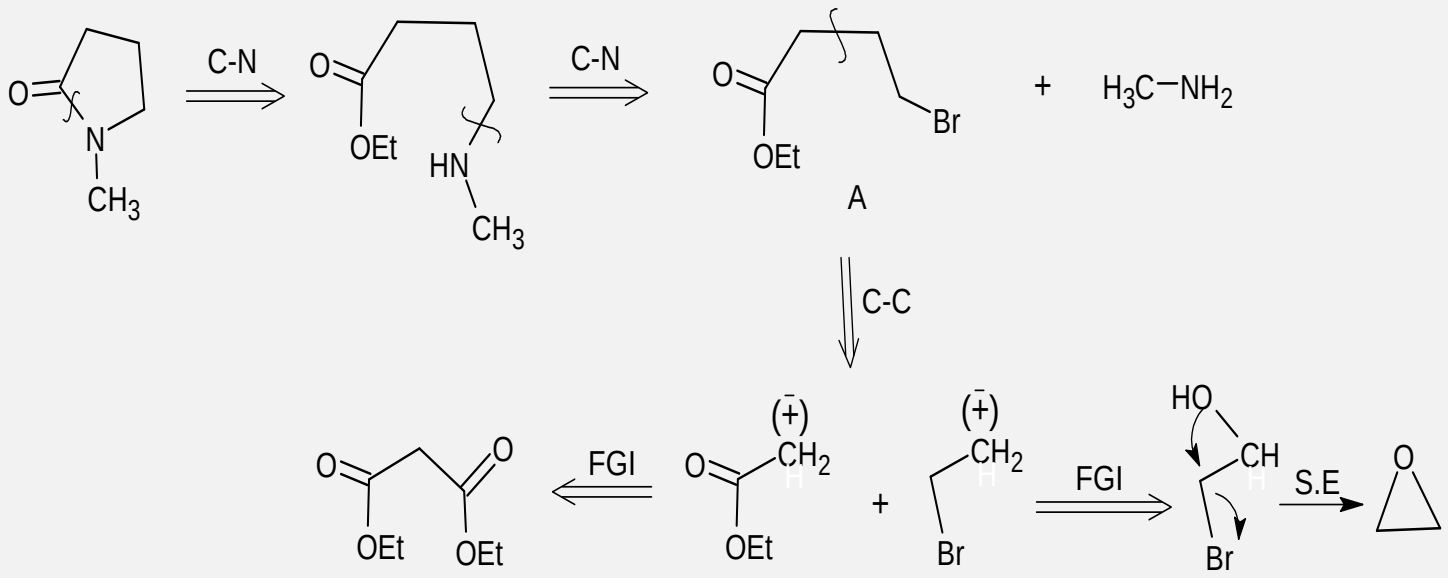
BÖLÜM 8

HETEROATOMLAR VE HETEROHALKALI (HETEROSİKLİK) BİLEŞİKLER

2. HETEROHALKALI (HETEROSİKLİK) BİLEŞİKLER

Moleküller arası (Inter-moleculer) reaksiyonlar, molekül-içi (Intra-moleculer) reaksiyonlardan hem daha hızlı hem de daha basittir. Örneğin, bir halkada C-N bağı oluşturmak için, hiçbir özel önlem almaya gerek olmadan, herhangi bir karbon elektrofili ile azot nükleofili kullanmak yeterlidir.

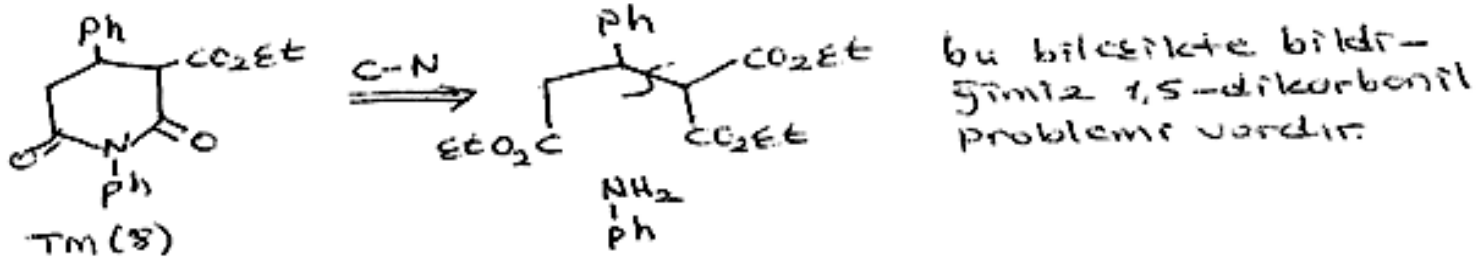
İki önemli parçalanma vardır:



Örnekler

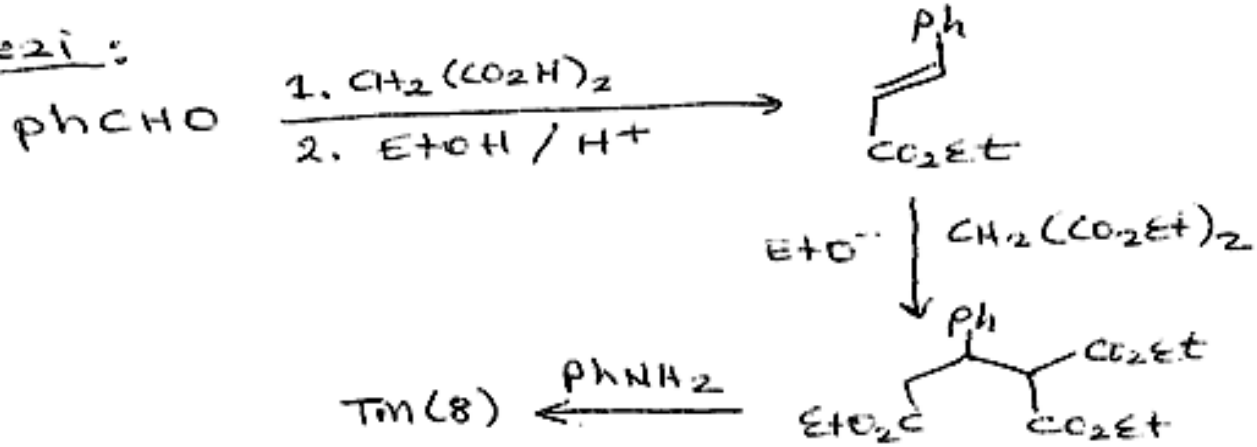
1. TM(8) bileşiğini analiz ediniz.

Analiz: Önce, her iki C–N bağı parçalanır



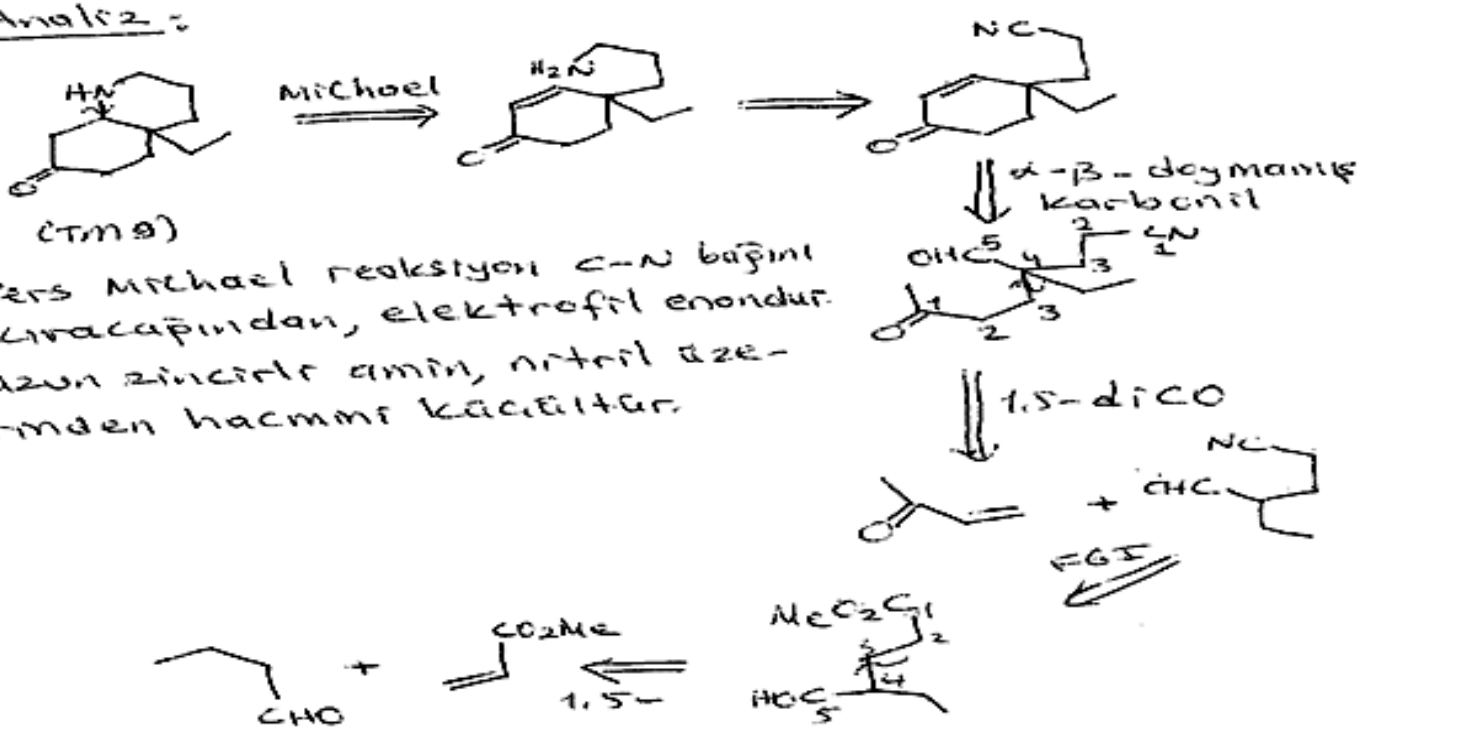
bu bileşikte bildiğimiz 1,5-dikarbonil problemi vardır.

Sentezi:



Örnek 2. TM(9) bileşiğinin sentez tasarımını yapınız.

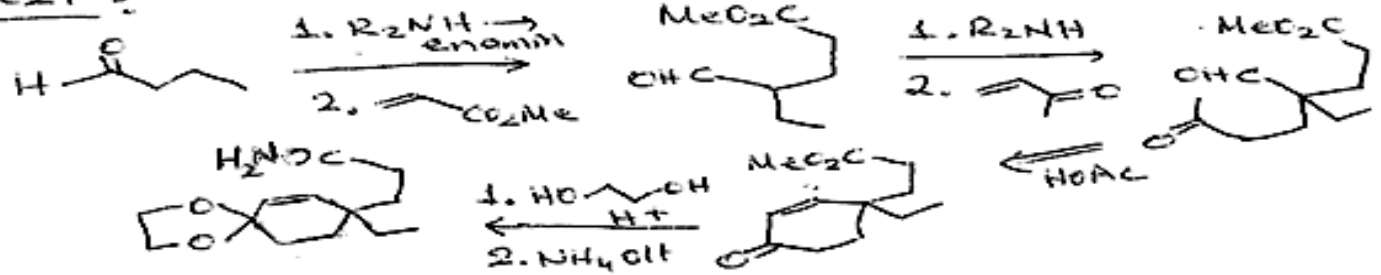
Analiz:

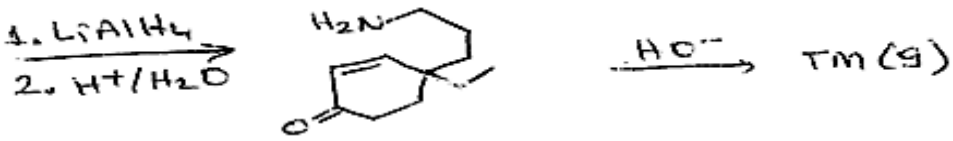


(TM9)

Ters Michael reaksiyon C–N bağını kıracağından, elektrofil enondur. Uzun zincirli amin, nitril üzerinden hacmini kaybeder.

Sentezi:

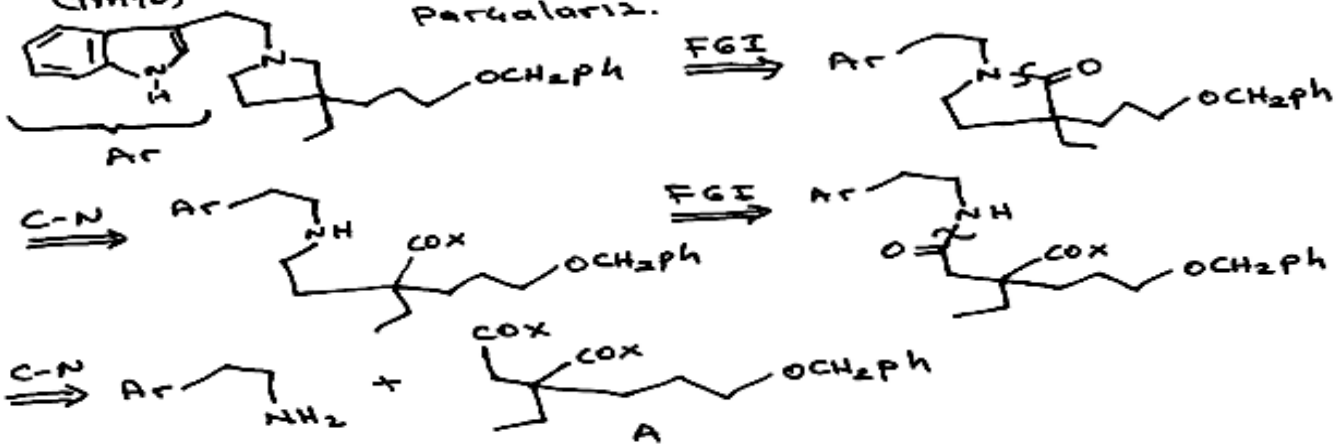




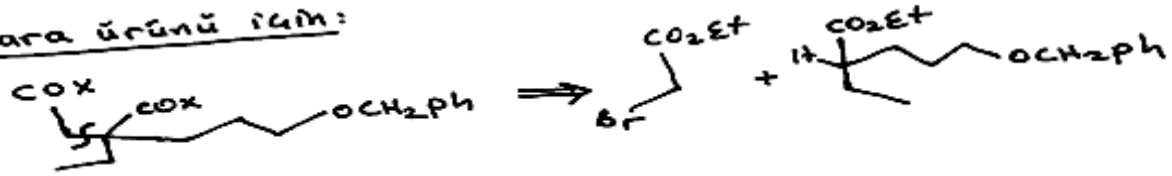
Örnek 3: Halkalaşma reaksiyonun oluşması sırasında, çok karmaşık yapılarda çok karmaşık parçalanmalar olacaktır anlamı çıkmamalıdır:
Aşağıdaki bileşiğin sentez tasarımını yapınız.

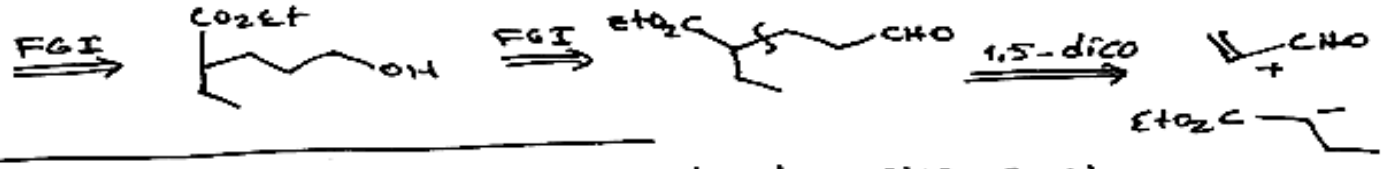
Analizi: 5 üyeli halkada (pirolidin) N atomunun her iki tarafına karbonil grubu yerleştirip, bağı parçalarız.

(TM10)

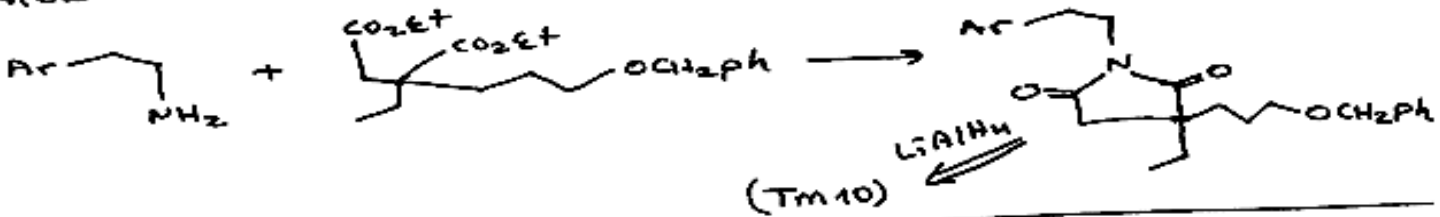


A ara ürünü için:

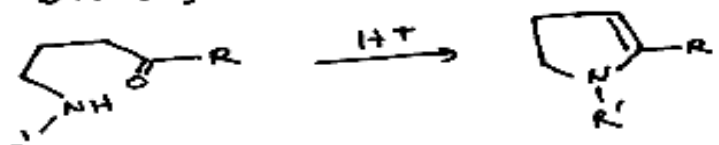




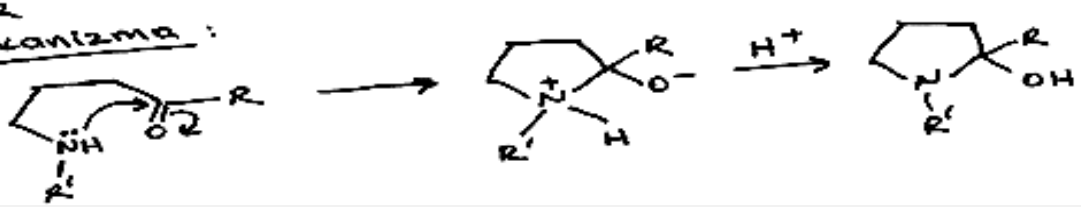
Sentez1 : X = OEt, olduğunda her iki C-N bağı oluşturma işleminin bir basamakta gerçekleştirğ literatürde (J. Amer. Chem. Soc, 1966, 88, 3656) belirtilmektedir. Aslında Sentez, umulduğundan daha basittir:

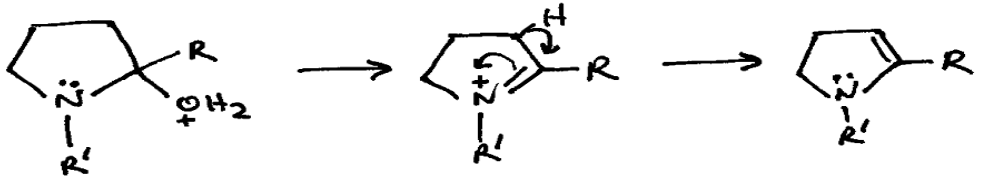


- Doymamış heterosiklik bileşiklerde uygulanabilen yararlı bir parçalanma daha vardır. Eğer, N (azot) atomu halkada bir çift bağa bağlı ise, siklik bir enamine sahip oluruz. Enamin, bir amin ve karbonil bileşiğinden elde edilebilir:

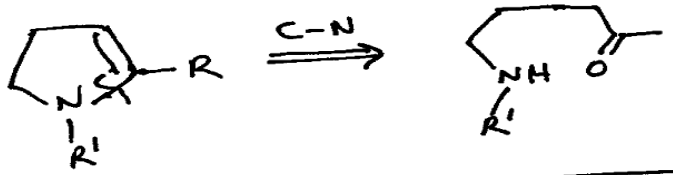


Mekanizma :



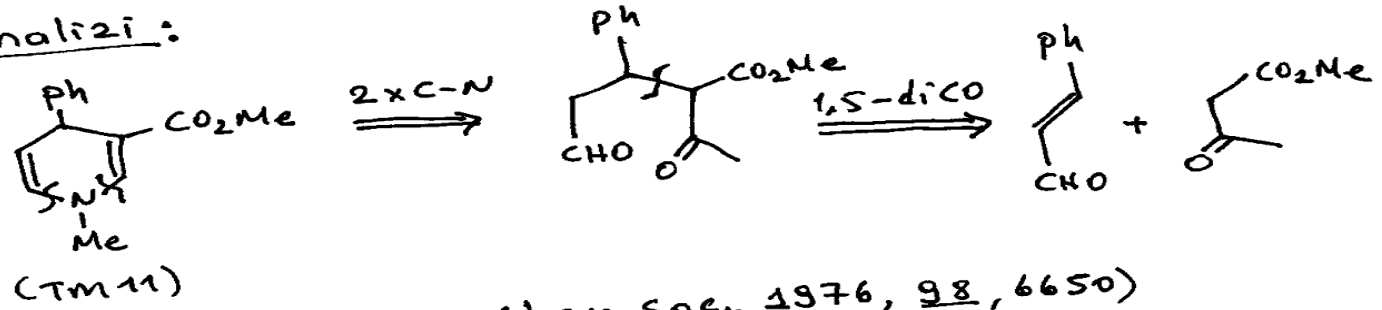


Bu reaksiyon ürününe karşı gelen parçalanma türü, C-N bağının koparılmasıdır.



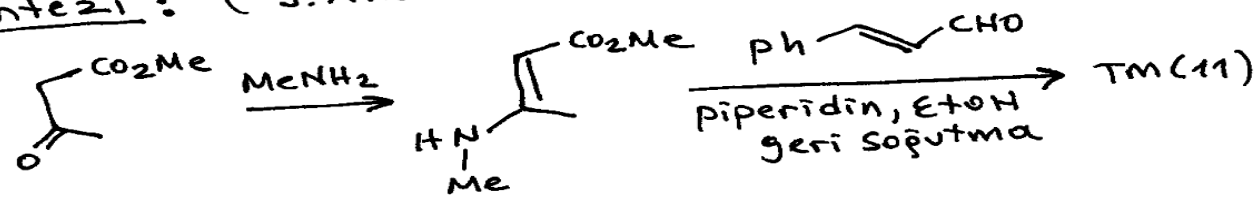
Örnek 4: TM(11) bileşiğini nasıl sentezlersiniz?

Analizi:



(TM11)

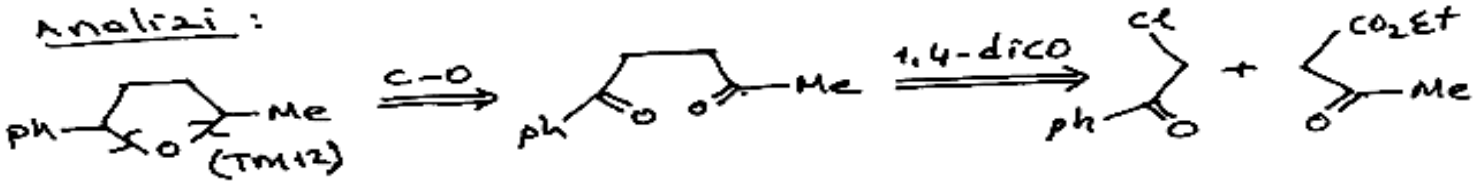
Sentezi: (J. Amer. Chem. Soc., 1976, 98, 6650)



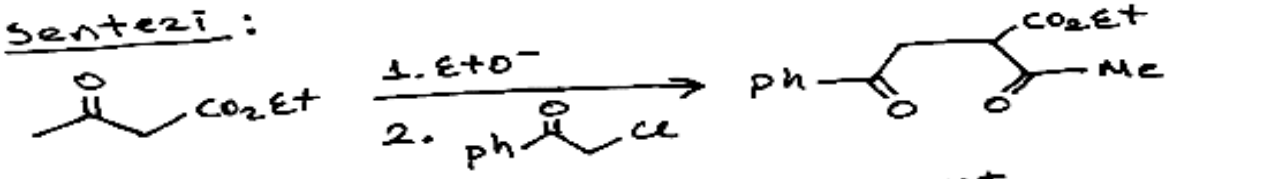
• Doymamış heterosiklik bileşiklerden çoğu, doğrudan dikarbonil bileşiklerinden elde edilebilir.

Örnek 5: TM(12) bileşiğini nasıl yaparsınız?

Analizi:

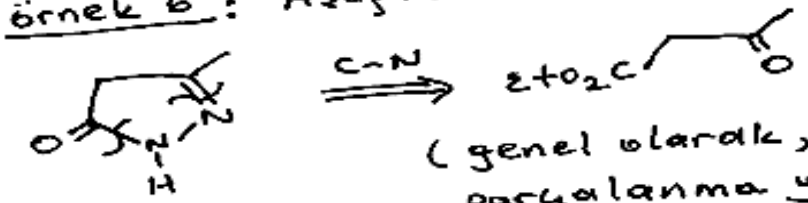


Sentezi:



• İki hetero atom içeren heterosiklik bileşiklerin parçalanması için çeşitli yollar vardır.

Örnek 6: Aşağıdaki bileşiğin analizini yapınız.

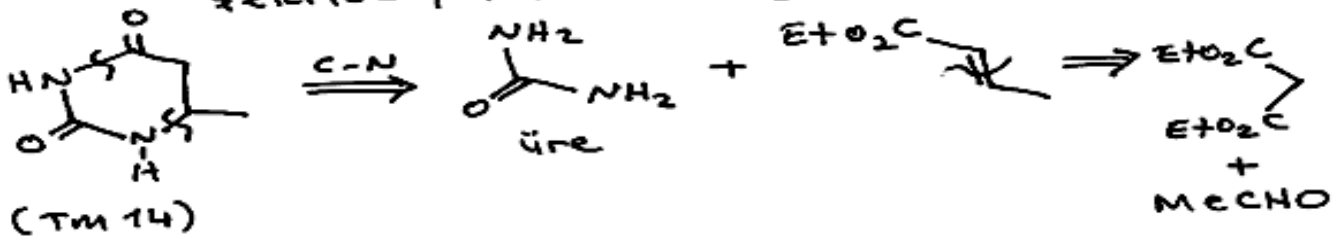


(genel olarak, hidrazin verecek parçalanma yapılır)

Sentezi: parçalanma ürünleri karıştırılarak elde edilir.

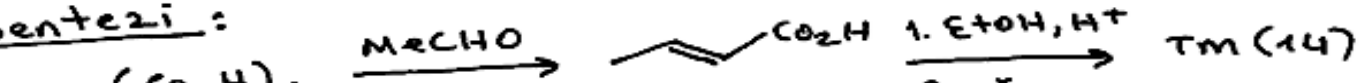
Örnek 7: TM (14) bileşiğinin sentez tasarımını yapınız.

Analizi: Basit elektrofilik parçalar oluşturu şekilde parçalanma yapılmalıdır:

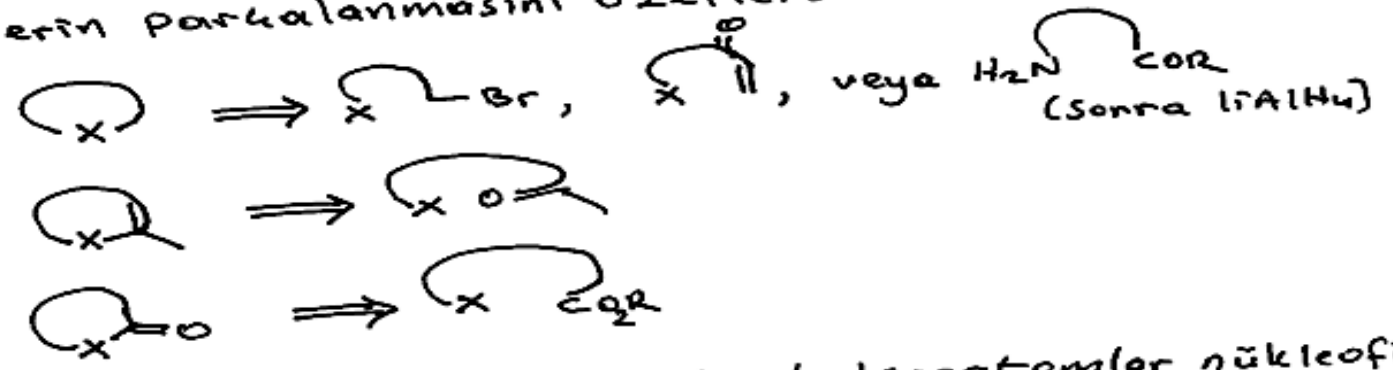


(TM 14)

Sentezi:



- Buraya kadar olan kısım için heterosiklik bileşiklerin parçalanmasını özetlersek:

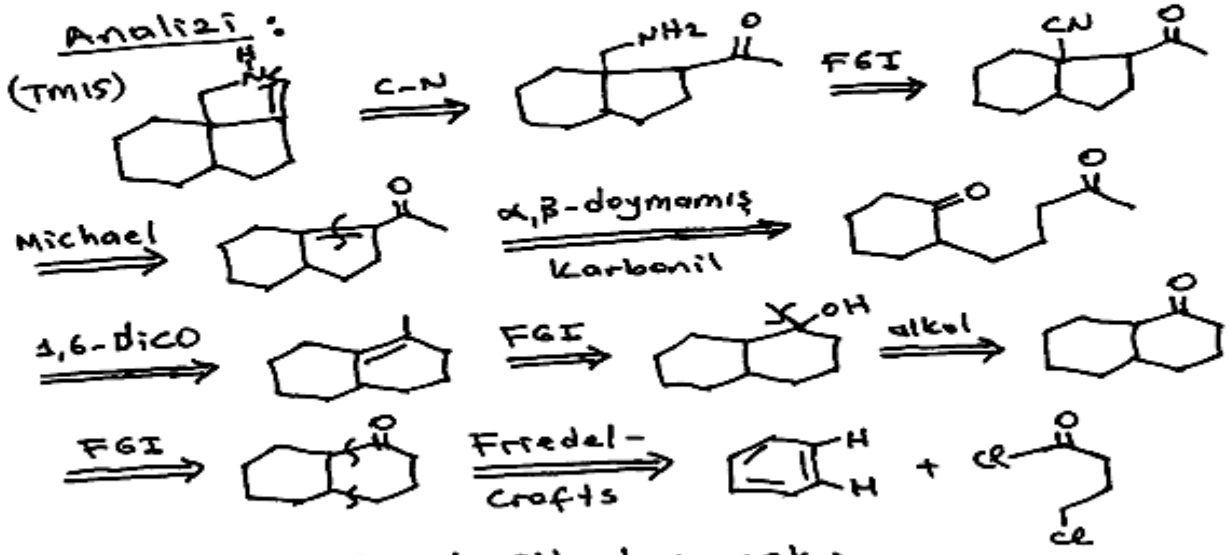


Bu reaksiyonların hepsinde heteroatomlar nükleofildir. Bunlara uygun elektrofiller seçilmelidir.

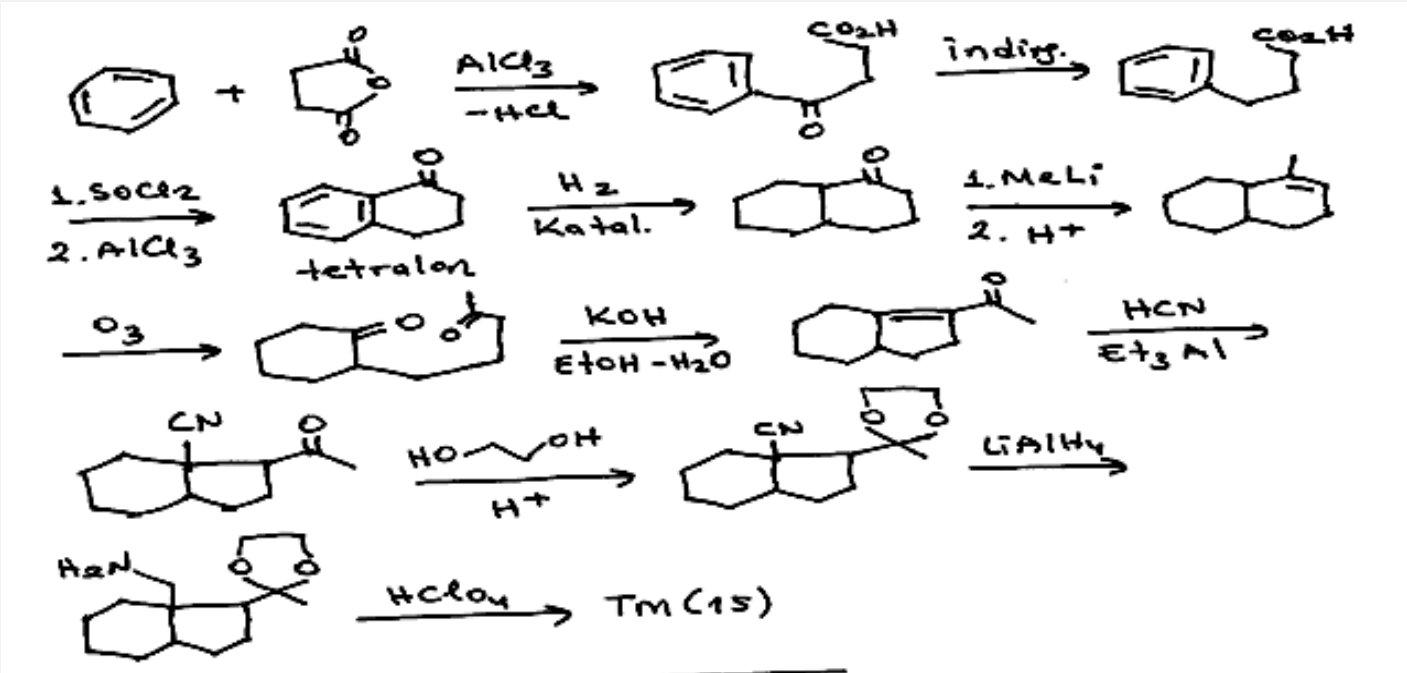
Heterosikliklerin sentezi için bir çok özel yöntemler vardır. Şimdi, heterosiklik halkada problem olabilecek moleküllerdeki parçalanmalarını gözönüne alarak örnekler üzerinde inceleyelim

Örnek 8: Basit başlangıç maddelerinden çıkarak Tm(15) bileşiğinin Sentez tasarımını yapınız.

Analizi:

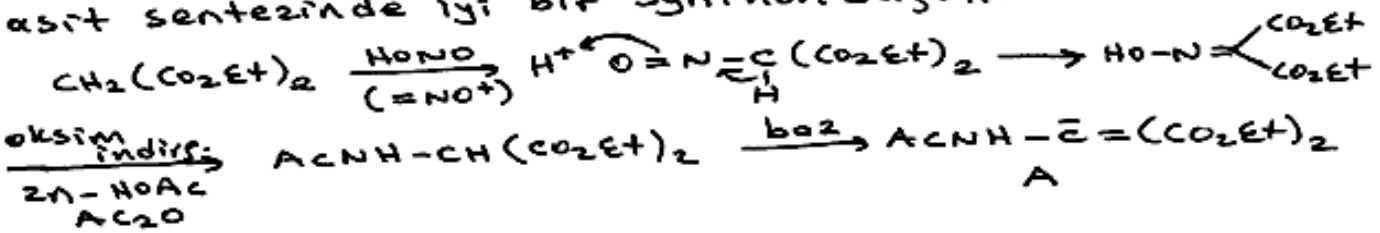


Sentezi: Sentezde ilk basamak; Siklohekzanon oluşması basamağıdır. Daha sonraki basamak; Johnson'un Conessine sentezinden adapte edilmiş reaksiyonları içerir (J. Amer. Chem. Soc., 1962, 84, 1485):



3. AMİNO ASİTLER

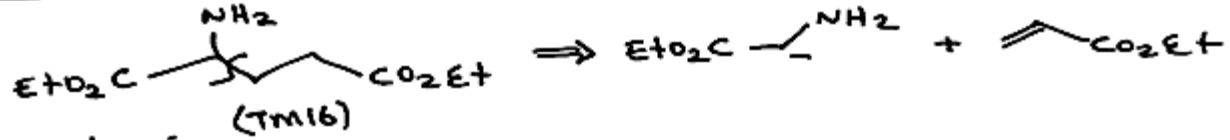
Daha önce, heteroatomun her zaman nükleofil olarak davrandığını söylemiştik. Ancak, N'un elektrofil olarak kullanıldığı bir durum vardır. Bu, amino asit sentezinde iyi bir synthon sağlar.



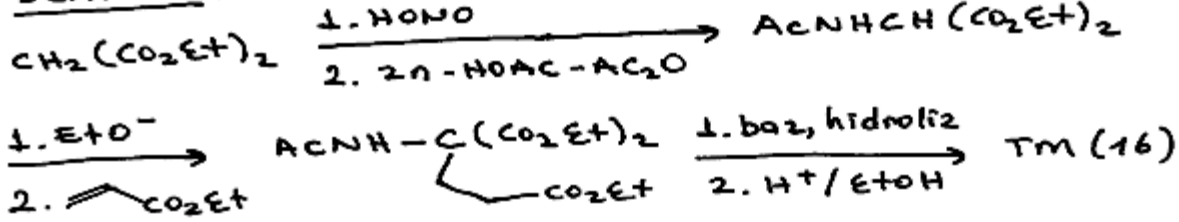
A anyonu, amino asit sentezinde (synthon) reaktif olarak kullanılmaktadır.

Örnek 9: Aşağıdaki aminoasidi (TM16) nasıl yaparsınız?

Analizi:



Sentezi:



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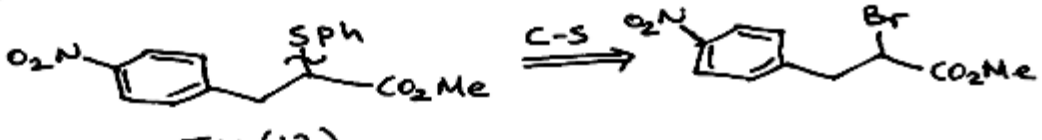
4. PROBLEMLER

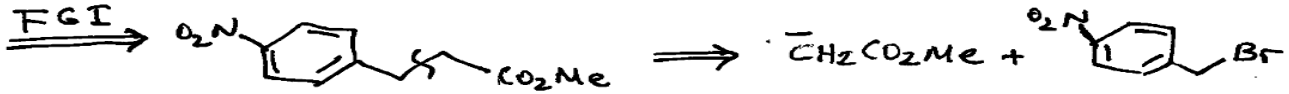
Heterosiklikler ve heteroatomlar ile ilgili bilgileri pekiştirmek için üç problem hazırlanmıştır. Bunlardan ilk ikisi kükürt içermektedir. Kükürt atomu, oksijen atomu gibi düşünülebilir.

Problem 1: TM(17) bileşiğinin sentez tasarımını yapınız.

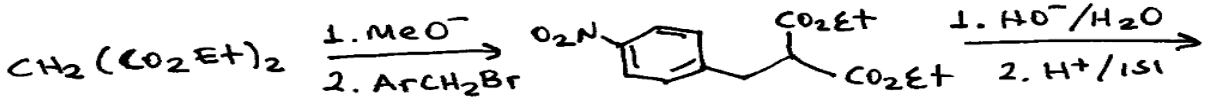
Analizi:



TM(17)

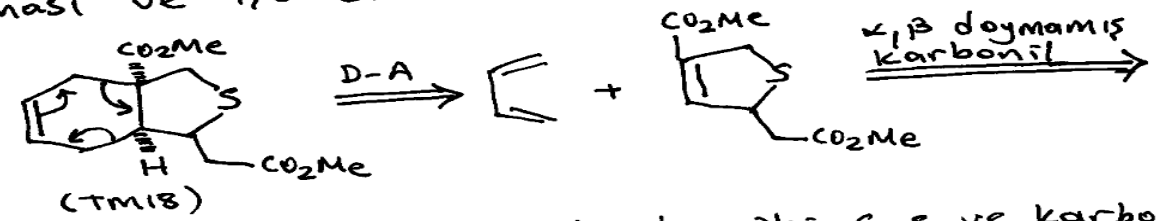


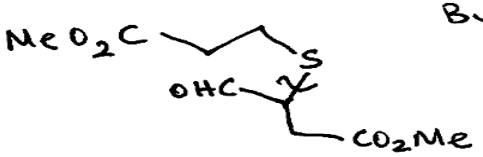
Sentezi: phSH kolayca hazırlanabilir.



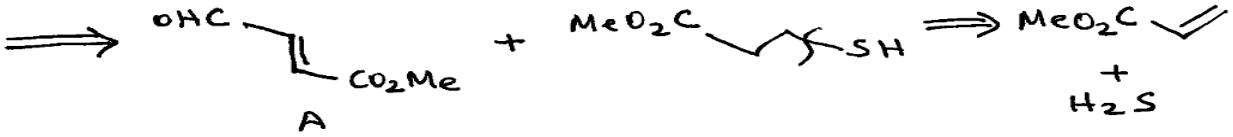
Problem 2: (TM 18) bileşiğinin sentez tasarımını yapınız.

Analizi: Bazı C-S bağları için Diels-Alder parçalanması ve 1,6-dikarbonil bağıntısı kullanılabilir:

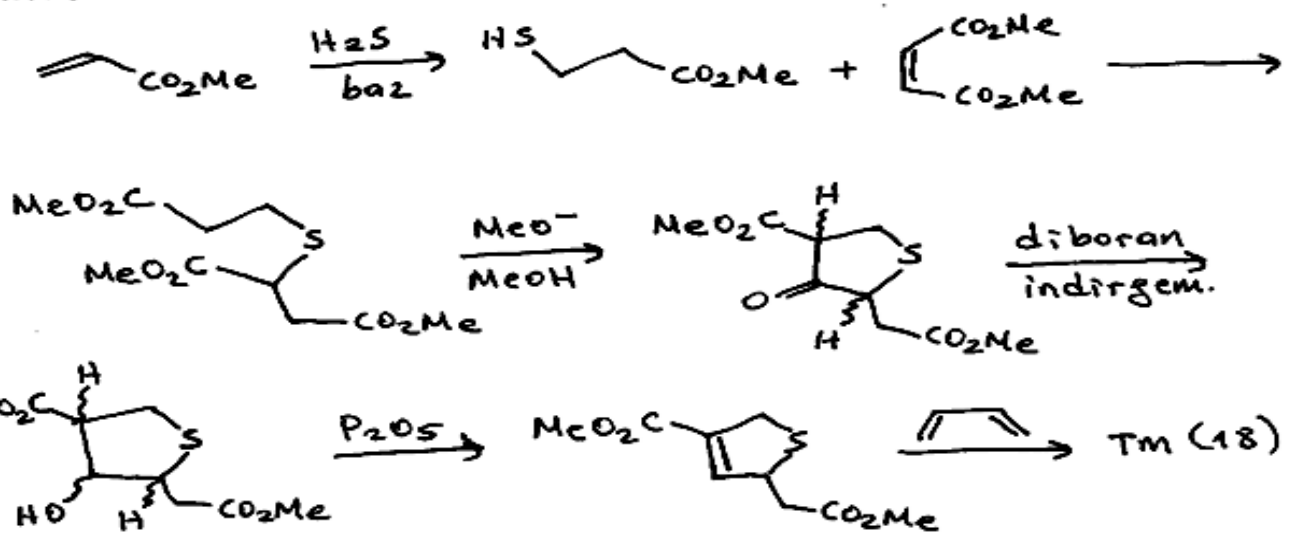




Burada, her iki C-S ve karbonil C-C bağları ters Michael reaksiyonu ile sıra ile parçalanır.

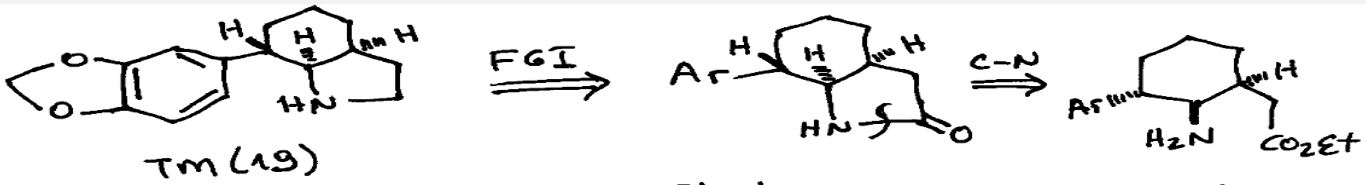


Sentezi: Öncelikle A reaktifinden (synthon) sentezе bağlamak oldukça zor olacaktır. Bunu kolaylaştırmak için diestere dönüştürmek gerekecektir. Bu bileşiğin gerçek sentezi Stork tarafından yapılmıştır (J. Amer. Chem. Soc., 1969, 91, 7780).



Problem 3: Aşağıdaki bileşiği (TM 19) analiz ederek sentezini yapınız.

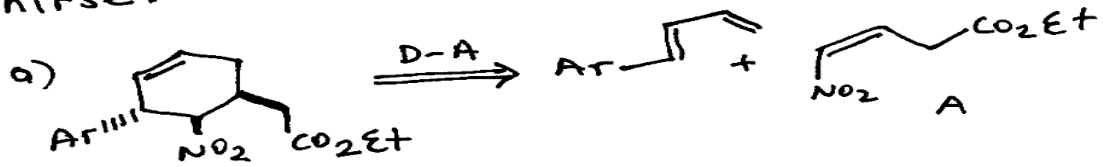
Analizi: Belkide şimdiye kadar çözülen soruların en zoru. Bir çok çözüm yolu öngörülebilir ve burada yalnızca biri verilecektir.

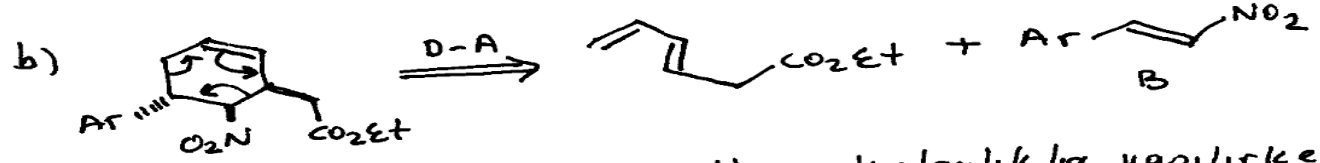


TM(19)

TM(19)'da N atomuna bağlı bir CH_2- grubu olduğundan, genel amin sentezinde olduğu gibi karbonil grubu yerleştirilir (FGI).

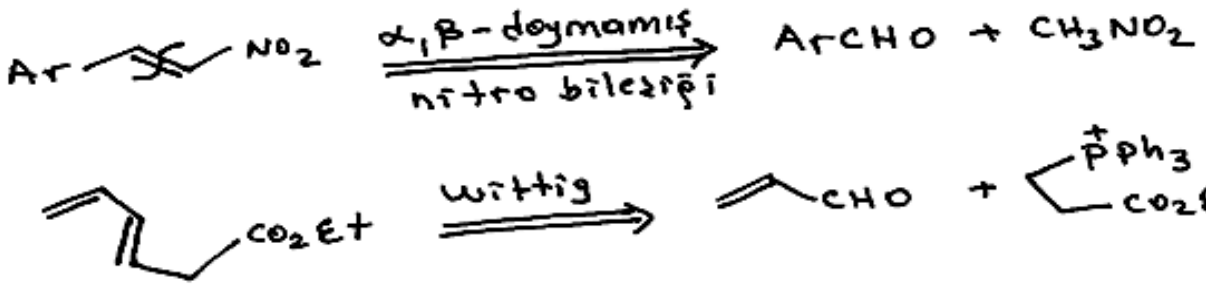
İkinci aşamada, altılı halkada parçalanma yapılmalıdır. Bunun için Diels-Alder reaksiyonu düşünülmelidir. Yerleştirilecek çift bağın yeri için iki alternatif yol vardır, eğer NH_2 grubunu ihtiyaç duyulan aktifleştirici bir gruba dönüştürmek istenirse:

a) 

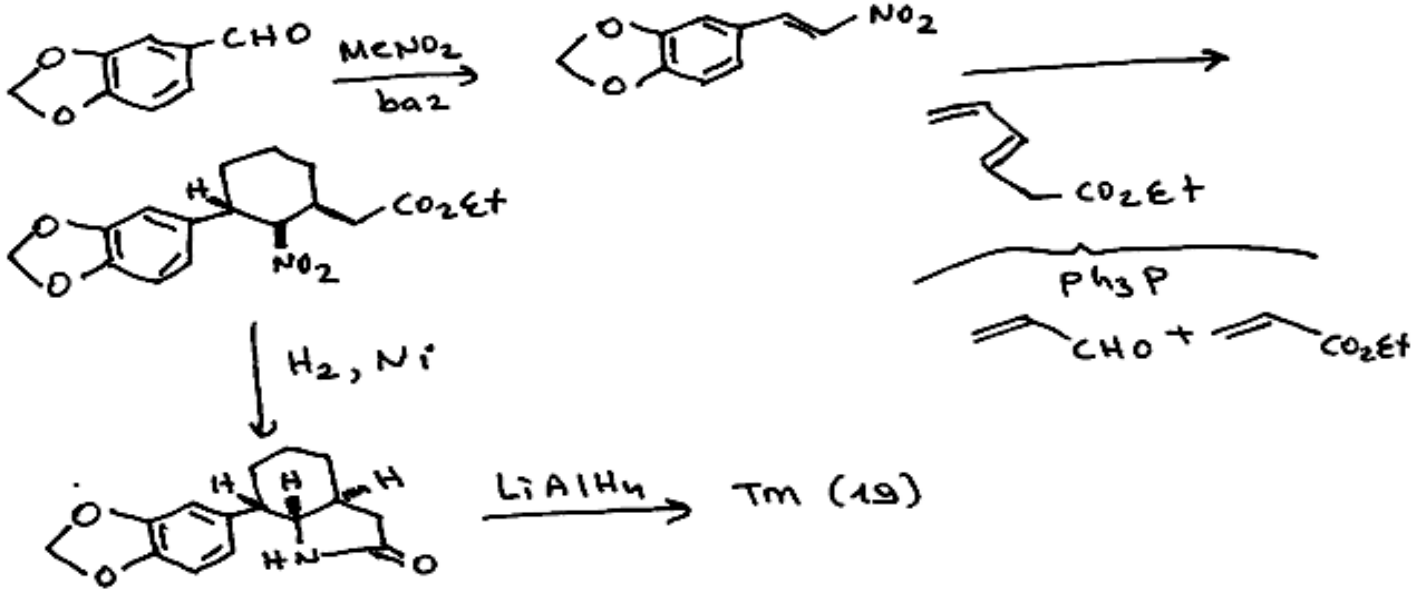
b) 

(b) yoluyla trans-nitro-alken kolaylıkla yapılırken (a) yoluyla elde edilen cis-nitroalken (A) sentezi zor olacaktır.

Şimdi (b) yoluna göre analizini düşünelim:

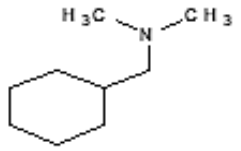


Sentezi: Sentezi, α-lycorane sentezinde kullanılan yöntemi içerir (J. Amer. chem. soc., 1962, 84, 4951).



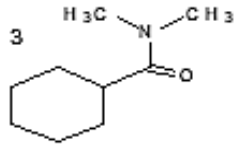
Bölüm 8. Bileşiklerin IUPAC adlandırması

TM 3



1-cyclohexyl-*N*,*N*-dimethyl methanamine

syf. 3

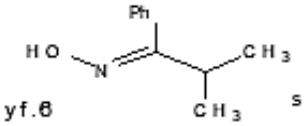


N,*N*-dimethylcyclohexane carboxamide

TM 4

N-benzyl-2-methyl-1-phenylpropan-1-amine

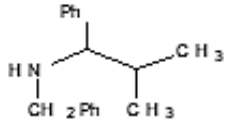
syf.6



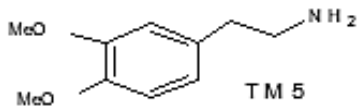
syf. 6

(1Z)-2-methyl-1-phenylpropan-1-one oxime

syf.6

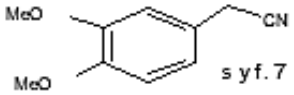


N-benzyl-2-methyl-1-phenylpropan-1-amine



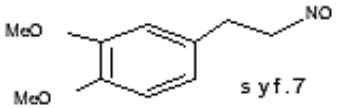
TM 5

2-(3,4-dimethoxyphenyl)ethanamine



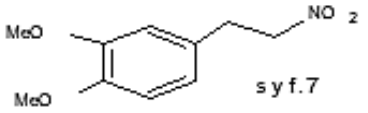
syf.7

(3,4-dimethoxyphenyl)acetonitrile



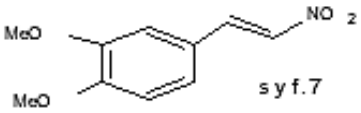
syf.7

1,2-dimethoxy-4-(2-nitrosoethyl)benzene



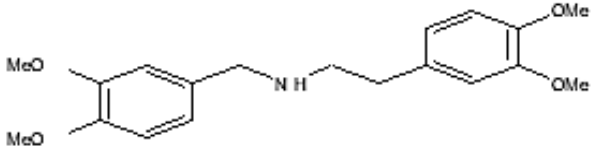
syf.7

1,2-dimethoxy-4-(2-nitroethyl)benzene



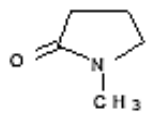
syf.7

1,2-dimethoxy-4-[(*E*)-2-nitrovinyl] benzene



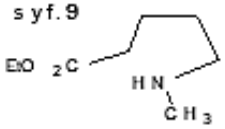
N-(3,4-dimethoxybenzyl)-2-(3,4-dimethoxyphenyl)ethanamine

syf.9



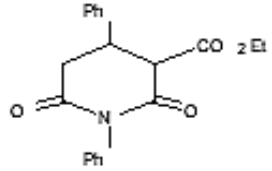
1-methylpyrrolidin-2-one

syf.9



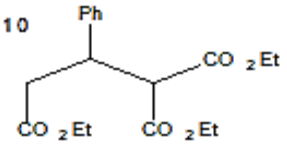
ethyl 5-(methylamino)pentanoate

TM 8



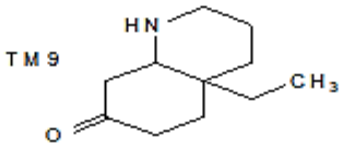
ethyl 2,6-dioxo-1,4-diphenylpiperidine-3-carboxylate

syf.10



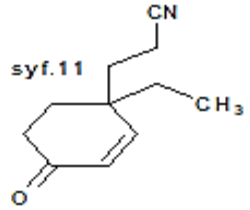
triethyl 2-phenylpropane-1,1,3-tricarboxylate

TM 9



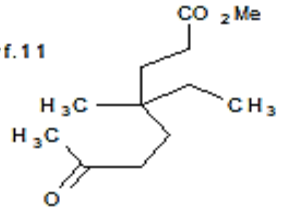
4a-ethyloctahydroquinolin-7(1*H*)-one

syf.11

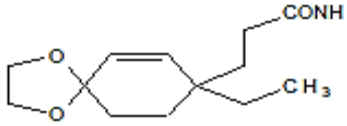


3-(1-ethyl-4-oxocyclohex-2-en-1-yl) propanenitrile

syf.11

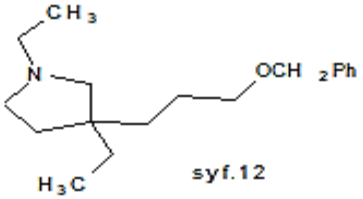


methyl 4-ethyl-4-methyl-7-oxooctanoate



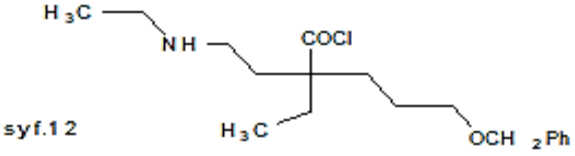
syf.11

3-(8-ethyl-1,4-dioxaspiro[4.5]dec-6-en-8-yl)propanamide



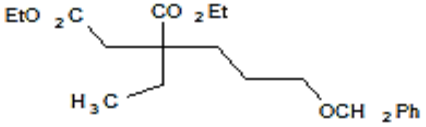
syf.12

3-[3-(benzyloxy)propyl]-1,3-diethylpyrrolidine



syf.12

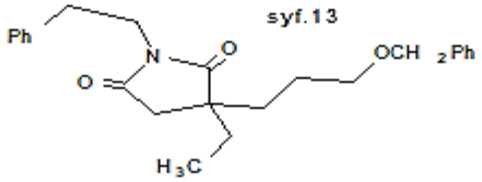
5-(benzyloxy)-2-ethyl-2-[2-(ethylamino)ethyl] pentanoylchloride



syf.13

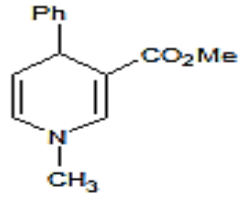
diethyl 2-[3-(benzyloxy)propyl]-2-ethylsuccinate

syf.13

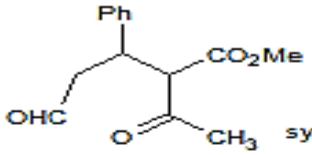


3-[3-(benzyloxy)propyl]-3-ethyl-1-(2-phenylethyl) pyrrolidine-2,5-dione

syf.14



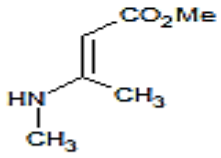
Methyl 1-methyl-4-phenyl-1,4-dihydropyridine-3-carboxylate



syf.14

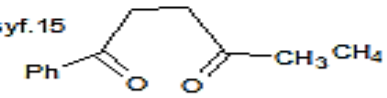
methyl 2-acetyl-5-oxo-3-phenylpentanoate

syf.14



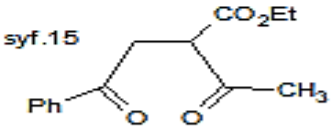
methyl (2*E*)-3-(methylamino)but-2-enoate

syf.15



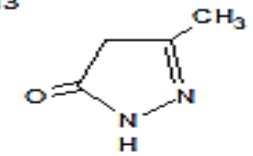
1-phenylpentane-1,4-dione

syf.15

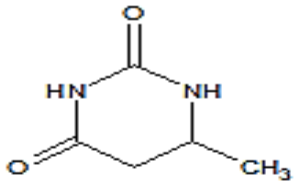


ethyl 2-acetyl-4-oxo-4-phenyl butanoate

TM13



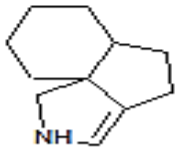
5-methyl-2,4-dihydro-3*H*-pyrazol-3-one



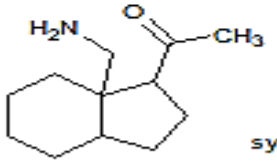
syf.15

6-methyldihydropyrimidine-2,4(1*H*,3*H*)-dione

TM15

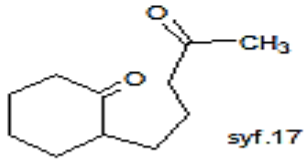


2,4,5,5a,6,7,8,9-octahydro-1*H*-indeno[1,7a-*c*]pyrrole



syf.17

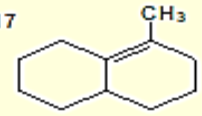
1-[7a-(aminomethyl)octahydro-1*H*-inden-1-yl]ethanone



syf.17

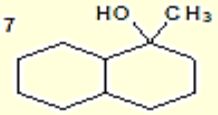
2-(4-oxopentyl)cyclohexanone

syf.17



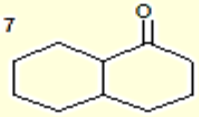
8-methyl-1,2,3,4,4a,5,6,7-octahydro naphthalene

syf.17



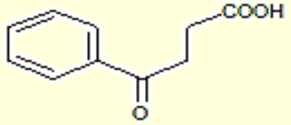
1-methyldecahydronaphthalen-1-ol

syf.17



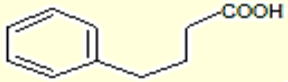
octahydronaphthalen-1(2*H*)-one

syf.18

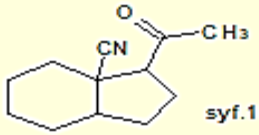


4-oxo-4-phenylbutanoic acid

syf.18



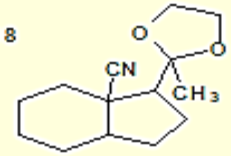
4-phenylbutanoic acid



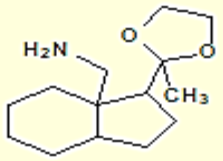
syf.18

3-acetyloctahydro-3a*H*-indene-3a-carbonitrile

syf.18

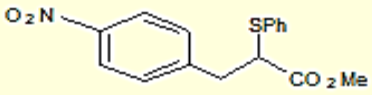


3-(2-methyl-1,3-dioxolan-2-yl)octahydro-3a*H*-indene-3a-carbonitrile

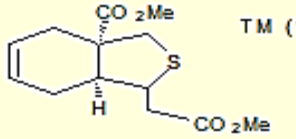


1-[3-(2-methyl-1,3-dioxolan-2-yl)octahydro-3a*H*-inden-3a-yl]methanamine

TM (17)

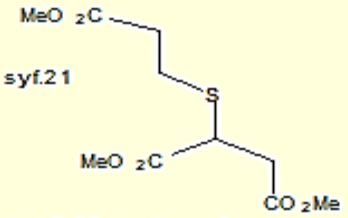


methyl 3-(4-nitrophenyl)-2-(phenylthio) propanoate



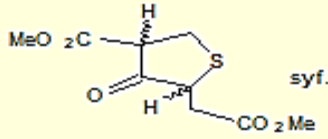
TM (18)

methyl (3a*R*,7a*S*)-1-(2-methoxy-2-oxoethyl)-1,4,7,7a-tetrahydro-2-benzothiophene-3a(3*H*)-carboxylate



syf.21

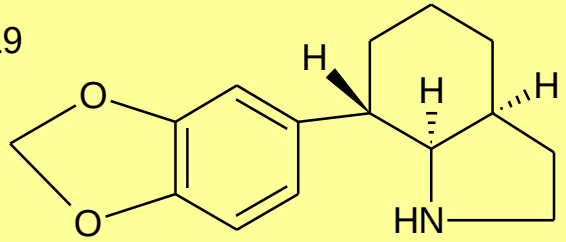
dimethyl 2-[(3-methoxy-3-oxopropyl)thio]succinate



syf.21

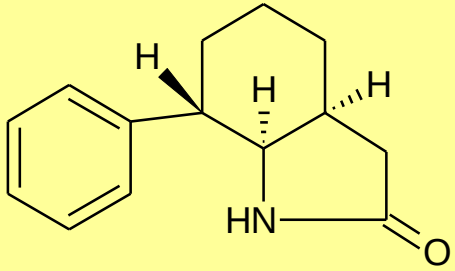
methyl 5-(2-methoxy-2-oxoethyl)-4-oxotetrahydrothiophene-3-carboxylate

TM19



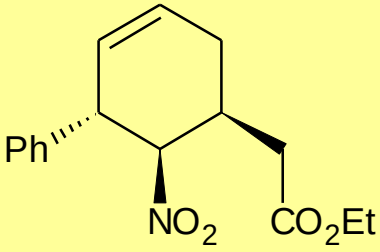
(3a*S*,7*S*,7a*R*)-7-(1,3-benzodioxol-5-yl) octahydro-1*H*-indole

syf.22

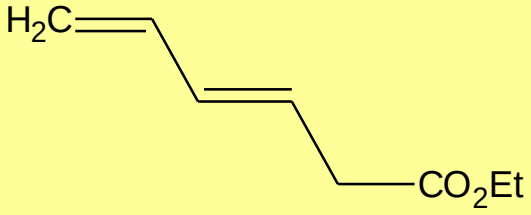


(3a*S*,7*S*,7a*R*)-7-phenyloctahydro-2*H*-indol-2-one

syf.22



ethyl [(1*S*,5*S*,6*R*)-6-nitro-5-phenylcyclohex-3-en-1-yl]acetate



ethyl (3*E*)-hexa-3,5-dienoate

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