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Abstract

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SYNTHESIS AND SOME TRANSFORMATIONS OF β-SUBSTITUTED ACROLEINS

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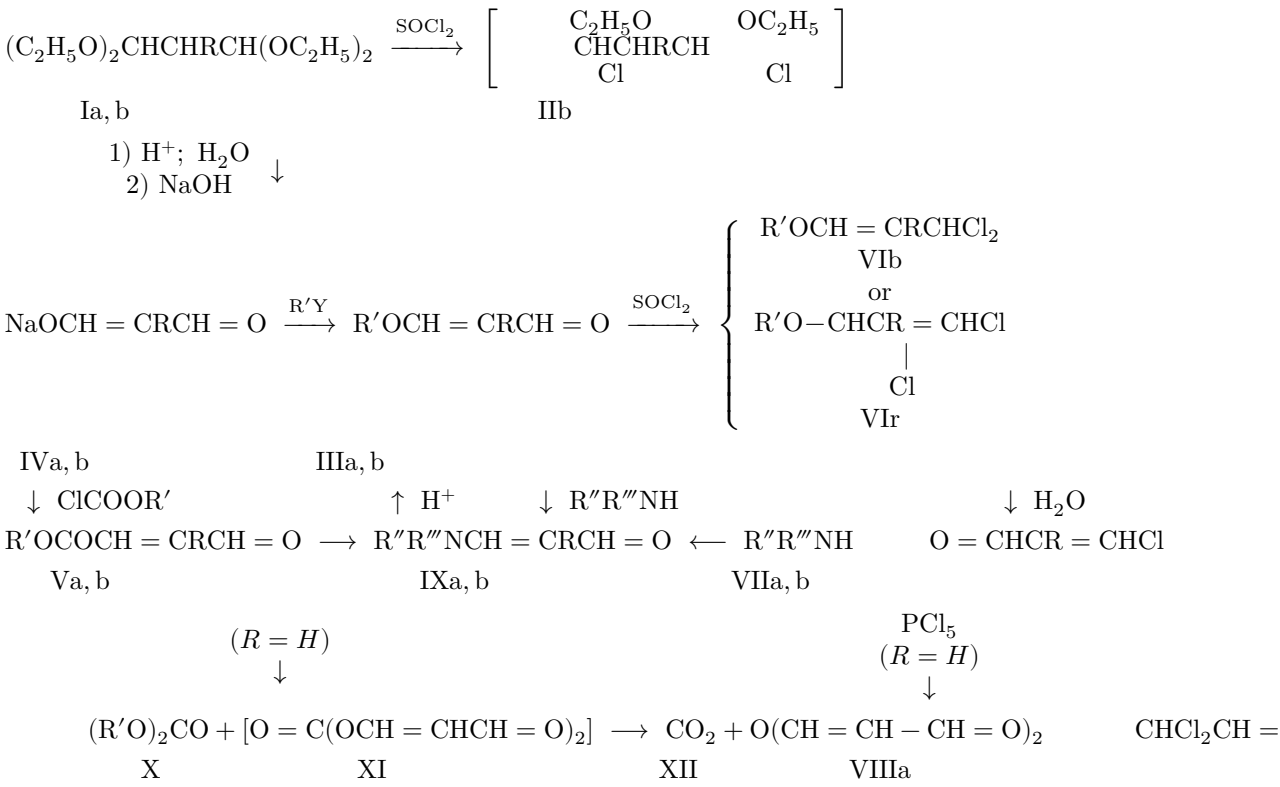
In the present brief communication* we describe methods of preparation, some properties, and reactions of β-substituted acroleins $XCH = CRCH = O$ ($R = H, Alk, Ar$; $X = OR', OCOOR', NH_2, NR'R'', Cl$, etc.), functional derivatives of the enolic form of malondialdehyde or of its homologs. β-Substituted acroleins are vinylogs of the corresponding derivatives of formic acid (its esters, mixed anhydrides, amides, acid chloride, etc.), which is reflected in some methods of their preparation and in their properties. Individual representatives or analogs of these little-studied compounds have recently acquired great importance as pharmacological ([1]) and chemotherapeutic ([2]) preparations and as key substances for the synthesis of carotenoids ([3]), photosensitizers ([4]), and heterocyclic compounds ([5]).

We have previously shown ([6]) that, under the action of thionyl chloride or other acid chlorides on the tetraacetal of malondialdehyde (Ia), a relatively stable di-(α-chloro ether) (IIa) is formed. In attempting to extend this reaction to the full acetals of homologs of malondialdehyde (Ib) ([7]), we established that the corresponding di-(α-chloro ethers) (IIb) cannot be isolated, owing to the ease of their conversion (with loss of hydrogen chloride and alkyl halide) into β-alkoxyacroleins (IIIb) ([8]). This reaction constitutes a simple method for obtaining β-alkoxyacroleins (IIIb), an interesting type of compound about which, prior to our work ([9–11]), there were only brief mentions in the literature ([12,13]). β-Alkoxyacroleins (III), as vinylogs of formic acid esters, were also obtained by us through the interaction of salts of homologs of malondialdehyde (IVb) with alkyl halides, dialkyl sulfates, or esters of arylsulfonic acids ([10]). In all these cases we were unable to detect the formation of products of C-alkylation; evidently, the alkylation of salts of β-dialdehydes (IV) proceeds mainly, if not exclusively, without transfer of the reaction center.



a) $R = H$; b) $R = CH_3,\ C_2H_5,\ iso\text{-}C_3H_7,\ C_6H_5$;
$R' = Alk$; R'' and $R''' = H,\ Alk,\ Ar$;
$Y = Br,\ J,\ OSO_3Alk,\ OSO_2Ar$.

All these routes did not give satisfactory results in attempts to obtain the relatively unstable unsubstituted β-alkoxyacroleins (IIIa).**

* The results of these investigations will be published in greater detail in a series of other papers.

** The recently described preparation of α-methyl-β-ethoxyacrolein by saponification of the corresponding acetal (Ib) with calculated amount of water ([3]) is likewise suitable only for the synthesis of substituted β-alkoxyacroleins (IIIb) ([14]).

Subsequently we found yet another route for the synthesis of β-alkoxyacroleins, which proved to be the most general. It was found that, in the presence of catalytic amounts of acids, alkyl β-acroleinyl carbonates (V) (see Table 1), formed as a result of the reaction of malondialdehyde salts (IV) with chloroformates[^15] with evolution of carbon dioxide, are readily

Table 1

Mixed carbonates
R′OCOCH=CRCH=O (V)

R	R′	Yield, %	m.p., °C	b.p., °C (mm)	C, % found	C, % calc.	H, % found	H, % calc.
H	C_2H_5	76.5	15–16	61–63.5 (1.5)	50.15	49.86 50.00	5.62	5.29 5.55
H	*n*-C_4H_9	83.0		85.5–87 (1)	56.23	56.22 55.82	7.14	7.15 7.02
H	C_6H_5	77.0	41–42	119–120 (2)	62.96	62.24 62.49	4.10	4.14 4.16
H	$CH_2C_6H_5$	71.0	52.5–54		64.42	64.48 64.07	4.81	4.65 4.85
CH_3	CH_3	70.0	64–65		50.01	50.27 50.00	5.48	5.27 5.55
iso-C_3H_7	CH_3	80.0	43–44		55.48	55.54 55.82	7.30	7.24 7.02

converted into β-alkoxyacroleins (III)[^11]. In this way labile unsubstituted β-alkoxyacroleins (IIIa) were obtained and characterized for the first time.

β-Alkoxyacroleins (III) (see Table 2) are liquids distilling in vacuo without decomposition; compounds that do not contain substituents at the α-carbon are hydrolyzed extremely readily. The rate of hydrolysis decreases with increasing R′ and, especially, in the presence of an alkyl radical R in the α-position to the carbonyl group. A considerable exaltation of molecular refraction (2–3 units) and an anomalously high boiling point of the β-alkoxyacroleins indicate an increased polarity of the molecule, caused by conjugation of the free electron pair of the alkoxy oxygen through the double bond with the carbonyl group

Table 2

β-Alkoxyacroleins
R′OCH=CRCH=O (III)

R	R′	Yield, %	b.p., °C (mm)	C, % found	C, % calc.	H, % found	H, % calc.
H	CH_3	73.4	35.5–37.0 (1.5)*	55.8855.70	55.80	7.007.04	7.02
H	C_2H_5	80.0	48–49 (2.5)	60.0860.23	59.98	7.937.82	8.05
H	*n*-C_4H_9	49.0	68–68.5 (2)	65.3765.35	65.59	9.419.35	9.44
H	$CH_2C_6H_5$	59.0	120–123 (2)	74.4274.25	74.05	6.416.52	6.21
CH_3	CH_3	87.5	57–59 (2)	59.9059.69	59.98	7.997.93	8.05
CH_3	C_2H_5	83.3	60–61 (3)	63.5463.36	63.15	8.948.86	8.83
C_2H_5	C_2H_5	54.6	70–72 (3)	65.4265.62	65.59	9.219.39	9.44

* m.p. 14–15°.

$$O{=}CH{-}CR{=}CH{-}OR'$$

The presence of such conjugation may explain the unusual ease of hydrolysis of the alkoxy group, which is diminished by the inductive effect of α-alkyl substituents, as well as the decreased electrophilic reactivity of the carbonyl group. The latter is manifested, for example, in the fact that for β-alkoxyacroleins we were unable to obtain hydrazones, semicarbazones, or oximes; instead, the corresponding cyclization products—pyrazole or isoxazole derivatives—were isolated[^16]. It is possible that in all these cases the first stage of the reaction is substitution of the alkoxy group.

The reaction of β-alkoxyacroleins (III) with thionyl chloride, phosgene, or other acid halides leads to the formation of compounds,

to which either the structure of 1-alkoxy-3,3-dichloropropenes-1 (VIc) or the structure of their allylic isomers, 1-alkoxy-1,3-dichloropropenes-2 (VId), may be assigned [17]. In both cases we have a new type of allylic compounds, containing three different electronegative substituents in the terminal positions of the allylic triad. At present we cannot make a final choice between the structures (VIc) and (VId)*, but the results of a study of the IR spectra, which because of lack of space will be discussed in another communication, make the structure (VId) more probable. The allylic compounds (VI) (see Table 3) are unstable,

strongly fuming liquids in air, distilling with partial decomposition in vacuo, and very readily hydrolyzed by water with formation of the corresponding β-chloroacroleins (VII).

Table 3

Alkoxydichloropropenes R′OCH=CRCHCl$_2$ (VIc) or (R′O)CR=CHCl (VId)

R	R^1	Yield, %	b.p., °C (mm)	d_4^{20}	n_D^{20}	Cl′, %, found	Cl′, %, calcd.	β-Chloroacrolein (X), after hydrolysis, %
H	CH_3	70.0	55–59 (30)	1.4700	1.2289	25.55*; 25.40	25.13	49.0
CH_3	CH_3	78.4	65–68 (30)	1.1025	1.4701	21.95; 22.02	22.87	57.1
CH_3	C_2H_5	80.7	68–70 (12)	1.0920	1.4645	20.47; 20.67	20.97	–
C_2H_5	C_2H_5	62.0	71–75 (10)	1.1036	1.4690	19.11; 19.02	19.34	71.0
iso-C_3H_7	C_2H_5	50.7	73–76 (6)	1.0695	1.4635	17.47; 17.20	17.99	73.0

* Found, %: C 34.18; 33.82; H 4.37; 4.40
$C_4H_6OCl_2$. Calculated, %: C 34.00; H 4.28

The β-chloroacroleins (VII, R = H, CH_3, or C_2H_5) obtained by us by this method were identical with substances recently synthesized by other routes [18,19]. α-Phenyl-β-chloroacrolein (VIII, R = C_6H_5), m.p. 23–24° (literature data [19]: m.p. 25–26°), was also obtained in 42.4% yield, although it was not possible to isolate the corresponding allylic compound (VI, R = C_6H_5). The α-isopropyl-β-chloroacrolein first isolated by us (yield 57.6%) had the following constants: b.p. 45–47° (20 mm), n_D^{20} 1.4670.

Found, %: C 54.73; 55.00; H 7.06; 7.02; Cl 26.34; 26.36
C_6H_9OCl. Calculated, %: C 54.34; H 6.84; Cl 26.74

The synthesis of β-chloroacroleins (VIIb) by this route acquires practical significance because the allylic compounds (VIb) can be obtained directly from acetals

of homologs of malondialdehyde (Ib) by treating the latter with an excess of thionyl chloride [17], without isolation of the intermediately formed di-(α-chloro ethers) (IIb) and β-alkoxyacroleins (IIIb).

By the action of phosphorus pentachloride, β-chloroacrolein (VIIa) was converted into 1,1,3-trichloropropylene-2 (VIII), b.p. 136–137°, n_D^{20} 1.4935, d_4^{20} 1.3895, corresponding in constants to the higher-boiling form of this compound (literature data [20]: b.p. 136.2–136.8°, n_D^{20} 1.4965, d_4^{20} 1.3898).

Among β-aminoacroleins (IX), compounds with a tertiary nitrogen atom (IX, R″ and R‴—radicals) have until now been available and studied mainly; they were obtained by addition of amines to propargyl aldehyde [21] or by the action of a complex of dimethylformamide with phosgene on alkenyl ethers [13]. Using the principle of vinylogy, we obtained a series of β-aminoacroleins (IX) [22] (see Table 4) from β-alkoxyacroleins (III), alkyl β-acroleylcarbonates (V), and β-chloroacroleins (VII). It was established that the most convenient and general route is the action of amines on β-alkoxyacroleins (III). Secondary amines (including such weak bases as diphenylamine), primary amines (the mild reaction conditions make it possible to leave the aldehyde group unaffected), and ammonia can be used as the amines. In the latter case, β-aminoacroleins with a primary amino group are formed—

* The possibility that a mixture of allylic isomers is present also cannot be excluded.

···(vinyl formamide) (23), a type of compound that had not previously been obtained. The results of a study of the structure, properties, and reactions of these compounds will be reported separately.

In addition to the transformation of mixed carbonates (V) into β-alkoxyacroleins (III) under the influence of acid catalysts described above, we also found another possible direction of their decomposition, occurring spontaneously on storage and proceeding especially readily and rapidly for (V, R = H, R′ = C_6H_5). The first stage of the transformation is probably the disproportionation of the mixed carbonate (V) into two symmetrical carbonates X and XI, of which the latter, being unstable, is converted with evolution of carbon dioxide into di-β-acroleyl ether (XII), m.p. 105° (with decomposition).

Table 4

β-Aminoacroleins $R''R'''NCH=CRCH=O$ (IX)

R	R″	R‴	Yield, %	M.p., °C	B.p., °C (mm)	N, % found	N, % calc.
H	H	H	70.0	105–106*		19.88	19.71
H	H	H	70.0	105–106*		20.05**	19.71

R	R″	R‴	Yield, %	M.p., °C	B.p., °C (mm)	N, % found	N, % calc.
CH_3	H	H	51.7	108–109		16.48	16.45
CH_3	H	H	51.7	108–109		16.21	16.45
C_2H_5	H	H	53.8	105–106		13.73	14.12
C_2H_5	H	H	53.8	105–106		13.94	14.12
C_6H_5	H	H	81.6	97–100		9.39	9.52
C_6H_5	H	H	81.6	97–100		9.56	9.52
H	H	CH_3	60.0	41–43	85–87 (1.5)	16.66	16.45
H	H	CH_3	60.0	41–43	85–87 (1.5)	16.67	16.45
H	H	C_2H_5	55.5	22–25	90–94 (1)	14.09	14.12
H	H	C_2H_5	55.5	22–25	90–94 (1)	14.19	14.12

* Sublimes in vacuum.
** Found %: C 50.73; 50.74; H 7.09; 6.95
C_3H_5ON. Calculated %: C 50.69; H 7.09

Found %: C 57.09; 57.23; H 4.74; 4.59
$C_6H_6O_3$. Calculated %: C 57.14; H 4.75

Methyl β-acroleyl carbonate (V, R=H, R′=CH_3) is converted on storage into the same di-β-acroleyl ether (XII), but in this case the transformation proceeds considerably more slowly.

The two possible directions of decomposition of alkyl β-acroleyl carbonates (V): into β-alkoxyacroleins (III) and into di-β-acroleyl ether (XII), are probably transformations vinylogous to the two recently discovered pathways of decomposition of mixed anhydrides of formic and carbonic acids

RCOCOR′

with formation of esters

RCOR′

and anhydrides $(RCO)_2O$ (24).

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Note: Figure translations are in progress. See original paper for figures.