Synthesis of Heterocyclic Ketene N,O-Acetals and Their Reactions with α,β-Unsaturated Esters

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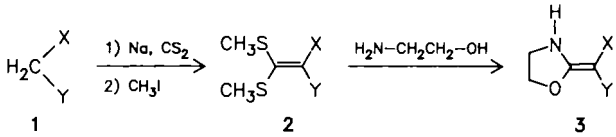
Ketene dithioacetals 2 react with 2-aminoethanol or 1-amino-2-propanol to afford the corresponding substituted 2-methyleneoxazolidines 3 and 4. In some cases, 3 and 4 react with α,β-unsaturated esters to give 5*H*-oxazolo[3,2-*a*]pyridine derivatives 5 by an electrophilic addition and cyclocondensation sequence.

Synthese von heterocyclischen Keten-N,O-acetalen und ihre Reaktionen mit α,β-ungesättigten Estern

Ketendithioacetale **2** reagieren mit 2-Aminoethanol oder 1-Amino-2-propanol zu den entsprechenden substituierten 2-Methylenoxazolidinen **3** und **4**. Diese ergeben in einigen Fällen mit α,β-ungesättigten Estern 5*H*-Oxazolo[3,2-*a*]pyridin-Derivate über eine Additions- und Cyclokondensations-Sequenz.

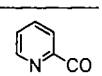
Heterocyclic ketene aminals are versatile starting materials for the synthesis of a wide variety of fused heterocycles. Although their synthesis and reactions have received much attention[1-18], the synthesis and reactions of their corresponding sulfur and oxygen analogues – heterocyclic ketene N,S- and N,O-acetals – have only been studied in a few cases[3-7,19-22]. Recently, the synthesis and some reactions of heterocyclic ketene N,S-acetals have been reported by us[23]. Here, we describe the synthesis of some new heterocyclic ketene N,O-acetals and their reactions with α,β-unsaturated esters. Using the latter reaction, several 5*H*-oxazolo[3,2-*a*]pyridine derivatives can be synthesized.

Heterocyclic ketene N,O-acetals **3a–i** are synthesized by the reaction of ketene dithioacetals **2a–i** with 2-aminoethanol. The starting materials **2** are prepared by the reaction of active methylene compounds **1** with sodium hydride and carbon disulfide, followed by methyl iodide in a one-pot reaction. When both X and Y are electron-withdrawing groups, **3a–c** may be obtained by reaction of **2a–c** with 2-aminoethanol in boiling absolute ethanol. In the case of **2d–i**, where only one electron-withdrawing group, an aroyl group, is present, **3d–i** can not be obtained by this method, not even in boiling toluene or *N,N*-dimethylformamide. This differs from the reaction of **2** with 1,2-ethanediamine or 2-aminothioethanol; in these cases heterocyclic ketene aminals[24] or ketene N,S-acetals[23] are easily formed. **3d–i** can be obtained from **2d–i** with 2-aminoethanol in the presence of metallic sodium in order to increase the nucleophilicity of the 2-aminoethanol.

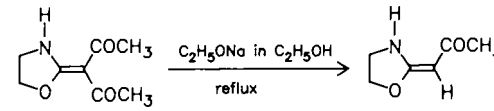


1 2 3

1-4	a	b	c	d	e	f
X	CH_3CO	CH_3CO	CH_3CO_2	C_6H_5CO	4-$CH_3C_6H_4CO$	4-$CH_3C_6H_4CO$
Y	CH_3CO	CH_3CO_2	CN	H	H	H

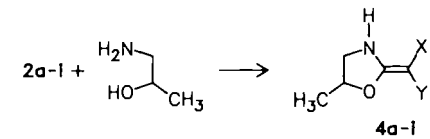
1-4	g	h	i
X	4-ClC_6H_4CO		
Y	H	H	H

Heterocyclic ketene N,O-acetal **3j** is synthesized by the reaction of **3a** with sodium ethoxide, eliminating one acetyl group.



3a 3j

Heterocyclic ketene N,O-acetals **4** are similarly obtained from the reaction of **2** with 1-amino-2-propanol.



4a-l

The constitutions of the products **3** and **4** were confirmed by the elemental analyses and mass spectra. Only one set of signals was observed in the product ^{1}H- and ^{13}C-NMR spectra, indicating that these compounds are not a mixture. The absence of methine or methylene proton signals and the presence of a nitrogen proton signal in the ^{1}H-NMR spectra of the products exclude the structure of tautomer **A**. The presence of the ketonic or ester carbonyl carbon signal in the ^{13}C-NMR spectra of the products also excludes the structure of tautomer **B**. The stereochemical problem of distinguishing *E* or *Z* isomers of **3** and **4** is solved by the intra-

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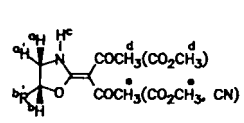
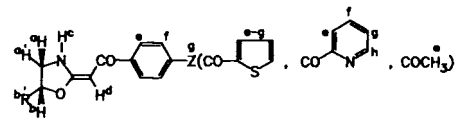
Table 1. ^{1}H-NMR data (δ values, J in Hz) of **3** and **4** in $CDCl_3$ with TMS as internal standard



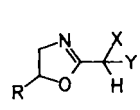
3, 4, a–c



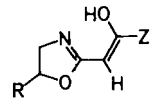
3, 4, d–j

	H^a	$H^{a'}$	H^b	$H^{b'}$	H^c	H^d	H^e	H^f	H^g	H^h
3a		3.81	4.62 (J = 8.0)		11.22 (s)		2.36 (s)			
3b		3.76	4.58 (J = 8.2)		11.05 (s)	2.36 (s)	3.69 (s)			
3c		3.82	4.64 (J = 8.0)		8.51 (s)	3.68 (s)				
3d		3.58	4.29 (J = 8.0)		9.70 (s)	5.58 (s)		7.33–7.90 (m)		
3e		3.71	4.40 (J = 8.0)		9.32 (s)	5.56 (s)	7.71 (d)	7.13 (d)	2.33 (s)	
3f		3.68	4.37 (J = 8.0)		9.15 (s)	5.47 (s)	7.70 (d)	6.77 (d)	3.74 (s)	
3g		3.77	4.47 (J = 8.0)		8.72 (s)	5.49 (s)	7.74 (d)	7.30 (d)		
3h		3.73	4.44 (J = 8.3)		8.99 (s)	5.46 (s)		6.91–7.49 (m)		
3i		3.70	4.46 (J = 8.0)		9.15 (s)	6.03 (s)	7.69–7.93 (m)		7.25–7.47 (m)	8.49–8.56 (m)
3j		3.70	4.41 (J = 8.0)			4.92 (s)	2.02 (s)			
4a	3.90	3.38	4.99 (sext)	1.54 (d)	11.10 (s)	2.36 (s)				
	$J_{aa'}$ = 10.0, J_{ab} = 8.0, $J_{a'b}$ = 8.0									
4c	3.97	3.43	5.08 (sext	1.52 (d)	8.55 (s)	3.73 (s)				
	$J_{aa'}$ = 9.6, J_{ab} = 8.4, $J_{a'b}$ = 7.6									
4d	3.80	3.25	4.69 (sext)	1.40 (d)	9.65 (s)	5.38 (s)		7.20–7.82 (m)		
	$J_{aa'}$ = 9.6, J_{ab} = 8.0, $J_{a'b}$ = 7.2									
4e	3.81	3.28	4.76 (sext)	1.44 (d)	9.19 (s)	5.48 (s)	7.65 (d)	7.08 (d)	2.32 (d)	
	$J_{aa'}$ = 9.0, J_{ab} = 8.4, $J_{a'b}$ = 7.8									
4f	3.81	3.27	4.76 (sext)	1.45 (d)	9.35 (s)	5.47 (s)	7.74 (d)	6.80 (d)	3.76 (s)	
	$J_{aa'}$ = 9.0, J_{ab} = 7.8, $J_{a'b}$ = 7.8									
4g	3.80	3.30	4.81 (sext)	1.46 (d)	9.40 (s)	5.46 (s)	7.72 (d)	7.27 (d)		
	$J_{aa'}$ = 9.0, J_{ab} = 8.2, $J_{a'b}$ = 8.0									
4h	3.82	3.29	4.78 (sext)	1.43 (d)	9.35 (s)	5.45 (s)		6.94–7.52 (m)		
	$J_{aa'}$ = 9.0, J_{ab} = 8.0, $J_{a'b}$ = 7.6									
4i	3.83	3.29	4.75 (sext)	1.43 (d)	9.96 (s)	6.14 (s)	7.48–8.03 (m)		6.93–7.72 (m)	8.43–8.51 (m)
	$J_{aa'}$ = 9.2, J_{ab} = 8.0, $J_{a'b}$ = 7.2									

molecular hydrogen bond formation. In general, compounds with intramolecular hydrogen bonds are more stable. Intramolecular hydrogen bond formation in **3** and **4** is proven by the downfield shift (δ = 8.51–11.22, see Table 1) of the NH signal in the ^{1}H-NMR spectra. This suggests that **3c–j** and **4c–i** might be in *E* configuration and **3b** in *Z* configuration. The ^{1}H- and ^{13}C-NMR data of **3** and **4** are listed in Tables 1 and 2, respectively.

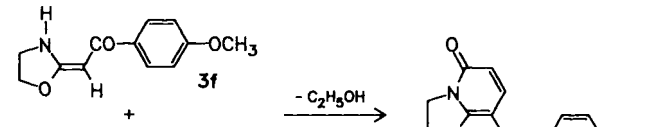


A



B

From the spectral data listed in Tables 1 and 2 and in the experimental part, the bathochromic shift of the carbonyl and double bond absorption in the IR spectra and the upfield shift of the carbonyl carbon signal in the ^{13}C-NMR spectra are due to conjugation of the carbonyl group with the double bond and the nitrogen and oxygen atoms. Ketene N,O-acetals **3** show the characteristic A_2B_2 pattern in the ^{1}H-NMR spectra due to the $-NH-CH_2-CH_2-O-$ structural moiety, while in ketene N,O-acetals **4**, $H^{aa'}$ and H^b form an ABX system, and H^b is further split by the vicinal protons of the methyl group.



3f

5a

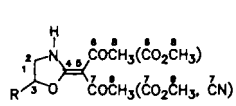
3, 4

5b–h

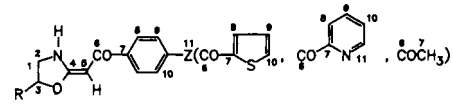
5	b	c	d	e	f
R	H	H	H	H	CH_3
X	C_6H_5CO	4-$CH_3C_6H_4CO$	4-ClC_6H_4CO		4-$CH_3C_6H_4CO$

5	g	h
R	CH_3	CH_3
X	4-$CH_3OC_6H_4CO$	4-ClC_6H_4CO

Table 2. ^{13}C-NMR data (δ values) of **3** and **4** in $CDCl_3$ with TMS as internal standard



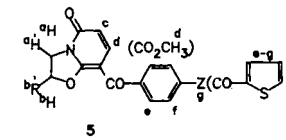
3, 4, a–c



3, 4, d–j

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11
3a		42.2	67.9	171.5	103.6	196.3		31.2			
3b		42.3	68.2	171.1	88.2	196.0	167.4	29.7	50.5		
3d		43.0	67.3	170.6	74.0	187.4	139.9	128.1	126.7	130.5	
3e		43.0	67.3	170.6	73.8	187.4	137.2	128.8	126.8	140.8	21.4
3f		43.0	67.2	170.4	73.4	186.7	132.5	128.6	113.2	161.6	55.2
3g		43.0	67.5	170.8	74.0	186.1	136.6	129.2	128.3	138.3	
3h		42.9	67.3	169.8	73.3	180.1	146.9	129.1	126.7	127.4	
3j		42.9	67.2	169.4	101.4	194.2	28.7				
4a	19.5	48.3	77.4	170.8	98.9	196.2		31.1			
4d	19.4	49.1	76.2	169.8	73.8	187.0	139.8	127.7	126.4	130.1	
4f	19.9	49.5	76.4	170.1	73.3	186.7	132.5	128.7	113.3	161.6	55.2
4h	19.4	49.4	76.4	169.6	73.4	180.8	147.2	128.8	126.7	127.2	

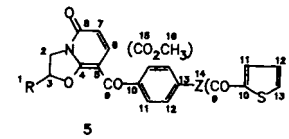
Table 3. ^{1}H-NMR data (δ values, J in Hz) of **5** in $CDCl_3$ with TMS as internal standard



5

	H^a	$H^{a'}$	H^b	$H^{b'}$	H^c	H^d	H^e	H^f	H^g
5a	4.23		4.70 (J = 9.0)		6.03 (d)	7.61 (d)	7.57 (d)	6.82 (d)	3.79 (s)
5b	4.25		4.66 (J = 8.5)		6.41 (s)	3.52 (s)		7.18–7.76 (m)	
5c	4.27		4.57 (J = 8.0)		6.47 (s)	3.53 (s)	7.60 (d)	7.14 (d)	2.37 (s)
5d	4.28		4.68 (J = 8.0)		6.47 (s)	3.59 (s)	7.65 (d)	7.32 (d)	
5e	4.29		4.74 (J = 9.0)		6.47 (s)	3.59 (s)		6.97–7.67 (m)	
5f	4.31	3.82	5.13 (sext)	1.50 (d)	6.47 (s)	3.58 (s)	7.68 (d)	7.22 (d)	2.39 (s)
	$J_{aa'}$ = 12.0, J_{ab} = 8.2, $J_{a'b}$ = 8.0								
5g	4.31	3.73	5.03 (sext)	1.48 (d)	6.36 (s)	3.54 (s)	7.61 (d)	6.77 (d)	3.78 (s)
	$J_{aa'}$ = 11.6, J_{ab} = 8.0, $J_{a'b}$ = 7.8								
5h	4.38	3.80	5.09 (sext)	1.49 (d)	6.43 (s)	3.64 (s)	7.70 (d)	7.38 (d)	
	$J_{aa'}$ = 12.0, J_{ab} = 8.0, $J_{a'b}$ = 7.6								

Table 4. ^{13}C-NMR data (δ values) of **5** in $CDCl_3$ with TMS as internal standard



5

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	C-16
5a		43.4	69.2	158.6	99.1	143.2	110.4	162.9	189.2	131.0	131.3	113.4	160.6	55.4		
5b		43.4	69.3	157.1	97.0	145.5	112.6	159.1	189.9	138.0	128.7	128.3	132.8		165.9	52.6
5e		43.8	69.5	156.8	97.1	144.9	113.1	159.3	181.8	146.9	134.0	127.9	133.2		165.6	52.8
5f	20.0	49.7	79.1	156.6	97.5	145.9	112.3	159.4	189.5	135.6	129.1	129.0	143.7	21.6	165.9	52.6
5h	20.0	49.5	79.3	156.9	103.6	145.6	112.6	159.3	188.6	136.4	130.3	128.5	139.1		165.9	52.7

Among the ^{13}C-NMR spectral data, the upfield shift of C-5 is noteworthy (δ = 73.3–103.6); it indicates that the electron density is higher at this carbon and nucleophilic attack of this carbon on an electron-deficient group may be expected, as in ketene aminals and ketene N,S-acetals. In the reaction with α,β-unsaturated esters, aroyl-substituted heterocyclic ketene aminals and ketene N,S-acetals react smoothly with propiolic esters, acetylenedicarboxylic esters,

and even with acrylic esters, to form fused biheterocycles by an electrophilic addition and cyclocondensation sequence[12-17,23]. In the reaction of aroyl-substituted heterocyclic ketene N,O-acetals with ethyl propiolate, only the more reactive 4-methoxybenzoyl-substituted ketene N,O-acetal **3f** can react with ethyl propiolate to give the 5*H*-oxazolo[3,2-*a*]pyridine derivative **5a** in satisfactory yield, and other aroyl-substituted ketene N,O-acetals react sluggishly with this reagent. However, aroyl-substituted ketene N,O-acetals react smoothly with the more active electrophile dimethyl acetylenedicarboxylate in refluxing ethanol to give the oxazolidine ring-fused biheterocycles in good to excellent yields.

The structure of the products **5** was established from the spectral data and elemental analyses. The ^{1}H- and ^{13}C-NMR data of **5** are listed in Tables 3 and 4, respectively.

Altogether, this reaction provids a new and convenient method for the synthesis of biheterocycles containing an α-pyridone fused with an oxazolidine ring.

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Experimental

Melting points are not corrected. – IR spectra: Perkin-Elmer 782. – UV spectra: Hitachi 340. – ^{1}H-NMR spectra: Varian EM-360 L. – ^{13}C-NMR spectra: Jeol FX-100 and Varian XL-200. – MS: AEI MS-50. – Elemental analyses: Analytical Laboratory of the Institute.

2-(Diacetylmethylene)oxazolidine (**3a**): A mixture of 8.16 g (40 mmol) of **2a** and 3.05 g (50 mmol) of 2-aminoethanol in 30 ml of absolute ethanol was heated for 10 h at reflux, until no odor of methanethiol was evolved. After partial removal of the solvent, 2.90 g (43%) of **3a** crystallized, m.p. 130–132°C. – IR (KBr): $\tilde{\nu}$ = 3210 cm^{-1} (NH), 1615 (C=O), 1587, 1550. – UV (ethanol): λ_{max} (lg ε) = 270 nm (4.10). – MS: *m/z* = 169 [M$^+$].

$C_8H_{11}NO_3$ (169.2) Calcd. C 56.79 H 6.56 N 8.28
Found C 57.05 H 6.58 N 7.93

(Z)-2-[Acetoxy(acetyl)methylene]oxazolidine (**3b**): As described for **3a**, 3.00 g (54%) of **3b**, m.p. 132–134°C, was obtained from 6.60 g (30 mmol) of **2b** and 2.24 g (40 mmol) of 2-aminoethanol in 30 ml of ethanol. – IR (KBr): $\tilde{\nu}$ = 3205 cm^{-1} (NH), 1670 (ester C=O), 1610 (C=O), 1555. – UV (ethanol): λ_{max} (lg ε) = 276 nm (4.10), 240 (3.99). – MS: *m/z* = 185 [M$^+$].

$C_8H_{11}NO_4$ (185.2) Calcd. C 51.89 H 5.99 N 7.56
Found C 51.91 H 5.93 N 7.38

(E)-2-[Acetyl(cyano)methylene]oxazolidine (**3c**): As described for **3a**, 0.46 g (55%) of **3c**, m.p. 149–151°C, was obtained from 1.02 g (5 mmol) of **2c** and 0.37 g (6 mmol) of 2-aminoethanol in 25 ml of ethanol. – IR (KBr): $\tilde{\nu}$ = 3330 cm^{-1} (NH), 2220, 2202 (CN), 1675 (ester C=O), 1615, 1595. – UV (ethanol): λ_{max} (lg ε) = 260 nm (4.17). – MS: *m/z* = 168 [M$^+$].

$C_7H_8N_2O_3$ (168.2) Calcd. C 50.00 H 4.80 N 16.66
Found C 49.48 H 4.86 N 16.85

(E)-2-(Benzoylmethylene)oxazolidine (**3d**): 0.14 g (6 mmol) of sodium was added to a solution of 0.37 g (6 mmol) of 2-aminoethanol in 3 ml of dry tetrahydrofuran with stirring. When the sodium had reacted, a solution of 1.12 g (5 mmol) of **2d** in 10 ml of dry tetrahydrofuran was added, and the mixture was heated for 10 h at reflux, until no odor of methanethiol was evolved. The whole mixture was poured into 20 ml of water and extracted with chloroform (10 ml × 3). The extract was dried with anhydrous sodium sulfate, and after removal of the solvent the crude product was recrystallized from methanol; yield 0.60 g (63%), m.p. 104–106°C. – IR (KBr): $\tilde{\nu}$ = 3260 cm^{-1} (NH), 1620 (C=O), 1575, 1529, 1500. – UV (ethanol): λ_{max} (lg ε) = 322 nm (4.23), 242 (3.84). – MS: *m/z* = 189 [M$^+$].

$C_{11}H_{11}NO_2$ (189.2) Calcd. C 69.82 H 5.86 N 7.40
Found C 69.67 H 5.82 N 7.34

(E)-2-[(4-Methylbenzoyl)methylene]oxazolidine (**3e**): As described for **3d**, 1.20 g (59%) of **3e**, m.p. 177–179°C, was obtained from 2.38 g (10 mmol) of **2e**, 0.74 g (12 mmol) of 2-aminoethanol, and 0.28 g (12 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3280 cm^{-1} (NH), 1618 (C=O), 1598, 1570, 1522, 1508. – UV (ethanol): λ_{max} (lg ε) = 320 nm (4.08), 256 (3.70). – MS: *m/z* = 203 [M$^+$].

$C_{12}H_{13}NO_2$ (203.2) Calcd. C 70.92 H 6.45 N 6.89
Found C 70.92 H 6.40 N 6.67

(E)-2-[(4-Methoxybenzoyl)methylene]oxazolidine (**3f**): Like **3d**, 0.66 g (60%) of **3f**, m.p. 140–142°C, was obtained from 1.27 g (5 mmol) of **2f**, 0.37 g (6 mmol) of 2-aminoethanol, and 0.14 g (6 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3270 cm^{-1} (NH), 1620 (C=O), 1595, 1580, 1515. – UV (ethanol): λ_{max} (lg ε) = 322 nm (4.32), 268 (3.76). – MS: *m/z* = 219 [M$^+$].

$C_{12}H_{13}NO_3$ (219.2) Calcd. C 65.74 H 5.98 N 6.39
Found C 65.78 H 6.05 N 6.22

(E)-2-[(4-Chlorobenzoyl)methylene]oxazolidine (**3g**): As for **3d**, 1.34 g (60%) of **3g**, m.p. 197–200°C, was obtained from 2.59 g (10 mmol) of **2g**, 1.22 g (20 mmol) of 2-aminoethanol, and 0.28 g (12 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3270 cm^{-1} (NH), 1621 (C=O), 1570, 1521. – UV (ethanol): λ_{max} (lg ε) = 324 nm (4.32), 228 (4.11). – MS: *m/z* = 223 [M$^+$].

$C_{11}H_{10}ClNO_2$ (223.7) Calcd. C 59.07 H 4.51 N 6.26
Found C 59.09 H 4.50 N 6.29

(E)-2-[(2-Thiophenecarbonyl)methylene]oxazolidine (**3h**): Like **3d**, 0.58 g (59%) of **3h**, m.p. 117–120°C, was obtained from 1.15 g (5 mmol) of **2h**, 0.74 g (12 mmol) of 2-aminoethanol, and 0.14 g (6 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3260 cm^{-1} (NH), 1615 (C=O), 1535, 1515. – UV (ethanol): λ_{max} (lg ε) = 336 nm (4.22), 262 (3.64), 240 (sh). – MS: *m/z* = 195 [M$^+$].

$C_9H_9NO_2S$ (195.2) Calcd. C 55.36 H 4.65 N 7.17
Found C 55.10 H 4.52 N 7.14

(E)-2-(Picolinoylmethylene)oxazolidine (**3i**): As described for **3d**, 0.47 g (49%) of **3i**, m.p. 162–165°C, was obtained from 1.13 g (5 mmol) of **2i**, 0.74 g (12 mmol) of 2-aminoethanol, and 0.14 g (6 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3290 cm^{-1} (NH), 1620 (C=O), 1580, 1560, 1525. – UV (ethanol): λ_{max} (lg ε) = 334 nm (4.21), 236 (4.03). – MS: *m/z* = 190 [M$^+$].

$C_{10}H_{10}N_2O_2$ (190.2) Calcd. C 63.14 H 5.30 N 14.73
Found C 62.95 H 5.44 N 14.60

(E)-2-(Acetylmethylene)oxazolidine (**3j**): 0.85 g (5 mmol) of **3a** was heated at reflux in a sodium ethoxide solution (0.12 g of sodium in 10 ml of absolute ethanol) for 10 h. After removal of ethanol, the residue was dissolved in 10 ml of water, and the solution was neutralized with dilute hydrochloric acid and extracted with chloroform (3 × 10 ml). The extract was dried with anhydrous sodium sulfate; after removal of the solvent 0.25 g (39%) of **3j**, m.p. 106–108°C, was obtained. – IR (KBr): $\tilde{\nu}$ = 3250 cm^{-1} (NH), 1630

(C=O), 1550, 1500. – UV (ethanol): λ_{max} (lg ε) = 228 nm (4.22). – MS: *m/z* = 127 [M^+].

$C_6H_9NO_2$ (127.1) Calcd. C 56.68 H 7.14 N 11.02
Found C 56.35 H 7.33 N 10.82

2-(Diacetylmethylene)-5-methyloxazolidine (**4a**): As described for **3a**, 2.60 g (47%) of **4a**, m.p. 118–120°C, was obtained from 6.12 g (30 mmol) of **2a** and 2.25 g (30 mmol) of 1-amino-2-propanol in 30 ml of ethanol. – IR (KBr): $\tilde{\nu}$ = 3239 cm^{-1} (NH), 1600 (C=O), 1550. – UV (ethanol): λ_{max} (lg ε) = 270 nm (4.34). – MS: *m/z* = 183 [M^+].

$C_9H_{13}NO_3$ (183.2) Calcd. C 59.00 H 7.15 N 7.56
Found C 59.16 H 7.07 N 7.68

(E)-2-[Acetyl(cyano)methylene]-5-methyloxazolidine (**4c**): As for **3a**, 0.74 g (81%) of **4c**, m.p. 152–154°C, was obtained from 1.02 g (5 mmol) of **2c** and 0.38 g (5 mmol) of 1-amino-2-propanol. – IR (KBr): $\tilde{\nu}$ = 3330 cm^{-1} (NH), 2205 (CN), 1665 (ester C=O), 1605. – UV (ethanol): λ_{max} (lg ε) = 254 nm (4.42). – MS: *m/z* = 182 [M^+].

$C_8H_{10}N_2O_3$ (182.2) Calcd. C 52.74 H 5.53 N 15.38
Found C 52.72 H 5.41 N 15.25

(E)-2-(Benzoylmethylene)-5-methyloxazolidine (**4d**): As for **3d**, 0.63 g (31%) of **4d**, m.p. 68–70°C, was obtained from 2.24 g (10 mmol) of **2d**, 1.80 g (24 mmol) of 1-amino-2-propanol, and 0.28 g (12 mmol) of sodium in tetrahydrofuran. – IR (KBr): $\tilde{\nu}$ = 3240 cm^{-1} (NH), 1615 (C=O), 1590, 1575, 1526, 1500. – UV (ethanol): λ_{max} (lg ε) = 320 nm (4.24), 240 (4.01). – MS: *m/z* = 203 [M^+].

$C_{12}H_{13}NO_2$ (203.2) Calcd. C 70.92 H 6.45 N 6.89
Found C 70.36 H 6.40 N 6.93

(E)-5-Methyl-2-[(4-methylbenzoyl)methylene]oxazolidine (**4e**): As described for **3d**, 0.24 g (22%) of **4e**, m.p. 108–110°C, was obtained from 1.19 g (5 mmol) of **2e**, 0.45 g (6 mmol) of 1-amino-2-propanol, and 0.14 g (6 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3260 cm^{-1} (NH), 1615 (C=O), 1570, 1539, 1505. – UV (ethanol): λ_{max} (lg ε) = 322 nm (4.30), 250 (3.84). – MS: *m/z* = 217 [M^+].

$C_{13}H_{15}NO_2$ (217.3) Calcd. C 71.86 H 6.96 N 6.45
Found C 71.57 H 6.78 N 6.25

(E)-2-[(4-Methoxybenzoyl)methylene]-5-methyloxazolidine (**4f**): Like **3d**, 0.50 g (43%) of **4f**, m.p. 118–121°C, was obtained from 1.27 g (5 mmol) of **2f**, 0.90 g (12 mmol) of 1-amino-2-propanol, and 0.14 g (6 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3250 cm^{-1} (NH), 1615 (C=O), 1590, 1575, 1515. – UV (ethanol): λ_{max} (lg ε) = 322 nm (4.34), 270 (3.98). – MS: *m/z* = 233 [M^+].

$C_{13}H_{15}NO_3$ (233.3) Calcd. C 66.93 H 6.48 N 6.00
Found C 66.82 H 6.48 N 6.19

(E)-2-[(4-Chlorobenzoyl)methylene]-5-methyloxazolidine (**4g**): Like **3d**, 0.53 g (45%) of **4g**, m.p. 126–128°C, was obtained from 1.30 g (5 mmol) of **2g**, 0.90 g (12 mmol) of 1-amino-2-propanol, and 0.14 g (6 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3290 cm^{-1} (NH), 1620 (C=O), 1575, 1530, 1510. – UV (ethanol): λ_{max} (lg ε) = 326 nm (4.28), 248 (4.06). – MS: *m/z* = 237 [M^+].

$C_{12}H_{12}ClNO_2$ (237.7) Calcd. C 60.64 H 5.09 N 5.89
Found C 60.46 H 5.14 N 5.89

(E)-5-Methyl-2-[(2-thienylcarbonyl)methylene]oxazolidine (**4h**): As described for **3d**, 0.52 g (50%) of **4h**, m.p. 115–117°C, was obtained from 1.15 g (5 mmol) of **2h**, 0.90 g (12 mmol) of 1-amino-2-propanol, and 0.14 g (6 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3275 cm^{-1} (NH), 1620 (C=O), 1540, 1505. – UV (ethanol): λ_{max} (lg ε) = 335 nm (4.28), 262 (3.74). – MS: *m/z* = 209 [M^+].

$C_{10}H_{11}NO_2S$ (209.3) Calcd. C 57.39 H 5.30 N 6.69
Found C 57.19 H 5.35 N 6.54

(E)-5-Methyl-2-(picolinoylmethylene)oxazolidine (**4i**): As described for **3d**, 0.36 g (35%) of **4i**, m.p. 106–108°C, was obtained from 1.13 g (5 mmol) of **2i**, 0.90 g (12 mmol) of 1-amino-2-propanol, and 0.14 g (6 mmol) of sodium. – IR (KBr): $\tilde{\nu}$ = 3280 cm^{-1} (NH), 1618 (C=O), 1580, 1560, 1530. – UV (ethanol): λ_{max} (lg ε) = 336 nm (4.31), 240 (3.80). – MS: *m/z* = 204 [M^+].

$C_{11}H_{12}N_2O_2$ (204.2) Calcd. C 64.69 H 5.92 N 13.72
Found C 64.64 H 5.74 N 13.55

2,3-Dihydro-8-(4-methoxybenzoyl)-5H-oxazolo[3,2-a]pyridin-5-one (**5a**): A mixture of 153 mg (0.7 mmol) of **3f** and 69 mg (0.7 mmol) of ethyl propiolate in 5 ml of ethanol was heated for 2 d at reflux. After partial removal of ethanol, **5a** crystallized; yield 100 mg (53%), m.p. 184–186°C. – IR (KBr): $\tilde{\nu}$ = 1680 (amide C=O), 1650 (C=O), 1605, 1520. – UV (ethanol): λ_{max} (lg ε) = 320 nm (4.38), 290 (sh). – MS: *m/z* = 271 [M^+].

$C_{15}H_{13}NO_4$ (271.3) Calcd. C 66.41 H 4.83 N 5.16
Found C 66.26 H 4.78 N 5.01

Methyl 2,3-Dihydro-8-benzoyl-5-oxo-5H-oxazolo[3,2-a]pyridin-7-carboxylate (**5b**): A mixture of 132 mg (0.7 mmol) of **3d** and 100 mg (0.7 mmol) of dimethyl acetylenedicarboxylate in 5 ml of methanol was heated for 2 d at reflux. After partial removal of methanol, **5b** crystallized; yield 180 mg (86%), m.p. 148–150°C. – IR (KBr): $\tilde{\nu}$ = 1742 cm^{-1} (ester C=O), 1660 (amide C=O), 1630 (C=O), 1615, 1525. – UV (ethanol): λ_{max} (lg ε) = 328 nm (4.04), 300 (sh), 258 (4.08). – MS: *m/z* = 299 [M^+].

$C_{16}H_{13}NO_5$ (299.3) Calcd. C 64.21 H 4.38 N 4.68
Found C 64.20 H 4.20 N 4.64

Methyl 2,3-Dihydro-8-(4-methylbenzoyl)-5-oxo-5H-oxazolo[3,2-a]pyridine-7-carboxylate (**5c**): As described for **5b**, 130 mg (83%) of **5c**, m.p. 184–186°C, was obtained from 102 mg (0.5 mmol) of **3e** and 71 mg (0.5 mmol) of dimethyl acetylenedicarboxylate. – IR (KBr): $\tilde{\nu}$ = 1718 cm^{-1} (ester C=O), 1660 (amide C=O), 1630 (C=O), 1595, 1515. – UV (ethanol): λ_{max} (lg ε) = 326 nm (4.07), 270 (4.12). – MS: *m/z* = 313 [M^+].

$C_{17}H_{15}NO_5$ (313.3) Calcd. C 65.17 H 4.83 N 4.47
Found C 65.05 H 4.89 N 4.33

Methyl 8-(4-Chlorobenzoyl)-2,3-dihydro-5-oxo-5H-oxazolo[3,2-a]pyridine-7-carboxylate (**5d**): As for **5b**, 100 mg (60%) of **5d**, m.p. 225–228°C, was obtained from 112 mg (0.5 mmol) of **3g** and 71 mg (0.5 mmol) of dimethyl acetylenedicarboxylate. – IR (KBr): $\tilde{\nu}$ = 1715 cm^{-1} (ester C=O), 1660 (amide C=O), 1630 (C=O), 1597, 1570, 1515. – UV (ethanol): λ_{max} (lg ε) = 328 nm (4.13), 266 (4.08). – MS: *m/z* = 333 [M^+].

$C_{16}H_{12}ClNO_5$ (333.7) Calcd. C 57.58 H 3.63 N 4.20
Found C 57.62 H 3.62 N 4.27

Methyl 2,3-Dihydro-5-oxo-8-(2-thiophenecarbonyl)-5H-oxazolo[3,2-a]pyridine-7-carboxylate (**5e**): Like **5b**, 100 mg (66%) of **5e**, m.p. 172–174°C, was obtained from 98 mg (0.5 mmol) of **3h** and 71 mg (0.5 mmol) of dimethyl acetylenedicarboxylate. – IR (KBr): $\tilde{\nu}$ = 1730 cm^{-1} (ester C=O), 1678 (amide C=O), 1600 (C=O), 1520. – UV (ethanol): λ_{max} (lg ε) = 330 nm (4.10), 274 (3.96), 232 (sh). – MS: *m/z* = 305 [M^+].

$C_{14}H_{11}NO_5S$ (305.3) Calcd. C 55.07 H 3.63 N 4.59
Found C 54.76 H 3.93 N 4.85

Methyl 2,3-Dihydro-2-methyl-8-(4-methylbenzoyl)-5-oxo-5H-oxazolo[3,2-a]pyridine-7-carboxylate (**5f**): As described for **5b**, 150 mg (92%) of **5f**, m.p. 153.5–155.5°C, was obtained from 109 mg (0.5 mmol) of **4e** and 71 mg (0.5 mmol) of dimethyl acetylenedicarboxylate. – IR (KBr): $\tilde{\nu}$ = 1727 cm^{-1} (ester C=O), 1668 (amide

C=O), 1637 (C=O), 1600, 1520. – UV (ethanol): λ_{max} (lg ε) = 328 nm (4.12), 270 (4.24). – MS: *m/z* = 327 [M^+].

$C_{18}H_{17}NO_5$ (327.3) Calcd. C 66.04 H 5.24 N 4.28
Found C 65.87 H 5.21 N 4.05

Methyl 2,3-Dihydro-8-(4-methoxybenzoyl)-2-methyl-5-oxo-5H-oxazolo[3,2-a]pyridine-7-carboxylate (**5g**): As for **5b**, 200 mg (83%) of **5g**, m.p. 169.5–170.5°C, was obtained from 163 mg (0.7 mmol) of **4f** and 100 mg (0.7 mmol) of dimethyl acetylenedicarboxylate. – IR (KBr): $\tilde{\nu}$ = 1735 cm^{-1} (ester C=O), 1668 (amide C=O), 1615 (C=O), 1597, 1528. – UV (ethanol): λ_{max} (lg ε) = 326 nm (4.14), 294 (4.21). – MS: *m/z* = 343 [M^+].

$C_{18}H_{17}NO_6$ (343.3) Calcd. C 62.97 H 4.99 N 4.08
Found C 62.87 H 4.96 N 4.01

Methyl 8-(4-Chlorobenzoyl)-2,3-dihydro-2-methyl-5-oxo-5H-oxazolo[3,2-a]pyridine-7-carboxylate (**5h**): As described for **5b**, 150 mg (86%) of **5h**, m.p. 193–196°C, was obtained from 119 mg (0.5 mmol) of **4g** and 71 mg (0.5 mmol) of dimethyl acetylenedicarboxylate. – IR (KBr): $\tilde{\nu}$ = 1730 cm^{-1} (ester C=O), 1680 (amide C=O), 1630 (C=O), 1600, 1580, 1522. – UV (ethanol): λ_{max} (lg ε) = 328 nm (4.24), 266 (4.20). – MS: *m/z* = 347 [M^+].

$C_{17}H_{14}ClNO_5$ (347.7) Calcd. C 58.71 H 4.06 N 4.03
Found C 58.83 H 3.95 N 3.86

CAS Registry Numbers

2a: 15908-50-6 / **2b**: 29866-43-1 / **2c**: 3490-92-4 / **2d**: 13636-88-9 / **2e**: 41467-27-0 / **2f**: 33868-76-7 / **2g**: 41467-26-9 / **2h**: 41467-29-2 / **2i**: 78570-34-0 / **3a**: 121373-62-4 / **3b**: 121373-63-5 / **3c**: 121373-64-6 / **3d**: 121373-65-7 / **3e**: 121373-66-8 / **3f**: 121373-67-9 / **3g**: 121373-68-0 / **3h**: 121373-69-1 / **3i**: 121373-70-4 / **3j**: 121373-71-5 / **4a**: 121373-72-6 / **4c**: 121373-73-7 / **4d**: 121373-74-8 / **4e**: 121373-75-9 / **4f**: 121373-76-0 / **4g**: 121373-77-1 / **4h**: 121373-78-2 / **4i**: 121373-79-3 / **5a**: 121373-80-6 / **5b**: 121373-81-7 / **5c**: 121373-82-8 / **5d**: 121373-83-9 / **5e**: 121373-84-0 / **5f**: 121373-85-1 / **5g**: 121373-86-2 / **5h**: 121373-87-3 / 2-aminoethanol: 141-43-5 / 1-amino-2-propanol: 78-96-6 / ethyl propiolate: 623-47-2 / dimethyl acetylenedicarboxylate: 762-42-5

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