POLYHETERO[3,3]-SIGMATROPIC REARRANGEMENT OF *O*(*S*)-METHYL-*S*(*O*)ALLYL-*N*-(9-ACRIDINYL)IMINOTHIOCARBONATES

Pavol Kristian, Slávka Hočová, Juraj Bernát, Tatiana Bušová, and Igor Chomča

Department of Organic Chemistry, P. J. Šafárik University, 041 67 Košice, The Slovak Republic

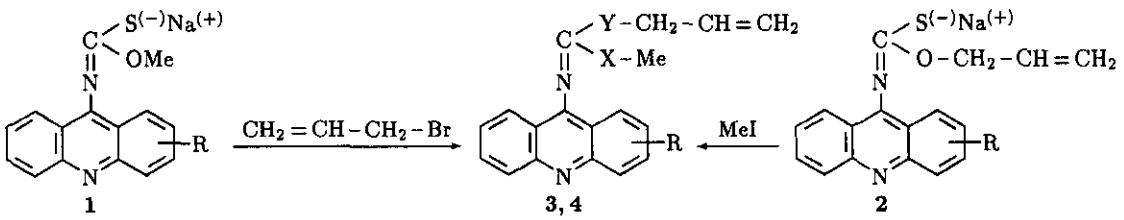
(Dedicated to Professor Koji Nakanishi on the occasion of his 75th birthday)

Abstract – A new synthetic route to *N*-allyl-*N*-(9-acridinyl)thiocarbamic acid *O*-methyl esters (**5a–c**) and *S*-methyl esters (**6a, b**) *via* $S \rightarrow N$ ($O \rightarrow N$) allylic transposition of *O*(*S*)-methyl-*S*(*O*)-allyl-*N*-(9-acridinyl)iminothiocarbonates (**3a–c, 4a, b**) was elaborated. The reaction represents a new convenient method for the synthesis of this type of acridine compounds.

In our previous paper[1] we have reported the synthesis and fluorescence properties of *O*-methyl-*S*-alkyl-*N*-(9-acridinyl)iminothiocarbonates. In this work we focused our attention to the syntheses of *O*(*S*)-methyl-*S*(*O*)allyl-*N*-(9-acridinyl)iminothiocarbonates (**3a–c, 4a, b**) in order to obtain starting compounds for polyhetero[3,3]-sigmatropic rearrangements. The aim was to demonstrate that the reaction could be applied for synthesis of *N*-allyl-*N*-(9-acridinyl)thiocarbamic acid *O*-methyl esters (**5a–c**) and *S*-methyl esters (**5a–c**) resp., which could not be obtained by the so far known synthetic methods. Despite many literature data concerning this problem,[2,3] the known methods are not of general use. The most allylic rearrangements have been performed by thermal catalysis or by catalysis of Pd(II) salts.

The starting *O*-methyl-*S*-allyl-*N*-(9-acridinyl)iminothiocarbonates (**3a–c**) were prepared according our previous paper[4] by the reaction of allyl bromide with the sodium acridinyliminothiocarbonate (**1a–c**). *O*-Allyl-*S*-methyl-*N*-(9-acridinyl)iminothiocarbonates (**4a, b**) were obtained by the addition of sodium alloxide on 9-isothiocyanatoacridines and subsequent alkylation of the obtained sodium salts (**2a, b**) with methyl iodide (Scheme 1).

The thermal rearrangement in xylene and catalytic rearrangement with Pd(II) salts in acetonitrile or THF were unsuccessful. However, we found out, that $S \rightarrow N$ and $O \rightarrow N$ allylic rearrangement gave satisfactory results by refluxing of 9-acridinyliminothiocarbonates (**3a–c, 4a, b**) in xylene using $PdCl_2(MeCN)_2$ as catalyst (Scheme 2).

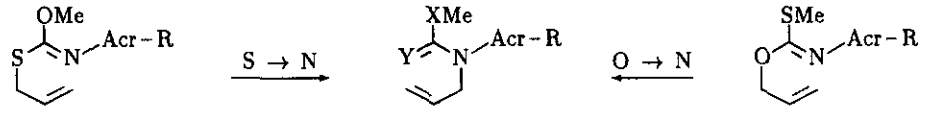


R: **1a**(H), **1b**(2-Me), **1c**(4-Me)

3a–c: X = O, Y = S
4a, b: X = S, Y = O
R: **3a**(H), **3b**(2-Me), **3c**(4-Me)
4a(H), **4b**(2-Me)

R: **2a**(H), **2b**(2-Me)

Scheme 1



R: **3a**(H), **3b**(2-Me), **3c**(4-Me)
Acr = 9-acridinyl

5a–c X = O, Y = S
6a, b: X = S, Y = O
R: **5a**(H), **5b**(2-Me), **5c**(4-Me)
6a(H), **6b**(2-Me)

R: **4a**(H), **4b**(2-Me)

Scheme 2

Futhermore we have proved, that the *O→N* rearrangement takes place with better results and faster than *S→N* one, which have been thought to be a catalyst poison owing to strong coordination of **5a–c** to the Pd(II) central atom.[5] In spite of relative low yields, this is up to day the only successful method for their preparation. The pure products obtained by rearrangement (**5a–c, 6a, b**) are crystaline compounds with higher melting points and lower fluorescence as compared with the starting ones (**3a–c, 4a, b**).

The structure of the synthetized compounds was unambiguously confirmed by their ^{1}H and ^{13}C NMR and MS spectra (see experimental).

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra (δ, ppm) were measured on Bruker AMX (600 MHz) (**4a, 6a**) and ARX (300 MHz) instruments at 298 K. Chemical shifts are expressed in ppm relative to TMS as internal standard. MS spectra were taken on an Finnigan MAT 90 spectrometer with chemical ionization. Elemental analyses were performed on a Perkin-Elmer CHN 2400 analyzer. The starting compounds (**3a–c**) were prepared according to ref.[6]

Preparation of *O*-allyl-*S*-methyl-*N*-(9-acridinyl)iminothiocarbonates (4a, b). General Procedure. Powdered sodium alloxide (*2.40 g, 0.03 mol*) was added to intensively stirred solution of 9-isothiocyanatoacridine (0.01 mol) in dry ether (30 mL) at rt. The end of the reaction

was followed by TLC on silica plates, eluent benzene–hexane (5 : 1), UV detection at 366 nm. The separated hygroscopic sodium salt (**2a, b**) was filtred off, washed with ether (30 mL) and suspended in dry dichloromethane (30 mL). Methyl iodide (1.42 g, 0.01 mol) was added and the stirring was continued at rt for next 0.5 h. The precipitate of NaI was removed by filtration and the filtrate was concentrated *in vacuo*. The product (**4a**) was crystalized from the mixture n-hexane–ether in the form of pale yellow crystals. The compound (**4b**) forms a yellow oil.

***O*-Allyl-*S*-methyl-*N*-(9-acridinyl)iminothiocarbonate (4a):** mp 57–60 °C ; yield 60%. Anal. Calcd for $C_{18}H_{16}N_2OS$: C, 69.95; H, 5.23; N, 9.06. Found: C, 69.27; H, 5.08; N, 8.82. MS *m/z* (rel intensity): 309.1 (100, M^+). ^{1}H NMR ($CDCl_3$) δ: 2.34 (s, 3H, SCH_3), 5.20 (ddd, J = 5.6, 1.2, and 1.1 Hz, 2H, CH_2), 5.45 (ddt, J = 10.5, 1.5, and 1.1 Hz, 1H, H-*cis*, $=CH_2$), 5.56 (ddt, J = 17.2, 1.5, and 1.2 Hz, 1H, H-*trans*, $=CH_2$), 6.23 (ddt, J = 17.2, 10.5, and 5.6 Hz, 1H, CH=), 7.41–8.21 (m, 8H, AcrH). ^{13}C NMR ($CDCl_3$) δ: 13.9 (SCH_3), 70.3 (CH_2), 118.4 ($=CH_2$), 132.2 (CH=), 159.6 (C=N).

***O*-Allyl-*S*-methyl-*N*-(2-methyl-9-acridinyl)iminothiocarbonate (4b):** oil; yield 63%. Anal. Calcd for $C_{19}H_{18}N_2OS$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.08; H, 5.50; N, 8.31. ^{1}H NMR ($CDCl_3$) δ: 2.40 (s, 3H, SCH_3), 2.56 (s, 3H, 2-CH_3), 5.25 (ddd, J = 5.8, 1.2, and 1.1 Hz, 2H, CH_2), 5.31 (ddt, J = 10.2, 1.5, and 1.1 Hz, 1H, H-*cis*, $=CH_2$), 5.75 (ddt, J = 17.1, 1.5, and 1.2 Hz, 1H, H-*trans*, $=CH_2$), 6.26 (ddt, J = 17.1, 10.2, and 5.8 Hz, 1H, CH=), 7.41–8.31 (m, 7H, AcrH).

Preparation of *N*-allyl-*N*-(9-acridinyl)thiocarbamic acid *O*-methyl esters (5a–c) and *S*-methyl esters (6a, b). General Procedure. A small amount of catalyst $PdCl_2(MeCN)_2$ was added to the solution of 9-acridinyliminothiocarbonate (**3a–c; 4a, b**) (0.01 mol) in dry *p*-xylene (5 mL). The reaction mixture was refluxed for 10 h. The course of the reaction was controlled by TLC on silica plates, till the reaction did not shaw further changes. After evaporation of the solvent, the crude product was directly subjected to a column chromatography (silica gel, benzene–acetone 10 : 1) to provide (**5a–c, 6a, b**) and a few starting compounds.

***N*-Allyl-*N*-(9-acridinyl)thiocarbamic acid *O*-methyl ester (5a):** mp 124–127 °C ; yield 23%. Anal. Calcd for $C_{18}H_{16}N_2OS$: C, 69.95; H, 5.23; N, 9.06. Found: C, 69.31; H, 5.10; N, 8.79. MS *m/z* (rel intensity): 309.5 (100, M^+). ^{1}H NMR ($CDCl_3$) δ: 3.78 (s, 3H, OCH_3), 4.88 (ddd, J = 6.9, 1.3, and 1.2 Hz, 2H, CH_2), 4.94 (ddt, J = 11.6, 1.6, and 1.2 Hz, 1H, H-*cis*, $=CH_2$), 5.09 (ddt, J = 17.4, 1.6, and 1.3 Hz, 1H, H-*trans*, $=CH_2$), 6.03 (ddt, J = 17.4, 11.6, and 6.9 Hz, 1H, CH=), 7.52–8.39 (m, 8H, AcrH). ^{13}C NMR ($CDCl_3$) δ: 58.6 (OCH_3), 58.9 (CH_2), 120.6 ($=CH_2$), 130.6 (CH=), 190.5 (C=S).

***N*-Allyl-*N*-(2-methyl-9-acridinyl)thiocarbamic acid *O*-methyl ester (5b):** mp 163–166 °C ; yield 23%. Anal. Calcd for $C_{19}H_{18}N_2OS$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.21; H, 5.46; N, 8.42. ^{1}H NMR ($CDCl_3$) δ: 2.58 (s, 3H, 2-CH_3), 3.79 (s, 3H, OCH_3), 4.94 (ddd, J = 6.9, 1.3, and 1.2 Hz, 2H, CH_2), 4.96 (ddt, J = 10.0, 1.6, and 1.2 Hz, 1H, H-*cis*, $=CH_2$), 5.13 (ddt, J = 16.9, 1.6, and 1.3 Hz, 1H, H-*trans*, $=CH_2$), 6.01 (ddt, J = 16.9, 10.0, and 6.9 Hz, 1H, CH=), 7.53–8.32 (m, 7H,

AcrH). ^{13}C NMR ($CDCl_3$) δ: 22.2 (2-CH_3), 58.6 (OCH_3), 58.8 (CH_2), 120.4 (=CH_2), 130.7 (CH=), 190.5 (C=S).

***N*-Allyl-*N*-(4-methyl-9-acridinyl)thiocarbamic acid *O*-methyl ester (5c):** mp 87–90 °C ; yield 42%. Anal. Calcd for $C_{19}H_{18}N_2OS$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.16; H, 5.49; N, 8.39. ^{1}H NMR ($CDCl_3$) δ: 2.95 (s, 3H, 4-CH_3), 3.76 (s, 3H, OCH_3), 4.93 (ddd, J = 6.9, 1.3, and 1.2 Hz, 2H, CH_2), 4.98 (ddt, J = 9.8, 1.7, and 1.2 Hz, 1H, H-*cis*, =CH_2), 5.14 (ddt, J = 17.0, 1.7, and 1.3 Hz, 1H, H-*trans*, =CH_2), 5.99 (ddt, J = 17.0, 9.8, and 6.9 Hz, 1H, CH=), 7.33–8.40 (m, 7H, AcrH). ^{13}C NMR ($CDCl_3$) δ: 18.5 (4-CH_3), 58.5 (OCH_3), 58.9 (CH_2), 120.1 (=CH_2), 130.7 (CH=), 190.6 (C=S).

***N*-Allyl-*N*-(9-acridinyl)thiocarbamic acid *S*-methyl ester (6a):** mp 105–107 °C ; yield 40%. Anal. Calcd for $C_{18}H_{16}N_2OS$: C, 69.95; H, 5.23; N, 9.06. Found: C, 69.33; H, 5.04; N, 8.76. MS *m/z* (rel intensity): 309.2 (100, M^+). ^{1}H NMR ($CDCl_3$) δ: 2.22 (s, 3H, SCH_3), 4.58 (ddd, J = 7.0, 1.3, and 1.2 Hz, 2H, CH_2), 4.92 (ddt, J = 10.2, 1.6, and 1.2 Hz, 1H, H-*cis*, =CH_2), 5.04 (ddt, J = 17.0, 1.6, and 1.3 Hz, 1H, H-*trans*, =CH_2), 5.96 (ddt, J = 17.0, 10.2, and 7.0 Hz, 1H, CH=), 7.54–8.35 (m, 8H, AcrH). ^{13}C NMR ($CDCl_3$) δ: 13.8 (SCH_3), 54.5 (CH_2), 120.5 (=CH_2), 132.1 (CH=), 170.2 (C=O).

***N*-Allyl-*N*-(2-methyl 9-acridinyl)thiocarbamic acid *S*-methyl ester (6b):** mp 130–132 °C ; yield 35%. Anal. Calcd for $C_{19}H_{18}N_2OS$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.28; H, 5.45; N, 8.36. ^{1}H NMR ($CDCl_3$) δ: 2.22 (s, 3H, SCH_3), 2.60 (s, 3H, 2-CH_3), 4.61 (ddd, J = 6.9, 1.3, and 1.2 Hz, 2H, CH_2), 4.95 (ddt, J = 11.0, 1.6, and 1.2 Hz, 1H, H-*cis*, =CH_2), 5.11 (ddt, J = 16.9, 1.6, and 1.3 Hz, 1H, H-*trans*, =CH_2), 6.02 (ddt, J = 16.9, 11.0, and 6.9 Hz, 1H, CH=), 7.52–8.35 (m, 8H, AcrH). ^{13}C NMR ($CDCl_3$) δ: 22.2 (2-CH_3), 54.1 (CH_2), 120.0 (=CH_2), 131.9 (CH=), 169.9 (C=O).

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