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CYCLOADDITIONS OF DIAZOESTERS TO α,β-UNSATURATED ALDEHYDES

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Abstract—The reaction of α,β-unsaturated aldehydes with diazoesters primarily gives unstable 1,3-dipolar adducts (1-pyrazolines) which evolve according to their substitution pattern: whenever there is a proton geminal to the formyl group, conjugation with the latter is highly favoured, yielding 3-formyl-2-pyrazolines which subsequently polymerize. On the other hand, if no proton is available for conjugation with the formyl group, two competitive reactions take place: tautomerisation into an ester conjugated pyrazoline and loss of nitrogen with formation of cyclopropanes, the latter reactionnal pathway being favoured with electronwithdrawing substituents.

If 1,3 dipolar additions of diazocompounds to activated olefins or acetylenes have been extensively investigated[1] and are presently well understood[2], much less is known about such additions to unsaturated conjugated aldehydes,[3] although those reactions were reported to give unidentified polymers.

Recently however, we have shown that the addition of diazoesters to propenal (acrolein) mostly give polyacetals resulting from a polymerization through the formyl group of intermediate 2-pyrazolines.[4]

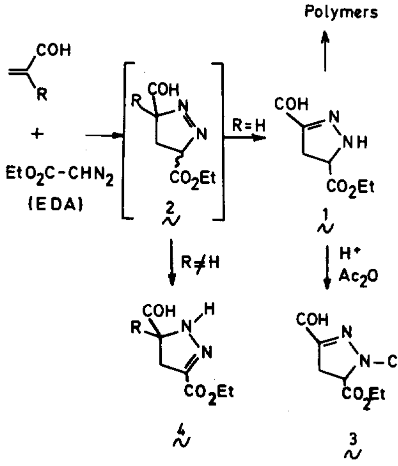
It is the goal of the present article to describe the structure of the unstable pyrazoline resulting from the 1,3 dipolar addition of ethyldiazoacetate (EDA) to acrolein, to determine the kinetic and thermodynamic parameters of this reaction, and to rationalize the effects of substitution on its course.

RESULTS

1. *Reactions of EDA with unsubstituted acroleins*

When 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 minimize 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 diazogroup, 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 1665 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 7.6 ppm (which disappears after addition of D_2O) together with an uncoupled aldehyde proton.

These data are consistent[5] with the structure of pyrazoline **1**, a tautomer of **2**, itself the result of a 1,3 dipolar addition of the diazoester to the olefinic bond of acrolein (Scheme 1, R = H).



Scheme 1.

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 **1** 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 $E_a^{\neq} = 13.6 \pm 0.8$ kcal m^{-1} and of the entropy of activation, $\Delta S^{\neq} = -33 \pm 4$ u.e., are also consistent with values usually found for 1,3 dipolar additions[7] and represent a final support for the mechanism as well.

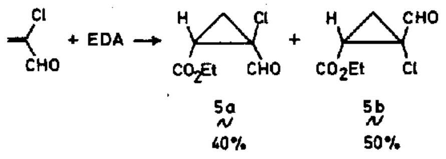
2. *Reactions of EDA with β*-substituted acroleins

Cinnamaldehyde and 2-butenal (crotonaldehyde) react with EdA at room temperature also to give polymeric materials. Although not isolated, evidence for the formation of unstable 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, cycloaddition reaction of diazocompounds 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-pyrazoline into a formyl-conjugated 2-pyrazoline of type **1**, 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 substituents.

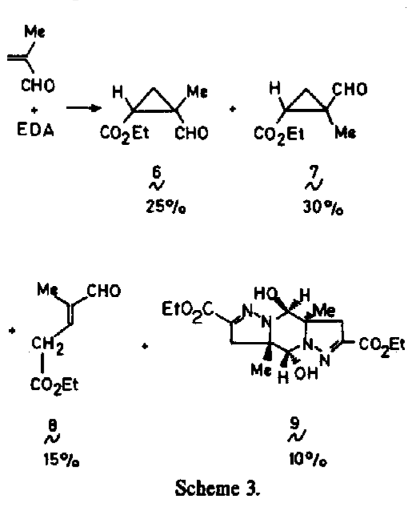
When α-chloroacrolein reacts with EDA in an inert solvent, (solution approximately $0.8\ m.l^{-1}$ in CCl_4) an almost quantitative evolution of nitrogen takes place and the isomeric cyclopropanes **5a** and **5b** are obtained in almost equivalent yields (Scheme 2).



Scheme 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 carbinolamine **9** a condensed molecule whose crystallographic characterization is reported elsewhere[8]. **9** is insoluble in most organic solvents and corresponds to a stereo-specific dimerization[9] of the 2-pyrazoline **4** (R = Me).



Scheme 3.

DISCUSSION

It becomes apparent from these experimental results that, substituted or not, α-β-unsaturated aldehydes react in a normal fashion with diazoesters, i.e. via 1,3 dipolar additions to give unstable intermediate 1-pyrazolines, the structure of which controls the further steps of the reaction.

Whenever 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-pyrazolines **1** 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) tautomerisation to a 5-formyl-2-pyrazoline of type **4**: (b) loss of nitrogen and formation of cyclopropanes. The decomposition of 1-pyrazolines is indeed a well established route to cyclopropanes and olefins.[10] That the latter possibility is favoured over any tautomerisation when the substituent is electronwithdrawing (as in α-chloroacrolein) is probably due to a stabilization of ionic intermediates and does not exclude a direct production of cyclopropanes *without* any formation of a 1-pyrazoline.

Indeed, unsymmetrical polarized olefins with unsaturated electronattracting substituents can react via a stepwise dipolar mechanism involving ionic addition to the double bond to give a zwitterionic intermediate which cyclized by nucleophilic displacement of N_2.[11]

Moreover, whenever 2-pyrazolines are formed, the presence of electrophilic groups such as the formyl one together with nucleophilic ring-nitrogens (either in 1- or 2-pyrazolines) promotes subsequent reactions so as to produce either polymers or oligomers according to the steric requirements of the reaction intermediates.[9]

EXPERIMENTAL

IR spectra were run as neat liquids (NaCl disks) on a Perkin-Elmer 21, and NMR spectra on a Varian HA 100 (^1H) or on a Brucker HFX – 90 (^{13}C, 23.9 MHZ) spectrometers. Chemical shifts are given in ppm (δ) relative to TMS as internal standard. The ^{13}C spectra are proton noise decoupled. VPC analysis were performed on a Varian Aerograph 1700 using a 6 ft × 0.125 column, 20% SE 30 on chromosorb *W* 30–60.

All starting materials and solvents were distilled before experiment.

The kinetic study was conducted by following the disappearence of the characteristic IR absorption of EDA at $2100\ cm^{-1}$.

5-Ethoxycarbonyl-3-formyl-2-pyrazolines **1**. To a soln of 3.4 ml (0.05 m) acrolein in 20 ml absolute hexane was slowly added a soln of 4.2 ml (0.04 m) EDA in 5 ml hexane. The mixture was well stirred at 20° for 2 hr and the soln siphonned off by means of a capillary.

The remaining yellow thick oil was then eluted on a silicagel column, first by benzene in order to eliminate the reactants in excess, then by a 4 : 1 mixture of ether-pentane at 2°. These last solvents were removed under reduce pressure at −20°, crude yield 80%. IR: 3400 (NH), 1735 (C = O ester), 1665 (conjugated C = O ald), 1550 (conjugated C = N); NMR ($CDCl_3$): $\delta = 9.57$, S, 1, COH; 7.6 (broad, S, 1, NH) 4.01 (q, 2, $C\underline{H}_2$–CH_3); 4.75–4.45 (m, 1, $C\underline{H}$–CO_2Et) 3.4–2.95 (m, 2, CH_2): 1.25 (t, 3, Me) (Found: C, 49.3; H, 5.8; N, 16.6. Calc for polymer; C, 49.3; H, 5.8; N, 16.5.

N - *Acetyl - 5 - ethoxycarbonyl - 3 - formyl - 2 - pyrazoline* **3**. To the crude **1** in 20 ml C_6H_6 was added 5 ml Ac_2O and 20 mg *p*-toluenesulfonic acid. The red soln was then heated for 12 hr at 50° and the product purified by chromatography on a silicagel column, yield 50%. IR: 1740 (C = O ester), 1672 (C = O acetyl), 1660 (conjugated C = O aldehyde), 1570 (conjugated C = N), no NH. NMR ^1H ($CDCl_3$): $\delta = 9.73$ (S, 1, –COH); 4.90 (q, 1, H_x); 4.17 (q, 2, $C\underline{H}_2 - CH_3$); 3.27 (q, 1, H_A, $J_{AX} = 12.6$ Hz); 3.01 (q, 1, H_B, $J_{BX} = 7$ Hz, $J_{AB} = 18$ Hz); 2.38 (S, 3, CH_3 acetyl); 1.23 (t, 3, $C\underline{H}_3$–CH_2–). ^{13}C ($CDCl_3$) $\delta = 247$ ppm (C = O acetyl); 184 (C = O aldehyde); 166 (C = O ester); 151 (C_3); 61 (CH_2) 58 (Me acetyl); 33 (C_5); 20 (C_4); 14 (Me ester).

Reactions of EDA with β-substituted acroleins. The reactions with crotonaldehyde and cinnamaldehyde were performed using the same experimental conditions as with acrolein. After 5 days, the polymers were precipated by addition of hexane and then dried under vacuum.

Reaction of EDA with α-chloroacrolein. α-Chloroacrolein was prepared according to Ref. 12, using 1,2-dichloroethane as solvent, and the reaction with EDA performed at room temp both in CCl_4 and in dichloroethane. The cyclopropanes **5** and **6** were isolated by preparative VPC after a preliminary distillation IR (mixture): 2860 cm^{-1} (CH ald) 1740 (C = O ester), 1725 (C = O ald), 1030 and 858 (cycle).

(E) - 1 - *Chloro* - 1 - *formyl* - 2 - *ethoxycarbonyl cyclopropane* **5**. NMR ($CDCl_3$) $\delta = 9.63$ (*S*, 1, –CHO), 4.21 (q, 2, $C\underline{H}_2$–CH_3); 2.77–2.43 (m, 1, ring) and 2.07–1.77 (m, 2, ring) 1.31 (t, 3, CH_3).

(Z) - 1 - *Chloro* - 1 - *formyl* - 2 - *ethoxycarbonyl cyclopropane* **6**. $\delta = 9.24$ (S, 1, –CHO); 4.15 (q, 2, $C\underline{H}_2$–CH_3); 2.7–1.55 (m, 3, ring, ABC); 1.27 (t, 3, Me).

Reactions of EDA with α-methylacrolein. To a soln of 1.7 ml (2 . 10^{-2} m) methacrolein in 20 ml benzene was added 2.1 ml EDA (2 . 10^{-2} m). The mixture was then stirred and kept at 40° for 12 hr. The evolution of N_2 reached 85% of the theoretical amount. The white ppt was collected and recrystallized in acetone, m.p. 219–224°. IR (Kbr): 3497 cm^{-1} (S, –OH), 1668 (S, C = O ester), 1547 (S, C = N), 1340 (S), 1292 (m), 1266 (S), 1250 (m), 761 (S), 752 (S), 732 (m). NMR (DMSO-$\underline{d}_6$): 6.47 (d, 1, $\underline{J}$ = 3.75 Hz, OH); 5.08 (d, 1, $\underline{J}$ = 3.75, CH): 4.10 (q, 2, $C\underline{H}_2$–CH_3), 3.28 and 2.50 (m, 2, $\underline{J}$ = 16.75, CH_2 (AB)); 1.24 (S, 3, CH_3); 1.16 (t, 3, CH_2–$C\underline{H}_3$). The isomeric cyclopropanes **6** and **7** were purified by VPC after a preliminary distillation (b.p. 45°, 1 mm Hg). (Found: C, 61.6; H, 7.8. Calc. for a mixture of **6** and **7**: C, 61.55, H, 7.69%). IR: 3060, 1735, 1720, 1029, 878 cm^{-1}.

(z) - 1 - *Formyl* - 1 - *methyl* - 2 - *ethoxycarbonyl cyclopropane* **6**. NMR ($CDCl_3$) $\delta = 9.09$ (S, 1, –CHO); 4.05 (q, 2, $C\underline{H}_2$–CH_3), 2.2–1.6 and 1.5–1.0 (m, 3H); 1.15 (S, 3, CH_3); 1.17 (t, 3, CH_2–$C\underline{H}_3$).

(E) - 1 - *Formyl* - 1 - *methyl* - 2 - *ethoxycarbonyl cyclopropane* **7**. $\delta = 8.66$ (S, 1, CHO); 4.05 (q, 2, $C\underline{H}_2$–CH_3); 2.3–1.8 and 1.6–1.1 (m, 3 H); 1.25 (S, 3, CH_3); 1.17 (t, 3, CH_2–$C\underline{H}_3$). Also isolated and purified in the same way was the:

1 - *Ethoxycarbonyl* - 3 - *formyl* - 2 - *butene* **8**. B.p. 54°, 1 mm Hg; IR: 1750 (C = O ester), 1700 (C = O ald), 1662 (C = C). NMR ($CDCl_3$): $\delta = 9.24$ (S, 1, CHO); 6.51 (txd, 1, H vinyl); 4.11 (q, 2, $C\underline{H}_2$–CH_3); 3.23 (dxd), 2, CH_2) 1.66 (d, 3, CH_3); 1.21 (t, 3, CH_2–$C\underline{H}_3$). The coupling constant ^3J_H vinyl-CH_2 = 3.23 Hz, ^4J_H vinyl-CH_3 = 1.5 Hz. (Found C, 61.3, H, 7.6. Calc. for $C_8H_{12}O_3$: C, 61.55, H, 7.69%).

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