REACTION OF β-DIMETHYLAMINOACROLEIN AMINAL WITH ALCOHOLS AND CH-ACIDS

Zh. A. Krasnaya and T. S. Stytsenko

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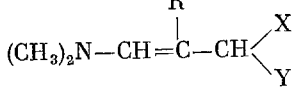
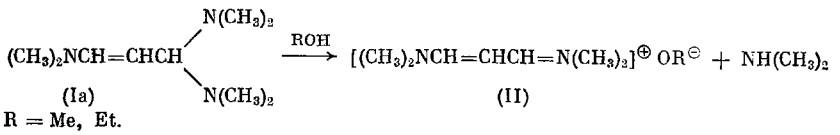
In a continuation of the study of synthesis of unsaturated ω-aminocarbonyl compounds using β-dimethylaminoacrolein derivatives of the type  (I), where R = H, CH_3, or C_6H_5, and X and Y = OCH_3 or $N(CH_3)_2$ [1-6], the present work is a study of the reaction of I with alcohols and CH-acids. β-Dimethylaminoacrolein aminal (Ia) in nonpolar solvents or without a solvent is in the undissociated form, according to PMR (Table 1) and UV spectra (Table 2). Since it is a strong base, Ia decomposes chloroform, and after several days is completely converted to 3-dimethylaminopropenylidenedimethylammonium chloride.

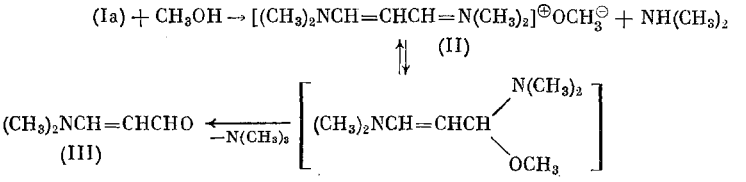
In the reaction with alcohols, as a result of protonation followed by evolution of dimethylamine, Ia is converted to a salt of 3-dimethylaminopropenylidenedimethylamine (II), in which the anion is an OR^- ion:



(Ia) R = Me, Et.

This conclusion follows from the fact that in the PMR spectrum taken in abs. CD_3OD ($6 \cdot 10^{-1}$ mole/liter), the proton signals of Ia have completely disappeared, and the proton signals of II appear (see Table 1). Along with these there also appear the proton signals of β-dimethylaminoacrolein (III). Formation of the mixture of II and III in abs. CH_3OH is confirmed by the appearance of two absorption maxima in the UV spectrum, at 285 (ε 28,000) and 312 nm (ε 20,000), that belong to III and II, respectively. The conversion of Ia to III is significantly accelerated by gentle heating. The III : II ratio is ~1 : 3 at 0°C, ~1 : 1 at 28°C.

In very dilute alcoholic solution ($6 \cdot 10^{-5}$ M), salt II is more stable than in the concentrated solution ($6 \cdot 10^{-1}$ M), and its conversion to III is significantly slower. The UV spectrum of such a solution contains one absorption maximum, at 312 nm (ε 42,700), that belongs to II, only after heating for many hours at 30°C does a shoulder form at 285 nm that belongs to III. The formation of III from Ia may be represented by the scheme:



The presence of $NH(CH_3)_2$ and $N(CH_3)_3$ in the $6 \cdot 10^{-1}$ M solution of Ia in methanol was confirmed by GLC analysis.

It should be noted that in concentrated alcoholic solution other β-dimethylaminoacrolein derivatives, e.g., Ib [R = CH_3, X = OCH_3, Y = $N(CH_3)_2$], Ic [R = C_6H_5, X = OCH_3, Y = $N(CH_3)_2$], and Id (R = H, X = Y = OCH_3), are easily converted to the aldehyde $(CH_3)_2NCH = C(R)CHO$, according to the PMR spectra; while in very dilute alcoholic solution they are converted to the salt $[(CH_3)_2NCH = C(R)CH = N(CH_3)_2]^+OCH_3^-$, according to UV spectra; when R = CH_3, λ_{max} = 325 nm (ε 38,600), and when R = C_6H_5, λ_{max} = 324 nm (ε 34,600) [4].

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TABLE 1. PMR Spectra of $(\overset{a}{CH_3})_2N\overset{b}{C}H{=}\overset{c}{C}H\overset{d}{C}H[\overset{e}{N}(CH_3)_2][\overset{f}{N}(CH_3)_2]$ (Ia)

Chemical shifts, δ, ppm: $(CH_3)_2N$, a	$(CH_3)_2N$, e, f	b	c	d	J, Hz: b, c	J, Hz: c, d	Solvent
2,5	2,05	5,76	3,81	2,53	14	9	None
2,66	2,35	6,04	4,0	3,32	14	9	$CDCl_3$ *
2.52	2,1	5,73	3,8	2,48	14	9	CCl_4
3.08 and 3.25		7,66	5,33	7,66	12	12	Abs. CD_3OD †,‡

*After some days there appeared signals of $[(\overset{a}{CH_3})_2N\overset{b}{C}H = \overset{c}{C}H\overset{d}{C}H = \overset{a}{N}(CH_3)_2]^+Cl^-$ (25%): 3.14 and 3.36 ($N(CH_3)_2$), 5.26 (H^c) and 8.49 (H^b and H^d), $J_{b,c} = J_{c,d} = 12$ Hz.

†These signals belong to the protons of $(\overset{a}{CH_3})_2N\overset{b}{C}H = \overset{c}{C}H\overset{d}{C}H = N(\overset{a}{CH_3})_2$

‡The spectrum also contains signals of $(CH_3)_2N\overset{\beta}{C}H = \overset{\alpha}{C}HCHO$ (III): 2.82 and 3.08 ($N(CH_3)_2$), 5.03 (H^α), 7.31 (H^β), and 8.78 (CHO), $J_{\alpha,\beta} = 12.5$, $J_{\alpha\text{-}CHO} = 9$ Hz; and also signals of $(CH_3)_3N$ and $(CH_3)_2NH$, 2.25.

In contrast to the salts described above, salts of type II with the anions of inorganic acids (I, Cl, ClO_4) are stable in alcoholic solution, and are converted to III only by alkaline reagents.

In the study of the reaction of Ia with CH acids, we discovered that here, just as with alcohols, salts of type II are formed, but with the anion of the CH acid. The formation of such salts as reaction intermediates has already been proposed [9].

From equimolar amounts of Ia and dimethyl malonate, without solvent or in abs. ether, at 20°C the colorless crystalline salt IV is rapidly formed in 80-90% yields; its structure is confirmed by elemental analysis and the UV and PMR spectra. When IV is heated for a short time (5 min, 80-90°C), there is a vigorous evolution of $NH(CH_3)_2$ and the diene δ-dimethylamino diester VI, previously obtained in [1, 9], is formed. In the conversion of IV to VI, the intermediate is apparently the diamine V:

$$(Ia) + CH_2(COOMe)_2 \xrightarrow[-HN(CH_3)_2]{} \underset{(IV)}{[(CH_3)_2NCH{=}CH{-}CH{=}N(CH_3)_2]^{\oplus}\,CH(COOMe)_2^{\ominus}} \rightarrow$$

$$\rightarrow \left[\underset{(V)}{(CH_3)_2NCH{=}CHCH(N(CH_3)_2)CH(COOMe)_2}\right] \xrightarrow[-HN(CH_3)_2]{} \underset{(VI)}{(CH_3)_2NCH{=}CHCH{=}C(COOMe)_2}$$

We previously separated analogous diamines in the condensation of Ia with macrocyclic ketones [6]. It is interesting that the mass spectrum of salt IV contains an intense ion with m/z 127 that corresponds to cation II, and an ion with m/z 213 that is M^+(VI); these are probably related to the partial conversion of IV to VI in the mass spectrometer.

In the reaction of Ia with methyl nitroacetate, the resulting salt $[(CH_3)_2NCH = CHCH = N(CH_3)_2]^+ \cdot NO_2\bar{C}HCOOMe$ (VIIa) is stable and when heated at 80°C for 4 h is not converted to the δ-dimethylamino nitroester previously described by us [1].

The analogous stable salts $[(CH_3)_2NCH = C(R)CH = N(CH_3)_2]^+ \cdot CF_3CO\bar{C}HCOCF_3$ (VIIb) (R = H) and (VIIc) ($R = CH_3$) are formed smoothly by the reaction of Ia and Ib with hexafluoroacetylacetone.

In contrast to the malonic and nitroacetic esters, the anions of which are weakly nucleophilic, such "weak" acids as acetone and 3-methyl-2-azafluorene react with Ia under the same conditions to form the diene amines VIII and IX directly in 85-90% yield. Apparently, the salts formed with the strongly nucleophilic anions in the first stage of the reaction are very easily converted to the thermodynamically stable VIII and IX.

The main product of the reaction between Ia and $CNCH_2CN$, which proceeds rapidly at 20°C, is the diene δ-dimethylaminodinitrile X [9]. This agrees with the fact that cyano derivatives are easily ionized, but the corresponding carbanions add a proton more rapidly than would be expected from the value of the dissocia-

TABLE 2. UV Spectrum of $(CH_3)_2NCH{=}CH{<}^{N(CH_3)_2}_{N(CH_3)_2}$ (Ia)

Solvent	λ_{max}, nm	ε
Hexane	220 (plateau)	9000
	275	4140
Abs. ether	220 (plateau)	8800
	270	2400
	312	800
Abs. CH_3OH *	312	42 700

*According to [8], $[(CH_3)_2NCH = CHCH = N(CH_3)_2]^+ClO_4^-$ has λ_{max} in C_2H_5OH 310 nm (ε 54,700).

tion constant [10]. Along with X, the product contains salt XI and ketenimine XII in ~5 : 1 : 1 ratio (PMR). The structure of XII, which was separated by preparative TLC, was established from UV, IR, PMR, and mass spectra.

$$(Ia) + CH_2(CN)_2 \rightarrow \begin{cases} [(CH_3)_2NCH{=}CHCH{=}N(CH_3)_2]^{\oplus}\overset{\ominus}{C}H(CN)_2 \\ \quad (XI)\ \lambda_{max}\ 312\ nm \\ (CH_3)_2NCH{=}CHCH{=}C(CN)_2 \\ \quad (X)\ \lambda_{max}\ 376\ nm \\ (CN)_2CHCH{=}CHCH{=}C(CN)_2 \\ \quad (XIII) \end{cases}$$

$$NH{=}C{=}CCH{=}CHCH{=}C(CN)_2$$
$$\quad\quad |$$
$$\quad\quad CN$$
$$(XII)\ \lambda_{max}\ 445\ nm$$

The formation of XII may be explained by the replacement of a $N(CH_3)_2$ group by the $\overline{C}H(CN)_2$ anion, and the nitrile-ketenimine tautomerism in the tetranitrile XIII [11].

It should be noted that the reaction of Ia with methyl cyanoacetate proceeds analogously; according to the UV spectra the reaction products are $(CH_3)_2NCH{=}CHCH{=}C{<}^{CN}_{COOCH_3}$ (λ_{max} 385 nm), the corresponding salt (λ_{max} 312 nm), and the ketenimine $NH{=}C{=}CCH{=}CHCH{=}C{<}^{CN}_{COOCH_3}$ (λ_{max} 455 nm), in ~10 : 2 : 1 ratio.

EXPERIMENTAL

PMR spectra were obtained on DA-60IL (60 MHz) and Tesla BS-497 (100 MHz) apparatus with HMDS as internal standard. UV spectra were obtained on a Specord UV-VIS apparatus, IR on a UR-20 apparatus.

$NH(CH_3)_2$ and $N(CH_3)_3$ were identified by GLC at 60°C in a glass capillary 60 m by 0.23 mm, with PEG 40 m-KF stationary phase, Khrom-4 chromatograph with flame-ionization detector, and N_2 carrier gas.

Compound Ia was obtained by the procedure of [12]*, Ib by [4], and Ic by [5].

Reaction of Ia with $CHCl_3$. A solution of 0.3 g of Ia in 2 ml of $CHCl_3$ was kept for 3 days, then evaporated in vacuum. There was obtained 0.22 g of dimethylaminopropenylidenedimethylammonium chloride; mp 192-193°C (after washing with hexane), cf. [13], λ_{max} in C_2H_5OH 312 nm (ε 48,000); PMR data correspond to those given in Table 1. Found: Cl 22.32%. $C_7H_{15}N_2Cl$. Calculated: Cl 21.9%.

*Under the conditions given in [12] for the synthesis of the aminal acetal $(CH_3)_2NCH{=}CHCH{<}^{N(CH_3)_2}_{OCH_3}$ mainly Ia is formed.

Reaction of Ia with Methyl Malonate. When 1.7 g of Ia and 1.3 g of methyl malonate were mixed in 10 ml of abs. ether, a colorless precipitate was quickly formed, which was separated and washed with abs. ether. There was obtained 2.2 g of salt IV. UV spectrum: λ_{max} in C_2H_5OH, 312 nm (ε 31,300). PMR (CD_3OD, δ, ppm): 3.07 and 3.24 ($N(CH_3)_2$), 3.27 ($COOCH_3$), 3.58 (CH), 5.3 (H^{β}), 7.66 (H^{α} and H^{γ}), $J_{\alpha,\beta} = J_{\beta,\gamma} = 12$ Hz. Found: C 55.24; H 8.28; N 10.73%. $C_{12}H_{22}N_2O_4$. Calculated: C 55.79; H 8.58; N 10.85%.

When 0.8 g of IV was heated to 80-90°C, it melted with evolution of dimethylamine, then crystallized when cool. There was obtained 0.65 g of VI, which agreed with the known sample [1, 14] in melting point and UV and PMR spectra.

Reaction of Ia with Methyl Nitroacetate. A mixture of 0.15 g of Ia and 0.1 g of methyl nitroacetate was washed with abs. ether for 10 min. There was obtained 0.2 g of VIIa as a yellowish oil, n_D^{20} 1.5212. UV: λ_{max} in C_2H_5OH, 312 nm (ε 28,200). PMR ($CDCl_3$, δ, ppm): 3.0 and 3.27 ($N(CH_3)_2$), 3.45 ($COOCH_3$), 5.51 (H^{β}), 6.4 (CH), 8.0 (H^{α} and H^{γ}), $J_{\alpha,\beta} = J_{\beta,\gamma} = 12$ Hz.

Reaction of Ic and Ib with $CF_3COCH_2COCF_3$. Ic, 1.72 g, was added gradually to 2.1 g of $CF_3COCH_2COCF_3$ in 4 ml of abs. ether. After 1 min the mixture was evaporated. There was separate 2.8 g of VIIc (after washing with ether–hexane mixture), mp 74-75°C. UV: λ_{max} in C_2H_5OH, 322 nm (ε 60,000). PMR (CD_3OD, δ, ppm): 2.08 (CH_3), 3.22 ($N(CH_3)_2$), 5.51 (CH), 7.34 (H^{α} and H^{γ}). Found: N 8.00%. $C_{13}H_{18}N_2O_2F_6$. Calculated: N 8.05%.

Salt VIIb was obtained analogously, mp 59-60°C. UV: λ_{max} in C_2H_5OH, 312 nm (ε 66,600). PMR (CD_3OD, δ, ppm): 3.02 and 3.22 ($N(CH_3)_2$), 5.24 (H^{β}), 5.49 (CH), 7.64 (H^{α} and H^{γ}), $J_{\alpha,\beta} = J_{\beta,\gamma} = 12$ Hz. Found: N 8.90%. $C_{12}H_{16}N_2O_2F_6$. Calculated: N 8.39%.

Reaction of Ia with Acetone. An equimolar mixture of Ia and acetone was held at 20°C (a) without solvent (b) in abs. ether, and (c) in abs. CH_3OH. The course of the reaction was followed by means of the UV spectrum: 6-dimethylamino-3,5-hexadiene-2-one, VIII, has λ_{max} at 380 nm [2], the salt 3-dimethylaminopropenylidenedimethylamine at 312 nm, and aldehyde III at 285 nm. The results are as follows:

Solvent	Reaction time	Reaction product
None	2 h	VIII†
Abs. ether	3 days	VIII
Abs. CH_3OH	3 days	VIII : III ~ 1 : 1

Reaction of Ia with 3-Methyl-2-azafluorene. To 2.7 g of 3-methyl-2-azafluorene was added 2.85 g of Ia and vigorous evolution of $HN(CH_3)_2$ began at once. The mixture was heated for 15 min at 30°C, cooled, and treated with abs. ether. The precipitate was filtered off and washed with abs. ether. There was obtained 3.5 g (89%) of 3-methyl-9-(δ-dimethylaminobutadienylidene)-2-azafluorene, IX, as a bright orange precipitate, mp 76-84°C from benzene–hexane mixture. UV: λ_{max} in C_2H_5OH, 248 (ε 21,000) and 440 nm (ε 17,300). From PMR spectrum ($CDCl_3$, δ, ppm) IX is a 1:3 mixture of two isomers, A and B, (at the α, β double bond): 2.58 (CH_3), 2.78 ($N(CH_3)_2$), 5.9 (H^{γ}_A), 5.85 (H^{γ}_B), 6.77 (H^{δ}_A), 6.74 (H^{δ}_B), 7-7.86 (H^{β} and Ph protons), 8.74 (H^{1}_A) and 8.97 (H^{1}_B). $J_{\alpha,\beta} = J_{\beta,\gamma} = 12$ Hz (both isomers). Found: C 82.34; H 7.10; N 10.48%. $C_{18}H_{18}N_2$. Calculated: C 82.4; H 6.92; N 10.68%.

Reaction of Ia with Malonodintrile. To 1.5 g of malonodinitrile in 15 ml. of abs. ether was added 4 g of Ia. A precipitate formed immediately; it was washed with abs. ether and filtered off. A precipitate 3 g, was obtained, which by PMR, shown below, contains a 5:1:1 mixture of X, XI, and XII. λ_{max} in C_2H_5OH, 312, 376, and 445 nm. Recrystallization from methanol yielded 2.0 g of X, mp 130-132°C, compare [9], λ_{max} in C_2H_5OH, 376 nm (ε 49,300). PMR of X (δ, ppm, $CDCl_3$): 2.93 and 3.14 (6 H, $N(CH_3)_2$), 5.47 m (1 H, H^{γ}), 7.1 d (1 H, H^{δ}), 7.17 d (1 H, H^{β}), $J_{\beta,\gamma} = J_{\gamma,\delta} = 12$ Hz. IR (KBr, ν, cm^{-1}): 1565 s. broad, 1635 s. broad (C = C), 2200 s. and 2210 s. (CN).

Compound XII was separated from the mother liquor by preparative TLC on SiO_2 (14:1 C_2H_5OH:NH_4OH) as a bright orange precipitate, mp 158-160°C, λ_{max} in C_2H_5OH, 445 nm (ε 78,900). PMR of XII (δ, ppm, $CDCl_3$ + CD_3OD): 6.02 t (1 H, H^{γ}), 7.06 broad d (2 H, H^{β}, and H^{γ}), $J_{\beta,\gamma}$ and $J_{\gamma,\delta}$ = 12 and 13 Hz.

IR spectrum (KBr, ν, cm^{-1}): 1565 s.br (C=C), 2205 s.br (conjugated CN), 3180 m.br (NH). Mass spectrum (m/z): 168 $(M)^+$. During TLC in SiO_2 (C_2H_5OH : NH_4OH, 14 : 1) X gave a pale yellow spot (R_f 0.57) when developed in I_2; XII gave a bright yellow spot (R_f 0.8) without development. PMR spectrum of XI (δ,

*VIII was separated in the usual way.

ppm, $CDCl_3$): 3.08 and 3.28 (12 H, $N(CH_3)_2$), 5.13 t (1H, H^β), 7.45 d (2H, H^α and H^γ) in the 3-3.3 region ($\underline{CH}(CN)_2$) $J_{\alpha,\beta} = J_{\beta,\gamma} = 12$ Hz.

Reaction of Ia with Methyl Cyanoacetate. To 0.1 g of methyl cyanoacetate was added 0.17 g of Ia. A yellow precipitate formed immediately. Abs. ether, 1 ml, was added and 0.14 g of a mixture of three products, described above, was filtered off.

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CONCLUSIONS

1. In the reaction of alcohols with β-dimethylaminoacrolein aminal and α-methyl(phenyl)-β-dimethylaminoacrolein aminal-acetal, salts of 3-dimethylaminopropenylidenedimethylamine are formed, which in concentrated solution are easily converted to α,β-unsaturated β-dimethylaminoaldehydes.

2. In the reaction of β-dimethylaminoacrolein aminal with CH acids, salts of 3-dimethylaminopropenylidenedimethylamine are formed with the CH acid anions; these are intermediates in the formation of diene δ-dimethylamines. Moreover, the reaction of malonodinitrile and methyl cyanoacetate forms diene ketenimines.

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