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ETHYLENIC ACYL CYANIDES III† : BASE INDUCED SELF-CONDENSATION OF ETHYLENIC ACYL CYANIDES.

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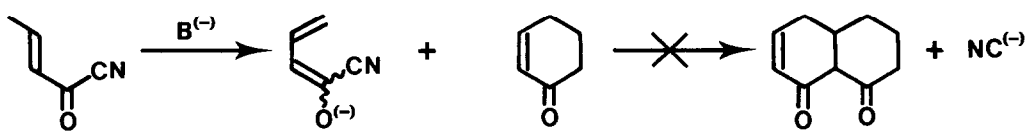
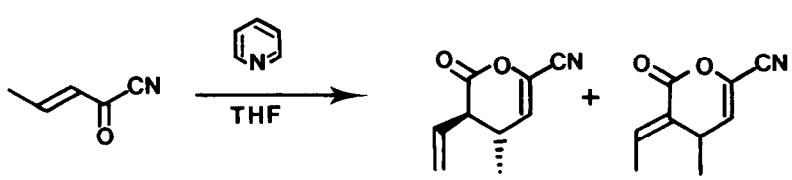
Summary : *Tertiary amines promote formation of ethylenic acyl cyanide enolates which add with high chemo-selectivity on acyl cyanides giving unsaturated δ-lactones.*

In connection with a project on the synthesis of a bicyclic enedione as 3, we tried to react crotonyl cyanide enolate 2 (methyl crotonate d^5-reagent (2)) with cyclohexenone. However, we were unsuccessful using a variety of experimental conditions which might reasonably be expected to have given 3. For example, with potassium t-butoxide in t-butanol solution, cyclohexenone is recovered with new products which result from enolate addition on crotonyl cyanide :



1 2 3

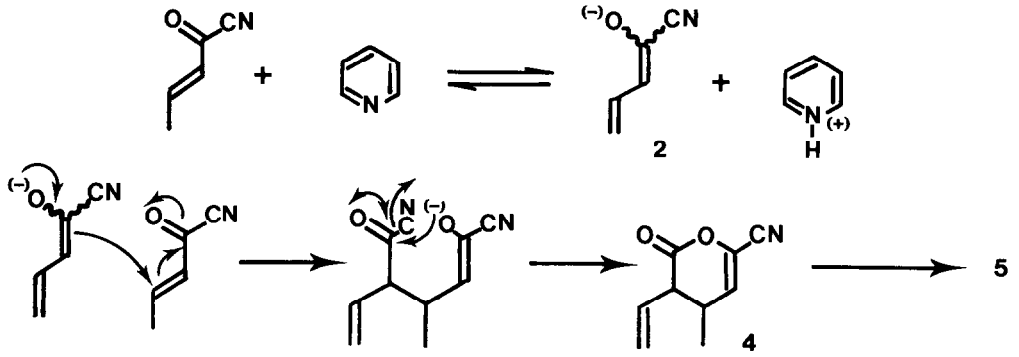
The highest yield for this self-condensation (87 %) is observed under *exceptionally mild conditions* : pyridine/THF; 0°→ r.t.; 3 days; 4/5 : 15/85 (3) :



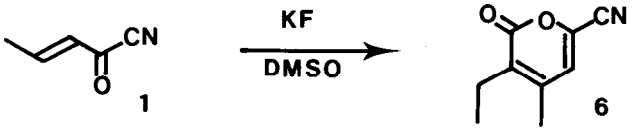
1 4 5

A mechanistic scheme that accommodates these, and other observations discussed below, is so illustrated (d^3-reagent on a^4-reagent (2)):

†Part II : see ref. 1.

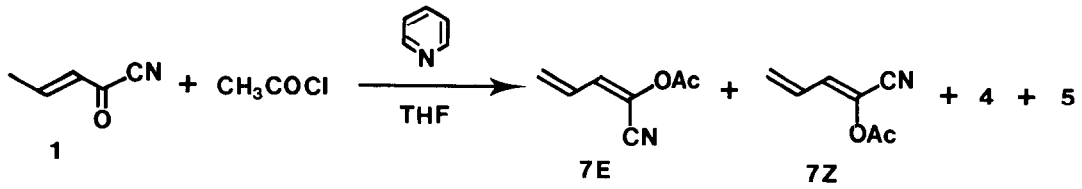


This base induced reaction can take place in DMSO with a catalytic amount of KF (4). In this case, pyranone 6 is the sole product (90 %)(during storage, the lactones 4 and 5 are isomerised to very large white crystals of the pyrone 6) :

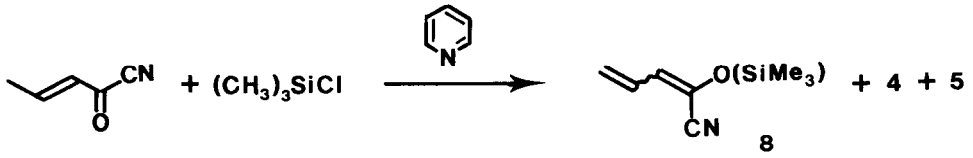


Even when the above reaction was carried out with 1 mol equivalent of crotonyl cyanide and 10 mol equivalents of methyl vinyl ketone (with pyridine/THF), the major products are 4 and 5. Only small quantities of other, as yet unidentified, condensation products were formed.

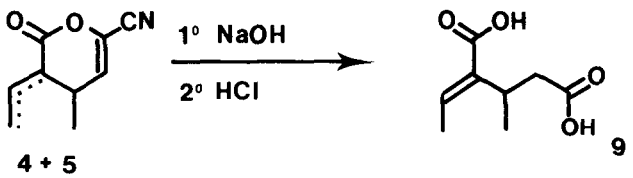
The enolate 2 can be trapped by condensation with acetyl chloride (2 mol equivalents, pyridine/THF) giving 2-acetoxy 2,4-pentadiennitrile 7 (30-35 %; E/Z ≃ 1/1 (5)(7)), but 4 and 5 are still the major products (60 %) :



Condensation with trimethylchlorosilane leads to the known 2-(trimethylsilyloxy)-2,4-pentadiennitrile 8 (8) also in low yield (20-25 %)(4, 5, yield : 60 %) :

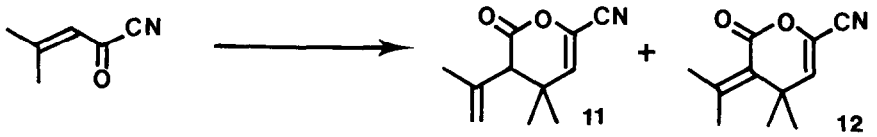


Hydrolysis (basic medium) of the lactones 4 and 5 lead quantitatively to glutaric acid derivative 9 :

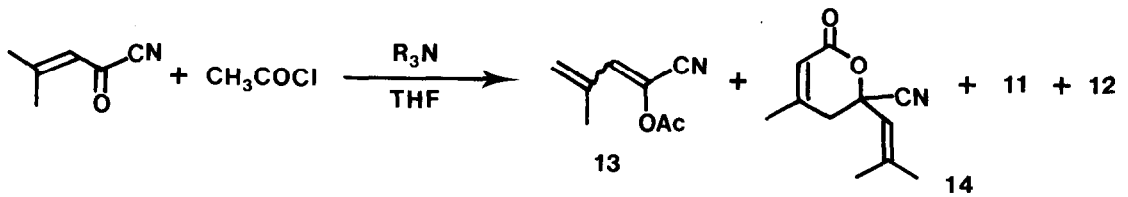


4 + 5 9

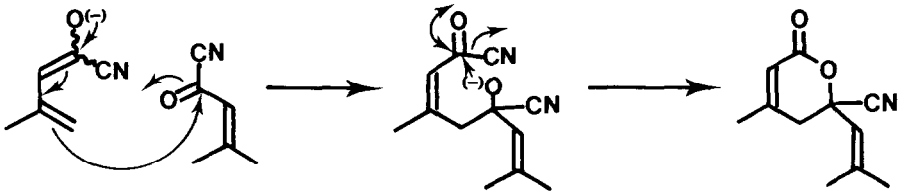
Comparable results are also obtained with the senecioyl cyanide 10. Condensation in presence of pyridine, triethylamine or KF/DMSO leads to a mixture of lactones 11 and 12 (overall yield : 80 % ; with pyridine or triethylamine, 11/12 : 40/60 ; with KF/DMSO, 11/12 : 65/35) :



Attempts to obtain 2-acetoxy-4-methyl-2,4-pentadien-nitrile 13 by condensation with acetyl chloride (2 mol equivalent, pyridine or triethylamine/THF) lead to a complex mixture of 13 (yield 20-25 % -with pyridine-; 15 % -with triethylamine-; one isomer), 11+12 (yield 60 % -with pyridine-; 10 % -with triethylamine-), and a new self-condensation product 14 (yield 10 % -with pyridine- ; 65 % -with triethylamine-)(overall yield : 85-90 %) :

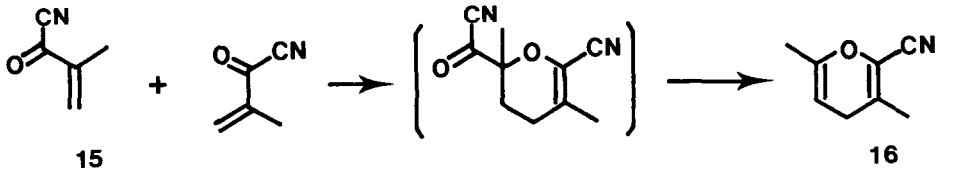


The formation of the lactone 14 can be explained by a 1,2-addition of enolate on senecioyl cyanide (d^5-reagent on a^2-reagent (2)(9)) (a slight difference in the solvent used can lead to a modification of 1,2 *versus* 1,4 addition, for an example see (12)) :



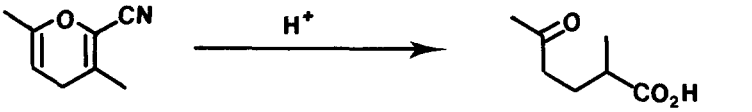
These observations show a high chemo-selectivity and confirm that ethylenic acyl cyanides are very good acceptors (1)(13)(14).

In addition, we have observed during the preparation of methacryloyl cyanide 15 a rather special DIELS-ALDER reaction. During the condensation of methacryloyl chloride with cuprous cyanide (15), the major product (yield : 60 %) is the pyran 16 resulting from the loss of CO + HCN :



15 16

Hydrolysis (20 % hydrochloric acid) of the pyran 16 leads quantitatively to the γ-keto-acid 17 :



16 17

REFERENCES and NOTES :

1 A. JELLAL, J.P. ZAHRA and M. SANTELLI, *Tetrahedron Lett.*, 1983,1395.

2 D. SEEBACH, *Angew. Chem. Int. Ed. Eng.*, 18, 239 (1979)

3 Anhydrous pyridine (25 ml) and anhydrous THF (10 ml) were cooled (0°C) under nitrogen and acyl cyanide (10 mmol) in anhydrous THF (15 ml) was slowly added. The solution was allowed to stir at r.t. for 3 days. Hydrolysis and extractive work-up (acidic) with diethyl ether gave lactones.

4 Potassium fluoride (60 mg), DMSO (25 ml) and THF (5 ml) were cooled (0°C) under nitrogen and acyl cyanide (10 mmol) in anhydrous THF (10 ml) was slowly added. The solution was allowed to stir at r.t. for 3 h. Hydrolysis and extractive work-up with diethyl ether gave lactones.

5 1-Acetoxy-1-cyano-1,3-butadiene 7 had the potential of serving as vinylketene equivalent in DIELS-ALDER reaction (vinylketenes add on the ethylenic compounds according to π2s + π2a process (6).

6 R.W. HOLDER, H.S. FREIMAN and M.F. STEFANCHIK, *J. Org. Chem.*, 41, 3303 (1976)

7 Enolisation of propionyl cyanide lead to Z/E ratio of 65/35 (8)

8 U. HERTENSTEIN, S. HUNIG, H. REICHELT and R. SCHALLER, *Chem. Ber.*, 115, 261 (1982)

9 The lithium dienolates of α,β-unsaturated carbonyl compounds react with most electrophiles selectively at the α-position (d^5-reagent (2))(10). For an example of γ-alkylation see 11.

10 I. FLEMING, J. GOLDHILL and I. PATERSON, *Tetrahedron Lett.*, 1979, 3205.

11 W. OPPOLZER, H.F. STRAUSS and D.P. SIMMONS, *ibid.*, 1982, 4673.

12 E.J. COREY and C. RUCKER, *ibid.*, 1982, 719.

13 Ethylenic acyl chlorides lead by treatment with tertiary amines to neutral vinylketenes (6)

14 S. HUNIG and R. SCHALLER, *Angew. Chem. Int. Ed. Eng.*, 21, 36 (1982)

15 A. JELLAL and M. SANTELLI, *Tetrahedron Lett.*, 1980, 4487.

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