Reactions of Amide Anions with α-Bromo-amides

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Summary The reactions of α-bromoisobutyramides with the anions from amides and a thioamide afford oxazolidin-4-ones and a thiazolidin-4-one, respectively; these are useful intermediates for preparation of ester derivatives.

α-BROMO-*N*-BENZYL-PROPIONAMIDE (**1**) and -ISOBUTYRAMIDE (**2a**) undergo hydride-catalysed self-condensation to produce 2-amino-2-bromoalkyloxazolidin-4-ones (**3**); from these heterocycles the ester derivatives (**4**) and (**5**) were obtained.[1] We considered that the reaction of a halogeno-

TABLE Bromo-amide cyclization products from amide or thioamide anions.

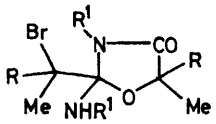
Anion precursor	Bromo-amide	Products[a,b]	R^2	R^3	M.p./°C	% Yield[c]
$MeCONHCH_2Ph$	(**2a**)	(**6a**)	Me	CH_2Ph	98—100	40
$H_2C{=}CMe{-}CONHCH_2Ph$	"	(**6b**)	$H_2C{=}CMe$	CH_2Ph	73—75	58
PhCONHMe	"	(**6c**)	Ph	Me	97—99	56
PhCONHPh	"	(**6d**)	Ph	Ph	103—105	66
$MeCONHCH_2Ph$	(**2b**)	(**6e**)[b]	Me	CH_2Ph	50—52	35
$MeCSNHCH_2Ph$	(**2a**)	(**7**)	Me	CH_2Ph	94—95	81

[a] All products gave satisfactory elemental analyses and spectra. [b] $R^1 = CH_2Ph$ except for (**6e**) where $R^1 = Bu^t$. [c] Yields were not optimized.

amide with the conjugate base of a molecule of the same compound was a possible pathway to the formation of the oxazolidinones (**3**). We therefore thought it possible that

$MeCRBrC(:O)NHR^1$

(**1**) R = H, $R^1 = CH_2Ph$
(**2a**) R = Me, $R^1 = CH_2Ph$
(**2b**) R = Me, $R^1 = Bu^t$



(**3**)

$Me_2C(NHR^1)CO_2CMe_2CONHR^1$

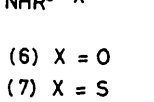
(**4**)

$BrCRMeCO_2CRMeCONHR^1$

(**5**)

R = H or Me, $R^1 = CH_2Ph$

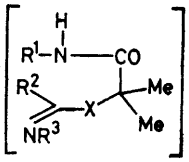
the conjugate base of a different amide might also react with an α-halogeno-amide to produce an oxazolidinone. Accordingly, we treated representative amides and a thioamide with sodium hydride in anhydrous tetrahydrofuran at room temperature followed, after hydrogen evolution had ceased, by α-bromo-*N*-benzylisobutyramide (**2a**) or, in one case, α-bromo-*N*-t-butylisobutyramide (**2b**). 2-Substituted 2-amino-oxazolidin-4-ones (**6a**—**e**) and the thiazolidin-4-one (**7**) were obtained (Table). The heterocycles (**6**) were transformed into the ester derivatives (**8**) upon mild acid hydrolysis. The hydrolytic behaviour of (**7**) is still under investigation.



(**6**) X = O
(**7**) X = S

$R^2CO_2CMe_2CONHR^1$

(**8**)



(**9**)

We suggest that, in the present reaction, the oxygen (or sulphur) end of the amide conjugate anion is alkylated by the sp^3 carbon of the α-bromo-amide, and the nitrogen of the conjugate base of the postulated intermediate (**9**) thus formed adds nucleophilically to the C=N bond.

Spiro-oxazolidinones were considered to arise through a similar mechanism in reactions of the 2-methylcyclohexane-1,3-dione anion with α-halogeno-acetanilides or -propionanilides.[2] Talaty *et al.* have described the formation of pyrrolinones in the reaction of alkynyl-lithium reagents with α-halogeno-amides or α-lactams, stressing the possibility of obtaining heterocycles bearing bulky aliphatic substituents.[3]

Our results indicate that some α-halogeno-amides, either capable [*e.g.* (**2b**)] or incapable [*e.g.* (**2a**)] of producing stabilized α-lactams,[4] afford heterocyclic derivatives. Studies on the scope and limitations of the reactions of α-halogeno-amides with anions, as well as with neutral reagents, will be reported elsewhere.

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