Thienoquinolizidinones. Synthesis and Rearrangement into New Piperidino[1,2-*a*][1,3] or [1,4]diazepinones Fused to a Thiophene Ring

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A convenient route to thienoquinolizidinones is described starting from ethyl pipecolinate and suitable halogenomethylthiophenes or 3-chloromethylbenzothiophene. The Schmidt reaction and the Beckmann rearrangement of oximes of these ketones led to piperidino[1,2-*a*][1,3] or [1,4]diazepines fused to a thiophene ring.

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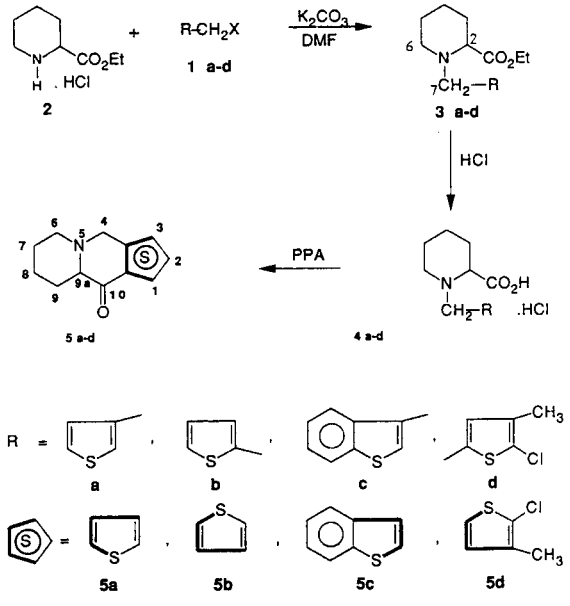
In connection with other works in this laboratory [1,2] we have recently developed a convenient and high yield sequence for the synthesis of thienoindolizidinediones [3] which were precursors of pyrrolidino[*a*]thieno[*e*][1,3]diazepinediones [4].

We showed that the Beckmann rearrangement of the thienoindolizidinones oximes yielded pyrrolidino[*a*]thieno[*e*]-[1,3]diazepines but also some thieno[*c*]naphthyridines, due to the fragility of the lactam ring in the starting compounds. Now, we wish to report the synthesis and reactivity of thieno[*b*]quinolizidinones.

Condensation of the suitable halogenomethylthiophenes **1a,b,d** or 3-chloromethylbenzo[*b*]thiophene **1c** with ethyl pipecolinate hydrochloride **2** in the presence of dimethylformamide and an equivalent of potassium carbonate gave the aminoesters **3a-d** in good yields (68-87%). These compounds could be distilled but analytical samples were obtained as their hydrochloride salts. Hydrolysis of **3a-d** to the corresponding carboxylic acids is achieved in hydrochloric acid solution in good yields (67-76%). These aminoacids were purified as their hydrochloride salts **4a-d**.

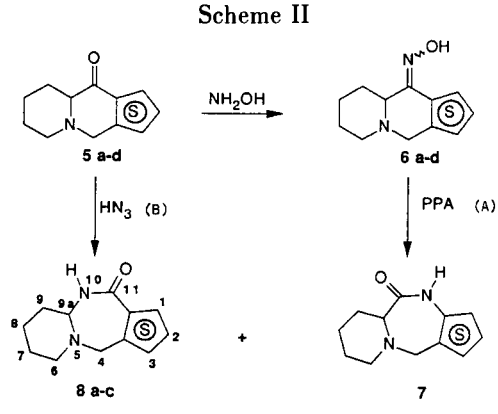
Scheme I



Cyclization to the thieno[*b*]quinolizidinones or [1]benzothieno[*b*]quinolizidinone was brought about through a cyclodehydration reaction. Thus, stirring the aminoacids **4a-d** in polyphosphoric acid under nitrogen atmosphere at 95-100° during seven hours, the reaction mixture turned from a colorless to a dark red viscous oil. A careful workup at 20° afforded the thieno[*b*]quinolizidinones **5a-d** in good yields (40-60%). These compounds are stable in contrast to naphtho[*b*]quinolizidinones [5] or phenantro[*b*]quinolizidinones [6].

The intermediates and final aminoketones have been characterized by ir, nmr spectra and microanalysis. Details are reported in the experimental, but there are some features of interest. Thus, in the ^{1}H nmr spectra we observe the non-equivalence of the methylene protons between the thiophene nucleus and the nitrogen atom in aminoesters **3a-d**, in aminoacids **4a-d** as well as in thieno-[*b*]quinolizidines **5a-d**. This non-equivalence of the H-4 axial (*ax*) and equatorial (*eq*) protons has been described before in thieno[*e*]indolizidines [3] and is in accordance with the observation made by Sollhuber [5] that the *ax* and

Scheme II



eq protons of a methylene group α to the nitrogen in quinolizidines have a marked difference in chemical shifts. This allows us to assign to compounds **5a-d** a *trans* quinolizidine configuration. The strong absorption band at 2700-2800 cm^{-1} observed in the ir spectra of these compounds is characteristic for the *trans* quinolizidine ring [7]. In compounds **3a-d** and **4a-d** we can also suggest a restricted rotation about the thiophene C-7 bond.

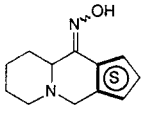
The ^{13}C chemical shifts assignment of ketones **5a-d** was made from analogy with that of thienoindolizidinones [4] as well as by comparing with chemical shifts of *trans* quinolizidine [9] and substituted thiophenes [10].

From ketones **5a-d**, it was interesting to study the Schmidt rearrangement and the Beckmann rearrangement of the corresponding oximes under similar conditions to those used with thieno[*e*]indolizidinone oximes previously reported [4]. Thus, ketones **5a-c** heated with hydroxylamine hydrochloride in the presence of sodium acetate afforded the corresponding oximes **6a-c** in good yields (65-71%). Under these conditions ketone **5d** did not react, however using pyridine as the solvent and base we isolated a small amount of oxime **6d** (26% yield). In all cases only one isomer was obtained.

The configuration of oximes **6a** and **6c** can be explained by an intramolecular hydrogen bond between the hydrogen of the oxime group and the sulfur atom of the thiophene ring. Analogous considerations had been proposed for thienoindolizidinone oximes [3]. It seems that the piperidine ring hinders the formation of the oxime **6b (B)** because with a pyrrolidine ring [3] a mixture of oximes was obtained: **A** = 60% and **B** = 40% respectively. This fact is accentuated with compound **6c**, since the indolizidinone oxime analogue is a mixture of isomers (**A** = 80% and **B** = 20%). Nevertheless, **6d (B)** is the single oxime isolated as with a pyrrolidine ring [3], the methyl group on the thiophene ring hinders the formation of oxime **6d** and so the yield is low (26%). In that case it is interesting to note that

Table 1

Configuration of the oxime group **6**, percentage of each and yield

Oxime	Configuration* (Yield %)	
		
6	**isomer A**	**isomer B**
N°	**A**	**B**
6a	100 (65)	0
6b	100 (65)	0
6c	100 (71)	0
6d	0	100 (26)

*Determined in the crude product by ^1H nmr spectroscopy (200 MHz).

Table 2

^1H nmr chemical shifts of esters **3 a-d** in deuteriochloroform, δ (ppm)

Compound N°	H-6ax	H-6eq	H-2	H-7	H-aromatique
3a	2.17dt	2.95dt	3.08dd	3.56d 3.77d	7.05dd (H-4') 7.09dd (H-2') 7.26dd (H-5')
3b	2.33dt	2.99dt	3.20dd	3.84d 3.96d	6.88dd (H-3') 6.94dd (H-4') 7.22dd (H-5')
3c	2.12dt	2.93dt	3.12 t	3.60d 4.00d	7.20 s (1H) 7.22-7.38 m (2H) 7.76d (1H), 8.12d (1H)
3d	2.34dt	2.97dt	3.22 t	3.67d 3.82d	6.55 s (1H)

Table 3

^1H nmr chemical shifts of acids **4 a-d** in DMSO-d_6, δ (ppm)

Compound N°	H-6ax	H-6eq	H-2	H-7	H-aromatique
4a	2.90-3.18m	3.20-3.58m	3.86 t	4.35d 4.46d	7.32dd (1H) 7.68dd (1H) 7.77dd (1H)
4b	2.95-3.20m	3.30-3.55m	3.87 t	4.58d 4.68d	7.13dd (1H) 7.36dd (1H) 7.77dd (1H)
4c	3.05-3.28m	3.30-3.50m	4.24dd	4.63d 4.75d	7.40-7.56m (2H) 8.08 d (1H) 8.14d (1H), 8.17s (1H)
4d	2.98-3.25m	3.28-3.58m	3.98dd	4.49d 4.60d	7.16 s (1H)

Table 4

^1H nmr chemical shifts of ketones **5 a-d** and oximes **6 a-c** in DMSO-d_6

Compound N°	CH_2	H-9eq	H-6ax H-6eq	H-9a	H-4ax H-4eq	H-aromatique
5a	1.20-1.90m	2.10-2.20m	2.32m 2.96dd	2.85dd	3.50dd 4.01d	7.15d 8.05d
5b	1.22-1.90m	2.06-2.25m	2.34 m 2.96dd	2.83dd	3.69dd 4.16d	7.29d 7.46d
5c	1.25-1.90m	2.12-2.32m	2.43m 3.07dd	3.00dd	3.66dd 4.37d	7.45-7.67m 7.98dd 8.11dd
5d*	1.25-1.90m	2.06-2.22m	2.28m 2.93dd	2.81dd	3.58dd 4.06d	
6a	1.25-1.90m	2.15-2.45m	2.30m 2.99d	3.11d	3.42d 3.95d	7.67d 6.98d
6b	1.25-1.84m	2.15m	2.28 m 2.92d	3.04d	3.56d 4.01d	7.95d 7.35d
6c	1.25-1.90m	2.27d	2.33m 3.07d	3.14d	3.49d 4.22d	7.36-7.52m 7.80dd 7.99dd

*2.29 (s, 3H, CH_3).

in the ^1H nmr spectrum of **6d** the H-9a proton is shifted downfield (δ = 4.23 ppm) compared to that of the corresponding ketone **5d** (δ = 2.81 ppm), while in the other ox-

Table 5

^{13}C nmr chemical schifts of ketones **5 a-d** and oximes **6 a-c** in DMSO-d_6, δ (ppm)

N°	CH_2	C-1	C-2	C-3	C-3a	C-4	C-6	C-9a	C-10	C-10a
5 a	23.3,24.6,26.0	-	135.1	126.5	151.0	53.5	54.8	66.8	189.4	133.1
5 b	23.2,24.7,25.9	123.6	124.9	-	153.4	52.4	54.6	66.5	190.7	134.7
5 c	23.3,24.6,26.0	-	141.5	136.2	146.7	51.8	54.8	67.1	191.2	132.6
5 d	23.1,24.5,25.7	132.9	122.3	131.4	151.2	52.1	54.4	67.1	190.6	131.4
6 a	23.0,24.6,27.6	-	130.3	124.3	140.1	54.4	54.6	61.1	147.3	122.9
6 b	22.8,24.7,27.6	129.4	122.1	-	142.3	53.2	54.1	60.9	146.6	127.3
6 c	23.0,24.7,27.7	-	141.1	134.7	134.7	52.8	54.7	61.3	148.0	123.4

Table 6

Analytical and IR spectral Data of diazepines **8 a-c** and **7**

Compound N°	Yield % A	Yield % B	mp°C	IR ν cm^{-1} KBr NH	IR ν cm^{-1} KBr C=O	Formula	Analysis Calcd/Found C%	H%	N%
8 a	50	64	163-164	3152	1614	$C_{11}H_{14}N_2OS$	59.42 59.26	6.36 6.16	12.60 12.48
8 b	45	77	206-207	3164	1630	$C_{11}H_{14}N_2OS$	59.42 59.52	6.36 6.34	12.60 12.46
8 c	60	53	222-223	3140	1626	$C_{15}H_{16}N_2OS$	66.14 66.35	5.93 5.90	10.29 10.25
7	0	32	235-236	3182	1666	$C_{12}H_{15}ClN_2OS$	53.22 53.23	5.59 5.52	10.35 10.23

* See scheme II.

imes **6a-c** we observe only a deshielding of +0.25 ppm. This chemical shift difference for **6d** (δ = +1.42 ppm) would be due to the close proximity of the hydroxy group of the oxime.

The Beckmann rearrangement of the oximes **6a-d** using the usual method (polyphosphoric acid at 140°) led to the expected diazepines **8a-c** and **7**. Actually in the case of oxime **6a-c** the *anti* piperidine group is migrating so we isolated the three [1,3]diazepinones **8a-c**, while with oxime **6d** the *anti* thiophene group is migrating to afford the [1,4]diazepinone **7**. In contrast to previous investigations [3] no isomerization of the oxime has been observed. The structures of diazepinones **7** and **8a-c** were supported by analytical and spectral data (ir, ^1H and ^{13}C nmr). Details are reported in the experimental, but there are some features of interest. The signal of the H-9a proton is a multiplet for **8a-c** as in the analogous pyrrolidino[*a*]thieno[*e*]-[1,3]diazepinones [3] while it is a doublet of doublet for **7**. Actually in the [1,4]diazepinone **7** this proton is only coupled with two non-equivalent protons (*axial* and *equatorial*) at C-9 (J = 6.2 and 2.5 Hz respectively). The chemical shift difference (δ = +0.24 ppm) between proton H-9a of

Table 7

^1H nmr chemical shifts of diazepines **8 a-c** and **7** in DMSO-d_6, δ (ppm)

Compound N°	$(CH_2)_3$	H-9a	H-4ax H-4eq	H-6ax H-6eq	N-H	H-aromatique
8 a	1.25-1.90m	4.58-4.72m	3.94d 4.28d	2.80m 2.42d	7.82s	6.92d 7.68d
8 b	1.20-1.78m	3.84-3.95m	4.01d 4.09d	2.76m 2.38dd	8.05s	7.28d 7.40d
8 c	1.32-2.00m	4.64-4.78m	4.29d 4.51d	2.94m 2.48d	8.12s	7.34-7.56m 7.83dd 7.98dd
7	1.00-1.80m	2.57dd	3.58d 3.99d	2.72m 2.33m	9.75s	-

Table 8

^{13}C nmr chemical schifts of diazepines **8 a-c** and **7** in DMSO-d_6, δ (ppm)

N°	CH_2	C-1	C-2	C-3	C-3a	C-4	C-6	C-9a	C-11	C-11a
8 a	18.1,25.3,30.0	-	130.9	128.7	142.1	56.1	45.0	67.2	164.4	135.0
8 b	20.7,25.1,29.9	128.4	123.9	-	141.2	52.1	49.0	68.3	166.8	135.9
8 c	18.2,25.4,29.9	-	139.3	138.6	136.5	54.3	45.2	66.9	164.9	135.2
7	22.5,25.6,27.1	128.7	120.8	-	119.5	50.7	54.1	62.3	172.1	135.5

* 122.5, 123.2, 124.4, 126.6 ; ° 11.2

[1,4]diazepinone **7** and the ketone **5d** is much lower than those observed for [1,3]diazepinones **8a-c** by comparison with the corresponding ketones **5a-c** (δ = 1.1 to 1.8 ppm). Furthermore the chemical shift for the N-H proton of **7** is shifted downfield (δ = 9.75 ppm) compared to **8b** (δ = 8.05 ppm). The ^{13}C nmr spectra also confirm the structures of compounds **5-8**. As expected the chemical shift of carbon C-3a in [1,4]diazepine **7** (δ = 119.5 ppm) is shifted upfield compared to ketone **5d** (δ = 151.2 ppm) or oxime **6d** (δ = 137.1 ppm). Furthermore the chemical shifts of carbons C-3a, C-4, C-9 and C-11 of the [1,3]diazepinones **8** are similar to those observed in the pyrrolidinothieno[1,3]-diazepinones previously reported [4].

To confirm our results the Schmidt rearrangement of ketones **5a-d** afforded a successful route to tricyclic diazepines **8a-c** and **7** (Scheme II). The product of the reaction on α-tetralone had been previously characterized as exclusively the one from aryl rearrangement [11,12]. Alkyl rearrangement was only reported in certain cases [11,13] for 5-substituted tetralones. The Schmidt rearrangement in an usual manner (ketone in solution of dichloromethane, sodium azide, concentrated sulfuric acid, room temperature) of thieno[*b*]quinolizidinones **5a-c** gave the piperidino[*a*]thieno[*e*][1,3]diazepinones **8a-c** (alkyl rearrangement) and ketone **5d** gave the piperidino[*a*]thieno[*e*][1,4]-diazepine **7** (aryl rearrangement). This is a new example of

an alkyl rearrangement. To confirm this result, the Schmidt rearrangement of thienoindolizidinediones previously reported [3] and thienoindolizidinones are in progress.

EXPERIMENTAL

Melting points are uncorrected. The infrared spectra of solids (potassium bromide) were recorded on a Beckman IR 20 spectrometer. The nmr spectra were recorded on a Bruker AC-200 spectrometer (200 MHz) in DMSO-d_6 using tetramethylsilane (^{1}H) or DMSO-d_6 (^{13}C, δ = 39.5 ppm) as the internal standards. Ascending thin layer chromatography was performed on precoated plates of silica gel 60 F 254 (Merck) and the spots visualized using the uv lamp or iodine vapor. E. Merck silica gel 60 F (70-300 mesh) was used for column chromatography. The elemental analyses were carried out by the microanalysis laboratory of INSA at Rouen, F 76130 M^r.S^r.Aignan.

(±)-Ethyl 2-Piperidinecarboxylate Hydrochloride (**2**).

(±)-2-Piperidinecarboxylic acid (55.5 g, 0.43 mole) was suspended in ethanol (400 ml) and heated to 60°. Thionyl chloride (91.6 g, 0.77 mole) was added dropwise over 30 minutes. The resulting solution was stirred at room temperature for 6 hours and then cooled. The precipitate was filtered and washed with ether to give 75.0 g (90%) of ester hydrochloride **2**, mp 220-222° ([14] gives 202-203°).

Ethyl *N*-Thienylmethylpiperidine-2-carboxylates **3a-d**. General Procedure.

A mixture of **2** (27.1 g, 0.14 mole), potassium carbonate (20.7 g, 0.15 mole) and thienylmethyl halide **1a-d** (0.13 mole) in dry distilled dimethylformamide (300 ml) was stirred overnight at 60°. The resulting suspension was poured into 1*N* hydrochloric acid (1 *l*) and extracted with ether (3 x 100 ml). The aqueous layer was cooled with ice, basified with 40% sodium hydroxide and reextracted with dichloromethane (4 x 200 ml). The organic phase was washed with saturated brine, dried (sodium sulfate), filtered and concentrated to an oil. Distillation under reduced pressure afforded the esters **3a-d**. Their ^{1}H nmr data are given in Table 2.

The hydrochloride salts of the piperidine esters **3** were precipitated from solutions of the bases in dry ether by the dropwise addition of a solution of hydrogen chloride in dry ether (8%) with vigorous stirring.

Ethyl *N*-(3-Thienylmethyl)-2-piperidinecarboxylate (**3a**).

This compound was obtained in a yield of 87%, $bp_{0.3}$ 115-117°. The hydrochloride salt was crystallized from acetone-ether, mp 123-125°.

Anal. Calcd. for $C_{13}H_{20}ClNO_2S$: C, 53.87; H, 6.97; N, 4.83. Found: C, 53.93; H, 7.26; N, 4.79.

Ethyl *N*-(2-Thienylmethyl)-2-piperidinecarboxylate (**3b**).

This compound was obtained in a yield of 83%, $bp_{0.1}$ 124-126°. The hydrochloride salt of **3b** was crystallized from acetone-ether, mp 151-152°.

Anal. Calcd. for $C_{13}H_{20}ClNO_2S$: C, 53.87; H, 6.97; N, 4.83. Found: C, 53.94; H, 6.99; N, 4.69.

Ethyl *N*-(3-[1]Benzothienylmethyl)-2-piperidinecarboxylate (**3c**).

This compound was obtained in a yield of 68%, $bp_{0.1}$ 162-164°. The hydrochloride salt of **3c** was crystallized from acetone-ether, mp 155-156°.

Anal. Calcd. for $C_{17}H_{22}ClNO_2S$: C, 60.07; H, 6.54; N, 4.12. Found: C, 59.99; H, 6.53; N, 3.95.

Ethyl *N*-(2-Chloro-3-thienylmethyl)-2-piperidinecarboxylate (**3d**).

This compound was obtained in a yield of 82%, $bp_{0.1}$ 136-139°. The hydrochloride salt of **3d** was crystallized from acetone-ether, mp 134-135°.

Anal. Calcd. for $C_{14}H_{21}Cl_2NO_2$: C, 54.91; H, 6.91; N, 4.57. Found: C, 55.04; H, 6.62; N, 4.69.

N-Thienylmethyl-2-piperidinecarboxylic Acid Hydrochlorides **4a-d**. General Procedure.

A mixture of esters **3a-d** (0.1 mole) in 10*N* hydrochloric acid (700 ml) was refluxed for 4 hours. The resulting solution was evaporated to dryness to give a solid. Crystallization from a mixture acetone-methanol-ether gave the hydrochlorides of acids **4a-d** as white crystals. Spectral data of compounds **4** are given in Table 3.

N-(3-Thienylmethyl)-2-piperidinecarboxylic Acid Hydrochloride (**4a**).

This compound was obtained in a yield of 76%, mp 191-192°.

Anal. Calcd. for $C_{11}H_{16}ClNO_2S$: C, 50.46; H, 6.17; N, 5.35. Found: C, 50.14; H, 5.97; N, 4.93.

N-(2-Thienylmethyl)-2-piperidinecarboxylic Acid Hydrochloride (**4b**).

This compound was obtained in a yield of 69%, mp 143-145°.

Anal. Calcd. for $C_{11}H_{16}ClNO_2S$: C, 50.46; H, 6.17; N, 5.35. Found: C, 50.11; H, 6.46; N, 5.10.

N-(3-[1]Benzothienylmethyl)-2-piperidinecarboxylic Acid Hydrochloride (**4c**).

This compound was obtained in a yield of 76%, mp 216-218°.

Anal. Calcd. for $C_{15}H_{18}ClNO_2S$: C, 57.77; H, 5.83; N, 4.49. Found: C, 57.58; H, 5.68; N, 4.32.

N-(2-Chloro-3-thienylmethyl)-2-piperidinecarboxylic Acid Hydrochloride (**4d**).

This compound was obtained in a yield of 67%, mp 238-240°.

Anal. Calcd. for $C_{12}H_{17}Cl_2NO_2S$: C, 46.45; H, 5.53; N, 4.52. Found: C, 46.78; H, 5.55; N, 4.58.

Thieno[*b*]quinolizidinones **5a-d**. General Procedure.

A suspension of acids **4a-d** (15 mmoles) in polyphosphoric acid (80 g) was stirred under nitrogen, in a parafin bath at 95-100° during 7 hours. The reaction mixture turned from a colorless to a dark red viscous oil. The solution was poured slowly into ice water (200 ml), and basified, at 20° with 40% sodium hydroxide, to *p*H 8-9. The mixture was extracted with dichloromethane (3 x 100 ml). The organic phase was washed with saturated brine, dried (sodium sulfate), filtered and concentrated to a dark solid. Recrystallization from appropriate solvent afforded ketones **5a-d**. The ^{1}H and ^{13}C nmr spectral data are given in Tables 4 and 5.

Thieno[2,3-*b*]quinolizidin-10-one (**5a**).

This compound was obtained in a yield of 47%, mp 82-83° (from cyclohexane); ir: 2958, 2920, 2844, 2762, 2735, 1658 (C=O) cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}NOS$: C, 63.73; H, 6.33; N, 6.76. Found: C, 63.88; H, 6.53; N, 6.66.

Thieno[3,2-*b*]quinolizidin-4-one (**5b**).

This compound was obtained in a yield of 51%, mp 108-109° (from cyclohexane); ir: 2952, 2850, 2802, 2750, 1650 (C=O) cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}NOS$: C, 63.73; H, 6.33; N, 6.76. Found: C, 63.93; H, 6.61; N, 6.74.

[1]Benzothieno[2,3-*b*]quinolizidin-12-one (**5c**).

This compound was obtained in a yield of 62%, mp 143-144° (from ethanol); ir: 2918, 2850, 2800, 2758, 1650 (C=O) cm^{-1}.

Anal. Calcd. for $C_{15}H_{15}NOS$: C, 70.01; H, 5.87; N, 5.44. Found: C, 69.73; H, 6.06; N, 5.21.

2-Chloro-3-methylthieno[3,2-*b*]quinolizidin-4-one (**5d**).

This compound was obtained in a yield of 40%, mp 89-90° (from light petroleum ether); ir: 2922, 2842, 2790, 2745, 1662 (C=O) cm^{-1}.

Anal. Calcd. for $C_{12}H_{14}ClNOS$: C, 56.35; H, 5.53; N, 5.48. Found: C, 56.55; H, 5.47; N, 5.43.

General Procedure for Oximes **6a-c**.

A mixture of corresponding ketone **5a-c** (4.8 mmoles), hydroxylamine hydrochloride (0.69 g, 10 mmoles), and sodium acetate (0.82 g, 10 mmoles) in aqueous ethanol (60%) was refluxed for 10 hours. Ice water cooling afforded a white crystalline precipitate, which was collected, washed with aqueous ethanol (50%) and recrystallized from a suitable solvent. The ^1H and ^{13}C nmr spectra of oximes **6a-c** are given in Tables 4 and 5.

10-Oximinothieno[2,3-*b*]quinolizidine (**6a**).

This compound was obtained in a yield of 65%, mp 250-252° (from ethanol): ir: 2930, 2850 (C-H), 1603 (C=N) cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}N_2OS$: C, 59.42; H, 6.36; N, 12.60. Found: C, 59.33; H, 6.54; N, 12.46.

4-Oximinothieno[3,2-*b*]quinolizidine (**6b**).

This compound was obtained in a yield of 65%, mp 247-248° (from DMSO-water); ir: 2956, 2920, 2820 (C-H), 1610 (C=N) cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}N_2OS$: C, 59.42; H, 6.36; N, 12.60. Found: C, 59.25; H, 6.53; N, 12.54.

12-Oximino[1]benzothieno[2,3-*b*]quinolizidine (**6c**).

This compound was obtained in a yield of 71%, mp 254-256 dec (from DMSO); ir: 2920, 2845 (C-H), 1610 (C=N) cm^{-1}.

Anal. Calcd. for $C_{15}H_{16}N_2OS$: C, 66.14; H, 5.93; N, 10.29. Found: C, 66.36; H, 5.95; N, 10.05.

2-Chloro-3-methyl-4-oximinothieno[3,2-*b*]quinolizidine (**6d**).

A mixture of ketone **5d** (0.9 g, 3.5 mmoles) and hydroxylamine hydrochloride (0.97 g, 14 mmoles) in dry pyridine (20 ml) was refluxed 6 hours. After evaporation of the solvent, water (50 ml) and ether (50 ml) was added to the residue. The organic layer was separated and the mixture was extracted with ether (3 x 100 ml). The combined organic phases were washed with saturated brine, dried (sodium sulfate) and evaporated. The resulting residue was triturated with cold ether (10 ml). Recrystallization of the solid from benzene-hexane gave 0.25 g (26%) of oxime **6d**, mp 193-195°; ir: 2930, 2948, 1625 cm^{-1}; ^1H nmr (DMSO-d_6): δ 1.12-1.92 (6H, m, $(CH_2)_3$), 2.78-3.08 (2H, m, CH_2), 3.55 (1H, d, H-10$_{ax}$), 4.13 (1H, d, H-10$_{eq}$, J = 16.0 Hz), 4.23 (1H, d, H-4a, J = 9.6 Hz), 11.09 (1H, s, =NOH); ^{13}C nmr (DMSO-d_6): δ 14.4 (q, CH_3), 18.9, 20.7, 24.5 (t, CH_2), 44.4 (t, C-10), 52.6 (t, C-8), 54.9 (d, C-4a), 121.3 (s, C-2), 127.6 (s, C-3a), 132.0 (s, C-3), 137.1 (s, C-10a), 152.8 (s, C-4).

Anal. Calcd. for $C_{12}H_{15}N_2ClOS$: C, 53.22; H, 5.59; N, 10.35. Found: C, 53.50; H, 5.33; N, 10.25.

4*H*-Piperidino[1,2-*a*]thieno[2,3-*e*][1,3]diazepin-11(10*H*)-one (**8a**), 11*H*-Piperidino[1,2-*a*]thieno[3,2-*e*][1,3]diazepin-4(5*H*)-one (**8b**), 5*H*-Piperidino[1,2-*a*][1]benzothieno[2,3-*e*][1,3]diazepin-12(11*H*)-one (**8c**), 2-Chloro-3-methyl-11*H*-piperidino[1,2-*a*]thieno[3,2-*e*]-[1,4]diazepin-5(4*H*)-one (**7**).

A. Beckmann Rearrangement of Oximes **6a-d**.

Finely powdered oxime **6a-d** (9 mmoles) was quickly added to hot (140°), stirred polyphosphoric acid (40 g). The mixture was vigorously stirred for 2 hours. The hot mixture was decanted over crushed ice (100 ml) and basified at 20° with 40% sodium hydroxide to *p*H 8-9. The aqueous solution was extracted with dichloromethane (3 x 100 ml). The organic phase was washed with saturated brine, dried (sodium sulfate), filtered and concentrated to give a solid. Crystallization from ethanol afforded the pure [1,3]diazepinones **8a-c** and [1,4]diazepinone **7**.

B. Schmidt Rearrangement of Ketones **5a-d**.

A well stirred solution of the corresponding ketone **5a-d** (3.5 mmoles) in dichloromethane (25 ml) was treated dropwise with 98% sulfuric acid (3.2 ml), with cooling in an ice bath, for 10 minutes. After sodium azide (0.65 g, 10 mmoles) was added for 30 minutes, and the reaction mixture was stirred at room temperature for 6 hours. The mixture was decanted over crushed ice (100 ml) and basified with potassium carbonate to *p*H 8-9. The aqueous solution was extracted with dichloromethane (3 x 100 ml). The organic phase was washed with saturated brine, dried (sodium sulfate), filtered and concentrated to give a solid. Crystallization from ethanol afforded diazepines **8a-c** and **7** as white crystals.

Physical, spectral and analytical data of [1,3]diazepinones **8a-c** and [1,4]diazepinone **7** are summarized in Tables 6, 7 and 8.

REFERENCES AND NOTES

[1] A. Daich, F. Povazanec and B. Decroix, *J. Heterocyclic Chem.*, **28**, 1911 (1992).

[2] A. Daich and B. Decroix, *J. Heterocyclic Chem.*, **28**, 1881 (1991).

[3] S. Marchalin, B. Decroix and J. Morel, *Acta Chem. Scand.*, **47**, 287 (1993).

[4] S. Marchalin and B. Decroix, *J. Heterocyclic Chem.*, **30**, 667 (1993).

[5] M. Fernandez, G. G. Trigo and M. Sollhuber, *Heterocycles*, **24**, 1589 (1986).

[6] G. G. Trigo, E. Galvez and M. Sollhuber, *J. Heterocyclic Chem.*, **17**, 69 (1980).

[7] F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958).

[8] B. Chauncy and E. Gellert, *Aust. J. Chem.*, **23**, 2503 (1970).

[9] M. Sugiura and Y. Sasaki, *Chem. Pharm. Bull.*, **22**, 2988 (1976).

[10] K. Fujieda, K. Takahashi and T. Sone, *Bull. Chem. Soc. Japan*, **58**, 1587 (1985).

[11] P. A. Smith, *J. Am. Chem. Soc.*, **70**, 320 (1948).

[12] S. Uyeo, H. Irie, A. Yoshitake and A. Ito, *Chem. Pharm. Bull.*, **13**, 427 (1965).

[13] W. L. Nelson, D. D. Miller and R. S. Wilson, *J. Heterocyclic Chem.*, **6**, 131 (1969).

[14] A. Warren, A. Reckhow and D. S. Tarbell, *J. Am. Chem. Soc.*, **74**, 4960 (1952).