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Medizinische Chemie
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Antibacterials: Focus on Quinolones

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Table 1. The major groups of pathogenic bacteria

Morphological type	Family	Genus	Gram stain	Oxygen utilization *
Cocci	Micrococcaceae	<i>Micrococcus</i>	+	A
		<i>Staphylococcus</i>	+	A/F – AN
	Streptococcaceae	<i>Streptococcus</i>	+	F – AN
	Peptococcaceae	<i>Peptococcus</i>	+	AN
		<i>Peptostreptococcus</i>	+	AN
	Neisseriaceae	<i>Neisseria</i>	–	A
Veillonellaceae	<i>Veillonella</i>	–	AN	
Rods	Enterobacteriaceae	<i>Escherichia</i>	–	F – AN
		<i>Shigella</i>	–	F – AN
		<i>Salmonella</i>	–	F – AN
		<i>Citrobacter</i>	–	F – AN
		<i>Klebsiella</i>	–	F – AN
		<i>Enterobacter</i>	–	F – AN
		<i>Ersinia</i>	–	F – AN
		<i>Serratia</i>	–	F – AN
		<i>Hafnia</i>	–	F – AN
		<i>Edwardsiella</i>	–	F – AN
		<i>Proteus</i>	–	F – AN
		<i>Providencia</i>	–	F – AN
		<i>Morganella</i>	–	F – AN
		<i>Yersinia</i>	–	F – AN
		Vibrionaceae	<i>Vibrio</i>	–
	Pasteurellaceae	<i>Aeromonas</i>	–	F – AN
		<i>Pasteurella</i>	–	F – AN
	Pseudomonadaceae	<i>Haemophilus</i>	–	F – AN
		<i>Pseudomonas</i>	–	A
	Legionellaceae	<i>Legionella</i>	–	A
	Neisseriaceae	<i>Moraxella</i>	–	A
		<i>Acinetobacter</i>	–	A
		<i>Brucella</i>	–	A
		<i>Bordetella</i>	–	A
	Bacteroidaceae	<i>Bacteroides</i>	–	AN
		<i>Fusobacterium</i>	–	AN
<i>Leptotricha</i>		–	AN	
Bacillaceae	<i>Bacillus</i>	+	AN	
	<i>Clostridium</i>	+	AN	
	<i>Listeria</i>	+	A	
	<i>Erysipelothrix</i>	+	A	

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Morphological type	Family	Genus	Gram stain	Oxygen utilization*	
Actinomycetes and related organisms	Propionibacteriaceae	<i>Corynebacterium</i>	+	A/F – AN	
		<i>Propionibacterium</i>	+	AN	
		<i>Eubacterium</i>	+	AN	
	Actinomycetaceae	<i>Actinomyces</i>	+	FA	
	Mycobacteriaceae	<i>Mycobacterium</i>	+	A	
	Nocardiaceae	<i>Nocardia</i>	+	A	
Rickettsias and Chlamydias	Rickettsiaceae	<i>Rickettsia</i>	–	P	
		<i>Coxiella</i>	–	P	
	Bartonellaceae	<i>Bartonella</i>	–	P	
	Anaplasmataceae	<i>Grahamella</i>	–	P	
		<i>Anaplasma</i>	NR**	P	
	Chlamydiaceae	<i>Haemobartonella</i>	–	P	
		<i>Eperythrozoon</i>	–	P	
		<i>Chlamydia</i>	–	P	
	Mycoplasmas	Mycoplasmataceae	<i>Mycoplasma</i>	–	FA
			<i>Ureaplasma</i>	–	FA
Acholeplasmataceae		<i>Acholeplasma</i>	NR**	FA	
Spirochetes	Spirochaetaceae	<i>Treponema</i>	–	AN	
		<i>Borrelia</i>	–	AN	
		<i>Leptospira</i>		A	

* A = Aerobic; AN = Anaerobic; F – AN = Facultative anaerobic; A/F – AN = Aerobic or facultative anaerobic growth;
P = Parasitic usually require host cells for growth.
** NR = Gram stain not revealed.

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Classification of Antibiotics 1

1. β -Lactame

1. Natural Penicillins (Penicillin G)
2. Semisynthetic Penicillins
 1. Oxacillin, Ampicillin, Amoxicillin
3. Natural Cephalosporins: Cephalosporin C
4. Semisynthetic Cephalosporin: Cephalexin
5. Cephamycine: 7 α -methoxy-C.
6. 1-Oxacephems
7. Clavulanic Acid
8. Peneme
9. Carbapeneme
10. Nocardicine
11. Monobactams

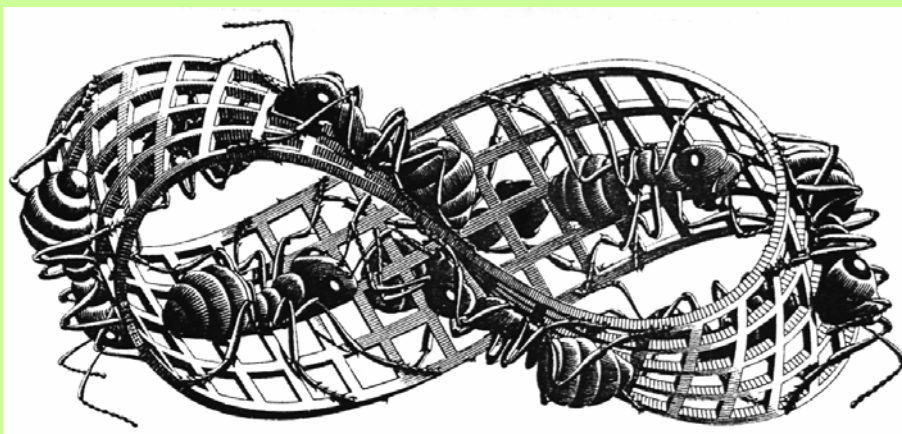
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Klassifikation der Antibiotika 2

2. Tetracyclins
3. Aminoglycosides
4. Nucleosides
 1. N-Nucleosides
 2. C-Nucleosides
 3. Carbocyclic Nucleosides
5. Macrolides
 1. 12-membered
 2. 14-membered
 3. 16-membered
6. Ansamycine
7. Peptides: Bleomycine
8. Various others

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A Model of DNA



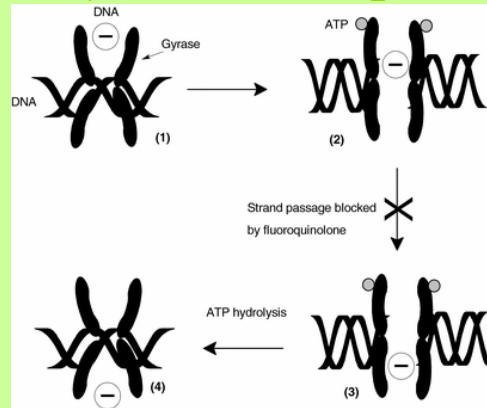
Martin Escher

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Web Link: Mechanism of Action of Quinolones

<http://www.baytril.com/index.cfm/page/8>

http://www.medscape.com/viewarticle/418293_3



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Quinolones

- The first and only fully synthetic antibiotics

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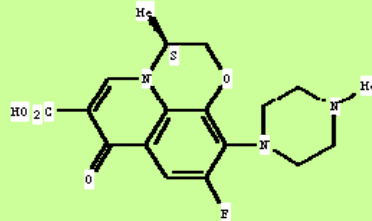
4th Gen. Quinolones

Agent

Levofloxacin^(S, R, 7)

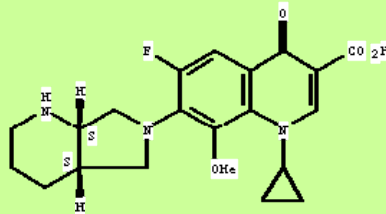
Topoisomerase

Topoisomerase IV



Moxifloxacin^(R)

DNA gyrase

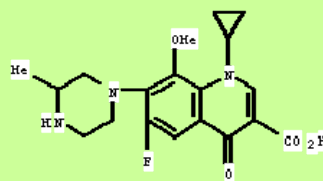


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4th Gen. Quinolones

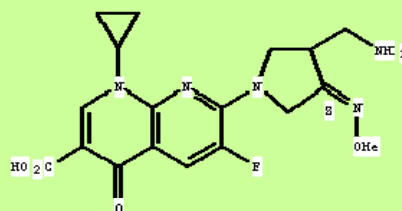
Gatifloxacin^(R, R, 4)

DNA gyrase



Gemifloxacin^{(7), (R)}

Topoisomerase IV⁽⁷⁾

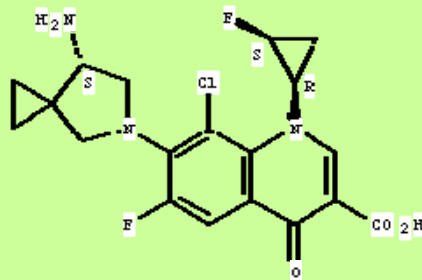


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4th Gen. Quinolones: Sitafloxacin

Sitafloxacin®
9. 03

Both



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DNA-Supercoiling

Creates torsional tension

Eucarionten:

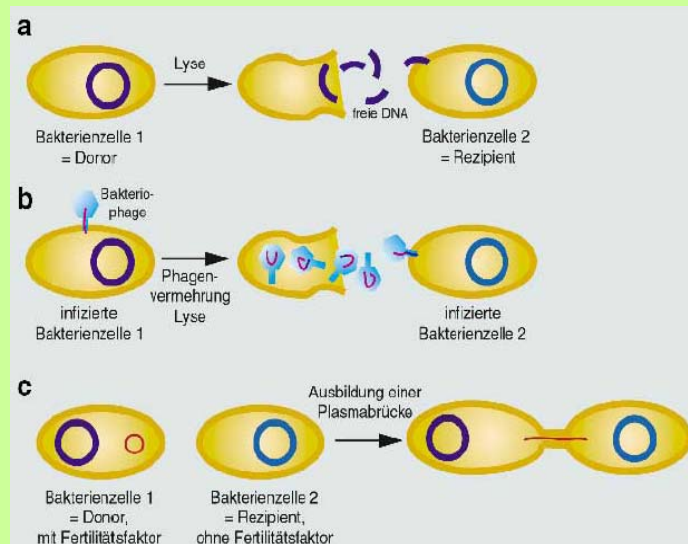
Folding and coiling of DNA via DNA-histon-complex -> chromosome

Procarionten:

Activation for:

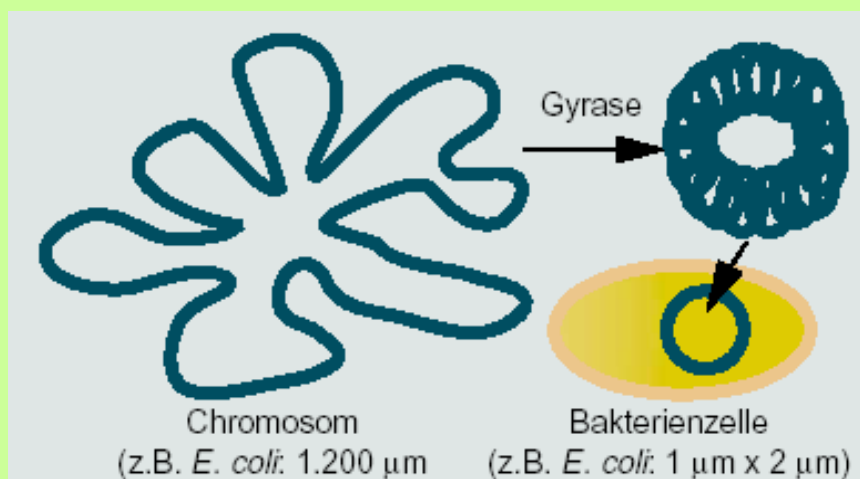
- Replikation
- Transkription
- Recombination

Genes can be transferred between bacteria



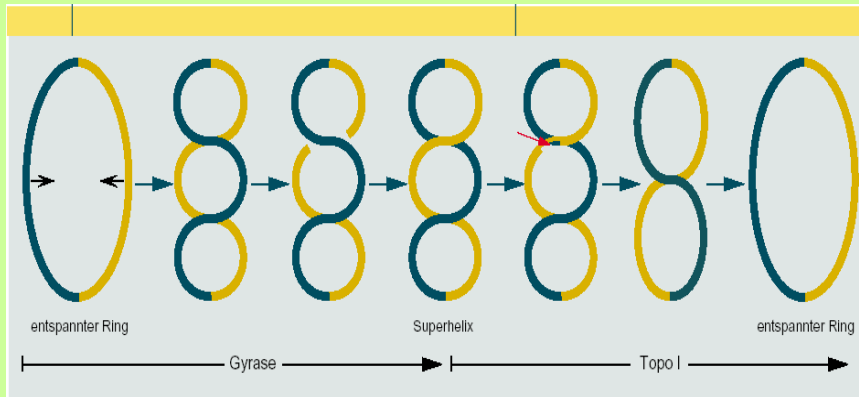
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Packing of cyclic bacterial DNA



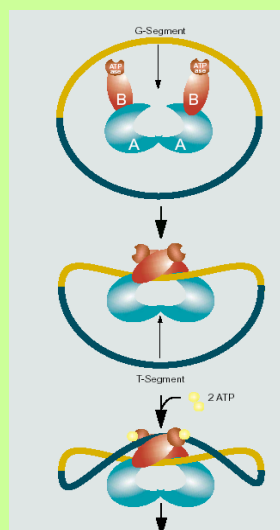
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Wirkung der Gyrase bzw. Topoisomerase I



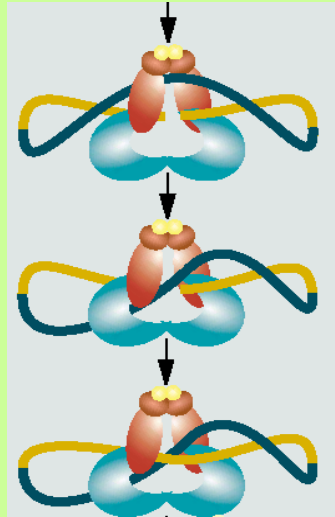
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Reaktion der Typ II-Topoisomerase



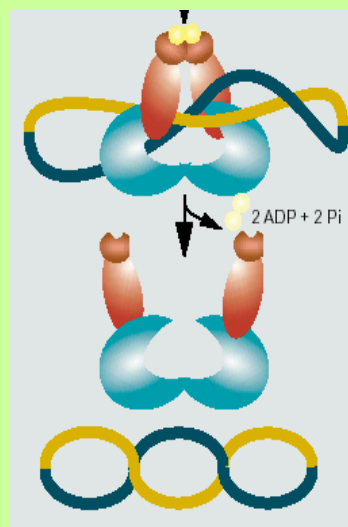
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Reaktion der Typ II- Topoisomerase



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Reaktion der Typ II- Topoisomerase



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Spaltsequenz der Gyrase



R = Purinbase

Y = Pyrimidinbase

N = jedes Nukleotid möglich

[] = seltener vorhandenes Nukleotid

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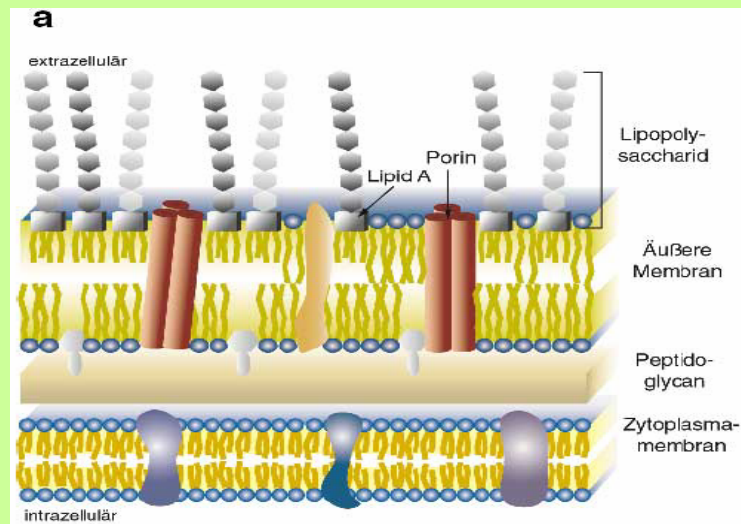
Internet-Links

Protein Datenbank: <http://www.expasy.org/>

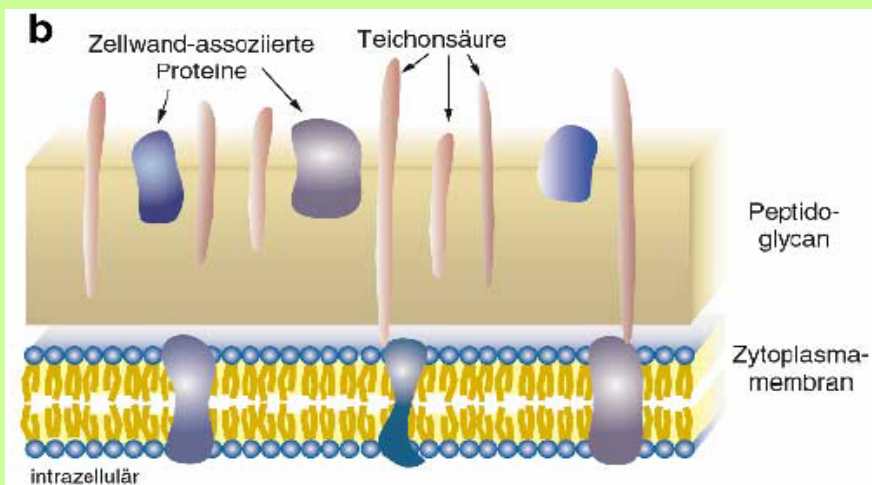
National Center for Biotechnology
Information <http://www.ncbi.nlm.nih.gov/>

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Zellwand Gram-negativer Eubakterien



Zellwand Gram-positiver Eubakterien

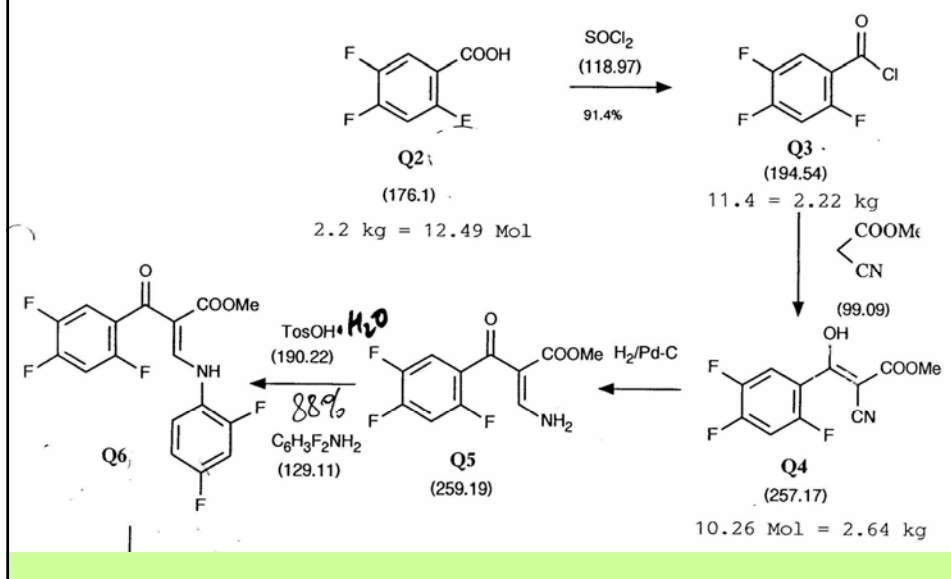


Einteilung der Topoisomerasen

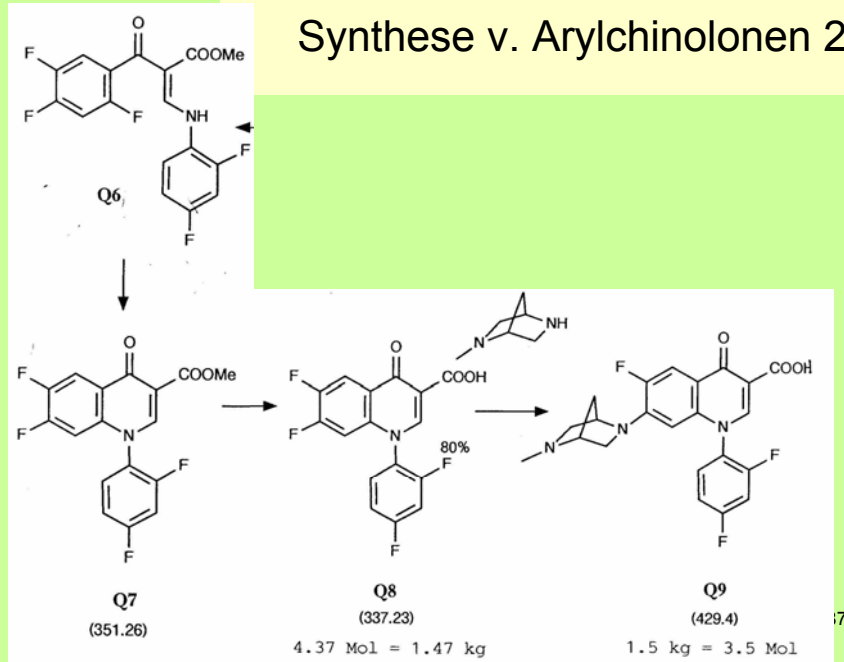
Klassifizierung	Struktur	Wichtigste Reaktion
Typ-I-Topoisomerase		
Bakterien	Topoisomerase I	eine Untereinheit
	Topoisomerase III	eine Untereinheit
Eukaryonten	Topoisomerase I	eine Untereinheit
	Topoisomerase III (Isoenzyme α mit 2 Isoformen und β mit 3 Isoformen)	eine Untereinheit
Typ-II-Topoisomerase (ATP-abhängig)		
Bakterien	Topoisomerase II (Gyrase)	Tetramer aus 2 GyrA- und 2 GyrB-Untereinheiten
	Topoisomerase IV	Tetramer aus 2 ParC- und 2 ParE-Untereinheiten
Eukaryonten	Topoisomerase II (Isoenzyme α und β mit 2 Isoformen)	Dimer aus identischen Untereinheiten
		Relaxation negativ superhelikaler DNA

Aus: Wang, J.C.: DNA Topoisomerasen, *Annu. Rev. Biochem.*, 65 (1996), 635–692.

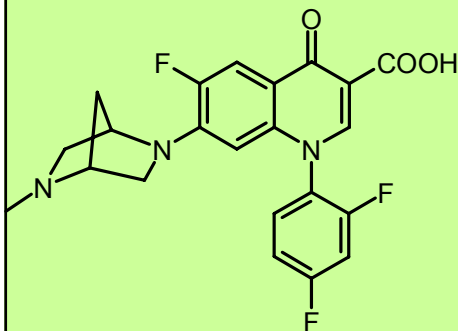
Synthese v. Arylchinolonen 1



Synthese v. Arylchinolonen 2



1991 ...



Die kg Synthese...



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1991 ...



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