197. Diazoaldehyde Chemistry

Part 1

Transdiazotization of Acylacetaldehydes in Neutral-to-Acidic Medium. A Direct Approach to the Synthesis of α-Diazo-β-oxoaldehydes[1])

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(12.VII.94)

First ever non-deformylating transdiazotization of acylacetaldehydes was achieved: the reactions of 2-azido-1-ethylpyridinium tetrafluoroborate (**4**) with acylacetaldehydes **3** proceeded partially without deformylation to yield 16 new α-diazo-β-oxoaldehydes **1** along with diazomethyl ketones **2**, especially in the presence of NaOAc (*Scheme 1*, *Tables 1* and *2*). The product distribution was substituent-dependent and could be correlated quantitatively. This new diazotization reaction appears as an alternative, direct, and more general method for the synthesis of these diazooxoaldehydes. α-Oxocycloalkanecarbaldehydes **5** gave only traces (if any) of α-diazocycloalkanones **7**, and rearrangement products **6** were isolated (*Scheme 2*). Mechanisms of the reactions are discussed (*Schemes 4* and *5*).

Introduction. – The diazo function adds fascinating properties to organic compounds. Although a number of α-diazo-β-dicarbonyl compounds are known (for synthetic methods and numerous examples, see [1]), only three representatives of α-diazo-β-oxoaldehydes **1**, which are available *via* low-yield and multi-step methods, appear in the literature. The synthesis of diazomalonaldehyde (**1a**, R = H) *via* amine diazotization [2] seems to be an incovenient route to compounds of this type, due to the multi-step and low-yield syntheses of the unstable α-amino-β-oxoaldehydes [3]. *Vilsmeier-Haack* formylation of diazomethyl ketone **2**, which allowed the syntheses of ethyl (formyl)diazoacetate (**1b**, R = EtO) [4] [5] and (benzoyl)diazoacetaldehyde (**1c**, R = Ph) [4] each in 25% yield based on the starting **2b** and **2c**, respectively, was not successful with diazomethane [4], diazoacetaldehyde (**2a**, R = H) [2a], and diazoacetone (**2d**, R = Me) [4]. Therefore, a general method is necessary for the syntheses of α-diazo-β-oxoaldehydes.

$$\underset{\mathbf{1}}{RCO{-}CN_2{-}CHO} \qquad \underset{\mathbf{2}}{RCO{-}CHN_2}$$

Our interest in these compounds is due to the versatility of their use in organic syntheses. The available literature includes mainly the syntheses of dioxalenes, dihydrofurans, and 1,3-oxazoles [5] [6], which were in turn used as starting materials for various 3-substituted furans and pyrroles [6a, b] and for some antibiotics [6a, d]. Reactions leading to triazoles and thiadiazoles were reported [2a] [4]. Syntheses of triazolyl-

[1]) Abstracted from the Ph. D. Thesis by *Ö. S.*, Istanbul, 1994.

methylenepenemcarboxylates were patented [7]. *Wolff* rearrangement of these compounds was also a point of interest [2a] [4] [8], and this led to a recent elegant synthesis of γ-pyrone (4*H*-pyran-4-one) [6b]. In addition, the isolation of novel 'carbene dimers' [2a] [6c] confers on this class of diazo compounds the suitability to be precursors of a lovely chemistry.

In the present study, we approached to the synthetic problem using the diazo-transfer method [9] which is shown retrosynthetically below.

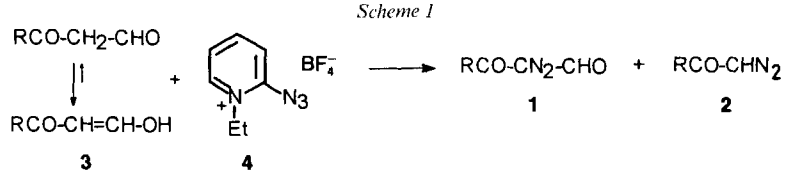
$$\underset{\mathbf{1}}{RCO{-}CN_2{-}CHO} \Rightarrow \underset{\mathbf{3}}{RCO{-}CH_2{-}CHO} + R'{-}N{=}N_2$$

This route is a challenging one, since it is generally used to synthesize diazomethyl ketones **2** from the sodium salts of **3** and sulfonyl azides, representing a deformylating diazo transfer [9] [10]. The reason for the choice of this route was the mechanistic uncertainty of the deformylation: If the genuine intermediate of the reaction is a triazene, and if the diazomethyl ketones **2** result from the solvolysis of the initially formed α-diazo-β-oxoaldehydes **1** under basic conditions [10], one should be able to synthesize the latter using the transdiazotization reagents in neutral and acidic media.

The most common reagents for diazo transfer in neutral and acidic medium are the azidinium salts [11]; one of them, *i.e.*, 2-azido-1-ethylpyridinium tetrafluoroborate (**4**), was recently prepared *in situ* from relatively inexpensive starting materials [12]. Although the presence of dihydrotriazole intermediates for some specific reactions of azidinium salts was reported [13] [14], the general diazo-transfer mechanism using these reagents was proposed to involve triazene intermediates [11], and this was considered as an additional clue for a probable non-deformylating diazo transfer.

Results. – The 2-azido-1-ethylpyridinium tetrafluoroborate (**4**) was chosen as the reagent for the diazo transfer in neutral-to-acidic medium[2]), and the reactivity of this azide towards acylacetaldehydes **3** was investigated under six different conditions (*Scheme 1*, *Table 1*). When no additives were used, the solution of **4**, prepared *in situ* from NaN_3 and 2-chloro-1-ethylpyridinium tetrafluoroborate in $MeOH/H_2O$, was added directly to **3** in MeOH (see *Exper. Part*). The formation of diazomethyl ketones **2** as the only products, except in the case of the three *ortho*-substituted **1n**, **1o**, and **1s** (R = aryl), is a strong indication of dihydrotriazole intermediates in the reaction. This was more evident on observing the very different reactivities of α-oxocycloalkanecarbaldehydes

Scheme 1



[2]) (Azidochloromethylidene)dimethylammonium chloride [15a, b] is not a cheaper alternative. On the other hand, azidoformamidinium chloride, which can be prepared *in situ* from the very cheap aminoguanidinium hydrogen carbonate [15c], was also used in preliminary experiments: reactions of this *in situ* prepared azide with **3c** in aq. MeOH (pH 4–5, AcOH/AcONa) gave remarkable **1c**/**2c** ratios, but very low yields. When the isolated azide [15d] was reacted with **3c** in aq. MeCN for one week without buffer, no **1c** or **2c** was found, and a tetrazolopyrimidine derivative was isolated in low yield.

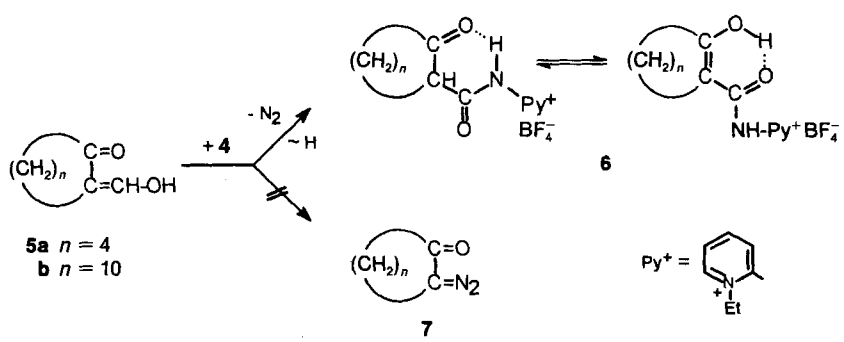
Table 1. *Transdiazotizations of Acylacetaldehydes* **3** *to Diazooxoaldehydes* **1** *and Diazomethyl Ketones* **2** *According to* Scheme 1[a])[b])

	R	100 × **1**/(**1** + **2**)					
		no additive	*A*	*B*	*C*	*D*[c])	*E*
3b	EtO					39.0[d])[e])	
c	Ph	0.0	4.33	10.10	3.30[f])	12.0[g])	26.10[c])
d	Me					61.0[d])[e])	53.0[c])[d])[h])
e	i-Pr	0.0	8.50				35.7[c])[i])
f	Me_2CHCH_2	0.0	12.40				26.0[i])
g	*t*-Bu	0.0	≈ 0.7[i])	≈ 1.40[i])			7.25[i])
h	4-Me–C_6H_4	0.0	2.00				15.90[c])
i	4-MeO–C_6H_4	0.0	1.55	3.57	1.75[j])		10.75[c])
j	4-F–C_6H_4	0.0	4.85				28.60
k	4-Cl–C_6H_4	0.0	6.25				52.55[c])
l	4-Br–C_6H_4	0.0	6.50	14.52	3.43[k])		47.85
m	3,4-Cl_2–C_6H_3	≈ 0.7	23.15	33.46	8.40		74.0
n	2,4-Cl_2–C_6H_3	5.7	72.44	79.10			86.05
o	2,4-Br_2–C_6H_3	24.9	74.43				94.90
p	2,4-$(MeO)_2$–C_6H_3	0.0					3.20[c])[j])
q	3-NO_2–C_6H_4	≈ 1.0[l])	33.30	47.35			
r	4-NO_2–C_6H_4	≈ 1.0[m])	34.00	58.35			
s	2,4,6-Me_3–C_6H_2	16.15	41.35				92.40[c])
t	Naphthalen-1-yl	0.0	6.08				37.90[c])
u	Naphthalen-2-yl	0.0	3.85				19.10[c])
v	3,5-Me_2-Furan-2-yl	0.0	≈ 0.7[i])				3.42[c])[j])

[a]) Transfer yield (**3**→**1** + **2**) at least 85–90%, unless otherwise stated; ratios **1**/(**1** + **2**) from ^{1}H-NMR. [b]) For reaction conditions *A–E*, see text or *Exper. Part.* [c]) Oxoaldehyde was generated *in situ* (see *Exper. Part.*). [d]) Data not realiable due to the volatility and probable side reactions of **2b** or **2d**. [e]) Transfer yield *ca.* 15%. [f]) 15% **3c** unreacted (^{1}H-NMR). [g]) Transfer yield *ca.* 70–75%. [h]) Transfer yield *ca.* 50–60%. [i]) Data not reliable. [j]) 34% **3i** unreacted (^{1}H-NMR). [k]) 23% **31** unreacted (^{1}H-NMR). [l]) 14% **3q** unreacted (^{1}H-NMR). [m]) 30% **3r** unreacted (^{1}H-NMR).

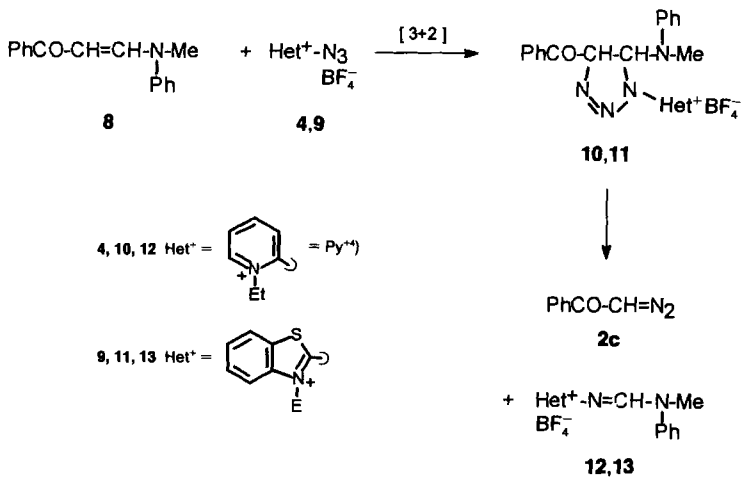
5a, b under the same conditions and under all other conditions which will be discussed below: no formation of diazoketones **7** but rearrangement under evolution of N_2 occurred, yielding products **6a, b** (*Scheme 2*). Such a reaction path was not observed for acylacetaldehydes **3** (*Scheme 2*). The α-oxocycloalkanecarbaldehydes **5a, b** underwent also, to some extent, rearrangement, when they were reacted with tosyl azide (up to 5% in case of **5a** and up to 40% in case of **5b**) [16].

Scheme 2



The 1,3-dipole character of the azidinium salts was further evidenced by reacting pyridinium salt **4** or benzothiazolium salt **9** with β-(*N*-methylanilino)acrylophenone (**8**), which is isolelectronic with the enolic acylacetaldehydes **3**. The expected diazoacetophenone (**2c**) and the formamidine derivative **12** and **13**, formed *via* **10** and **11**, respectively, were isolated from the reaction mixtures in good yields (*Scheme 3*). The reaction is analogous with the ones reported for sulfonyl azides [17].

Scheme 3



The reaction of acylacetaldehydes **3** with **4** at pH 4.3–4.4, using AcOH/AcONa buffer, failed to give rearrangement products *via* acid-catalyzed dihydrotriazole decomposition (for the decompositions of dihydrotriazoles by acid, see [18]); instead, considerable amounts of diazooxoaldehydes **1** were observed[3]) (*Table 1*, conditions *A*). The results of the reactions under conditions *B* and *D* at essentially the same pH value, but using two- and six-fold concentrated buffers, revealed a buffer-concentration effect: the diazooxoaldehyde formation ratios were almost doubled or tripled as compared to conditions *A*, and this was promising from the preparative point of view. This effect also showed that the role of AcOH/NaOAc was not only due to pH adjustment but that those additives also acted as reaction participants.

The influence of the AcOH component of the buffer additive on the formation of **1** was found to be less pronounced, as evidenced by the product distributions obtained under conditions *C*, *i.e.*, at pH 3.9–4.0, with the same amount of AcOH but ¼ amount of NaOAc compared to conditions *B* (see *Exper. Part*): the formation of **1** was greatly suppressed, even in comparison to conditions *A*. This result apparently suggested the use of NaOAc alone as additive.

Indeed, when NaOAc was used as the only additive (conditions *E*, pH 7.4–7.8) the highest **1**/(**1** + **2**) ratios were obtained (*Table 1*). Thus, the reaction of **3** and **4** under

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[3]) A third product other than **1c** and **2c** was isolated from some of the reactions of **3c** with erratic yields (0–20%). The compound was spectroscopically identical to authentic 3,5-dibenzoylpyrazole [19]. Under our diazo-transfer conditions, reaction of **2c** and **3c** to yield this product was unsuccessful. Whether this compound is arising from the transdiazotization of dimerized **3c** is unknown.

conditions *E* represents a mild and direct preparative method for α-diazo-β-oxoaldehydes **1** and shows that transdiazotization of acylacetaldehydes **3** can proceed without deformylation. The obtained 16 new α-diazo-β-oxoaldehydes **1** include acetyldiazoacetaldehyde (**1d**) which was not available to *Stojanovic* and *Arnold* [4]. Some spectral characteristics of **1b–v** are shown in *Table 2*.

Although most yields of **1** were modest, the simplicity of our procedure counterbalances this drawback. *E.g. Vilsmeier* formylation of **2c** gave a 25% yield of **1c** [4], **2c** being obtained either *via* diazomethane acylation or *via* deformylating diazo transfer in 70–80% yield; thus, the overall yield of **1c** *via* the multi-step route was 18–20%, comparable to our yield (19%). Furthermore, *Table 2* shows much higher yields for other diazooxoaldehydes. The isolation of **1g**, **1p**, and **1v** was not successful due to their low formation ratios. Optimization studies for higher yields are in progress.

Table 2. *Some Data of α-Diazo-β-oxoaldehydes* **1**

	R	Yield [%][a]	IR[b]		^{1}H-NMR[c]
			$\tilde{\nu}$ (C=N=N)	$\tilde{\nu}$ (CO)	δ (CHO) ($\omega_{1/2}$)
1b	EtO	2–3[d]	2148[e]	1715, 1665[e]	9.70
c	Ph	19.0	2173, 2135[f]	1652, 1615[f]	9.78
d	Me	19.2	2162, 2136[e]	1672, 1641[e]	9.75 (3.7)
e	i-Pr	19.9	2156, 2143	1674, 1645	9.78 (3.1)
f	Me_2CHCH_2	20.0	2156, 2132	1674, 1641	9.76 (2.5)
g	*t*-Bu	–	2155, 2139[g]	1669[g]	9.96[g]
h	4-Me–C_6H_4	11.9	2166, 2135	1661, 1633	9.78
i	4-MeO–C_6H_4	7.2	2166, 2133	1663, 1634	9.80
j	4-F–C_6H_4	23.7	2168, 2137	1665, 1633	9.76
k	4-Cl–C_6H_4	45.7	2168, 2133	1665, 1637	9.74
l	4-Br–C_6H_4	42.5	2166, 2133	1667, 1635	9.73
m	3,4-Cl_2–C_6H_3	58.9	2176, 2158	1668, 1634	9.73
n	2,4-Cl_2–C_6H_3	72.7	2172, 2141	1670, 1639	9.44 (15.4)
o	2,4-Br_2–C_6H_3	88.3	2168, 2141	1671, 1641	9.40 (26.9)
p	2,4-$(MeO)_2$–C_6H_3	–	2159[g]	1659[g]	9.66[g]
q	3-NO_2–C_6H_4	33.0[h]	2180 (sh), 2164, 2130	1672, 1634	9.74
r	4-NO_2–C_6H_4	50.2[h]	2170, 2136	1669, 1634	9.71
s	2,4,6-Me_3–C_6H_2	76.7	2162, 2135	1665, 1636	9.00 (7.0)
t	Naphthalen-1-yl	29.7	2162, 2135	1662, 1632	9.55 (3.7)
u	Naphthalen-2-yl	13.0	2160, 2129	1662, 1630	9.85
v	3,5-Me_2-Furan-2-yl	–	2149[g]	1642[g]	10.12[g]

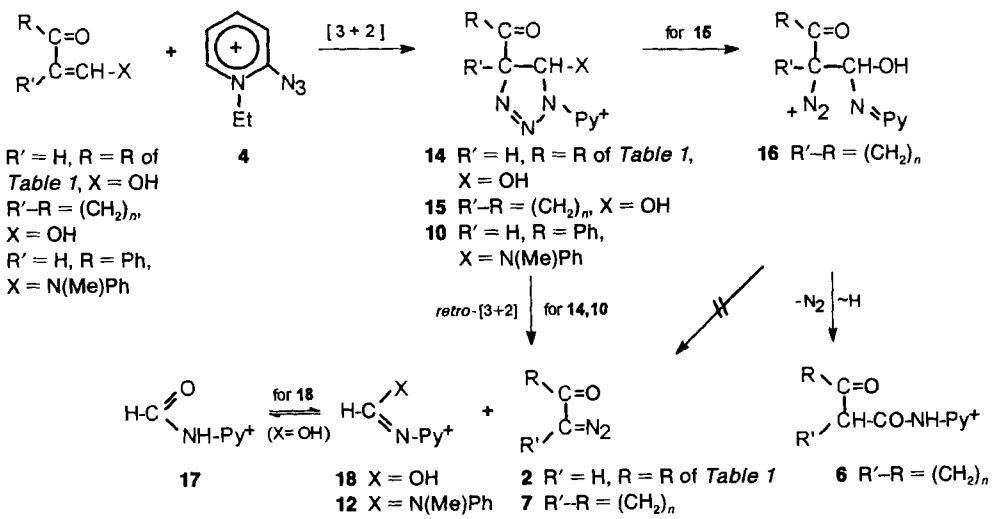
[a]) Conditions *E*; yields after isolation. [b]) In CH_2Cl_2 or $CHCl_3$. [c]) In $CDCl_3$; $\omega_{1/2}$, band width at half height; $\omega_{1/2}$ usually 1.83 Hz, higher values (in parentheses) are very possibly due to a hindered internal rotation which will be subject to another study. [d]) From conditions *D*. [e]) Taken as film. [f]) Taken as KBr pellet. [g]) From the spectra of crude reaction mixtures. [h]) From conditions *B*.

The action of NaOAc is somewhat surprising, considering the lability of α-diazo-β-oxoaldehydes (for the Et_3N-catalyzed cleavage of **1a**, see [20a]; for the base-catalyzed cleavage of α-diazo-β-dicarbonyl compounds, see [20b]). Mechanisms of the reactions are discussed below.

Discussion. – It is apparent that the formation of the diazomethyl ketones **2** from acylacetaldehydes **3**, and the rearrangement of α-oxocycloalkanecarbaldehydes **5** pro-

ceed *via* the dihydrotriazole intermediates **14** and **15**, respectively (*Scheme 4*). The products obtained from **5** suggest that **15** is transformed to the diazonium structure **16** by ring opening. This also reveals the elimination inability of the CH(OH)–N=Py group[4]) from **16** to form an α-diazocycloalkanone **7**. In contrast, dihydrotriazole **14** does not undergo ring opening to a diazonium structure, and the diazomethyl ketone **2** could arise from a synchronous cycloelimination (*retro*-[3 + 2]) reaction. Substitution of the H-atom in **14** (R′ = H) with the electron-releasing alkyl group at C(α) of **15** might be responsible for this different reactivity, the alkyl group at C(α) stabilizing the neighboring cation in **16**. The reaction of the aminoenone **8** with **4** (or **9**) should also proceed *via* the *retro*-[3 + 2] decomposition[5]) of the dihydrotriazole intermediate **10** or **11**.

Scheme 4[4])[a])



[a]) For convenience, the counterions BF_4^- are omitted.

The product distributions obtained under conditions *A*–*C* and *E* show an apparent substituent dependency (see *Table 1*). Increasing electron-withdrawing character of the acyl R group causes higher **1**/(**1** + **2**) formation ratios. A search for a quantitative relationship between the data resulted in a good correlation using the *Hammett* equation in the benzoylacetaldehyde series (conditions *A*: $\rho = 1.48$, $n = 9$, $r = 0.9946$, $c = \pm 0.09$; conditions *B*: $\rho = 1.40$, $n = 6$, $r = 0.9917$, $c = \pm 0.10$; conditions *C*: $\rho = 0.78$, $n = 4$, $r = 0.9709$, $c = \pm 0.09$; conditions *E*: $\rho = 1.63$, $n = 7$, $r = 0.9908$, $c = \pm 0.12$). While the ρ values obtained under the conditions *A* and *B* are similar in magnitude, the ones obtained under conditions *C* and *E* are the lowest and the highest, respectively. This might be a mathematical representation of the effectivenesses of AcOH and NaOAc.

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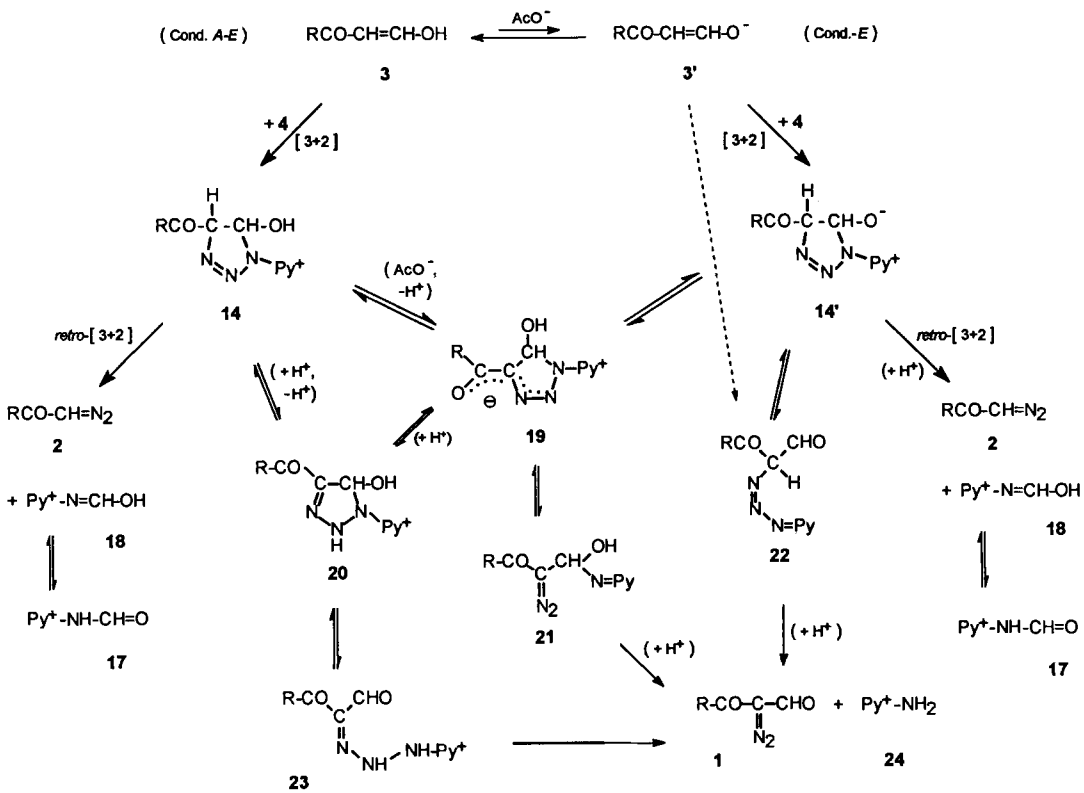
[4]) Py^+ and Py stand for the 1-ethylpyridin-1-ium-2-yl and 1-ethylpyridin-2-ylidene residue, respectively (see *Schemes 2* and *3*).

[5]) One does not have to agree with *Fusco et al.* [17a] that the reactions of enamines with sulfonyl azides proceed *via* ring opening of the dihydrotriazole intermediates. Competition of dihydrotriazole ring-opening and *retro*-[3 + 2] reactions seems to depend on the substituents of the enamine.

Since the *Hammett* correlation is usually applied to the data sets of reaction rates or equilibrium constants, this correlation of product distribution indicates the presence of two equilibrating intermediates in the diazo transfer. Each of these intermediates should be responsible for the formation of one of the products **1** and **2**. Taking this into consideration, we propose the mechanistic interpretation of the results shown in *Scheme 5*.

Scheme 5[4])[a])



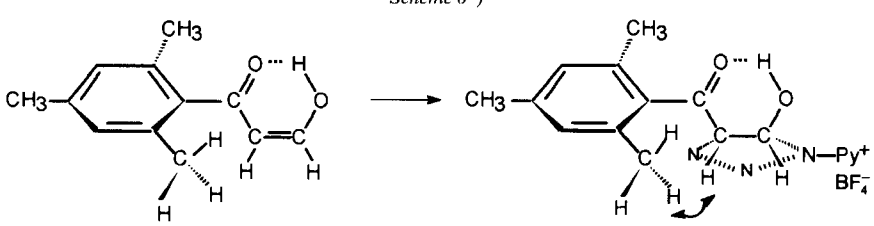
[a]) For convenience, the counterions BF_4^- are omitted.

We suggest that the 'first intermediate' of the reaction is dihydrotriazole **14**, and the origin of the substituent effect is the C–H acidity of **14**. The acidity of H–C(4), which is activated both by the RCO and the N=N groups is expected to increase with the increasing electron-withdrawing character of the acyl R group. Deprotonation of **14** should give the resonance-stabilized betaine **19** (see **14**⇌**19**). This 'second intermediate' then can recapture a proton to yield the tautomeric dihydrotriazole **20** (which can be assigned higher stability by analogy to the 4,5-dihydro-3*H*- and 1*H*-4,5-dihydropyrazoles [21]) and subsequently undergo ring opening to the triazene **23**, finally yielding **1** by an α-elimination of **24**. Conversion of **14** to **20** may also take place by a protonation-deprotonation sequence. The route **19**→**20**→**23**→**1** is reminiscent of the mechanism of a dihydrotriazole isomerization, which was proved to involve triazene intermediates, but

not diazo compounds [22]. On the other hand, the route **19**→**1** *via* the diazo intermediate **21** is reminiscent of *Huisgen*'s formulation of a dihydrotriazole→α-diazo-β-amino ester conversion aided by Et_3N [23]. Although it will be speculative, one may prefer the route **19**→**20**→**23** by analogy to the study of the *Regitz'* group, who presented a triazene-dihydrotriazole conversion as a mechanistic explanation of their results[6]).

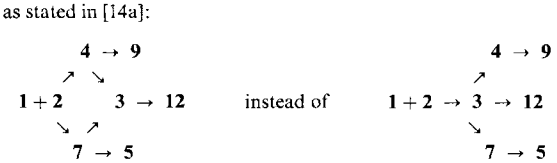
As a second alternative, one may consider the acidity of the enolic OH group of **3**, which is obviously prone to a substituent effect (see **3**⇌**3′**; especially a probable assumption of different reactivities for **3** and **3′**: **3′**→**22**→**1′** and **3**→**14**→**2**). If this is the case, it would be more difficult to explain the *ortho*-effect, *e.g.* especially the behavior of mesitoylacetaldehyde **3s** in the reaction without additive (see *Table 1*). To our knowledge, pK_a values of acylacetaldehydes are not listed, but one can use the pK_a values of corresponding benzoic acids for comparative purposes. In H_2O solution, the pK_a values of mesitoic and 4-nitrobenzoic acids are 3.43 and 3.44, respectively, thus being almost equal [24a]. Mesitoic acid is even a weaker acid than 4-nitrobenzoic acid in MeCN solution (pK_a 20.5 and 18.7, resp. [24b]). But the comparison of the reactivities of the corresponding aldehydes **3r** and **3s** shows independence from these pK_a values: In the reaction without additive, **3r** gives a **1r** formation ratio of 1, whereas **3s** gives a **1s** formation ratio as high as 16%. This difference can be better explained by the mechanisms proposed above considering the steric effects on the acidity of the dihydrotriazole's active H-atom (*Scheme 6*). Using *Dreiding* models, one can see that in dihydrotriazole **14s**, the active H-atom experiences steric hindrance from the *ortho*-Me groups. Thus, the relatively easier spontaneous deprotonation of **14s** is expected to yield the sterically more comfortable **19s** and the relevant C-atom reconverts to sp^2 hybridization from sp^3. The reactions of the 2,4-dihalogeno derivatives **3n** and **3o** can also be interpreted similarly. That such an *ortho*-effect was not observed in the reactions of **3p** may be due to the smaller volume of the MeO group (E_s values for Me, Br, Cl, and MeO are −1.24, −1.16, −0.97, and −0.55, resp. [25]). No steric effects were observed on the *Dreiding* models of **3p** and **14p** as well as of **3t** and **14t** and **3v** and **14v**.

Scheme 6[4])



3s **14s**

[6]) The results of *Regitz* and coworkers [14a] may also be formulated in the following way, using the original compound numbers as stated in [14a]:



Conclusion. – Whatever the mechanism is, the reaction of 2-azido-1-ethylpyridin-1-ium tetrafluoroborate (**4**) with β-oxoaldehydes **3** in the presence of NaOAc can be considered as a direct preparative method for α-diazo-β-oxoaldehydes **1**, which are potentially useful synthetic reagents. The more general nature of the present method is evidenced by the successful synthesis of acetyldiazoacetaldehyde (**1d**), which was not available by the existing methods [4]. The reactions of other active acetaldehydes, *e.g.* aryl-, vinyl-, sulfinyl-, sulfonyl-, and phosphorylacetaldehydes, as well as nitro- and cyanoacetaldehydes are under study.

The authors wish to express their gratitude to the *İ.T.Ü. Research Foundation* for financial support and to *Hoechst AG*, Germany, for a generous gift of a 2,4-dichloroacetophenone sample.

Experimental Part

1. *General.* The *2-acetyl-3,5-dimethylfuran* [26], *2,4-dibromoacetophenone* [27], *β-(N-methylanilino)acrylophenone* [28] (**8**), *2-chloro-1-ethylpyridinium tetrafluoroborate* [12] [29], *2-azido-1-ethylpyridinium tetrafluoroborate* [29] (**4**), *2-azido-3-ethylbenzothiazolium tetrafluoroborate* [29] (**9**), *ethyl formyldiazoacetate* [4] [5] (**1b**), and *benzoyldiazoacetaldehyde* [4] (**1c**) were prepared by literature procedures. The other starting materials were commercially available. pH's were measured with a *Metrohm-E-488* pH meter. IR Spectra: *JASCO-FT-IR-5300* spectrometer. NMR Spectra: δ in ppm, J in Hz; 200-MHz-*Bruker* instrument.

2. *β-Oxoaldehydes* (**3**) *and Their Sodium Salts.* Sodium enolates of **3** were prepared from the corresponding methyl ketones and ethyl or methyl formate using standard *Claisen* condensation techniques (with NaH or NaOMe in Et_2O, THF, or PhH). Yields were mostly higher than 85–90%. Free **3** were isolated by dissolving the sodium enolates in cold H_2O, discarding any impurities by extraction with CH_2Cl_2, acidifying with 10% excess of 2N AcOH, and extracting with CH_2Cl_2. After drying ($MgSO_4$) and evaporation, the residues were purified by distillation *in vacuo* or recrystallization from an appropriate solvent, whenever possible. Purification *via* the Cu chelates was especially avoided to prevent contamination with Cu compounds. To our knowledge, three of the obtained β-oxoaldehydes, *i.e.* **3o**, **3u**, and **3v** were not reported, neither free nor as their sodium salts.

(Z)-1-(2',4'-Dibromophenyl)-3-hydroxyprop-2-en-1-one (**3o**): Not isolated as Na salt. Yield 79%. M.p. 70–72° (petroleum ether/AcOEt 4:1). IR (KBr): 1627. ^{1}H-NMR ($CDCl_3$): 6.03 (*d*, J = 4.44, COCH=); 7.40 (*d*, ^3J(5',6') = 8.2, H–C(6')); 7.53 (*dd*, ^4J(3',5') = 1.74, H–C(5')); 7.81 (*d*, H–C(3')); 8.07 (*d*, CH=C*H*OH); 14.42 (br. *s*, OH).

(Z)-3-Hydroxy-1-(naphthalen-2'-yl)prop-2-en-1-one (**3u**): Yield 89% as Na salt. Hydroxy compound, m.p. 51–54° (petroleum ether AcOEt, 5:1). IR ($CHCl_3$): 1617. ^{1}H-NMR: 6.37 (*d*, J = 4.19, COCH=); 8.34 (*d*, CH=C*H*OH); 7.46–8.46 (*m*, 7 arom. H); 15.37 (br. *s*, OH).

(Z)-1-(3',5'-Dimethylfuran-2'-yl)-3-hydroxyprop-2-en-1-one (**3v**): Yield 83% as sodium salt. Orange, undistillable oil, when free. IR (neat): 1623. ^{1}H-NMR (60 MHz, CCl_4): 2.30 (*s*, Me–C(3'), Me–C(5')); 5.90 (*s*, H–C(4')); 5.92 (*d*, $J \approx 5$, COCH=); 7.40 (*d*, CH=C*H*OH); OH not observed.

3. *Transdiazotizations of* **3**: *Conditions* A–C *and No-Additive Conditions.* 3.1. *2-Azido-1-ethylpyridin-1-ium Tetrafluoroborate* (**4**) *Solution.* To the soln. of 1.605 g (7 mmol) of 2-chloro-1-ethylpyridinium tetrafluoroborate in 7 ml of MeOH and 4 ml of H_2O, cooled with ice/salt, 0.455 g (7 mmol) of NaN_3 were added in 1 portion. The bath was removed and the soln. allowed to warm to r.t. with continued stirring. This soln. of **4** was conditioned as described below.

No-Additive Conditions: No buffer reagent was added to the soln. of **4** which was used directly for the next step (pH *ca.* 5.3–5.5).

Conditions A: To the soln. of **4**, 0.43–0.45 ml of 2N NaOAc were added. This was followed by dropwise addition of 0.55–0.60 ml of AcOH to attain pH 4.3–4.4.

Conditions B: As described for conditions *A*, with 0.90 ml of 2N NaOAc and 1.10–1.20 ml of AcOH (pH 4.3–4.4; two-fold concentrated buffer compared to conditions *A*).

Conditions C: As described for conditions *A*, with 0.20 ml of 2N NaOAc and 1.10–1.20 ml of AcOH (pH 3.9–4.0; same amount of AcOH, but 1/4 amount of NaOAc, compared to conditions *B*).

3.2. *Diazo Transfer.* To a soln. of 5.7 mmol of acylacetaldehyde **3** in 3–5 ml of MeOH, the conditioned soln. of **4** was added in 1 portion (23% excess of **4**). The mixture was stirred at r.t. for 2.5 h. If **3** was not in soln. initially, it

completely dissolved usually within 30 min, when a yellow oil or sometimes a solid separated. After the mentioned period, 60 ml of H_2O were added, and the products were extracted with 3 × 15 ml of CH_2Cl_2. The org. phase was washed with H_2O, dried ($MgSO_4$), and filtered. A very small portion of this soln. was evaporated and the residue dissolved in $CDCl_3$ and analyzed by NMR to determine the product distribution. The mother liquor was evaporated and the residue subjected to rapid chromatography (silica gel *60*, petroleum ether/AcOEt 4:1) to remove the highly colored impurities. Early fractions of this filtration usually contained diazo mixtures enriched in **1**. Diazooxoaldehydes **1** were purified by prep. TLC, using hexane/Et_2O, hexane/AcOEt, or CCl_4/AcOEt mixtures. Distillation at 42°/0.3 Torr was also successful for **1d**. The results are summarized in *Tables 1* and *2*.

4. *Transdiazotizations of* **3b–d**: *Conditions* D. These reactions were performed after the experiments under conditions *A*, to study the reactivities of ethyl formylacetate (**3b**) and acetylacetaldehyde (= 3-oxobutanal; **3d**), which were not isolable in our hands[7]), at the same pH value. Benzoylacetaldehyde (**3c**) was also reacted under conditions *D* for comparison: A soln. of **4** was prepared from 8.71 g (38 mmol) of 2-chloro-1-ethylpyridinium tetrafluoroborate and 2.47 g (38 mmol) of NaN_3 in 35 ml of MeOH and 20 ml of H_2O as described in *3.1*. No buffer reagents were added. To a soln. of the sodium salt of **3b**, **c**, or **d** (33 mmol) in 25 ml of cold MeOH and 20 ml of cold H_2O, *ca.* 19 ml of AcOH was added to attain pH 4.6 (buffer concentration compared to conditions *A* is *ca.* 6-fold). To this buffered oxoaldehyde soln. was immediately added the above soln. of **4**, and the mixture was stirred for 2.5 h at r.t. Workup as described in *3.2*.

5. *Transdiazotizations in the Presence of NaOAc* (Conditions *E*). A soln. of 7 mmol of **4** in 7 ml of MeOH and 4 ml of H_2O was prepared as described for the no-additive conditions (see *3.1*), and 0.60 ml of 2N NaOAc were added. Separately, 0.775 g (5.7 mmol) of NaOAc · $3H_2O$ were dissolved in 1 ml of H_2O and 3–4 ml of MeOH, and 5.7 mmol of an isolated **3** were dissolved in this soln. (pH *ca.* 7.4–7.8). Alternatively, the soln. of **3** was prepared *in situ* by dissolving 5.7 mmol of the Na salt of **3** in 3–4 ml of MeOH and 1 ml of H_2O and adding 0.325 ml of AcOH (5.7 mmol). To this oxoaldehyde soln. was added the above prepared soln. of **4**. The mixture was stirred for 60–70 min at r.t. and worked up as described in *3.2*.

6. *Reactions of the Oxocycloalkanecarbaldehydes* **5a, b** *with Azidinium Salt* **4**. Reactions of **5a, b** under conditions *A*, *B*, and *E* and no-additive conditions (*Exper. 3* and *5*) proceeded with N_2 evolution. Formation of α-diazocycloalkanones **7** (if any) was detected at most up to 1–2% by IR.

Evaporation of the CH_2Cl_2 extracts from the reactions of **5b** under conditions *B* and no-additive conditions gave viscous yellow oils. Attempts on TLC separations proved unsuccessful. Probably the assumed product **6b** hydrolyzed within 2.5 h. IR (major bands): 3550, 3425, 3100, 3050, 2925, 2850, 1728, 1710, 1630, 1580. ^{1}H-NMR (crude substance): Py^+ residue.

Reaction of **5a** under conditions *A* and *B* and no-additive conditions gave results similar to those obtained with **5b**. The reaction performed under conditions *E* was stopped after 15 min to avoid a probable hydrolysis. The CH_2Cl_2 extract was evaporated, the residue titurated with benzene to remove the soluble impurities, and the semi-solid waxy residue identified as **6a** by NMR and IR.

N-(1'-Ethylpyridin-1'-ium-2'-yl)-2-oxocyclohexane-1-carboxamide Tetrafluoroborate (**6a**): Purity *ca.* 85% by NMR. IR (neat): 3622, 3316, 3098, 2949, 2870 (3700–2450 (br.)), 1714, 1645 (sh), 1634, 1580, 1548, 1500, 1454, 1441, 1392, 1354, 1287, 1149, 1057. ^{1}H-NMR ($CDCl_3$): 8.46 (*dd*, ^4J = 1.0, ^3J = 8.53, H–C(6')); 8.26 (*dd*, ^4J = 1.10, ^3J = 6.46, H–C(3')); 7.99 (*td*, ^4J = 1.65, ^3J = 8.05, H–C(4')); 7.19 (*td*, ^4J = 1.0, ^3J = 6.54, H–C(5')); 4.53 (*q*, *J* = 7.17, MeCH_2); 2.39 (*m*, 2H–C(6)); 1.9–1.3 (*m*, CH_2(3), CH_2(4), CH_2(5)); 1.55 (*t*, *Me*CH_2); 14.4 (br. *s*, NH or OH).

7. *Reaction of β-(*N*-Methylanilino)acrylophenone* (= *3-(*N*-Methylphenylamino)-1-phenylprop-2-en-1-one*; **8**) *with* **4**. A soln. of 1.874 g (8.2 mmol) of 2-chloro-1-ethylpyridinium tetrafluoroborate in 20 ml of MeOH was cooled to 0°, 0.533 g (8.2 mmol) of NaN_3 were added, and the mixture was allowed to warm to r.t. with continuous stirring. Then 1.92 g (8.1 mmol) of **8** were added (orange-red and almost homogenized soln. after 10 min, except for some undissolved NaCl). After 1 h at r.t., the mixture was evaporated at 40°, the viscous, oily, red residue repeatedly extracted with hot petroleum ether (30–50°) and hot Et_2O, and the combined extract concentrated and cooled: 0.68 g (57.5%) of pure *diazoacetophenone* (= 2-diazo-1-phenylethanone; **2c**). The extraction residue crystallized overnight. Trituration with AcOEt removed the color, giving a dirty yellow substance, from which nice colorless crystals of **12** were obtained upon careful recrystallization from (i-Pr)$_2$O/AcOEt/MeCN 30:30:5: 1.49 g (56.3%). M.p. 83.5–84°.

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[7]) Although we were not successful in isolating free **3b** and **3d**, there are reports dealing with successful isolation and characterization of these compounds [30a, b].

Similar results were obtained when the reaction was repeated in MeCN, using an isolated sample of **4**: 80% of **2c** and 89% of **12**, the latter mixed with an impurity (IR: peak at 3354 cm^{-1}).

N'-(1'-Ethylpyridin-1'-ium-2'-yl)-N-methyl-N-phenylformamidine Tetrafluoroborate (**12**): Purity *ca.* 85–90% (^{1}H-NMR). IR (KBr): 3052, 3013, 2936, 1614, 1587, 1543, 1520, 1491, 1370, 1353. ^{1}H-NMR ($CDCl_3$): 1.53 (*t*, $J = 7.2$, $MeCH_2$); 3.63 (*s*, MeN); 4.58 (*q*, $MeCH_2$); 8.07 (*td*, $^3J = 8.0$, $^4J = 1.43$, H–C(4')); 8.33 (*dd*, $^3J = 6.43$, $^4J = 1.43$, H–C(6')); 8.55 (*s*, N=CH–N); 7.25–7.58 (*m*, 7H).

8. *Reaction of* **8** *with 2-Azido-3-ethylbenzothiazolium Tetrafluoroborate* (**9**). To a soln. of 1.022 g (3.5 mmol) of **9** in 30 ml of MeCN was added a soln. of 0.8295 g (3.5 mmol) of **8** in 5 ml of MeCN (→brown; reaction almost immediately complete). The mixture was poured into 300 ml of Et_2O with stirring: brownish yellow precipitate of **13** (0.63 g, 47%). Recrystallization from toluene/MeCN 8:1. M.p. 165–168°. ^{1}H-NMR: purity 95%.

From the Et_2O mother liquor, pure **2c** was isolated in 55% yield.

N'-(3-Ethylbenzothiazol-3-ium-2-yl)-N-methyl-N-phenylformamidine Tetrafluoroborate (**13**): IR (KBr): 3050, 3000, 2965, 1605, 1582, 1530, 1492, 1460, 1447, 1400, 1360, 1340, 1296, 1280, 1268, 1220. ^{1}H-NMR ($CDCl_3$): 8.54 (*s*, N=CH–N); 7.38–7.80 (*m*, 9 arom. H); 4.58 (*q*, $J = 7.2$, $MeCH_2$); 3.77 (*s*, MeN); 1.51 (*t*, $MeCH_2$).

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