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CYCLOCONDENSATIONS OF DMF WITH α-HALOAMIDES, AN AZIRIDINONE, OR A Δ^2-1,2,3-TRIAZOLIN-5-ONE

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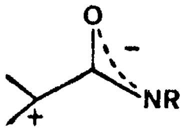
SUMMARY: The formation of oxazolidin-4-one derivatives from DMF and 2-bromo-isobutyramides (**3a,b**),the aziridinone **4a**, or the 1,2,3-triazolin-5-one **5a**, is reported. The possibility that a common dipolar intermediate cycloadds onto the carbonyl group of DMF, is considered.

During our studies on base-induced reactions of 2-bromo-carboxamides (**1**), we involved a zwitterion such as **2a,b**, possibly arising through the conjugate anion of **1** , in order to explain the trend observed in nucleophilic substitution and cyclo-condensation reactions.[1] The regioselectivity observed towards ambident anions may in fact indicate a charge-controlled reaction path.

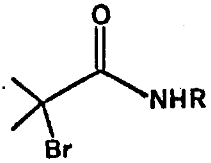
RR'BrCCONHR''

1 (R,R'=H or Me)

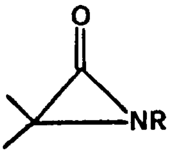


2	R
a	Me
b	CH_2Ph
c	tBu
d	CH_2SPh

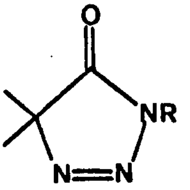
We report now on the outcome of base-induced reactions of α-bromo-isobutyramides with the dipolar aprotic partner DMF. We studied also thermal reactions of DMF i) with a moderately stable α-lactam (**4a**) previously suggested to be in equilibrium with a zwitterion (**2c**),[2] and ii) with triazolinone **5a**,[3] which we expected would yield a zwitterion such as **2b** through irreversible loss of nitrogen.[4,5]



3	R
a	Me
b	CH_2Ph

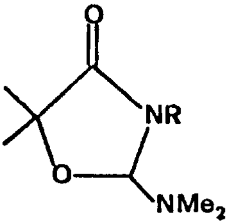


4	R
a	tBu
b	Ad



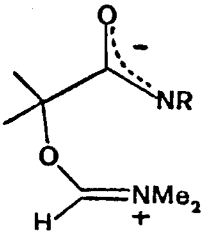
5	R
a	CH_2Ph
b	CH_2SPh
c	Ad

Accordingly, N-methyl- and N-benzyl-isobutyramide **3a,b** were treated with NaH in DMF:[6] the oxazolidinone derivatives **6a,b** were obtained in good yields (see Table). The aziridinone **4a** and the 1,2,3-triazolin-5-one **5a** were kept, in turn, in DMF at 20°C for 12 h, or at 30°C for 12 days, respectively: the corresponding oxazolidin-5-one derivatives **6b,c** were formed (see Table).



6	R
a	Me
b	CH_2Ph
c	tBu

Compounds **6** may arise from the different reagents through a non-concerted cycloaddition of a common intermediate such as zwitterions **2a-c** onto the carbonyl group of DMF. The betaine **7** may then represent the reactive intermediate of a two steps mechanism.[7]



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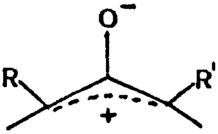

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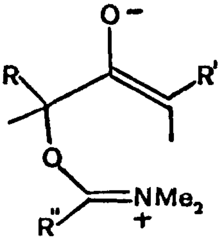

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In metal-promoted cyclo-coupling reactions of α,α'-dibromoketones with tertiary amides[8,9] the oxyallyl cation **11** and the adduct **12** have been suggested as reaction intermediates.[8] On the other hand, both in base-induced reactions of α-bromoacetamides[10] and in metal-induced reactions of α,α'-dibromoacetone,[8] no cyclocoupling was observed. The observed trend suggests that the stabilization of a positive charge by alkyl groups is important in both type of reactions.

The scope and limitations of the present research are under investigation in our laboratory.

TABLE. Yield, physical and spectroscopical data for compounds **6 a-c** . ^{1}H-NMR data are in $CDCl_3$.

Compound	Yield(%)[d]	m.p.(°C)	I.R.(KBr) $\nu_{C=O}$(cm^{-1})	^{1}H-NMR(δ)[a] CH	NMe$_2$	CMe$_2$	other H
6a	70	oil	1710	5.50	2.31	1.23,1.38	2.78 (Me)
6b	80[e], 85[f]	oil	1715	5.34	2.22	1.28,1.38	4.82,3.90(CH_2Ph)[b] 7.18-7.32 (Ph)[c]
6c	78	71-72	1695	5.64	2.28	1.28,1.35	1.42 (<u>t</u>Bu)

[a] All signals are singlets unless otherwise stated. - [b] AB system, J=14.4 Hz.
[c] Multiplet. - [d] All products gave satisfactory elemental analyses.
[e] Starting from **3b**. - [f] Starting from **5a**.

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REFERENCES AND FOOTNOTES

(1) P. Scrimin, F. D'Angeli, G. Cavicchioni, <u>Synthesis</u>, <u>1982</u>, 1092; G. Cavicchioni, P. Scrimin, A.C. Veronese, G. Balboni, F. D'Angeli, <u>J. Chem. Soc., Perkin Trans. 1,</u> <u>1982</u>, 2969, and references cited therein.

(2) Aziridinones and other heterocyclic analogues of methylene cyclopropanes may react in cycloaddition reactions as "externally stabilized" 1,3 - dipoles. G. L'Abbé, <u>Angew. Chem. Int. Ed. Engl.</u>, 1980, <u>19</u>, 276 and references therein.

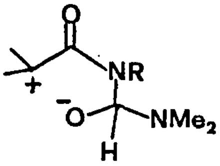
(3) The triazolinone **5a** was prepared from ethylisobutyrate and benzyl azide.[4] It is a colorless oil. I.R. (liquid film) 1735 cm^{-1} ; ^{1}H-NMR ($CDCl_3$), δ : 1.40 (s, 6H, 2Me); 4.95 (s, 2H, CH_2Ph); 7.26 (m, 5H, Ph).

(4) Triazolinone **5b** has been recently described to behave as a functional equivalent of a zwitterion such as **2d** : B. M. Trost, W. H. Pearson, <u>J. Amer. Chem. Soc.</u>, 1981, <u>103</u>, 2483.

(5) The photodenitrogenation of triazolinone **5c** to 1-adamantylaziridinone **4b** was also reported: H. Quast, B. Seiferling, <u>Tetrahedron Lett</u>. 1982, <u>23</u>, 4681.

(6) Procedure: A sample of the 2-bromo-isobutyramide (2 mmol) in DMF (5 ml) was added in 1 h to a stirred suspension of NaH (4 mmol) in DMF (10 ml). After further stirring (30 min) the mixture was concentrated in vacuo, and the residue was fractionated using a column of neutral alumina and ethyl acetate-toluene (1:4) as eluant.

(7) The final product (**6**) may alternatively form via a reverse addition, through betaine **8** . On the other hand, addition of a bromoamide anion **9** onto DMF



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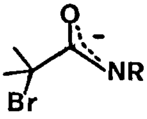

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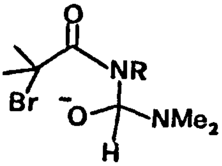

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would give the intermediate **10** . We think that these two alternative mechanisms are less likely to operate.

(8) H.M.R. Hoffmann, K.E. Clemens, E.A. Schmidt, R.H. Smithers, J. Amer. Chem. Soc., 1972, 94, 3201.

(9) R. Noyori, Y. Hayakawa, S. Makino, H. Takaya, J. Amer. Chem. Soc., 1973, 95, 4103.

(10) 2-Bromo-N-benzyl-acetamide, treated in the same conditions used for **3a,b** (Ref. 6), gave only N,N-dibenzyl-piperazin-2,6-dione (60 %).

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