A LIMITATION TO THE PREPARATION OF β,γ-UNSATURATED N,N-DIALKYL AMIDES
STARTING FROM β,γ-UNSATURATED ACID CHLORIDES[1]

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In the course of an investigation on the reactivity of β,γ-unsaturated acid chlorides (e.g. 2-methyl-3-butenoylchloride) with aliphatic primary and secondary amines, we observed that during the reaction, depending on the conditions and the amine structure, a double bond shift from the β,γ to the α,β position can occur.

This fact was unexpected since in the literature no limitation is reported to transform any acid chloride to the corresponding N-alkyl or N,N-dialkyl-amide. Furthermore the alcoholysis of β,γ-unsaturated acid chlorides in the presence of t.amines affords only β,γ-unsaturated esters[2].

We observed that, when 2-methyl-3-butenoylchloride (I) in pentane or diethylether at 0°C, was reacted with diisopropylamine (molar ratio (I)/amine = 1/2) by adding amine to (I), a reaction mixture containing prevailingly two isomers was produced.

To the first (Found: C, 72.02; H, 11.31; N, 7.78; Calcd. for $C_{11}H_{21}NO$: C, 72.08; H, 11.55; N, 7.64) on the basis of the I.R. (υ_{max} 1660, 1627, 840, 820 cm^{-1}) and N.M.R. spectra (100 Mc) in C_6D_6 (υ_a 141.7, υ_b 537.6, υ_c 171.3, υ_d 346,8, υ_e 116.9 c.p.s. from T.M.S.; J_{ab} 6.8, J_{ac} 1.2, J_{bc} 1.8, J_{de} 6.8 c.p.s.) and by comparison of its physical properties with those of an authentic sample of this compound, we assigned the structure of trans-N,N-diisopropyl-2-methyl-2-butenamide (II). (Fig. 1)

To the second component of the reaction mixture (Found: C, 72.17; H, 11.59; N, 7.82) on the basis of the I.R. (υ_{max} 1640, 1630, 995, 910 cm^{-1}) and the N.M.R. spectra (100 Mc) in C_6D_6 ($\upsilon_{a'} = \upsilon_{b'}$ 520, $\upsilon_{c'}$ 585, $\upsilon_{d'}$ 134, $\upsilon_{e'}$ 413.0, $\upsilon_{f'}$ 358, $\upsilon_{g'}$ 113, $\upsilon_{h'}$ 120 c.p.s. from T.M.S.) we assigned the structure of N,N-diisopropyl-2-methyl-3-butenamide (III) (Fig. 1).

The isomeric ratio (II)/(III) was 67/29.

By changing the reaction time and temperatures, the ratio is almost unaffected. However, when (I) was reacted with diisopropylamine at 0°C by adding (I) to amine, the product contained mostly amide (II) (94 %) besides amide (III) (5 %).

The molar ratio α,β unsaturated amide/β,ɣ unsaturated amide is largely affected by the structure of the amine used (Table 1).

In order to obtain some information about the mechanism of the above reactions the reactivity of (I) with amines-N-d was investigated. By reacting (I) with diethylamine-N-d the corresponding N,N-diethylamide was obtained; however the reaction of (I) with diisopropylamine-N-d provided a reaction mixture containing partially deuterated α,β unsaturated amide (II) and no deuterated β,ɣ unsaturated amide (III).

By comparison of the N.M.R. spectrum (100 Mc) of the partially deuterated α,β unsaturated amine with that of an authentic sample of <u>trans</u>-N,N-diisopropyl-2-methyl-4d$_1$-2-butenamide[3], we found that the former consists of the <u>trans</u>-N,N-diisopropyl-2-methyl-4d$_1$-2-butenamide (IV) (41 %), of <u>trans</u>-N,N-diisopropyl-2d$_1$ methyl-2-butenamide (V) (41 %) and of the amide (II) (18 %).

The results obtained cannot be explained on the basis of an isomerization of the β,ɣ unsaturated amide (III) as no isomerization of (III) to (II) was found maintaining (III) for 24 hours in the presence of diisopropylamine.

The formation of an intermediate unsaturated ketene, as has been observed in the reaction of α,β unsaturated acid chlorides with tertiary amines[2] must also be excluded. In fact by the most probable 1,2 addition[2] of the diisopropylamine-N-d, such a ketene should give rise to an β,ɣ unsaturated amide deuterated in position 2 which was not found in the reaction products.

From the results presented in Table 1 it is also clear that the different course of the reaction of (I) with the different secondary amines can not be explained only on the basis of the basic strength of the amines, because amines having almost the same dissociation constants[4] (e.g. diethylamine and diisopropylamine) lead to very different results.

Taking into account the products of the reaction of (I) with diisopropylamine-N-d, we think that the bulkiness of the secondary amine used plays an important role and that the reaction may proceed both by direct
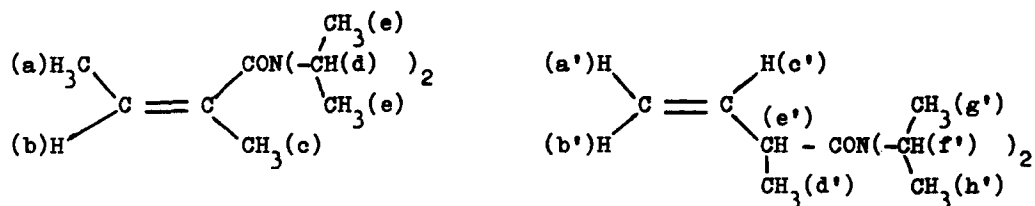
Fig. 1

$(a)H_3C$
$(b)H$
$C = C$
$CON(-CH(d))_2$ with $CH_3(e)$ above and $CH_3(e)$ below
$CH_3(c)$

$(a')H$
$(b')H$
$C = C$
$H(c')$
(e') $CH-CON(-CH(f'))_2$ with $CH_3(g')$ and $CH_3(h')$
$CH_3(d')$

Table 1

Products from reaction of 2-methyl-3-butenoylchloride (I) with amines

Amine	Products			
	β,γ unsaturated amide	%	α,β unsaturated amide	%
$(CH_3)_2CHNH_2$	$CH_2=CH-CH-CONHCH(CH_3)_2$ with CH_3	100	–	–
$(CH_3)_2NH$	$CH_2=CH-CH-CON(CH_3)_2$ with CH_3	100	–	–
$(C_2H_5)_2NH$	$CH_2=CH-CH-CON(C_2H_5)_2$ with CH_3	100	–	–
$(\overset{CH_3}{\underset{CH_3}{}}CH-CH_2)_2NH$	$CH_2=CH-CH-CON[CH_2CH(CH_3)_2]_2$ with CH_3	97	$CH_3-CH=C-CON[CH_2CH(CH_3)_2]_2$ with CH_3	3
$[(CH_3)_2CH-]_2NH$	$CH_2=CH-CH-CON[CH(CH_3)_2]_2$ with CH_3	29	$CH_3-CH=C-CON[CH(CH_3)_2]_2$ with CH_3 trans	67

nucleofilic attack of the amine on the chloroformylic group and through the
zwitterions (VI) and (VII)

(VI)   (VII)
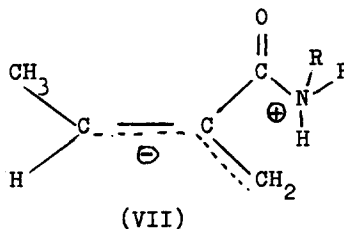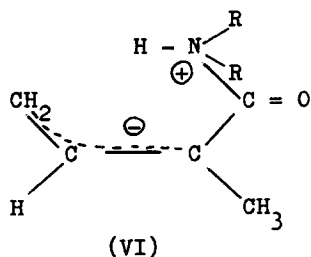
   Although the above possibility may also account for the course of the
reaction of (I) with different secondary amines, a definitive explanation
must await in our opinion further experimental work.

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References and Notes

1. We express our grateful thanks to Dr. A.L.Segre of Istituto di Chimica
   Industriale, Politecnico di Milano, for N.M.R. measurements.

2. T.Ozeki, M.Kusaka, Bull.Soc.Chem.Japan, 40, 2686 (1967).

3. This amide was prepared starting from trans-4d$_1$-2-methyl-2-butenoic acid
   obtained by isomerization with NaOD of 2-methyl-3-butenoic acid.

4. Although we make reference to K_b values in water, it is to be noticed
   that the base strength of an amine in water is, broadly speaking, a
   reliable index of its base strength in organic solvents [H.K.Hall Jr.,
   J.Phys.Chem., 60, 63 (1956)].