CYCLOADDITIONS OF DIAZOESTERS TO \( \alpha, \beta \)-UNSATURATED ALDEHYDES

A. F. NOEL,* J. N. BRAHAM, A. J. HUBERT and Pu TSENNÉ

Laboratoire de Chimie Macromoléculaire et de Catalyse Organique, Université de Liège, Sart Tilman
par 4000 Liège, Belgique

(Received in UK 5 May 1978; Accepted for publication 13 July 1978)

Abstract—The reaction of \( \alpha, \beta \)-unsaturated aldehydes with diazomethanes primarily gives unstable 1,3-dipolar adducts (1,3-diazo-2-propene) which either according to their substitution pattern or whether there is a planar cisoid substituent to the formyl group, conjugation with the latter is highly favoured, yielding 3-formyl-2-pyzrolines which subsequently polymerize. On the other hand, if no proton is available for conjugation with the formyl group, two competitive reactions take place: tautomisation into an ester conjugated pyrazoline and loss of nitrogen with formation of cyclopropanes, the latter racemational path being favoured with electronwithdrawn substituents.

If 1.3 dipolar additions of diazo compounds to activated olefins or acetylenes have been extensively investigated¹ and are presently well understood², much less is known about such additions to unsaturated conjugated aldehydes,³ although those reactions were reported to give unidentified products.

Recently however, we have shown that the addition of diazoesters to propenal (acrolein) mostly give polyacetaldehydes resulting from a polymerization through the formyl group of intermediate pyrazolines.⁴ It is the goal of the present article to describe the structure of the unstable pyrazoline resulting from the 1.3 dipolar addition of ethylidiazocacetate (EDCA) to acrolein, to determine the kinetic and thermodynamic parameters of this reaction, and to rationalize the effects of substitution on its course.

RESULTS

1. Reactions of EDA with unsaturated acroleins

EDA is added in equimolecular amount to acrolein in an apolar solvent such as hexane or carbon tetrachloride, a precipitate immediately separates out. However, the oily liquid so isolated is unstable and quickly evolves nitrogen at room temperature. So, in order to obtain satisfactory spectral and analytical data, all operations have to be carried out in the cold to mainntain what appeared to be oligomerization processes. Chromatography on silica gel at 0° yields a compound still contaminated by small amounts of oligomers formed in situ. However, the IR spectrum clearly shows, besides the lack of any diazo group, the presence of a non-conjugated ester function absorbing at 1735 cm⁻¹ and of a formyl group conjugated with an azomethine double bond respectively at 1663 and 1550 cm⁻¹. A broad absorption around 3400 cm⁻¹ is characteristic of associated NH vibrations. The NMR spectrum also shows the broad absorption of a secondary amine at 7.5 ppm (which disappears after addition of D2O together with an uncoupled aldehyde proton. These data are consistent with the structure of pyrazoline 1, a tautomiser of 2, itself the result of a 1,3 dipolar addition of the diazoester to the olefinic bond of acrolein (Scheme 1, R = H).

The 1-pyrazoline 2 itself is never observed, it very rapidly rearranges to the more stable 1 even below room temperature. Besides, isolated 1 gives polymers identical to those directly obtained from the reactants (EDA and acrolein), that proves the adduct to be the real monomer of these polymerization processes.

Moreover the synthesis of the N-acetyl derivative 3 from 2 further confirms the structure of 2; 3 is very stable and remains unaltered in boiling benzene for ten days.

It is interesting to note the regiospecificity of the double bond migration, 2 exclusively isomerizes to 1, no ester-conjugated 4 was ever detected when R = H. A kinetic study of the cycloaddition was carried out, the reaction is first-order in each reactant and second order overall. The values of the activation energy \( E_a = 13.6 \pm 0.8 \text{ kcal mol}^{-1} \) and of the entropy of activation, \( \Delta S^\circ = -33.4 \pm 2 \text{ cal K}^{-1} \text{ mol}^{-1} \) are consistent with values usually found for 1,3 dipolar additions¹ and represent a final support for the mechanism as well.

2. Reactions of EDA with \( \beta \)-substituted acroleins

Cinamaldehyde and 2-butenal (crotaldehyde) react with EDA at room temperature also to give polymeric...
matters. Although not isolated, evidence for the formation of unique 1,3-dipolar adducts was obtained by VPC. The IR spectra of the polymers are in agreement with those of the acrolein-EDA polymerization. Therefore, cyclodaddition reaction of diazoesters with these β-substituted acroleins seem to follow the same reaction pathway as acrolein itself.

3. Reaction of EDA with α-substituted acroleins

If α-substituted acroleins are used in order to prevent a further rearrangement of the initially formed 1-pyrrolizines into α-formyl-2-pyrrolizines of type I, then, completely different products are obtained and their relative ratios depend both on the concentration of the reactants in solution and on the nature of the substituent.

When α-chloroacrolein reacts with EDA in an inert solvent, (solution approximately 0.8 mol/l) in CCl4 an α-formyl-2-pyrrolizine takes place and the isomeric cyclopropanes 5a and 5b are obtained in almost equivalent yields (Scheme 2).

\[
\text{EDA} + \text{α-CHClC} = \text{CH2} \rightarrow \text{C}_2\text{H}_4\text{CH} = \text{CH} + \text{C}_2\text{H}_4\text{CH} = \text{CHCH}_2\text{CH} = \text{CH}_2
\]

At higher solution concentrations, polymerization also occurs to some extent (20-30%). On the other hand, the reaction of EDA with α-methylacrolein gives, in addition to the two isomeric cyclopropanes 6 and 7 (Scheme 3) a new α-β unsaturated aldehyde 8 and the carboxaldehyde 9 (dimer) of a condensed molecule whose crystallographic characterization is reported elsewhere. 9 Is insoluble in most organic solvents and corresponds to a stereo-specific dimerization of 2 the 2-pyrrolizine 4 (IR = Me).

EXPERIMENTAL

IR spectra were recorded using liquids (Nujol disks) on a Perkin-Elmer 21, and NMR spectra on a Varian HA 100 (H) or on a Bruker HFX-90 (100 MHz) spectrometer. Chemical shifts are given in ppm relative to TMS as internal standard.

The 13C spectra are proton noise decoupled. VPC analysis were performed on a Varian Aerograph 1700 using a 6 ft x 0.125 column, 205° C as temperature.

All starting materials and solvents were distilled before experiment.

The kinetic study was conducted by following the disappearance of the characteristic IR absorption of EDA at 2100 cm⁻¹.

5-Ethoxycarbonyl-3-formyl-2-pyrrolizine 1, to a solution of 3.4 ml (0.05 M) of 20 ml absolute hexane was slowly added a solution of 4.3 ml (0.04 M) of EDA in hexane. The mixture was well stirred at 20° for 2 h and the soln siphoned off by means of a capillary.

The yellowish thin oil was then eluted on a silicagel column, first by benzene in order to eliminate the reactants excess, then by a 1:1 mixture of petroleum ether. These last solvents were removed in vacuo at 60 °C and 0.01 mm pressure to 20 °C, crude yield 80%. IR: 3400 (NH), 1735 (C=O ester), 1643 (conjugated C=N); NMR (CDCl₃): δ = 9.7, 3.4, 0.12 (4, 2. CH₃, CH₂); δ = 1.25, 2.15 (m, 3, Me); (Found: C, 49.9; H, 10.4; N, 16.5; - N = CH₂ - 3-formyl-2-pyrrolizine 3.

The crude 1 in 20 ml CH₂Cl₂ was added 3 ml Ac₂O and 20 ml p-toluene sulfonic acid. The red oil was then heated for 30 min at 50 °C and the product purified by chromatography on a silica gel column, yield 50%. IR: 1740 (C=O ester), 1672 (C=O aldehydes), 1570 (conjugated C=N), 1540 (NH), 1460 (C=O aldehydes), 1570 (conjugated C=N), 1470 (CH₂Cl₂), 1370 (N = CH₂ - 3-formyl-2-pyrrolizine 3.

3. Reaction of EDA with α-substituted acroleins

When the C atom bearing the formyl group is monosubstituted, (acrolein or β subst acroleins), conjugation with this function always and exclusively takes place, yielding 3-formyl-2-pyrrolizines 4 which subsequently polymerize. As no (or very little) nitrogen evolution occurs, such a rearrangement is clearly a highly favoured pathway at room temperature.

On the other hand, if there is no geminal H to the formyl function (pyrazolines obtained from α-subst acroleins), then 2 competitive reactions occur: (a) tautomeration to a 5-formyl-2-pyrrolizine of type 4; (b) loss of nitrogen and formation of cyclopropanes. The decomposition of 1-pyrrolizines is indeed a well established route to cyclopropanes and olefins. 9 That the latter possibility is favored over any tautomeration when the substituent is electron withdrawing (as in α-chloroacrolein) is probably due to a stabilization of intermediate 1-pyrrolizines.

Indeed, unsymmetrical polarized olefins with unsaturated electroattracting substituents can react via a stepwise dipolar mechanism involving ionic addition to the double bond to give a zwitterionic intermediate which cyclizes by nucleophile displacement of N₂⁻.

Moreover, whenever 2-pyrrolizines are formed, the presence of electroattracting groups such as the formyl one together with nucleophile ring-opening either in 1-pyrrolizines or 2-pyrrolizines promotes subsequent reactions so as to produce either polymers or oligomers according to the steric requirements of the reaction intermediates.

REFERENCES