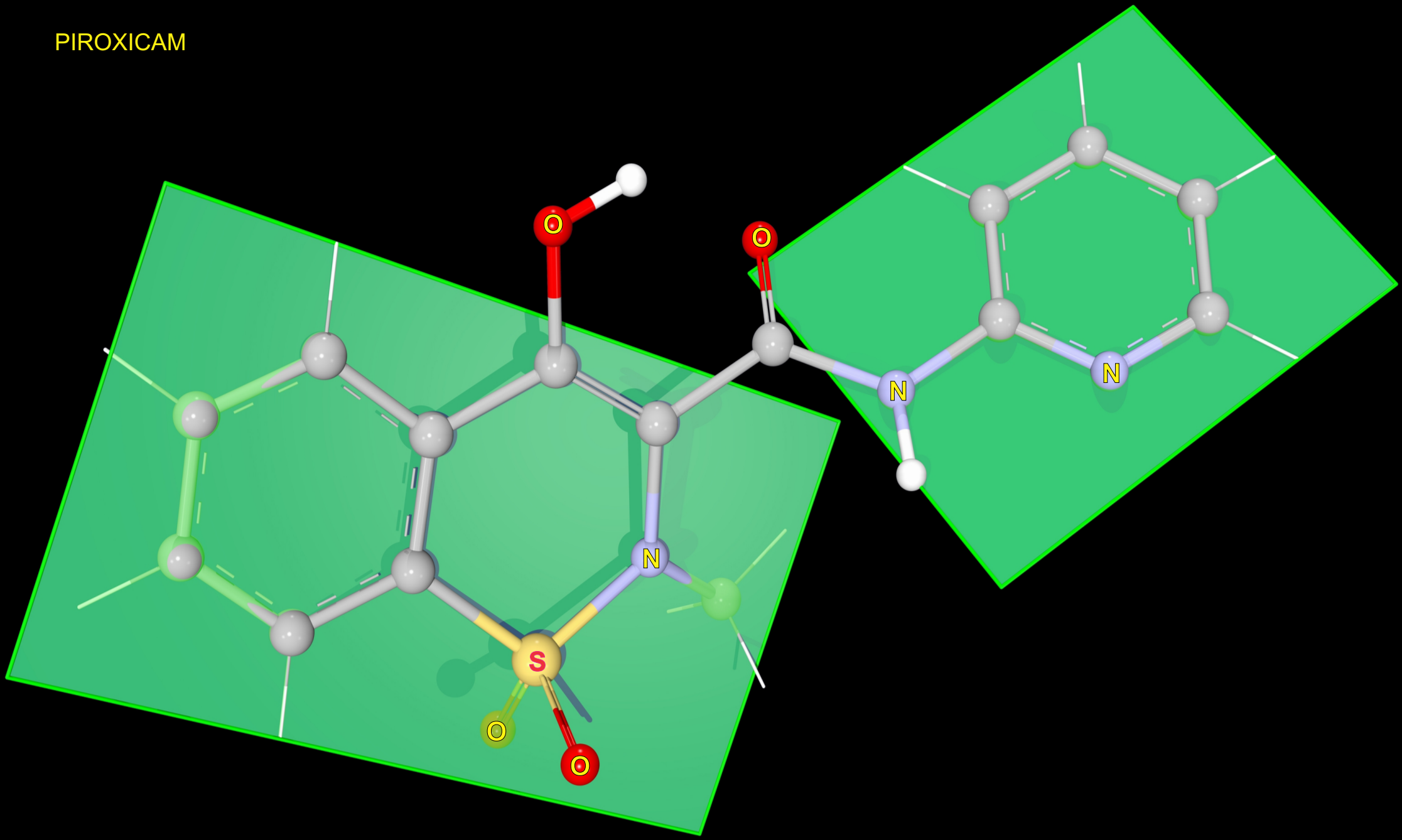
NE-STEROIDNI ANALGETICI 7. OKSIKAMI - DERIVATI SAHARINA

SINTEZA SAHARINA (METODA II)



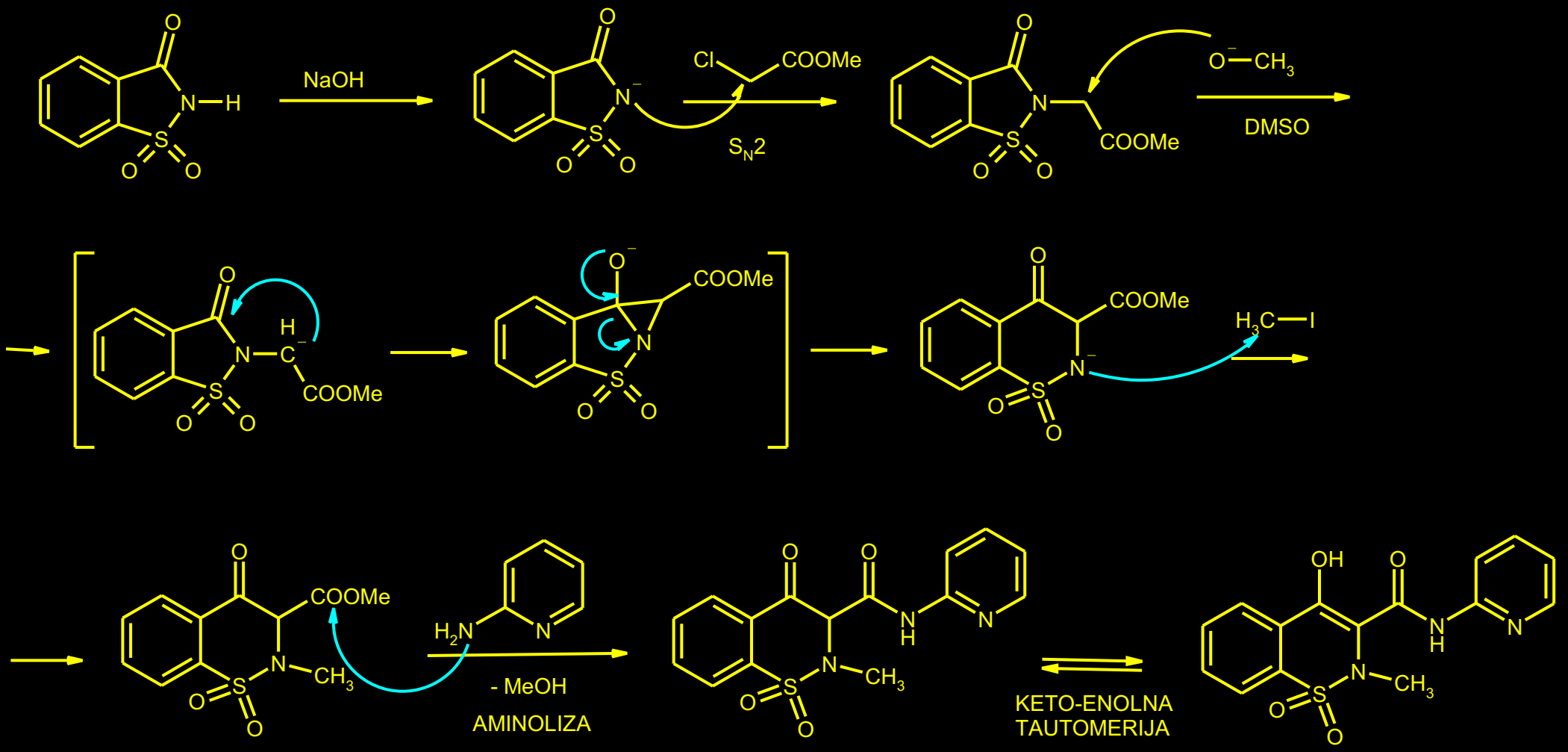
NE-STEROIDNI ANALGETICI 7. OKSIKAMI - DERIVATI SAHARINA

PIROXICAM



NE-STEROIDNI ANALGETICI 7. OKSIKAMI - DERIVATI SAHARINA

SINTEZA PIROXICAM-a



Monograph Number: 7589
Title: Piroxicam
CAS Registry Number: 36322-90-4
CAS Name: 4-Hydroxy-2-methyl-N-2-pyridinyl-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide
Additional Names: 3,4-dihydro-2-methyl-4-oxo-N-2-pyridyl-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide
Manufacturers' Codes: CP-16171
Trademarks: Artroxicam (Coli); Baxo (Toyama); Bruxicam (Bruschettini); Caliment (Apotex); Erazon (Krka); Feldene (Pfizer); Flogobene (Farge); Geldene (Pfizer); Improntal (Kabi); Larapam (Lagap); Pirkam (DAK); Piroflex (Lagap); Reudene (ABC); Riacen (Chiesi); Roxicam (Gramon); Roxiden (Pulitzer); Sasulen (Andreu); Solocalm (Microsules); Zunden (Luitpold)
Molecular Formula: C15H13N3O4S
Molecular Weight: 331.35.
Percent Composition: C 54.37%, H 3.95%, N 12.68%, O 19.31%, S 9.68%
Literature References: Non-steroidal anti-inflammatory with long half-life. Prepn (keto form): J. Lombardino, DE 1943265; idem, US 3591584 (1970, 1971 to Pfizer). Synthesis and biological properties: J. Lombardino, E. Wiseman, J. Med. Chem. 15, 848 (1972); J. Lombardino et al., ibid. 16, 493 (1973). Pharmacology: E. Wiseman et al., Arzneimittel-Forsch. 26, 1300 (1976). Evaluation of ulcerogenic effects in comparison with droxicam, q.v.: G. Palacios et al., Method Find. Exp. Clin. Pharmacol. 9, 353 (1987). Clinical pharmacology: L. Martinez et al., ibid. 10, 729 (1988). Review: eidem, in Pharmacological and Biochemical Properties of Drug Substances vol. 3, M. E. Goldberg, Ed. (Am. Pharm. Assoc., Washington, DC, 1981) pp 324-346. Review of pharmacology and therapeutic efficacy: R. N. Brogden et al., Drugs 22, 165-187 (1981); eidem, ibid. 28, 292-323 (1984). Symposium on clinical efficacy and safety: Am. J. Med. 81, Suppl. 5B, 1-55 (1986). Comprehensive description: M. Mihalic et al., Anal. Profiles Drug Subs. 15, 509-531 (1986).
Properties: Crystals from methanol, mp 198-200°. pKa 6.3 (2:1 dioxane-water). LD50 orally in mice: 360 mg/kg (Wiseman).
Melting point: mp 198-200°
pKa: pKa 6.3 (2:1 dioxane-water)
Toxicity data: LD50 orally in mice: 360 mg/kg (Wiseman)

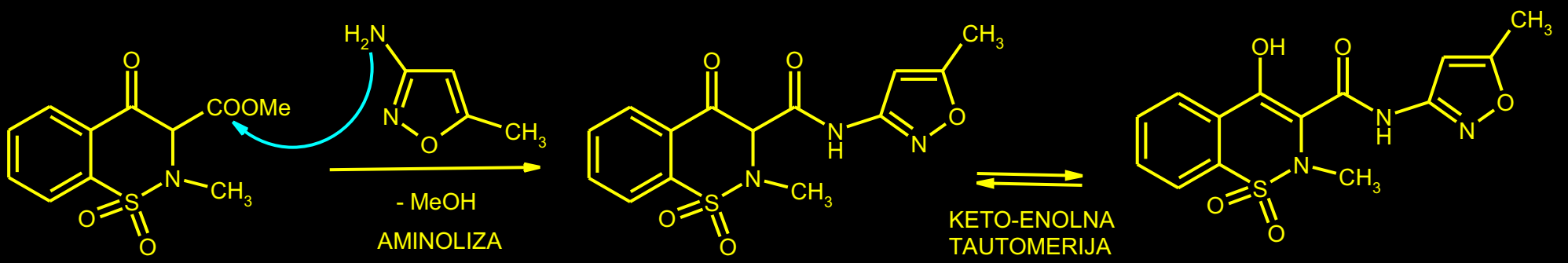
Derivative Type: Cinnamic acid ester
CAS Registry Number: 87234-24-0
Additional Names: Piroxicam cinnamate; cinnoxicam
Manufacturers' Codes: SPA-S-510
Trademarks: Sinartrol (SPA); Zelis (Proter); Zen (Prophin)
Molecular Formula: C24H19N3O5S
Molecular Weight: 461.50.
Percent Composition: C 62.46%, H 4.15%, N 9.11%, O 17.33%, S 6.95%

Derivative Type: Compd with □ -cyclodextrin
CAS Registry Number: 121696-62-6
Trademarks: Brexin (Chiesi); Cicladol (Master); Cycladol (Promedica)
Molecular Formula: C57H83N3O39S
Molecular Weight: 1466.34.
Percent Composition: C 46.69%, H 5.71%, N 2.87%, O 42.55%, S 2.19%

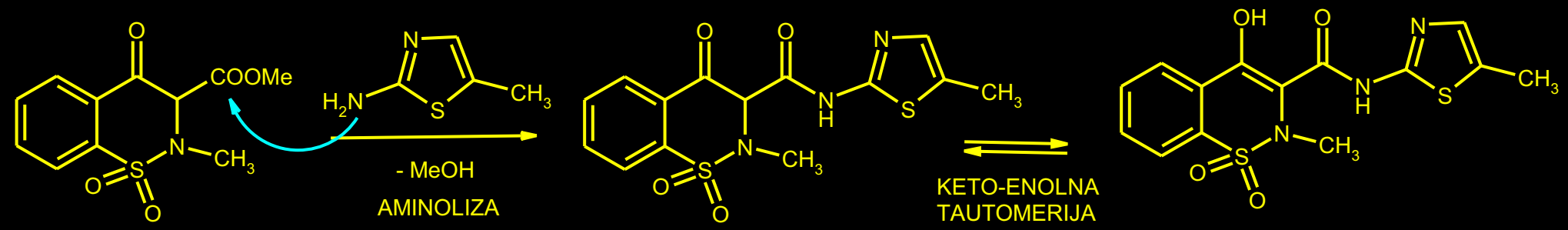
Therap-Cat: Anti-inflammatory.

NE-STEROIDNI ANALGETICI 7. OKSIKAMI - DERIVATI SAHARINA

ISOXICAM:



MELOXICAM

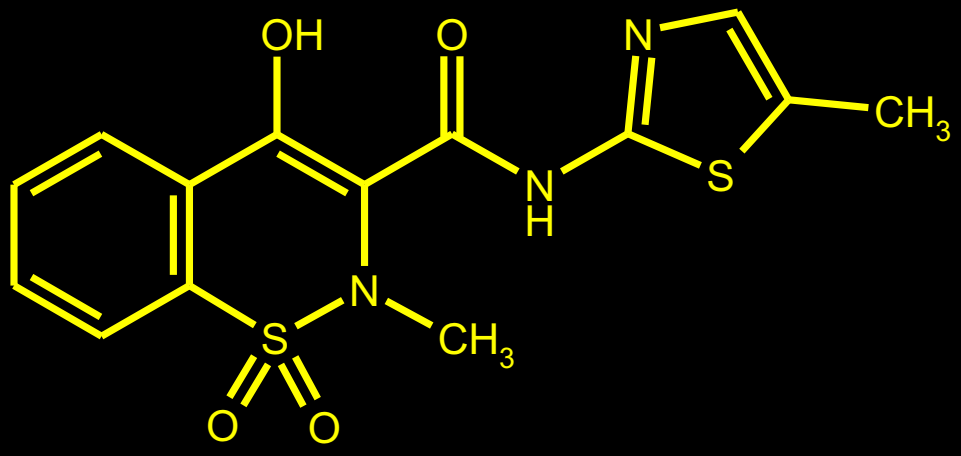


Monograph Number: 5260
Title: Isoxicam
CAS Registry Number: 34552-84-6
CAS Name: 4-Hydroxy-2-methyl-N-(5-methyl-3-isoxazolyl)-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide
Additional Names: 4-hydroxy-3-(5-methyl-3-isoxazolocarbamyl)-2-methyl-2H-1,2-benzothiazine 1,1-dioxide
Manufacturers' Codes: W-8495
Trademarks: Floxicam (Menarini); Maxicam (Parke-Davis); Pacyl (Warner-Lambert); Vectren (Warner-Lambert)
Molecular Formula: C14H13N3O5S
Molecular Weight: 335.34.
Percent Composition: C 50.14%, H 3.91%, N 12.53%, O 23.85%, S 9.56%
Literature References: Nonsteroidal anti-inflammatory drug with antipyretic and analgesic properties. Prepn: H. Zinnes et al., DE 2208351; eidem, US 3787324 (1972, 1974 both to Warner-Lambert). Anti-inflammatory properties: G. DiPasquale et al., Agents Actions 5, 256 (1975); ibid. 6, 748 (1976). Pharmacological studies: G. DiPasquale, D. Mellace, ibid. 7, 481 (1977); K. Rainsford, ibid. 573; G. DiPasquale et al., Res. Commun. Chem. Pathol. Pharmacol. 19, 529 (1978). Pharmacokinetics in man: E. U. Kölle et al., Arzneimittel-Forsch. 33, 582 (1983). Series of articles on pharmacology, safety and clinical efficacy: Am. J. Med. 79, Suppl. 4B, 1-42 (1985); Brit J. Clin. Pharmacol. 22, Suppl. 2, 107S-190S (1986). Review: Semin. Arthritis Rheum. 12, Suppl. 2, 153-183 (1982).
Properties: Crystals from 1,4-dioxane, mp 265-271° (dec).
Melting point: mp 265-271° (dec)

Derivative Type: Sodium salt
Molecular Formula: C14H12N3NaO5S
Molecular Weight: 357.32.
Percent Composition: C 47.06%, H 3.39%, N 11.76%, Na 6.43%, O 22.39%, S 8.97%
Properties: Crystals from ethanol. mp 270-272° (dec).
Melting point: mp 270-272° (dec)

Therap-Cat: Anti-inflammatory.

NE-STEROIDNI ANALGETICI 7. OKSIKAMI - DERIVATI SAHARINA



Monograph Number: 5848
Title: Meloxicam
CAS Registry Number: 71125-38-7
CAS Name: 4-Hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide
Trademarks: Metacam (Boehringer, Ing.); Mobic (Boehringer, Ing.)
Molecular Formula: C14H13N3O4S2
Molecular Weight: 351.41.
Percent Composition: C 47.85%, H 3.73%, N 11.96%, O 18.21%, S 18.25%
Literature References: Cyclooxygenase (COX-2) inhibitor. Prepn: G. Trummlitz et al., DE 2756113 (1979 to Thomae); eidem, US 4233299 (1980 to Boehringer Ingelheim). Pharmacology in horses: P. Lees et al., Brit. Vet. J. 147, 97 (1991). Physicochemical properties: R.-S. Tsai et al., Helv. Chim. Acta 76, 842 (1993). Veterinary trial in dogs: A. J. Henderson et al., Prakt. Tierarzt. 75, 179 (1994). Series of articles on pharmacology, mechanism of action and clinical efficacy: Brit. J. Rheumatol. 35, Suppl. 1, 1-77 (1996). Clinical trials of GI tolerability in arthritis: C. Hawkey et al., ibid. 37, 937 (1998); J. Dequeker et al., ibid. 946.
Properties: Crystals from ethylene chloride, mp 254° (dec). pKa: 4.08 in water; 4.24 ± 0.01 in water/ethanol (1:1); 4.63 ± 0.03 in water/ethanol (1:4). Log P (octanol/water): 3.02. LD50 orally in mice: 470 mg/kg (Trummlitz, 1980).
Melting point: mp 254° (dec)
pKa: pKa: 4.08 in water; 4.24 ± 0.01 in water/ethanol (1:1); 4.63 ± 0.03 in water/ethanol (1:4)
Log P: Log P (octanol/water): 3.02
Toxicity data: LD50 orally in mice: 470 mg/kg (Trummlitz, 1980)
Therap-Cat: Anti-inflammatory.
Therap-Cat-Vet: Anti-inflammatory.

NE-STEROIDNI ANALGETICI - SELEKTIVNI COX-2 INHIBITORI - POTENCIJALNO OPASNI KOD HRONIČNE PRIMENE

ROFECOXIB - POVUČEN SA TRŽIŠTA !!!