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Electrolytic Reduction of Azidochalcones

Electrolytic Investigations on Vinyl Azides, VI.

Dierk Knittel* and **V. Suryanarayana Rao**

Institut für Physikalische Chemie, Universität Hamburg, D-2000 Hamburg 13, Federal Republic of Germany

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Cathodic reduction of α-azidochalcones under slightly protic conditions proves to be an excellent method for a selective conversion of the azido function to an amino group without affecting other reducible parts of the molecules. The amino-propenones retain the *Z*-configuration about the C=C-bond of the starting material, whereas N-acetyl derivatives, obtained under mildly acetylating conditions, are partially isomerised. The low reduction potential of N,N-diacetyl-enamines of this type prevents their direct one step synthesis by electrolysis of azidochalcones under strongly acetylating conditions. The voltammetric behaviour of the azides and their reduction pathway is discussed.

(Keywords: α-Azidochalcones; Cathodic reduction; 2-Aminopropen-2-ones)

Elektrolytische Untersuchungen an Vinylaziden, 6. Mitt.

Elektrolytische Reduktion von Azidochalkonen.

Die kathodische Reduktion von α-Azidopropenon erweist sich als ausgezeichneter Weg, um selektiv zu Enaminen zu gelangen, ohne (wie chemische Reduktionsmittel) auch andere Gruppierungen anzugreifen. Durch die Kontrolle von Protonierungs- bzw. Acetylierungsschritten lassen sich die stabileren N-Acetylamine erhalten. Das niedrig liegende Reduktionspotential der N,N-Diacetylamino-propenone verhindert, daß sie in einer Einstufensynthese bei der Reduktion der Azidochalkone unter stark acylierenden Bedingungen erhältlich sind. Das voltammetrische Verhalten der Azide und ihr Reaktionsweg bei der kathodischen Reduktion werden diskutiert.

Introduction

The electrochemical investigation of α,β-unsaturated carbonyl compounds has been a continuously active area of reseach[1a–c].

Wawzonek et al.[1c] reported two one-electron steps in polarographic reduction e.g. of benzalacetophenone in aprotic media, whereas large scale electrolysis

resulted in polymer formation due to the starting material. Many other workers lead their interest into reductive coupling of such compounds giving β,β'-carbon bonded dimers[2a—c], depending on experimental parameters. Preferred coupling is reported to occur in N,N-dimethylformamide (*DMF*)[3].

The ketonic system of 2-azido-propenones, e.g. 2-azidochalcones, which should be very prone to *Michael*-type reactions, has been chosen for our investigation, the results of which are presented in this paper.

Studies on azidocinnamic esters—weakly activated olefinic carbonylgroups—showed that there is no attack on carbon during cathodic reduction as reported[4a, b]. In the ketonic system there might be the chance of effective carbon—carbon coupling. On the other hand, if in azidochalcones the olefinic skeleton is maintained, amino derivatives of chalcones may be obtained, which might find application in analytical chemistry[5].

Results and Discussion

Acetonitrile (*AN*) has been chosen as aprotic solvent for electrolysis because it is easy to remove. Since the azido group is likely to be attacked by strong nucleophiles[6], scavengers which react rapidly with anionic intermediates of cathodic reduction are required in the working solution. Ac_2O and proton donors like acetamide or *Ac*OH are used for this purpose.

A typical cyclovoltammogram (CV) of azidochalcone **2 a** in the solvent system employed is presented in Fig. 1.

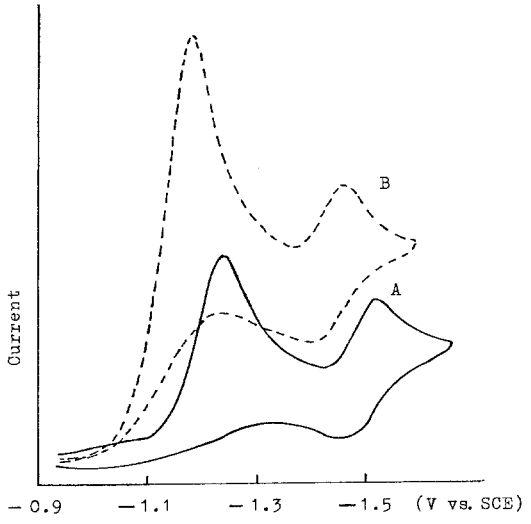


Fig. 1. CV of compound **2 a** in *AN*, 0.1 *M TEAB*, 200 mV s^{-1}, on Hg; ——— **2 a**; ———— with excess of Ac_2O

The appearance of a reversible step, following an irreversible one, is not very common in electroorganic chemistry. In the present case it may be interpreted as an EECCE-mechanism[7]. There will be electron transfer, release of nitrogen and probably protonation of anionic intermediates due to residual water or due to the supporting salt. If there is formation of a structure like keto-imino (e.g. **7** as shown in the reaction scheme) a reversible reduction may follow. Keto-imino compounds, substituted on N by aryl- or cyanogroups, are reported to be reversibly reducible in the range of —0.93 to —1.65 V[8a–c].

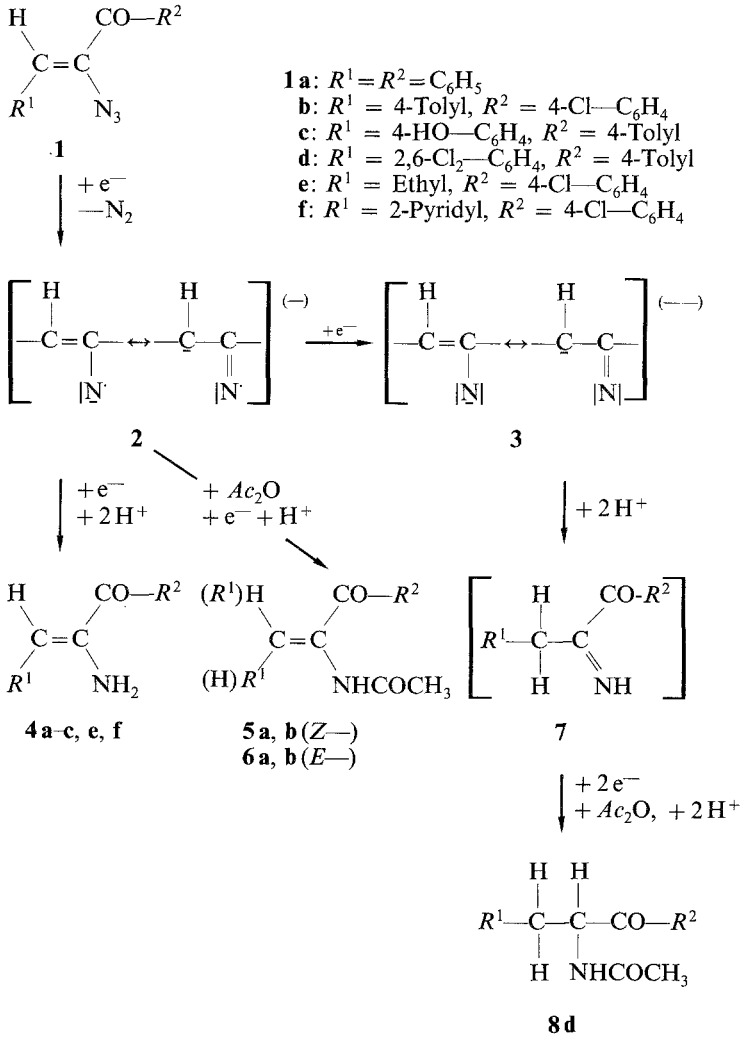


Table 1. *Reaction conditions and products of electrolysis of azidochalcones*

Substrate	E_{p1}[a]	E_{p2}[a]	method	E_{el}[b]	charge per mole	products (yield, %)	E_p[c]
1a	—1.21	—1.5	A	—1.25	2.5	**4a** (85)	—1.48
			B	—1.30	2	**5a** (40)	—1.41
						6a (30)	—1.41
1b	—1.33	—1.70[r]	A	—1.40	2.5	**4b** (85)	—1.72
		—1.68	B	—1.41	2.5	**5b** (40)	—1.68
						6b (30)	—1.68
1c	—1.50	—1.76	A	—1.55	2	**4c** (85)[d]	(—1.45)[e]
1d	—1.25	—1.69	A	—1.32	2.5	**8d** (70)	—1.75
1e	—1.35	—1.60	A	—1.38	2	**4e** (70)[d]	(—1.58)[e]
1f	—1.05	—1.35	A	—1.12	2.2	**4f** (88)[f]	—1.63

[a] Peak potential in CV, 50 mV s^{-1} on Hg vs. SCE.
[b] Potential of electrolysis.
[c] Peak potential for reduction of products.
[d] Isolated after acetylation.
[e] Peak potential of the acetylderivative.
[f] In *DMF*.
[r] Quasireversible. Method A: electrolysis with addition of *Ac*OH; method B: stoichiometric addition of azide, Ac_2O and *Ac*OH.

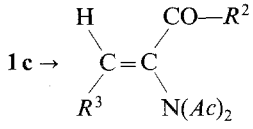
Other azidochalcones investigated differ from the behaviour of **2a** showing no reversible or quasireversible second peak in CV experiments even at scan rates up to 5 V s^{-1}. Logarithmic analysis of the first wave in polarography suggests a one-electron reduction. There is no linear relationship between current and concentration of the substrate even at millimolar level; coulometric data showed a consumption of 1.5 e^-/mol. Therefore "chemical complications" probably interfere with electrochemical reduction.

The reaction scheme proposed for the cathodic reduction of α-azidochalcones is shown below.

Results of large scale electrolysis under protonating conditions (method A), under aprotonic, strongly acetylating conditions (method B) and under mildly acetylating conditions (method C) are summarized in Table 1 together with experimental parameters and product yields.

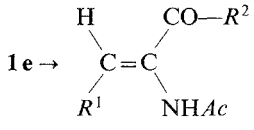
As can be seen from the results, electrolytic reduction following method A is a very useful way to synthesise 2-aminochalcones (**4a–c, f**) in excellent yields. With the exception of amine **4c** and **4f** there is no complication during product isolation. Compounds **4c** and **4f** are unstable towards normal isolation procedure as seen by chromatographic

control during workup. Therefore the crude electrolysis mixtures were acetylated immediately after extraction into CH_2Cl_2 and the acetyl derivatives (**9c**, **9f**) were analysed.



9c

R^2 = 4-Tolyl
R^3 = 4-Acetoxyphenyl



9e

$R^1 = C_2H_5$, R^2 = 4-Cl—C_6H_4

Electrolysis under strongly acetylating conditions, as successfully applied in the reduction of azidocinnamic esters[4a,b], consumed much more charge than required for a neat conversion to N,N-diacetyl-enamines and resulted in the formation of at least eight products formed in about equal amounts. Therefore no attempt has been made for isolation and identification.

2-(N,N-Diacetyl-)-propenones were prepared independently. Their reduction peaks in CV show that these derivatives are reduced at almost the same potential as the starting material (i.e. —1.38 V for the N,N-diacetyl compound **9b** derived from **2a**; —1.40 V for **9c**). Thus any diacetyl derivative formed in electrolysis will be reduced together with parent azidochalcone.

A mild acetylation method was developed in order to keep the reaction at the N-monacetyl stage, resulting in good yields. The *Z*- and *E*-isomers (**5** resp. **6**) are produced in almost equal ratios, whereas the amino compounds **4** retain the configuration of the starting material.

For highly substituted olefins it is not possible to predict which of the isomers is preferred in terms of thermodynamic stability. If there is some kinetic control during reductive acylation both isomers will result.

From the 2,6-dichlorophenyl compound **1d** the saturated acetyl derivative **8d** was obtained. The bulky groups prevent coplanarity of the aromatic ring with the double bond and favour protonation on C 3 which may lead to a keto-imino structure such as **7** being further reduced at the potentials applied (c.f.[8a—c]). For the azidochalcones no attack on C is observed on reductive acylation (cf. also results published on simple α,β-unsaturated carbonyl compounds[9a—c]).

The catalytic reduction of azidochalcones to enamines is not successful, since simultaneous reduction of the olefinic bond and/or the C=O group occurs—sometimes even accompanied by loss of aromatic halogen[10]. Also other chemical reductions of the azido function (e.g.

alkaline arsenite[11]) can not be applied because of the ease of retro-aldol reactions.

Therefore the electrochemical methods presented offer a very selective route to prepare 2-amino-propen-2-ones in excellent yields. N-Acetyl-enamides which in some cases are preferable because of chemical stability as compared with the free amines can also be obtained by carefully controlled protonation and acylation steps.

Experimental

All reagents used were of analytical grade. The chalcones were prepared according to known procedures[12]. *AN* was dried by passage through a column filled with activated alumina (Woelm Super B-I). The electrochemical measurements were made with the Electrochemistry System 170 from PAR. All potential values given are referred to a saturated calomel electrode, connected to the electrolyte by means of a salt bridge.

An electrolysis cell as employed in earlier work in azide reductions was used for electrosynthesis starting from the azidochalcones[13]. A mercury pool of 13 cm^3 was used as working electrode, concentration of supporting salt was 0.1 *M*. The temperature was maintained between 20–25 °C. Pre-electrolysis at the working potential in the solutions given below reduced background current to less than 10 mA. Usually several portions of about 0.5 m*M* of substrate were added until a total of 10 m*M* had been consumed. Starting current for each addition lies in the range of 500–700 mA.

Method A) protic conditions: 18 cm^3 *AN* + 2 cm^3 *Ac*OH as catholyte;

Method B) strongly acetylating conditions: 16 cm^3 *AN* + 4 cm^3 Ac_2O.

1 cm^3 of a mixture consisting of 5 m*M* azidochalcone, 5 m*M* Ac_2O and 5 m*M* *Ac*OH in 5 cm^3 of *AN* to 16 cm^3 of *AN*/*TEAB*-solution.

The anolyte consisting of *TEAB* in *AN* with cyclohexene added to remove bromine evolved during the anode process was replenished frequently during electrolysis. The progress of the electrolysis was monitored using HPLC analysis and CV. Electrolysis was stopped when the current for the last addition of substrate had fallen to about 10% of its initial value.

The electrolysis solution was evaporated and the supporting electrolyte precipitate by adding ethylacetate, ether or CH_2Cl_2. Any excess of Ac_2O or *Ac*OH was removed by treatment with $NaHCO_3$. For isolation of products "Flash-Chromatography" (40 μm silica particles, Fa. Baker) was used with eluting solvents consisting of mixtures of ethylacetate, petroleum ether and diisopropyl-ether. If products of electrolysis proved to be too labile for normal isolation procedures, the electrolysis mixtures were derivatized after evaporation of *AN* using acetylchloride and 2,4,6-collidine (e.g. with **4c**, **4f**).

1-(4-Chlorphenyl-)-2-azido-pentene-2-one-1 (**1f**)

Prepared according to[12] as pale yellow oil in 65% yield.

$C_{11}H_{10}ClN_3O$ (235.9).

^{1}H-NMR: δ 7.55 (A_2B_2), 5.72 (—CH=), 2.33 (mc, 2 H), 1.00 (t, 3 H). IR: 2 100 (N_3), 1 655 (CO) cm^{-1}.

1,3-Diphenyl-2-amino-propene-2-one-1 (**4a**)

By electrolysis of **1a** at —1.25 V following method A as yellow oil in 85% chemical yield.

$C_{15}H_{13}NO$ (223.3). Bp. 75–80 °C (0.5 mmHg).

^{1}H-NMR: δ 7.5 (mc, 10 H), 6.01 (s, —CH=), 4.47 (NH, 2 H). MS [*m*/e %]: 223 (M^+, 66), 195 (16), 118 (100), 105 (69), 91 (82). IR: 3350 (NH), 1620 (CO) cm^{-1}.

1-(4-chlorphenyl-)-2-amino-3-(4-tolyl-)-propene-2-one-1 (**4b**)

Electrolysing chalcone **1b** at —1.40 V according to method A yields 85% of **4b** as light yellow oil.

$C_{16}H_{14}ClNO$ (271.7). Bp. 80–84 °C (0.5 mmHg).

^{1}H-NMR: δ 7.2 (A_2B_2), 7.0 (mc, 4 H), 6.0 (s, —CH=), 4.4 (NH, 2 H), 2.33 (s, 3 H). MS [*m*/e %]: 271 (M^+, ^{35}Cl, 58), 236 (M^+-Cl), 139 (56), 132 (100), 117 (41), 111 (30).

1-(4-Chlorphenyl-)-2-acetamido-penten-2-one-1 (**9f**)

Electrolysing **1e** at —1.3 V (method A) results in a solution of enamine **4e** which is acetylated to give an overall yield of 70% of acetylamide **9f**.

$C_{13}H_{13}ClNO_2$ (250.8). Mp. 180 °C.

^{1}H-NMR: δ 7.46 (A_2B_2, +NH), 6.47 (t, 1 H, J = 8 Hz), 2.13 (N-acetyl), 2.1 (mc, 2 H), 1.06 (t, 3 H). MS [*m*/e %]: 251 (M^+, ^{35}Cl, 8), 209 (M^+-Cl, 16), 139 (24), 70 (37), 43 (100). IR: 3200 (NH), 1620 (CO) cm^{-1}.

1-(4-Tolyl-)-2-amino-3-(2-pyridyl-)-propen-2-on-1 (**4f**)

In 88% yield from azidochalcone **1f** by electrolysis at —1.4 V following method A. Yellow crystals.

$C_{15}H_{14}N_2O$ (238.2); Mp. 94–97 °C (*Me*OH).

^{1}H-NMR: δ 8.33 (m, 1 H), 7.43 (A_2B_2), 7.22 (mc, 3 H), 5.81 (—CH=), 2.33 (s, 3 H). MS [*m*/e %]: 238 (M^+, 17), 221 (9), 119 (100), 92 (52), 65 (38). IR: 3330, 3200 (NH), 1610 cm^{-1}.

Z-1,3-(Diphenyl-2-acetamido-propene-2-one-1 (**5a**)

$C_{17}H_{15}NO_2$ (265.3). Mp. 210–212 °C.

^{1}H-NMR: δ 8.2 (NH), 7.1 (mc, 10 H_{ar}—CH=), 6.60 (s, —CH=), 2.07 (s, (s, —CH=), 2.07 (s, N-acetyl). MS [*m*/e %]: 265 (40), 223 (88), 206 (31), 195 (39), 119 (100), 105 (39), 91 (37), 77 (62), 43 (69). IR: 3150 (NH), 1660, 1610 (CO) cm^{-1}.

E-1,3-Diphenyl-2-acetamido-propene-2-one-1 (**6a**)

By electrolysis of **1a** at —1.3 V following method B as white crystals in 35–40% yield together with 30–35% of the *E*-isomer **6a**.

$C_{17}H_{15}NO_2$ (265.3). Mp. 161 °C.

^{1}H-NMR: δ 8.2 (NH), 7.6 (mc, 10 H), 6.55 (s, —CH=), 1.98 (s, 3 H). MS [*m*/e %]: 265 (M^+, 23), 223 (M^+-ketene), 206 (30), 195 (26), 162 (29), 120 (51), 118 (100), 105 (82), 91 (46), 77 (72), 51 (23), 43 (87). IR: 3200 (NH), 1650, 1610 (CO) cm^{-1}.

Z-1-(4-Chlorphenyl-)-2-acetamido-3-(4-tolyl-)-propene-2-one-1 (**5b**)

$C_{18}H_{16}ClNO_2$ (309.8). Mp. 208–210 °C.

^{1}H-NMR: δ 7.44 (A_2B_2, +NH), 7.21 (A_2B_2), 6.50 (s, —CH=), 2.41 (s, N-acetyl), 2.12 (s, 3 H). MS [*m*/e%]: 313 (M^+, 29), 271 (56), 256 (16), 236 (16), 139 (39), 132 (100), 105 (49), 43 (59). IR: 3350 (NH), 1680, 1660 (CO) cm^{-1}.

E-1-(4-Chlorphenyl-)-2-acetamido-3-(4-tolyl-)-propene-2-one-1 (**6b**)

By electrolysing **1b** at —1.41 V following method C in 35–40% yield together with about 30% of the *E*-isomer **6b**.

$C_{18}H_{16}ClNO_2$ (309.8). Mp. 151 °C.

^{1}H-NMR: δ 7.43 (A_2B_2), 7.27 (mc, 4 H_{ar}, NH), 6.45 (—CH=), 2.20 (s, N-acetyl), 2.01 (s, 3 H). MS [*m*/e%]: 313 (42), 272 (57), 139 (28), 132 (56), 111 (27), 105 (23), 43 (100). IR: 3250 (NH), 1655, 1630 (CO) cm^{-1}.

1-(4-Tolyl-)-2-acetamido-3-(2,6-dichlorphenyl-)-propanone-2 (**8d**)

From **1d** following method A at —1.33 V in 70% yield.

$C_{18}H_{17}Cl_2NO_2$ (350.1). Mp. 190–195 °C.

^{1}H-NMR: δ 7.47 (A_2B_2), 7.18 (mc, 4 H_{ar}, NH), 6.00 (t, 1 H, J = 7 Hz), 3.25 (d, 2 H), 2.37 (s, N-acetyl), 1.87 (s, 3 H). MS [*m*/e%]: 349 (M^+, ^{35}Cl), 314 (2), 232 (34), 230 (53), 188 (100), 148 (34), 91 (38), 65 (20), 43 (58). IR: 3450 (NH), 1640, 1620 (CO) cm^{-1}.

1-(4-Chlorphenyl-)-2-(N,N-diacetylamino-)-3-(4-tolyl-)-propene-2-one-1 (**9b**)

Starting from the isolated mono-amide **5b** by acetylation with 2,4,6-trimethylpyridine and acetylchloride in CH_2Cl_2.

$C_{20}H_{18}ClNO_3$ (355.8). Mp. 210 °C.

^{1}H-NMR: δ 7.4 (A_2B_2), 7.2 (A_2B_2), 6.01 (s, —CH=), 2.37 (s, N,N-diacetyl), 2.0 (s, 3 H). MS [*m*/e%]: 355 (M^+, 1), 313 (-ketene, 7), 271 (-2 × ketene, 11), 167/11), 149 (30), 139 (27), 105 (24), 60 (24), 43 (100). IR: no NH, 1720 (CO) cm^{-1}.

1-(4-Tolyl-)-2-(N,N-diacetylamino)-3-(4-acetoxyphenyl-)-propene-2-one-1 (**9c**)

Electrolysing **1c** at —1.55 V following method A and chemical acetylation of the evaporated electrolysis solution as given for compound **9b** in an overall chemical yield of 85% as stable white crystals.

$C_{22}H_{21}NO_5$ (379.5). Mp. 221 °C.

^{1}H-NMR: δ 7.4 (A_2B_2), 7.2 (mc, 4 H), 6.81 (s, —CH=), 2.54 (s, O-acetyl), 2.31 (s, 2 × N-acetyl, CH_3). MS [*m*/e%]: 379 (M^+, 3), 337 (M^+-ketene, 61), 295 (—2 × ketene), 253 (M^+-3 × ketene, 73), 134 (12), 119 (41), 91 (34), 43 (100). IR: no NH, no OH, 1725, 1660, 1605 (CO) cm^{-1}.

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References

[1] a) *Pasternak R.*, Helv. Chim. Acta **31**, 48 (1948); b) *Wiemann J.*, Bull. Soc. Chim. Fr. **1964**, 2545; c) *Wawzonek S., Gunderson A.*, J. Electrochem. Soc. **111**, 324 (1964); d) *Baizer M. M.*, Tetrahedron **40**, 945 (1984).

[2] a) *Wiemann J., Bouguerra M. L.*, Ann. Chim. **2**, 35 (1967); b) *Grimshaw J., Rea E. F. J.*, J. Chem. Soc. C **1967**, 2628; c) *Baizer M. M., Petrovich J. P.*, in: Progress of Physical Organic Chemistry, Vol. 7 (*Streitwieser A.*, ed.). New York: J. Wiley. 1970.

[3] *Lamy E., Nadjo L., Saveant J. M.*, Norw. J. Chem. **3**, 21 (1979).

[4] a) *Knittel D.*, Monatsh. Chem. **115**, 1335 (1984); b) *Knittel D.*, Monatsh. Chem. **116**, 1133 (1985).

[5] *Raghava Naidu R.*, Talanta **22**, 614 (1975).

[6] *L'abbe G.*, Industrie Chim. Belge **T 34**, 519 (1969); Angew. Chem. **87**, 831 (1975).

[7] *Heinze J.*, Angew. Chem. **96**, 823 (1984).

[8] a) *Knittel D.*, Z. Naturf. **38 b**, 930 (1983); b) *Armand J., Boulares L., Pinson J., Souchay P.*, Bull. Soc. Chim. Fr. **1971**, 1918; c) *Pinson J.*, J. Armand, ibid. **1971**, 1764.

[9] a) *Lund H., Simonet J.*, C.R. Acad. Sci. Ser. C **277**, 1387 (1973); b) *Christensen L., Iversen P. E.*, Acta Chem. Scand. **B 33**, 352 (1979); c) *Shono T., Nishiguchi I. H., Ohmizu H.*, J. Amer. Chem. Soc. **99**, 7396 (1977).

[10] *Knittel D.*, Habilitationsarbeit, Universität Hamburg, 1985.

[11] *Ugi I., Perlinger H., Behringer L.*, Ber. **91**, 2330 (1958).

[12] *Knittel D., Hemetsberger H., Weidmann H.*, Monatsh. Chem. **101**, 161 (1970).

[13] *Knittel D., Henning A.*, Monatsh. Chem. **115**, 391 (1984).