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ENAMINE CHEMISTRY—XXII†

THE PREPARATION OF 4-ACYLAMINOPENT-3-EN-2-ONES AND THE CORRESPONDING ENAMINO-THIONES

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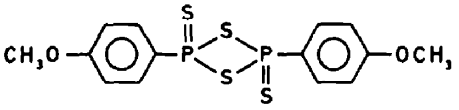
Abstract—Acylation of 4-aminopent-3-en-2-one, **5**, with different acid chlorides, RCOCl (R = Me, Me_2CH, Me_3C, C_6H_5, $ClCH_2$) gives only N-acylated products, **6**, in high yields. The N-acylated enaminones, **5**, are shown only to exist in the *Z*-s-*Z* form in solution. The UV spectra of **6** are discussed and an additional increment to the Dabrowski-Table[21] is given. The reaction of **6** with 2,4-bis(4-methoxyphenyl)-1,2,3,4-dithiadiphosphetane 2,4-disulfide, **2**, at room temperature in DME gives the corresponding enamino-thiones, **7**, in good yields. The ^1H and ^{13}C NMR spectra of **6** and **7** are discussed.

In the enaminone system[1,2] four geometrical isomers, *E*-s-*E*, *E*-s-*Z*, *Z*-s-*E* and *Z*-s-*Z*, are possible (for nomenclature, see Refs[1,2]). It has been reported[3] that 4-aminopent-3-en-2-one exists in both the *E*-s-*Z* and *Z*-s-*Z* form in solution and that the *E*-s-*Z* isomer is slowly transformed into the *Z*-s-*Z* one, which is stabilized by intramolecular H-bonding. Enaminones[1] have three nucleophilic centres at O, C and N; substitution at these sites has been investigated.[4–12] The preceding paper[13] of this series[14,15] has described the alkylation and acylation of ethyl 3-amino-2-butenoate, **1**, to give N- and/or C-alkylation and acylation products. The reaction of the N-acylated products with 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide, **2**,



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produced 2-substituted-4-methyl-1,3-thiazine-6-thiones, **3** (Scheme 1). The reaction of the C-acylated product with **2** gave the corresponding enamino-thione, **4**.

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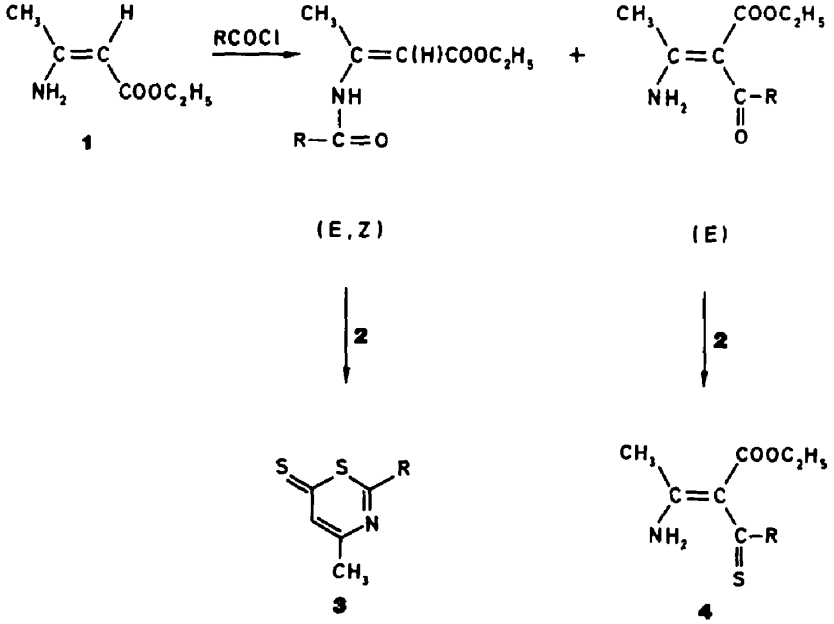
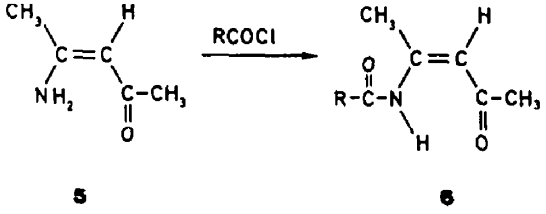


Scheme 1.

As a continuation of this work this paper will report on the acylation of 4-aminopent-3-en-2-one, **5**, and the subsequent thiation with **2**.

RESULTS AND DISCUSSION

4-Amino-3-en-2-one, **5**, was prepared[17,18] by condensing ammonia and pentane-2,4-dione. After distillation it was shown (^{1}H NMR) to exist only in the *Z*-s-*Z* form in $CDCl_3$ solution. Compound **5** was reacted with the following acid chlorides, RCOCl, R = Me (**a**), Me_2CH (**b**), Me_3C(**c**), C_6H_5 (**d**) and $CLCH_2$ (**e**), in ether at 0° by using pyridine as external base. The reaction was completed in one hour (see experimental) and only N-acylated products, **6**, were formed and isolated in high yields (Scheme 2, Table 2).



5 **6**

a) R = CH_3
b) R = $(CH_3)_2CH$
c) R = $(CH_3)_3C$
d) R = C_6H_5
e) R = $Cl-CH_2$

Scheme 2.

The ^{1}H NMR spectra of the compounds **6a–e** showed NH signals in the lowfield region (δ(NH) > 12), suggesting a strong intramolecular H- bonding between the amino group and the CO oxygen. Therefore these compounds are considered to exist in the *Z*-s-*Z* form in $CDCl_3$ solution. In strong polar solvents *N*-monosubstituted enaminones often show[6] C=C double-bond isomerisation,[19,20]

Z-s-*Z* ⇄ *E*-s-*Z* ⇄ *E*-s-*E*

but ^{1}H NMR spectra of **6** in DMSO ((d_6) solution did not show any isomerisation.

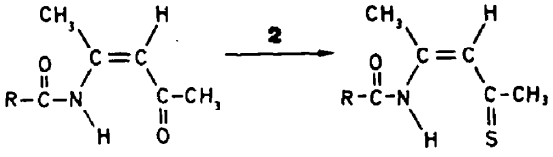
UV spectroscopy has been shown[20,21] to give excellent information on the structure of enaminones. Unfortunately data of N-acylated enaminones have not been given by the Dabrowski's increments.[21] As a consequence we measured the UV spectra of **6** (Table 1).

According to the ^{1}H NMR data the compounds **6** exist only in the *Z*-s-*Z* form. This is clearly reflected in the UV where solvent induced shifts of λ_{max} (Table 1) are small ($\Delta\lambda(\text{solvent})_{max} = \pm 6$ nm) as proposed by Dabrowski.[21] Although the small number of compounds investigated does not permit a rigorous regression analysis, an additional spectral increment can be proposed on the basis of the data collected for R equal to alkyl. The increment $\Delta\lambda$(nm) which can be added to the Dabrowski-Table[21] is

-NH-C(O)-Alk replacing -NH-Alk $\Delta\lambda = +76$ nm
(solvent cyclohexane, *Z*-s-*Z* isomer).

As only one compound is available for R equal to aryl (phenyl) no general tendency can be drawn. A remarkable bathochromic shift is observed giving rise to an increment value of $\Delta\lambda = 89$ nm. This is in accordance with similar increments given by Henning *et al.*[20] by substituting an alkyl group with a phenyl group.

The 4-acylaminopent-3-en-2-ones, **6a–d**, were reacted with **2**[16] under mild conditions in dimethoxy ethane (DME) giving fair to high yields of the corresponding enamino-thiones, **7a–d** (Scheme 3, Table 2). The thiation

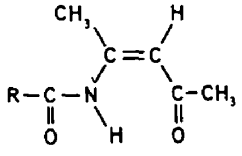


6 **7**

a) R = CH_3
b) R = $(CH_3)_2CH$
c) R = $(CH_3)_3C$
d) R = C_6H_5

Scheme 3.

Table 1. UV-Data for the enaminones **6** (λ_{max}, nm)*



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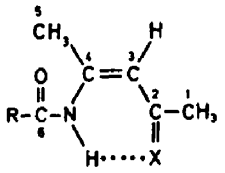
Solvent \ Compound	6a	6b	6c	6d	6e
C_6H_{12}	294	296	297	309	290
$(C_2H_5)_2O$	293	295	296	311	293
CH_3OH	293	295	296	317	291
H_2O	296	297	297	-	295

*log ε = 4.2 (6a, 6b, 6c, 6e); log (ε) = 4.1 (6d)

Table 2. Experimental and spectroscopic data for 4-acylaminopent-3-en-2-ones and the corresponding enamino-thiones



6 : X = O*
7 : X = S*

Comp.	X	Yield (%)	M.p.(°C) B.p.(°C/torr)	^{1}H NMR ($CDCl_3$) CH_3(1)	C=C^{H}	CH_3(5)	NH
6a	O	82	47	2.20	5.35	2.40	12.3
6b	O	74	70/2	2.15	5.30	2.40	12.4
6c	O	69	60/0.5	2.15	5.40	2.40	12.7
6d	O	70	80-81	2.15	5.40	2.50	13.4
6e	O	75	71	2.10	5.40	2.30	12.6
7a	S	30	oil	2.70	6.20	2.45	14.3
7b	S	90	-	2.60	6.20	2.40	14.3
7c	S	70	-	2.65	6.25	2.40	14.3
7d	S	60	70	2.70	6.30	2.60	14.8

*The microanalyses are in agreement with the calculated values

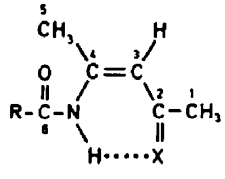
of the carboxamide function did not take place under these conditions. At elevated temperatures the yields of **7** were lowered while still no thiation of the carboxamide function were observed.

When R was equal to Me the yield of **7** was considerably lowered and an unidentified red compound was the main product (polymer?).

The structures of the 4-acylaminopent-3-ene-2-thiones, **7**, were proved by ^{1}H NMR and ^{13}C NMR. The ^{1}H NMR spectra showed NH signals in the lowfield region (δ(NH > 14)) suggesting the chelated *Z*-s-*Z* structure as for the corresponding enaminones, **6**. The ^{13}C NMR spectra showed >C=S resonances at δ = 223–225 and >C=O at δ = 167–178 clearly showing that thiation had taken place at the keto-group. This information was of course also at hand from the IR spectra.

As pointed out by Greenhill[1] unequivocal assignment exists for the Me groups Me(1) and Me(5). In an earlier paper[16] we observed a downfield shift at 0.5–0.7 ppm of the hydrogens α to the C=X group, X=O, S, by going

Table 3. ^{13}C NMR chemical shifts ($CDCl_3$) of **6** and **7**



6 : X = O
7 : X = S

Comp.	X	C_1	C_2	C_3	C_4	C_5	C_6
6a	O	29.6	198.6	104.4	154.5	20.9	168.7
6b	O	29.4	198.5	104.5	154.5	21.0	175.7
6c	O	29.6	198.8	105.0	155.5	21.3	177.8
6d	O	29.8	199.4	105.2	155.5	21.3	165.3
6e	O	30.0	199.2	106.7	153.0	21.1	165.7
7a	S	41.6	224.7	116.7	156.6	22.9	170.2
7b	S	41.7	224.5	117.4	157.3	23.3	177.8
7c	S	40.5	223.0	116.8	156.6	22.7	178.0
7d	S	41.9	225.0	118.5	157.7	23.8	167.0

from enaminone to enamino-thione. This observation makes it possible to assign the signals of the respective Me groups. It is found that the Me(1) shifts at higher field compared with the Me(5) group, simply since the former shows the proposed downfield shift by going from enaminone to enamino-thione. This is in accordance with the findings by Ostercamp[10] though his assignment relied on the fact that substituting the Me(1) group with a phenyl group would not affect the other Me group. This fact is not quite obvious, especially not for 4-aminopent-3-en-2-one. A downfield shift by 0.6 ppm was also observed for the vinylic hydrogen H(3) (Table 2).

The ^{13}C NMR spectra show a similar downfield shift[16] of 10–13 ppm for the α-carbon by going from enaminone to enamino-thione. This effect makes it possible to assign the signals of the C(1) and C(5) carbons, respectively.

Interestingly, it is found that the C(1) shifts at lower field (Table 3) for the compounds **6**, while the adjacent hydrogens shift at higher field compared to C(5). An explanation must await further investigations since several effects might operate; one of which is the alternating effect.[22] The remaining ^{13}C NMR data are straight forward and need no comments.

EXPERIMENTAL

^1H NMR spectra were recorded at 60 MHz on a Varian EM-360 spectrometer. ^{13}C NMR spectra were recorded at 20 MHz on a Varian CFT-20 spectrometer. TMS was used as internal standard and chemical shift are expressed in δ-values. $CDCl_3$ was used as solvent. IR spectra were recorded on a Beckman IR-18A spectrometer. UV spectra were recorded on a Varian CARY 219 spectrometer. Mass spectra were recorded on a Micromass 7070 Mass spectrometer operating at 70 eV using direct inlet. Elementary analyses were carried out by Novo Microanalytical Laboratory, Novo Industry A/S, Novo Allé, DK-2880 Bagsvaerd, supervised by Dr. R. E. Amsler. M.ps are uncorrected.

The enaminone **5** is known and prepared by passing ammonia through a warm solution of pentane-2,4-dione and subsequent distillation to give the *Z*-s-*Z* form.

General procedure for acylation of 4-aminopent-3-en-2-one, **5**. Compound **5** (0.2 mol) was dissolved in 140 ml dry ether in a 3-necked flask and cooled to 0°. 0.2 mol pyridine was added and then 0.2 mol of the appropriate acid chloride, dissolved in ether (25 ml), was added dropwise with stirring. After the addition was complete (0.5 hr), the mixture was usually refluxed for 0.5–1 hr. Then the mixture was treated with H_2O, washed with $NaHCO_3$(aq) and finally with H_2O and dried ($MgSO_4$). The solvent was removed (rotational evaporator) and the acylated products were isolated by either addition of light petroleum (precipitation) or distillation (Table 1). All products, **6a–e**, were characterized by means of ^1H NMR, ^{13}C NMR, IR, UV and MS. When unknown also be elementary analysis (**6b–c**).

General procedure for the preparation of enamino-thiones, **7a–d**. To 0.01 mol of **6**, in DME (20 ml) at room temp was added 0.005 mol of **2** with stirring. After the reaction was complete (tlc) (0.5–1.5 hr), the solvent was removed under reduced pressure. Tlhe residue was dissolved in CH_2Cl_2 and poured into 50 ml 1% NaOH. The aqueous phase was separated and then extracted several times with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with H_2O and dried ($MgSO_4$), followed by removal of CH_2Cl_2 under reduced pressure. The enamino-thiones, **7**, were purified by silica-gel column chromatography. An ether-light petroleum mixture was used for elution. The products were characterized by ^1H NMR, ^{13}C NMR, IR, UV, MS and elementary analyses.

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REFERENCES

[1]J. V. Greenhill, *Chem. Soc. Rev.* **6**, 277 (1977).
[2]J. B. Rasmussen, R. Shabana and S.-O. Lawesson, *Tetrahedron* **37**, 197 (1981).
[3]C. Kashima, M. Yamamoto and N. Sugiyama, *J. Chem. Soc.* (C) 111 (1970); and refs therein.
[4]G. H. Alt and A. J. Speziale, *J. Org. Chem.* **29**, 798 (1964).
[5]P. W. Hickmott and G. Sheppard, *J. Chem. Soc.* (C) 2112 (1971).
[6]L. Kozerski, *Tetrahedron* **32**, 1299 (1976).
[7]A. I. Meyers, A. H. Reine and R. Gault, *J. Org. Chem.* **34**, 698 (1969).
[8]G. H. Alt and A. J. Speziale, *Ibid.* **29**, 794 (1964).
[9]N. J. Leonard and J. A. Adamcik, *J. Am. Chem. Soc.* **81**, 595 (1959).
[10]D. L. Ostercamp, *J. Org. Chem.* **30**, 1169 (1965).
[11]L. Nilsson, *Acta Chem. Scand.* **B33**, 710 (1979).
[12]R. Helmers, *Tetrahedron Letters* 1905 (1966).
[13]R. Shabana, J. B. Rasmussen and S.-O. Lawesson, *Bull Soc. Chim. Belg.* **90**, 75 (1981).
[14]K. Clausen and S.-O. Lawesson, *Bull. Soc. Chim. Belg.* **88**, 305 (1979).
[15]K. Clausen and S.-O. Lawesson, *Nouv. J. Chim.* **4**, 43 (1980).
[16]R. Shabana, J. B. Rasmussen, S. O. Olesen an S.-O. Lawesson, *Tetrahedron* **36**, 3047 (1980).
[17]A. Combes and C. Combes, *Bull. Soc. Chim. Fr.* **7**(3), 778 (1892).
[18]W. Schroth and G. W. Fisher, *Chem. Ber.* **102**, 575 (1969).
[19]G. O. Dudek and G. P. Volpp, *J. Am. Chem. Soc.* **85**, 2697 (1963).
[20]H.-G. Henning, M. Bandlow, Y. Jedrych and R. Berlinghoff, *J. prakt. Chem.* **320**, 945 (1978).
[21]J. Dabrowski and K. Kamienska-Trela, *J. Am. Chem. Soc.* **98**, 2826 (1976), and refs therein.
[22]J. A. Pople and M. Gordon, *Ibid.* **89**, 4253 (1967).