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SYNTHESIS AND DIELS-ALDER REACTION OF TRANS-3-CYANOACROLEIN AND ITS ACETAL

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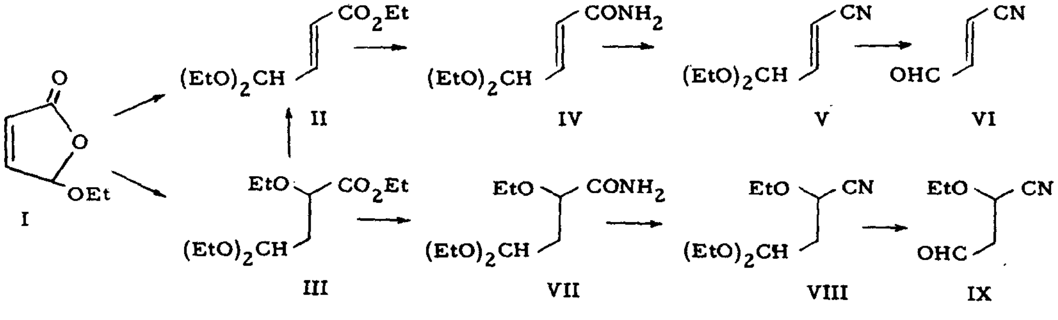
As a part of our studies on acylacrylic acids and derivatives (1), we have been attempting to synthesize trans-3-cyanoacrolein, a compound which promised to react as an active dienophile in the Diels-Alder reaction and seemed to be an attractive intermediate in organic synthesis. It has been only recently, in connection with the high polymer chemistry, that two synthesis of this compound have been described (2, 3).

We wish to report a new synthetic route to trans-3-cyanoacrolein and its diethylacetal, starting from cis-3-formylacrylic acid pseudoester (I) easily available from furfural (4), and the results obtained using them as dienophiles in Diels-Alder reaction.

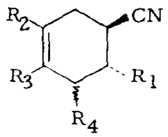


Conversion of cis-3-formylacrylic acid pseudoester (I) into ethyl 4,4-diethoxycrotonate (II) was previously reported by us (5, 6). However, a detailed examination of the reaction has shown that prolongued acid-catalyzed treatment of I with refluxing ethanol leads to an equilibrium mixture of II + III (38:62 by g. l. c. analysis), which can be separated by careful rectification (II: b. p. 108-110°/14 mm; III: b. p. 128-130°/16 mm). The trans configuration of II is confirmed on the basis of the n. m. r. spectrum, which shows 2 olefinic protons at 3.36 and 3.99 τ ($J_{2,3}$= 15.9 cps). The presence of the ethoxy substituent in the α-position of III can be proved from n.m.r. spectrum, in which the CH acetal proton at τ 5.36 appears as a triplet ($J_{3,4}$ = 5.8 cps). Simultaneous formation of II + III might be explained through an intermediate stage EtO-$\overset{+}{C}$H-CH=CH-COOEt, originated during cleavage of the ethoxylactone ring of I.

The acetal ester II reacts with cold conc. aqueous ammonia, yielding 4,4-diethoxycrotonamide (IV, 48 %), m. p. 104°, which on dehydration with phosphorus pentoxide, in the presence of triethylamine, gives 4,4-diethoxycrotononitrile (V, 70 % yield), b. p. 98°/15 mm, n_D^{21} = 1.4320 [i. r., $\bar{\nu}$ (cm^{-1}): 2225 (CN); 1640 (C=C); n. m. r., τ 8.83 (6H, CH_3); 6.50 (4H, CH_2O); 5.04 (1H, CH acetal); 4.33 (1 olef. H, C_2); 3.49 (1 olef. H, C_3); $J_{2,3}$ = 16.8 cps)]. Mild acid hydrolysis of cyano acetal V, at room temperature, gives 88 % of trans-3-cyanoacrolein (VI), b. p. 68°/15 mm, n_D^{22} = 1.4715 [i. r., $\bar{\nu}$ (cm^{-1}): 2870, 2770 (CH ald.); 2260 (CN); 1715 (C=O); 1625 (C=C); n. m. r., τ : 3.51 (1 olef. H, C_3); 3.11 (1 olef. H, C_2); $J_{2,3}$ = 16.9 cps; 0.37 (1H ald.)].

Similar reactions starting from III allow the preparation of the corresponding 2-ethoxy-3-formylpropionic derivatives VII, VIII and IX. However, ethanol elimination, in order to obtain the substituted acrylic series, is preferable done on the mixture II + III, directly prepared from I, thereby avoiding their separation. This mixture, heated in vacuo in the presence of $KHSO_4$, gives the acetal ester II in practically pure form (yield I $\rightarrow$ II + III $\rightarrow$ II, 72 %).

Trans-3-cyanoacrolein (VI) and diethyl acetal (V) react as dienophiles in the diene synthesis. From the results summarized in Table I follows that the trans-3-cyanoacrolein (VI) is an excellent dienophile, even reacting with a cis-1-substituted diene in an acceptable yield, whereas 4,4-diethoxycrotononitrile (V) is, as expected, a less active dienophile. With asymmetric dienes both possible structural isomers (A + B) are obtained, each as a mixture, in variable proportions,



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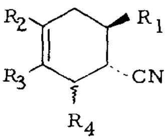

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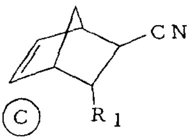

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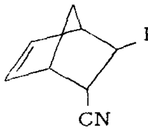

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TABLE I

Diene synthesis with trans-3-cyanoacrolein and its acetal

1. Adducts of trans-3-cyanoacrolein

diene	ratio[a]	temp. °C	t. hrs.	yield %	products (ratio)	R_1	R_2	R_3	R_4
butadiene	1:1[b]	100	4	100	A	CHO	H	H	H
isoprene	1:1[b]	95	15	100	A+B (58:42)[c]	CHO	Me	H	H
2,3-dimethyl-butadiene	1:1[b]	100	4	100	A	CHO	Me	Me	H
1-acetoxy-butadiene[d]	1:1[b]	95	18	68	A+B (85:15)[e]	CHO	H	H	OAc
cis-1-methoxy-butadiene	1:1[b]	105	18	43	A+B (84:16)[f]	CHO	H	H	OMe
cyclopentadiene	1:1[b]	20	1/12	100	C+D (66:34)	CHO	-	-	-

2. Adducts of 4,4-diethoxycrotononitrile

diene	ratio[a]	temp. °C	t. hrs.	yield %	products (ratio)	R_1	R_2	R_3	R_4
butadiene	3:1[g]	150	9	100	A	$(EtO)_2CH$	H	H	H
isoprene	1. 1:1[g]	135	10	45	A+B (50:50)	$(EtO)_2CH$	Me	H	H
2,3-dimethyl-butadiene	4:3[g]	100	9	60	A	$(EtO)_2CH$	Me	Me	H
1-acetoxy-butadiene[d]	4:3[b]	135	20	25	A+B (7:93)	$(EtO)_2CH$	H	H	OAc
cis-1-methoxy-butadiene	1. 1:1[g]	160	18	10	A+B (35:65)	$(EtO)_2CH$	H	H	OMe
cyclopentadiene	4:3[b]	100	5	80	C+D (78:22)	$(EtO)_2CH$	-	-	-

[a] Molar ratio diene:dienophile
[b] Benzene as solvent
[c] or 42:58
[d] Mixture of *cis* + *trans* isomers
[e] With simultaneous elimination of some AcOH in A
[f] With simultaneous elimination of some EtOH in A
[g] Without solvent

of geometrical isomers. The cyclopentadiene adducts appear as endo-exo mixtures (C + D). The structures of isomeric adducts and their relative ratios have been obtained by g.l.c. and n.m.r., whether directly or through convenient chemical transformations. In general, the Alder rules are obeyed and with 1-substituted dienes the -CHO group adopts the "ortho" orientation rather than the -CN group, and this **prefentially to the** $-CH(OEt)_2$ **group.** However, the rule of "maximum accumulation of unsaturation" does not seem an important factor in the case of cyclopentadiene/4,4-diethoxycrotononitrile adduct, where the bulky $-CH(OEt)_2$ group adopts the endo position in marked preference to the -CN group. This fact contrast with the addition of methyl 4,4-dimethoxycrotonate, which leads to a nearly equimolecular mixture of both possible adducts (7), and confirms the small orienting power of the -CN group, already brought in evidence before (8, 9, 10).

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