197. Diazoaldehyde Chemistry

Part 1

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

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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 -oxoalde-hydes 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], diazo-acetaldehyde (2a, R = H) [2a], and diazoacetone (2d, R = Me) [4]. Therefore, a general method is necessary for the syntheses of α -diazo- β -oxoaldehydes.

 $\begin{array}{ccc} \text{RCO-CN}_2 - \text{CHO} & \text{RCO-CHN}_2 \\ 1 & 2 \end{array}$

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, dihydro-furans, 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.

$$\frac{\text{RCO}-\text{CN}_2-\text{CHO} \Rightarrow \text{RCO}-\text{CH}_2-\text{CHO}+\text{R'}-\text{N}=\text{N}_2}{1}$$

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 medium²), 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 NaN₃ and 2-chloro-1-ethylpyridinium tetrafluoroborate in MeOH/H₂O, 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



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.

	R EtO	$100 \times 1/(1+2)$						
 3b		no additive A		В	С	D°)	E	
						39.0 ^d) ^e)		
с	Ph	0.0	4.33	10.10	3.30 ^f)	12.0 ^g)	26.10 ^c)	
d	Me					$61.0^{\rm d})^{\rm e}$	53.0 ^c) ^d) ^h)	
e	i-Pr	0.0	8.50				35.7°) ⁱ)	
f	Me ₂ CHCH ₂	0.0	12.40				26.0 ⁱ)	
g	t-Bu	0.0	$\approx 0.7^{\rm i}$)	$\approx 1.40^{i}$)			7.25 ⁱ)	
h	$4-Me-C_6H_4$	0.0	2.00				15.90 ^c)	
i	4-MeO-C ₆ H ₄	0.0	1.55	3.57	1.75 ⁱ)		10.75 ^c)	
j	$4-F-C_6H_4$	0.0	4.85				28.60	
k	4-ClC ₆ H ₄	0.0	6.25				52.55°)	
ł	$4-Br-C_6H_4$	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	
0	$2,4-Br_2-C_6H_2$	24.9	74.43				94.90	
р	$2,4-(MeO)_2-C_6H_3$	0.0					3.20 ^c) ⁱ)	
q	$3-NO_2-C_6H_4$	$\approx 1.0^{1}$)	33.30	47.35				
r	$4 - NO_2 - C_6 H_4$	$\approx 1.0^{\rm m}$)	34.00	58.35				
s	$2,4,6-Me_3-C_6H_2$	16.15	41.35				92.40°)	
t	Naphthalen-1-yl	0.0	6.08				37.90°)	
u	Naphthalen-2-yl	0.0	3.85				19.10 ^c)	
v	3,5-Me ₂ -Furan-2-yl	0.0	$\approx 0.7^{i}$)				$(3.42^{\circ})^{i})$	

Table 1. Transdiazotizations of Acylacetaldehydes 3 to Diazooxoaldehydes 1 and Diazomethyl Ketones 2 According to Scheme $1^{a})^{b}$

^a) Transfer yield $(3 \rightarrow 1 + 2)$ at least 85–90%, unless otherwise stated; ratios 1/(1 + 2) from ¹H-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**. ^c) Transfer yield *ca*. 15%. ^f) 15% **3c** unreacted (¹H-NMR). ^g) Transfer yield *ca*. 70–75%. ^h) Transfer yield *ca*. 50–60%. ⁱ) Data not reliable. ^j) 34% **3i** unreacted (¹H-NMR). ^k) 23% **31** unreacted (¹H-NMR). ¹) 14% **3q** unreacted (¹H-NMR). ^m) 30% **3r** unreacted (¹H-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].



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 sulforyl azides [17].



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 observed³) (*Table 1*, conditions A). The results of the reactions under conditions B and D at essentially the same pH value, but using twoand 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 $\frac{1}{4}$ 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

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.

	R	Yield [%] ^a)	IR ^b)	¹ H-NMR ^c)	
			\tilde{v} (C=N=N)	ν̃ (CO)	δ (CHO) ($\omega_{1/2}$)
16	EtO	2-3 ^d)	2148 ^e)	1715, 1665 ^e)	9.70
с	Ph	19.0	2173, 2135 ^f)	1652, 1615 ^f)	9.78
d	Me	19.2	2162, 2136 ^e)	1672, 1641°)	9.75 (3.7)
е	i-Pr	19.9	2156, 2143	1674, 1645	9.78 (3.1)
ſ	Me ₂ CHCH ₂	20.0	2156, 2132	1674, 1641	9.76 (2.5)
g	t-Bu	-	2155, 2139 ^g)	1669 ^g)	9.96 ^g)
h	$4 - Me - C_6 H_4$	11.9	2166, 2135	1661, 1633	9.78
i	$4 - MeO - C_6H_4$	7.2	2166, 2133	1663, 1634	9.80
j	$4 - F - C_6 H_4$	23.7	2168, 2137	1665, 1633	9.76
k	$4-Cl-C_6H_4$	45.7	2168, 2133	1665, 1637	9.74
1	$4-Br-C_6H_4$	42.5	2166, 2133	1667, 1635	9.73
m	3,4-Cl ₂ -C ₆ H 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)
0	$2,4-Br_2-C_6H_2$	88.3	2168, 2141	1671, 1641	9.40 (26.9)
р	$2,4-(MeO)_2-C_6H_3$	-	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	$4 - NO_2 - C_6 H_4$	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 ⁸)	1642 ^g)	10.12 ^g)

Table 2. Some Data of a-Diazo-β-oxoaldehydes 1

^a) Conditions *E*; yields after isolation. ^b) In CH₂Cl₂ or CHCl₃. ^c) In CDCl₃; $\omega_{1/2}$, 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 Et₃N-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 group⁴) 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] decomposition⁵) of the dihydrotriazole intermediate 10 or 11.



^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.

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.

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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*.



^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 $19 \rightarrow 20 \rightarrow 23 \rightarrow 1$ 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 $19 \rightarrow 1$ via the diazo intermediate 21 is reminiscent of *Huisgen*'s formulation of a dihydrotriazole $\rightarrow \alpha$ -diazo- β -amino ester conversion aided by Et₃N [23]. Although it will be speculative, one may prefer the route $19 \rightarrow 20 \rightarrow 23$ by analogy to the study of the *Regitz*' group, who presented a triazene-dihydrotriazole conversion as a mechanistic explanation of their results⁶).

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 $3 \rightleftharpoons 3'$; especially a probable assumption of different reactivities for 3 and 3': $3' \rightarrow 22 \rightarrow 1'$ and $3 \rightarrow 14 \rightarrow 2$). 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 δ). 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 sp² hybridization from sp³. 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.



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-1ium 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.

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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 Et₂O, THF, or PhH). Yields were mostly higher than 85–90%. Free 3 were isolated by dissolving the sodium enolates in cold H₂O, discarding any impurities by extraction with CH₂Cl₂, acidifying with 10% excess of 2N AcOH, and extracting with CH₂Cl₂. After drying (MgSO₄) 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.* **30**, **3u**, and **3v** were not reported, neither free nor as their sodium salts.

(Z)-1-(2',4'-Dibromophenyl)-3-hydroxyprop-2-en-1-one (30): Not isolated as Na salt. Yield 79%. M.p. 70–72° (petroleum ether/AcOEt 4:1). IR (KBr): 1627. ¹H-NMR (CDCl₃): 6.03 (d, J = 4.44, COCH=); 7.40 (d, ³J(5',5') = 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=CHOH); 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. $51-54^{\circ}$ (petroleum ether AcOEt, 5:1). IR (CHCl₃): 1617. ¹H-NMR: 6.37 (d, J = 4.19, COCH=); 8.34 (d, CH=CHOH); 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. ¹H-NMR (60 MHz, CCl₄): 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=CHOH); 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 NaN₃ 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 H₂O were added, and the products were extracted with 3×15 ml of CH₂Cl₂. The org. phase was washed with H₂O, dried (MgSO₄), and filtered. A very small portion of this soln. was evaporated and the residue dissolved in CDCl₃ 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/Et₂O, hexane/AcOEt, or CCl₄/AcOEt mixtures. Distillation at $42^{\circ}/0.3$ 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 hands⁷), 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 NaN₃ in 35 ml of MeOH and 20 ml of H₂O 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 H₂O, *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 \cdot 3 H_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 N₂ evolution. Formation of α -diazocycloalkanones 7 (if any) was detected at most up to 1–2% by IR.

Evaporation of the CH₂Cl₂ 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. ¹H-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-(I'-*Ethylpyridin-I'-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. ¹H-NMR (CDCl₃): 8.46 (*dd*, ⁴*J* = 1.0, ³*J* = 8.53, H–C(6')); 8.26 (*dd*, ⁴*J* = 1.10, ³*J* = 6.46, H–C(3')); 7.99 (*td*, ⁴*J* = 1.65, ³*J* = 8.05, H–C(4')); 7.19 (*td*, ⁴*J* = 1.0, ³*J* = 6.54, H–C(5')); 4.53 (*q*, *J* = 7.17, MeCH₂); 2.39 (*m*, 2H–C(6)); 1.9–1.3 (*m*, CH₂(3), CH₂(4), CH₂(5)); 1.55 (*t*, *Me*CH₂); 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 NaN₃ 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 Et₂O, 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)₂O/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% (¹H-NMR). IR (KBr): 3052, 3013, 2936, 1614, 1587, 1543, 1520, 1491, 1370, 1353. ¹H-NMR (CDCl₃): 1.53 (*t*, J = 7.2, MeCH₂); 3.63 (*s*, MeN); 4.58 (*q*, MeCH₂); 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*, 7 H).

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 (\rightarrow brown; reaction almost immediately complete). The mixture was poured into 300 ml of Et₂O with stirring: brownish yellow precipitate of 13 (0.63 g, 47%). Recrystallization from toluene/MeCN 8:1. M.p. 165–168°. ¹H-NMR: purity 95%.

From the Et₂O 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. ¹H-NMR (CDCl₃): 8.54 (s, N=CH–N); 7.38–7.80 (m, 9 arom. H); 4.58 (q, J = 7.2, MeCH₂); 3.77 (s, MeN); 1.51 (t, MeCH₂).

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