225. Nucleophilic 1,2-Shifts of Carboxamide Groups in the Benzil-Benzilic Acid Type Rearrangement of 4-Aryl-2,3-dioxobutyramides and of Quinisatine[1])

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Dedicated to Prof. *Tino Gäumann* on the occasion of his 60th birthday

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4-Aryl-2,3-dioxobutyramide hydrates **1** undergo the benzil-benzilic acid rearrangement to form (substituted) benzyltartronate monoamides **2**. For compound **1a** (Ar = Ph), it is demonstrated by isotopic labelling that the reaction occurs exclusively by migration of the $CONH_2$ group. Kinetic measurements with **1a–c** and with the cyclic amide quinisatine **6** show that the rearrangement of the carboxamide group, proceeding *via* an alkali-catalysed step, can reach a plateau in the $k_{obs.}/[OH^-]$ diagram (*cf.* the *Fig.*), due to complete formation of a mono-anion, and a further increase of rate attributable to the rearrangement of a bis-anion. Comparisons suggest that rearrangements involving an amide group are slower than those involving an ester group, and that, for this effect (as for others), the pre-equilibrium deprotonation of tbe hydrate is more important than a specific migration tendency.

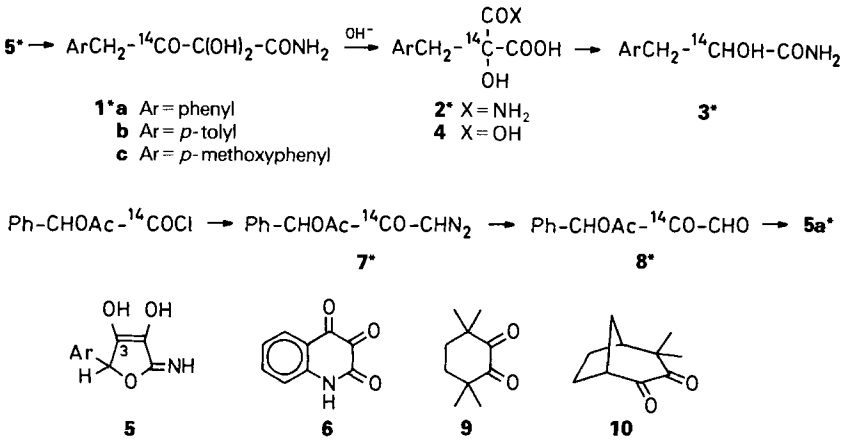
It is known [2] that electron-attracting groups are able to migrate in nucleophilic 1,2-shifts towards electron-deficient centres; this depends essentially upon the chemical and electronic character of the migration starting point and terminus. For instance ester groups ROOC have been demonstrated to migrate in *Wagner-Meerwein* [3], pinacol [4] and benzil-benzilic acid rearrangements [5]. We have found two cases of migration of carboxamide groups in the benzil-benzilic acid rearrangement of an open-chain compound, $Me-CO-CO-CONPh_2$ [6], and of a cyclic amide, quinisatine (**6**) [7]. On the other hand, *Kwart* and coworkers [8] have shown that there is no shift of the carboxamide group in the alkali-catalyzed rearrangement of alloxane and its *N*-substituted derivatives but exclusively cleavage of the C–N bond and migration of the N-group; *Smith* and *Kan* [9] found the same result for the rearrangement of phthalonimide.

In search of further cases of migration of carboxamide groups we have investigated the benzil-benzilic acid type rearrangement of 4-aryl-2,3-dioxobutyramides $Ar-CH_2-CO-CO-CONH_2$. These compounds, which form stable hydrates **1**, are easily accessible by reaction of aromatic aldehydes with glyoxal and cyanide ions [10] followed by acid hydrolysis of the cyclic products **5**[2]) [11]. When treated with aqueous alkali, **1a** (Ar = phenyl) yields *ca.* 90% benzyltartronamide (**2a**), the structure of which follows from its alkaline hydrolysis to benzyltartronic acid (**4a**) and its decarboxylation to

[1]) Reductones and Tricarbonyl Compounds, Part 32. Part 31: [1].

[2]) The intermediate products, formulated [10] as imino-enediols $-C(OH)=C(OH)-C(=NH)-$, very probably exist in their tautomeric forms $-CO-C(OH)=C(NH_2)-$. We use here the earlier published formula **5** for convenience.

Scheme



3-phenyllactamide (**3a**) *(Scheme)*. Both products **3a** and **4a** are known compounds. The substituted compounds **1b** and **1c** undergo the same reaction.

The formation of **2** from **1** shows that the C–N bond of the carboxamide group remains intact, in contrast to the results of the reaction of alloxane [8]. The reaction **1**→**2** can proceed, however, by migration of either the carboxamide group to C(3) or of the benzyl group to C(2). Both modes will lead to the same product. To distinguish between these two possibilities, we have used **1a***, isotopically labelled with ^{14}C in position 3[3]).

In the benzil-benzilic acid rearrangement **1a*** yielded **2a*** with nearly unchanged specific activity *(Table 1)*. CO_2 obtained from the decarboxylation of **2a*** was practically free of ^{14}C. Accordingly, nearly all radioactivity was found in **3a***. If the benzyl group had migrated in the rearrangement, the tracer would have been found in the carboxyl group of **2a*** and hence in the released CO_2. Thus, the result supports the migration of the $CONH_2$ group as observed before in the similar rearrangement reactions [6] [7][4]).

Table 1. *Benzil-Benzilic Acid Rearrangement of [3-^{14}C]-***1a** **(1a*)** *and of [1-^{14}C]-***1a**

Compound	Specific activity [nCi/mmol] of the starting material	
	[3-^{14}C]-**1a**	[1-^{14}C]-**1a**
1a	1.67 ± 0.30	1340 ± 20
2a	1.88 ± 0.30	1200 ± 20
3a	(2.64 ± 0.40)	1340 ± 20
$BaCO_3$	0.04 ± 0.02	1.5 ± 0.1

[3]) The precursor of **1a***, namely the cyclic compound **5a*** labelled in position 3 was prepared following a procedure indicated by *Weygand* and coworkers [12]: *O*-Acetylmandeloyl chloride, labelled in the ketone carbonyl group using a cyanhydrin reaction, was transformed *via* the diazo-ketone **7*** into (3-acetoxybenzyl) [2-^{14}C]glyoxal (**8***); the latter reacted with KCN to give **5a***, which was hydrolyzed by acid to yield **1a***.

[4]) As the result of the decarboxylation executed with **2a*** of low activity showed an uncertainty of > 2%, we confirmed our results using the more easily accessible [1-^{14}C]-**2a**, of higher activity, obtained by rearrangement of [1-^{14}C]-**1a**; the latter was prepared from benzaldehyde, glyoxal and K^{14}CN [10] followed by hydrolysis of [1-^{14}C]-**5a**.

As in other cases the preference of carboxamide over alkyl group migration can be explained by considering the difference between the carbonyl groups of **1**: the carbonyl group at C(2), being completely hydrated, is a poor migration terminus for the benzyl group, whereas the unhydrated carbonyl at C(3) is apt to accept a migrating nucleophile; this happens to be the carboxamide group. The third carbonyl group, that of the amide group, is too little electrophilic to be attacked by a migrating nucleophile. This seems to be the reason, too, why alloxane cannot undergo a proper benzil-benzilic acid rearrangement: the central carbonyl is completely hydrated and the lateral carbonyls belong to carboxamide groups; thus only the shift of an amino group occurs (by a not well-defined mechanism).

Kinetics. – In preceding kinetic investigations on rearrangements involving carboxamide-group migrations in the benzil-benzilic acid rearrangement we had found that for *N,N*-diphenyl-α,β-dioxobutyramide [6] the rate of rearrangement is proportional to $[OH^-]$, but tends towards a plateau at high pH values; for quinisatine (**6**) no clear order of dependence of the rearrangement rate upon $[OH^-]$ had been found [7]. We have now measured the rate of rearrangement of **1a–c** at different alkali concentrations; on the same occasion, we have extended the range of our former measurements with **6**, for which the course of the rearrangement had been established earlier [7].

To follow the reactions, we have determined the concentration of unreacted ketone by use of a dropping Hg electrode. Compounds **1a–c** show two polarographic reduction steps, one with a half wave potential > -1 V ($V_{½} = -0.6$ V for **1a**; -0.8 V for **1c**), and a second one at $V_{½} \approx -1.7$ V, *i.e.* close to the decomposition potential of the electrolyte. We chose a potential of -1.3 V as indicative of **1**. The rearranged product **2** and its anion do not show polarographic reduction, so one can follow the change in [**1**] by following the change in intensity of current i_l at a constant potential of -1.3 V.

We found that the reactions of **1a–c** were first-order in substrate concentration over *ca.* 3–4 half-lives[5]). The first-order rate constants $k_{obs.}$ depend upon the alkali concentration; for **1a** the dependence was found to be linear over the range of $[OH^-]$ studied, *i.e.* between 0.005M and 0.9M; for **1b**, there is linearity between 0.005 and 0.06M (a point at 0.1M possibly indicating the attainment of a plateau). The second-order rate constants are for **1a**: $k_{rearr.} = 6.1 \cdot 10^{-2} M^{-1}s^{-1}$; for **1b**: $k_{rearr.} = 5.7 \cdot 10^{-2} M^{-1}s^{-1}$. It is not surprising that the aryl substituents, rather remote from the reaction center, do not exert a significant influence on the rate. The rate/$[OH^-]$ profile of **1c** *(Figure)* showed a slight curvature with a plateau situated at pH *ca.* 12.5 and $k_{obs.}^{plateau}$ *ca.* $3 \cdot 10^{-3}s^{-1}$, indicating complete formation of the hydrate-mono-anion of **1c** in the pre-equilibrium and, at higher $[OH^-]$, by a new rise of $k_{obs.}$ incipient formation of the bis-anion $Ar-CH_2-CO-C(O^-)_2-CONH_2$. From the slope preceding the plateau, the second-order rate constant of the OH^--induced rearrangement of **1c**, $k_{rearr.} = 6.0 \cdot 10^{-2} M^{-1}s^{-1}$ (corresponding to the mono-anion), can be evaluated. The value of $k'_{rearr.}$ of the bis-anion seems to be similar in magnitude. The bis-anion should be, of course, much more reactive than the mono-anion, but it is present in low concentration in the second protonation/deprotonation equilibrium. In the case of **1c** these two effects seem nearly be canceled, *i.e.* $k_{rearr.} \approx k'_{rearr.}$

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[5]) The rearrangement was preceded by a short induction period (< 1 min), probably due to equilibration of different hydrate forms.

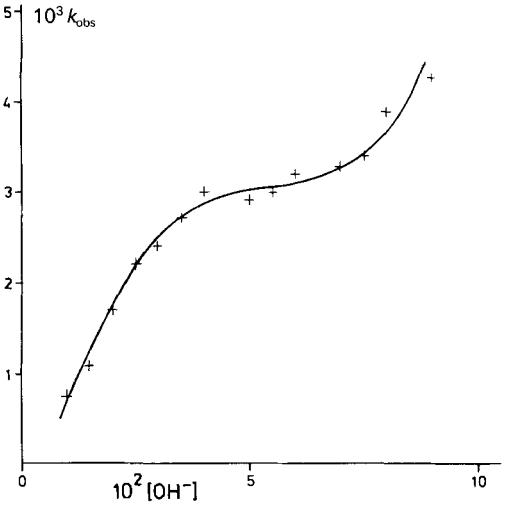

Fig. *Rearrangement of* **1c**: $k_{obs.}$ *as a function of* $[OH^-]$

With **6**, the new measurements confirm our earlier results (taking into account a slight difference in the reaction temperature); extending over a larger pH range, they show a rate profile $k_{obs.}/[OH^-]$ comparable to that of **1c**: the curve passes through the origin, but is linear only in the lowest $[OH^-]$ region measured, allowing to estimate $k_{rearr.} = k_{obs.}/[OH^-] = 4.1 \cdot 10^{-2} M^{-1}s^{-1}$. At $[OH^-] > 0.05M$ the slope of the curve diminishes; however, within the domain of (reasonably) constant ionic strength (0.025 to 0.6M) the expected plateau is not attained. Only at higher $[OH^-]$ (working with non-constant ionic strength), a turning point becomes visible (at pH *ca.* 14 and with $k_{obs.}^{plateau}$ *ca.* $10^{-2}s^{-1}$), which we attribute, as before, to (complete) formation of the hydrate anion of **6**. The subsequent rise of $k_{obs.}$ with increasing $[OH^-]$, due to incipient formation of the hydrate bis-anion of **6** (rather than salt effects[6])), shows an initial second order constant $k'_{rearr.} = k_{obs.}/[OH^-] \approx 2 \cdot 10^{-2} M^{-1}s^{-1}$.

Finally, our earlier measurements [6] with the diketoamide $Me-CO-C(OH)_2-CONPh_2$ can be evaluated to give, in the lower $[OH^-]$ range, a second-order rate constant $k_{rearr.} = 0.4 M^{-1}s^{-1}$; a plateau at pH *ca.* 13 and $k_{obs.}^{plateau} \approx 10^{-2}s^{-1}$ is due to completion of anion formation; a second increase of $k_{obs.}$ with $[OH^-]$ due to bis-anion formation was not observed in the pH range studied. These values are reasonably close to those measured for **1** and **6**, indicating that the size of the substituents linked to the N-atom does not play a major role for the rate of rearrangement.

Discussion. – As demonstrated before [1] [13], α,β-diketoesters undergo benzil-benzilic acid rearrangement by migration of the COOR group; their $k_{obs.}/[OH^-]$ rate profile is similar to that of the corresponding carboxamides as discussed above: a rate increase proportional to $[OH^-]$, followed by a plateau attributed to completion of formation of a mono-anion, and further rate increase due to the formation and rearrangement of a bis-anion. Similar rate profiles had been found in simpler cases of alkali-catalysed

[6]) A secondary deviation from linearity in this pH range, however, may be due to salt effects.

rearrangements [8] [14–17]. On the other hand, we had found that in COOR group migration the size of R (R = Et, i-Pr, *t*-Bu) does not play a significant role, neither for $k_{rearr.}$, nor for [OH^-] of the plateau of anion formation. The mean values (at 40 °C) for $MeCOC(OH)_2COOR$ are: $k_{rearr.} \approx 30 M^{-1}s^{-1}$; plateau at pH *ca.* 11 with $k_{obs.}^{plateau} \approx 3 \cdot 10^{-3}s^{-1}$; $k'_{rearr.} = 0.5–4 M^{-1}s^{-1}$. When comparing these results with those for amide-group migration (measured at 25°), one has to take in account the differences in reaction temperature. For identical temperature one can estimate for lower [OH^-] ranges that rearrangements involving ester groups occur *ca.* 10–20 times faster than those involving amide groups. This effect might, *a priori,* be attributed to higher acidity of the starting material (furnishing a higher concentration of the reacting mono-anion) and/or to larger intrinsic migration aptitudes. The pH values of the plateau of saturation show that the hydrates of esters are significantly more acidic (*ca.* 11) than the hydrates of the comparable amides (*ca.* 13), accounting for the rate difference in the lower [OH^-] range. On the contrary, there is no indication that specific migration aptitudes of groups influence the rate.

Table 2. *Rates of Benzil-Benzilic Acid Rearrangements*

Compound	Migrating group	Solvent[a])	Temp.	$k_{rearr.}$ [$M^{-1}s^{-1}$]	Ref.
PhCOCOPh	Ph	D–W	50°	$1.0 \cdot 10^{-4}$	[19]
			49.5°	$0.94 \cdot 10^{-4}$	[20]
3,3,6,6-Tetramethyl cyclohexane-1,2-dione (**9**)	R–CMe_2-(cycl.)	W	30°	$4 \cdot 10^{-5}$	[16]
Carbocamphenilonone (**10**)	R–CMe_2-(cycl.)	W	70°	$3.8 \cdot 10^{-5}$	[15]
$MeCOC(OH)_2COOR$	–COOR (R = Et, i-Pr, *t*-Bu)	W	40°	26–36	[1]
$MeCOC(OH)_2CONPh_2$	$-CONPh_2$	W	25°	0.41	[6]
$ArCH_2COC(OH)_2CONH_2$ (**1a–c**)	$-CONH_2$	A–W	25°	0.057–0.061	[b])
Quinisatine (**6**)	–CO–NHAr (cycl.)	W	25°	0.041	[b])
PhCO–CHO	H	W	25°	0.076	[21]
			35°	0.091	[17]
CHO–CHO	H	W	25°	*ca.* 0.9[c])	[14]

[a]) W: H_2O; D–W: dioxane/H_2O 2:1; A–W: EtOH/H_2O 1:1.
[b]) This work.
[c]) Estimated from third-order runs.

This conclusion is confirmed by comparison with other benzil-benzilic acid rearrangements wherein groups possessing no electron-attracting properties migrate [18–20] *(Table 2)*. In spite of large differences in reaction temperature and solvent one can estimate that the rates of the 'normal' rearrangements, involving migration of aryl or alkyl groups, are significantly slower than those of COOR and $CONR_2$. This corroborates the observation that in the benzil-benzilic acid rearrangement, electron-attracting groups, like COOR and $CONR_2$, are rather favoured compared with alkyl or aryl groups in the same molecule. This is contrary to the intuition that an electron-rich group should be more apt to migration, but it corresponds to the observations *a*) that in symmetrically substituted benzils and in arylglyoxals electron-attracting groups accelerate and donating groups retard the rearrangement [18] [21], and *b*) that in unsymmetrical benzils the more electron-attracting Ar migrates preferentially. The explanation is that electron-withdrawing groups favour hydration of the neighbouring carbonyl group and enhance the acidity of the hydrate, in the two pre-equilibrium steps preceding rearrangement; both effects promote the migration of the group bound next to $-C(OH)O^--$. In good accord with

this, glyoxal and phenylglyoxal, which are predominantly hydrated, and yield hydrates of relatively high acidity, show rapid rearrangement; in the arylglyoxals the (less hydrated) keto group is the preferential migration terminus thus defining direction of migration. All these observations confirm that differences in 'intrinsic migration aptitude' (if they exist at all) prove to be less important for the benzilic acid rearrangement than effects on the pre-equilibria.

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Experimental Part

General. See [22]. IR: *Beckman 4230* and *20A*. ^{1}H-NMR: *Bruker WP 80* and *WH 360*. MS: *Finnigan 1020*. Radioactivity measurements: *Packard Tricarb 3380* at the Institut de radiophysique appliquée, Lausanne. Elemental analyses: Mr. *E. Thommen*, Organisch-chemisches Institut, Universität Basel, and Mrs. *I. Beetz*, Kronach, FRG.

2-(α-Acetoxybenzyl)[2-^{14}C]glyoxal (1-Phenyl-2,3-dioxopropyl Acetate; **8***; *Method:* [12]). A soln. of *O*-acetyl[1-^{14}C]mandeloylchloride (6.03 g, 28.4 mmol), prepared [12] using K^{14}CN (6.6 mg, *ca.* 0.02 mCi; *Radiochemical Centre*, Amersham), in Et_2O (30 ml) was added dropwise at 0° to an Et_2O soln. of CH_2N_2 (1.5 fold excess), and stirred 1 h at 0° and 15 h at r.t. Solvent and excess CH_2N_2 were distilled, the oily residue was dissolved in dry Et_2O (20 ml). At −60°, ethylsulfenyl chloride (2.74 g, 28.4 mmol) in Et_2O (5 ml) was added dropwise and stirred 0.5 h at −60° and 15 h at r.t. The solvent was removed *in vacuo*, the oily residue was dissolved in 70% aq. AcOH (50 ml) and cooled to 0°. A soln. of Br_2 (4.84 g, 30 mmol) in AcOH (2 ml) was added, rapidly followed by dry AcONa (12.6 g). The mixture was stirred 3 h at r.t. and, after addition of H_2O (25 ml), extracted with petroleum ether (2 × 50 ml). The aq. phase was neutralized to pH 7 by addition of $KHCO_3$ and extracted with $CHCl_3$ (5 × 30 ml). The extract was dried (Na_2SO_4), the solvent removed and the residue distilled: 3.43 g (59%) of b.p. 100–123°/0.2 Torr.

4-Phenylhydroxy[3-^{14}C]tetronimide (3,4-Dihydroxy-2-phenyldihydro-5(2H)-furanimine; **5a***; *Method:* [12])[2]. A soln. of **8*** (5.04 g, 24.2 mmol) in dioxane (25 ml) was added dropwise at 0° under N_2 to a stirred soln. of KCN (4.70 g, 72.4 mmol) in 0.5N NaOH (25 ml). The brown soln. was stirred 10 min at r.t.; AcOH was added until pH 6, then the soln. was extracted with Et_2O (2 × 10 ml). Unlabelled **5a** (4.63 g, 24.4 mmol, prepared following [10]) was added; at 40° MeOH was added to make a homogenous soln. (*ca.* 50 ml). After cooling overnight to 0° the crystals were isolated and washed with cold Et_2O; the concentrated filtrate yielded a second crop of crystals. After recrystallization from MeOH/H_2O: 3.96 g **5a***, m.p. 171–173° (dec.). Spec. activity: see *Table 1*.

4-Phenyl-2,3-dioxo[3-^{14}C]butyramide-hydrate (**1a***) [11]. To a boiling mixture of 150 ml AcOH and 220 ml H_2O, **1a*** (3.32 g, 17.4 mmol) was added and refluxed for 1 h. The resulting yellow soln. was evaporated to dryness at 30–40° *in vacuo*; the residue was washed with Et_2O and recrystallized from acetone/Et_2O: 1.03 g (28%), m.p. 107–110° (dec.) [11]. Spec. activity: see *Table 1*. ^{1}H-NMR (acetone): 7.3 (*m*, arom.); 4.05 (*s*, CH_2); 6.16, 2.87 (*s*, both peaks disappear upon addition of D_2O: OH and NH_2).

Benzyl[2-^{14}C]tartronic Acid Monoamide (2-Carbamoyl-2-hydroxy-3-phenylpropionic Acid; **2a***). At 0°, **1a*** (0.45 g, 2.1 mmol) was dissolved in 2N NaOH (7 ml). The soln. rapidly lost its dark red colour; after 1 h at 0° it was saturated with NaCl and kept further 2 h at 0°. The precipitate (Na-salt of **2a***) was isolated, dissolved in H_2O (7 ml) at 0° and treated with cold 2N HCl. After 2 h at 0°, the precipitate was isolated and dried: 0.32 g (71%) **2a*** of m.p. 161–162° (recryst. from $CHCl_3$/Et_2O). Spec. activity: see *Table 1*. IR (KBr): 3410, 3280 (NH_2), 1730 (COOH), 1635 ($CONH_2$), 1550 (NH_2), 1125 (OH). ^{1}H-NMR ((D_6)DMSO): 7.3 (*m*, arom.); 3.17 (*s*, CH_2). MS: 209 (5, M^+), 191 (12, $M^+ - H_2O$), 174 (3), 165 (4, $M^+ - CO_2$), 163 (6), 118 (12), 105 (7), 91 (100, $C_7H_7^+$). Anal. calc. for $C_{10}H_{11}NO_4$ (209.2, non-radioactive): C 57.46, H 5.31, N 6.70; found: C 57.52, H 5.46, N 6.77.

3-Phenyl[2-^{14}C]lactamide (**3a***). Compound **2a*** (200 mg, 0.95 mmol) was heated for 20 min to 160° in a stream of N_2. CO_2 was precipitated as $BaCO_3$ (from $Ba(OH)_2$ soln.), which was washed with hot H_2O, EtOH, and Et_2O, and dried: 190 mg (99%); spec. activity: see *Table 1*. The decarboxylation residue was recrystallized two times from $CHCl_3$: 109 mg (70%) of m.p. 110–112° ([23]: m.p. 111–112°; no depression of mixed m.p. with authentic product prepared after [23]). IR (KBr): 3410, 3340, 1640 ($CONH_2$), 1595, 1495, 1085, (OH).

Benzyltartronic Acid (2-Benzyl-2-hydroxypropanedioic Acid; **4**). Inactive **2a** (0.60 g, 2.8 mmol) and 20% NaOH (10 ml) were heated for 6 h under reflux. The soln. was cooled, acidified with 2N HCl and submitted to continuous extraction with Et_2O for 24 h. The Et_2O extract was dried and the solvent was evaporated: 0.59 g (98%) of m.p. 144–146° ([24]: m.p. 143°).

4-Phenyl-2,3-dioxo[1-^{14}C]butyramide-hydrate ([1-^{14}C]-**1a**). 4-Phenyl-2-hydroxy[1-^{14}C]tetronimide (2.0 g, 10.5 mmol [25]) was heated in 40% aq. AcOH; the product was isolated and recrystallized as described above. Spec. activity: see *Table 1.*

Rearrangement and Decarboxylation of [1-^{14}C]-**1a**. Compound [1-^{14}C]-**1a** (0.45 g), treated with 2N NaOH (7 ml) as above, yielded 0.49 g (98%) of Na-salt of [1-^{14}C]-**2a**. To the Na-salt (0.43 g), dissolved in H_2O (6.5 ml), 2N HCl (4.8 ml) was added at 0°. As above, 0.36 g [1-^{14}C]-**2a** (93%) were isolated; spec. activity see *Table 1.* This compound (0.173 g, 0.84 mmol), heated as above, yielded 0.162 g $BaCO_3$ and, after recrystallization, 0.087 g (63%) [1-^{14}C]-**3a**; spec. activities see *Table 1.*

*4-(*p*-Tolyl)-2,3-dioxobutyramide* (**1b**). *4-(*p*-Tolyl)hydroxytetronimide* (*3,4-Dihydroxy-2-(*p*-tolyl)dihydro-5(2H)-furanimine;* **5b**) [10] (3.9 g, 19 mmol), suspended in AcOH (75 ml), was added under CO_2 to boiling 25% AcOH (300 ml). After 1 h under reflux, the solvent was evaporated *in vacuo*, and the residue washed with Et_2O and recrystallized from acetone/H_2O (2:5): 1.35 g (32%) **1b**, m.p. 122–123°. IR (KBr): 3435, 3300 (NH_2), 1742 (CO), 1670 ($CONH_2$), 1617, 1520. ^{1}H-NMR ((D_6)DMSO): 7.06 (*m*, arom. H); 3.90 (*s*, CH_2); 3.31 (*s*, *ca.* 1.5 H, disappears upon addition of D_2O, OH or NH_2); 2.25 (*s*, CH_3). MS: 223 (1, $M^+ + H_2O$), 205 (100, M^+), 177 (2, $M^+ - CO$), 161 (6, $M^+ - CO_2$), 133 (22, $M^+ - COCONH_2$), 132 (49), 105 (88, $CH_3C_7H_6^+$). Anal. calc. for $C_{11}H_{11}NO_3 \cdot H_2O$ (223.2): C 59.19, H 5.87, N 6.27, O 28.67; found: C 59.25, 59.31, H 5.87, 5.96, N 6.27, 6.26, O 28.69, 28.56.

Rearrangement of **1b**. Compound **1b** (1.0 g) was treated with 2N NaOH (15 ml) 1 h at 0°. The resulting suspension was acidified by adding 2N HCl (20 ml), filtered after 2 h standing at 0°; the precipitate was recrystallized from $CHCl_3$/EtOH (1:1): 0.6 g (60%), m.p. 152.5–153°. IR (KBr): 3450, 3420, 3300 (NH_2), 1725 (COOH), 1630 ($CONH_2$), 1120 (*HO* tert.). ^{1}H-NMR ((D_6)acetone): 7.2 (*m*, arom. H); 3.23 (*s*, CH_2); 2.32 (*s*, CH_3); *ca.* 5 (very br., disappears on addition of D_2O: NH_2 or OH). MS: 223 (2, M^+), 205 (18, $M^+ - H_2O$), 190 (9), 179 (2, $M^+ - CO_2$), 161 (3, $M^+ - CO_2 - H_2O$), 105 (100, $CH_3C_7H_6^+$). Anal. calc. for $C_{11}H_{13}NO_4$ (223.2): C 59.19, H 5.87, N 6.27; found: C 59.21, H 5.83, N 6.21.

p-*Methoxybenzyltartronic Acid Monoamide* (*2-Carbamoyl-2-hydroxy-3-(*p*-methoxyphenyl)propionic Acid;* **2c**). Compound **1c** [11] or its enol form [26] (3.4 g, 15.4 mmol) was kept standing in 2N NaOH (50 ml) 30 min at 0°; the soln. was saturated with NaCl and filtered, the precipitate was washed with EtOH and Et_2O and dried (*ca.* 3 g of Na-salt of **2c**). To the Na-salt (1.32 g) in H_2O (20 ml), 2N HCl (15 ml) was added at 0°; the precipitate (0.90 g) was recrystallized from $CHCl_3$/petroleum ether/EtOH: m.p. 148–149°. ^{1}H-NMR ((D_6)acetone): 7.1 (*q*, arom. H); 4.00 (*s*, CH_2); 3.81 (*s*, CH_3O); 6.15, 2.87 (*s*, both peaks disappear upon addition of D_2O: OH and NH_2). Anal. calc. for $C_{11}H_{13}NO_4 \cdot \frac{1}{2} H_2O$ (248.2): C 53.23; H 5.69, N 5.64; found: C 53.51, H 5.52, N 5.50.

3-(p-Methoxyphenyl)lactamid (**3c**). Compound **2c** (0.90 g) was decarboxylated 5 min at 150°; the residue was recrystallized from $CHCl_3$/petroleum ether: 0.70 g, m.p. 145°. Anal. calc. for $C_{10}H_{13}NO_3$ (195.2): C 61.53, H 6.72, N 7.17; found: C 61.60, H 6.70, N 7.05.

By acid hydrolysis of **3c**, *3-(*p*-methoxyphenyl)lactic acid* was formed; m.p. 87° (from Et_2O/petroleum ether); m.p. 104–105° (from $CHCl_3$/petroleum ether) ([27]: m.p. 88° (from AcOEt/petroleum ether)). Anal. calc. for $C_{10}H_{12}O_4$ (196.2): C 61.21, H 6.17; found: C 61.18, H 6.20.

Kinetics. – *Solns.: a*) 0.2N KOH and 0.2N KCl mixed at different ratios to yield aq. solns. of different pH at constant ionic strength, containing 0.0003% *Triton X100* to suppress polarographic maxima. *b*) 1.0N KOH diluted with 0.6N KCl at different ratios, containing 0.003% *Triton*. *c*) Aq. KOH 5.0N to 0.80N, containing *Triton*. *d*) 30 mg **1** in 2.5 ml EtOH (96%, daily fresh). *e*) 100 mg **6** in 2.5 ml H_2O + 1 ml DMF. All solns. were deoxygenated prior to use.

Table 3. *Rates of Alkaline Rearrangement of* **1a**, **1b**, *and* **1c** (polarography in EtOH/H_2O 1:1 at fixed potential of −1.3 V; $\mu = 0.1$; 25.0° ± 0.05°; each value represents the mean of 3 to 4 (for **1a** and **1b**) and *ca.* 2 (**1c**) measurements)

10^2 [OH^-]	$10^3 k_{obs.}$ [s^{-1}]			10^2 [OH^-]	$10^3 k_{obs.}$ [s^{-1}]		
	1a	**1b**	**1c**		**1a**	**1b**	**1c**
0.5	0.79	0.66	–	5.0	–	3.5	2.9
0.75	1.1	0.68	–	5.5	–	–	3.0
1.0	1.1	1.0	0.77	6.0	4.1	4.3	3.2
1.5	–	–	1.1	7.0	–	4.2	3.3
2.0	1.7	1.7	1.7	7.5	–	–	3.4
2.5	–	–	2.2	8.0	5.2	–	3.9
3.0	2.4	2.6	2.4	9.0	6.0	–	4.3
3.5	–	–	2.7	10.0	–	4.4	–
4.0	3.0	2.8	3.0				

Table 4. *Rates of Alkaline Rearrangement of* **6** (polarography in aq. soln. at fixed potential of −0.6 V; 25.0° ± 0.05°; each value represents the mean of 2 measurements)

$[OH^-]$	$10^3\ k_{obs.}\ [s^{-1}]$	$[OH^-]$	$10^3\ k_{obs.}\ [s^{-1}]$	$[OH^-]$	$10^3\ k_{obs.}\ [s^{-1}]$
0.025[a])	1.3	0.30[a])	10.4	2.0[b])	44
0.050[a])	2.5	0.40[a])	12.5	3.0[b])	77
0.10[a])	4.6	0.60[a])	14.9	4.0[b])	130
0.15[a])	6.6	0.80[b])	19	5.0[b])	250
0.20[a])	8.0	1.0[b])	23		

[a]) Ionic strength 0.6. [b]) Variable ionic strength.

Measurements: **1**: In a polarographic apparatus as described [6] [7] (*Polarecord Metrohm*, equipped for acceleration of droplet formation), 0.5 ml of soln. *d* were injected into a mixture of 10.0 ml of soln. *a* and 9.5 ml abs. EtOH at 25.0 ± 0.05° under N_2; the current was measured (starting after 1 min) at fixed potential of −1.3 V (against an AgCl electrode). **6**: 0.1 ml of soln. *e* injected into 20.0 ml of *b* or *c*; fixed potential: −0.6 V. Results: *Table 3* and *4*.

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