

Microwave-assisted synthesis of new aryliminothiazolylidene-2-thiazolidin-4-ones and their azarhodacyanines analogues

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Abstract: We here report an efficient microwave-assisted protocol for the synthesis of new aryliminothiazolylidene-2-thiazolidin-4-ones **6** and their azarhodacyanines derivatives **7** with quantitative yield from 2'-(methylthio)-4'-oxo-3*H*,4'*H*-[2,5-bithiazolylidene]-3'-ium tosylates **5** and 2-arylimino-5-(thiazol-2(3*H*)-ylidene)thiazolidin-4-ones **6**, respectively, using as starting material the 4-thiazoline-2-thiones **1** and 3-methyl-2-thioxo-1,3-thiazolidin-4-one **3**. The transformation of the tosylate salts **5** into their arylimino derivatives **6** has not been reported to date.

Keywords: Aryliminothiazolylidene-2-thiazolidin-4-ones; Azarhodacyanines; Microwave irradiation; DLC.

Introduction

It is well known that thiazole and fused heterocyclic thiazoles derivatives are found to be associated with various biological activities such as antibacterial, antifungal and anti-inflammatory activities¹⁻⁴. The 4-thiazolidinone derivatives have played an important role in medicinal chemistry. Moreover, the importance of the research carried out is due to their broad spectrum of biological activity, such as anti-HIV^{5,6}, antimycobacterial⁷, antiproliferative⁸, antimicrobial^{9,10}, anti-inflammatory^{11,12}, anticancer¹³, and antifungal¹⁴.

2-Heteroarylimino-1,3-thiazolidin-4-ones in particular thiazolimino- and benzothiazol imino-types, have been described in the literature and used as scaffolds for preparing a range antibacterial and antifungal compounds¹⁵⁻¹⁷, however, derivatives bearing a bis(thiazol-2(3*H*)-ylidene moiety as ring have not yet been known.

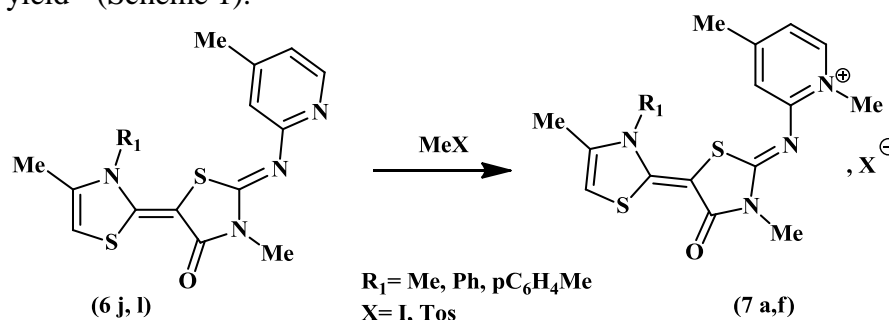
On the other hand, it has been reported in the literature that rhodacyanine dyes, designed by using the DLC (π -delocalized lipophilic cation) hypothesis¹⁸, exhibit potent *in vitro* antimalarial activity against *Plasmodium falciparum* and antitumor activity^{19,20}.

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Furthermore, the azarhodacyanines may be considered analogous to the rhodacyanine dyes and have been previously synthesized and designed as second generation of antimalarial rhodacyanines. Thus, these azarhodacyanines were obtained by condensation of 3-ethyl-5-(1-methylquinolin-2-ylidene)-2-(3-methylthio)-4-oxathiazolinium *p*-toluenesulfonate with 2-minomethylpyridinium salt in the presence of triethylamine, in refluxing acetonitrile for 12h in 71% yield²¹ (Scheme 1).



Scheme 1. 1-Methyl-2-{{[3-ethyl-5-(1-methylquinolin-2(1*H*)-ylidene)-4-oxothiazolidin-2-(pyridin-2-ylimino]methyl}pyridinium chloride (azarhodacyanine)

In view of the biological importance and in continuation of our previous work in which we have studied the beneficial effect of microwave irradiation on the condensation reaction for the synthesis rhodacyanines analogues²², we report herein an efficient microwave-assisted protocol for the synthesis of new aryliminothiazolylidene-2-thiazolidin-4-ones (**6**) from 2'-(methylthio)-4'-oxo-3*H*,4'*H*-[2,5-bithiazolylidene]-3'-ium tosylates (**5**). This method was developed previously in our laboratory²² and used the condensation of the starting material with aromatic amines in the presence of triethylamine.

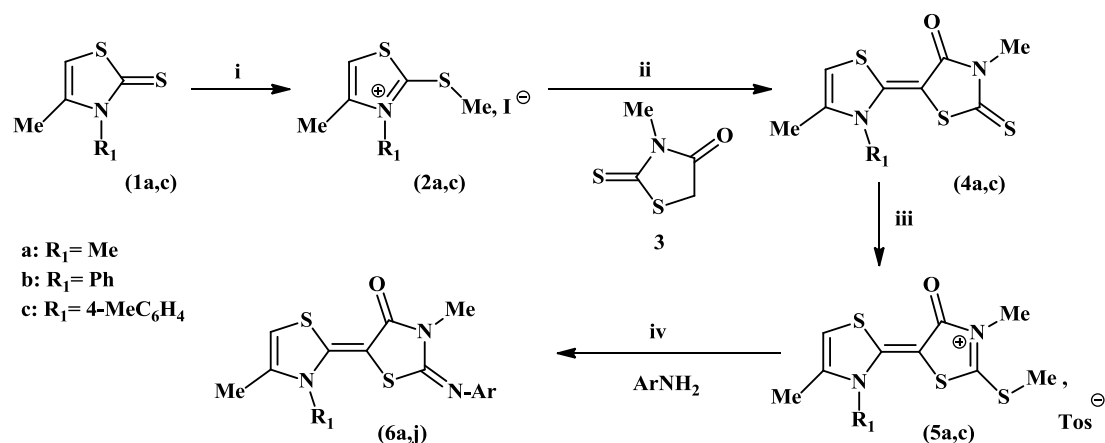
In this paper, 4-thiazoline-2-thione (**1**)²³ as starting material was transformed into aryliminothiazolylidene-2-thiazolidin-4-ones (**6**) which have not been reported to date. Hence, it is through of interest to accommodate 2-heteroarylimino-1,3-thiazolidin-4-ones and thiazole moieties in a single molecular framework and screen for their biologically activities.

The azarhodacyanines (**7a,f**) were obtained by simple quaternization from the corresponding aryliminothiazolylidene-2-thiazolidin-4-ones (**6j,l**).

Results and Discussion

Initially, a synthesis of 4-thiazoline-2-thione **1**²³⁻²⁶ by Hantzsch's cyclization is used for preparing the aryliminothiazolylidene-2-thiazolidin-4-ones **6** under microwave conditions (scheme 1). Two types of heating, conventional and the microwave activation were used.

The reaction under microwave was run at a frequency of 2.45 GHz with continuous irradiation power from 0 to 300W. The reaction temperature in the microwave cavity was measured with an IR captor (infrared thermometry) and the software algorithm regulates the microwave out-put power so that the preselected maximum temperature is maintained for the desired reaction/irradiation time. Synthesis of **6** was accomplished by a four-step sequence from 4-thiazoline-2-thiones **1**. *S*-methylation of **1** gave access to thiazolium salt **2** which was transformed into 5-(thiazol-2(3*H*)-ylidene)-2-thioxothiazolidin-4-ones **4** by condensation with *N*-methylrhodanine **3** in the presence of triethylamine. Activation by *S*-methylation of **4** furnished salt **5**²² (Scheme 2).



Scheme 2. Synthetic approach to obtain aryliminothiazolylidene-2-thiazolidin-ones (**6a,j**)

Reagents and conditions: (i) MeI (2 equiv), acetone, rt, 24 h. (ii) Et₃N (1.5 equiv), *N*-methylrhodanine (1 equiv), acetone, rt, 24 h. (iii) Methyl *p*-toluenesulfonate (MPTS) (3 equiv), DMF, 120°C, 4 h. (iv) **5** (1.2 equiv), ArNH₂ (1 equiv), Et₃N (1.5 equiv), MeCN, reflux, 4-8 h; MW: **5** (1.2 equiv), ArNH₂ (1 equiv), Et₃N (1.5 equiv), MeCN, 90°C, 8 to 12 min.

The target aryliminothiazolylidene-2-thiazolidin-4-ones (**6a,l**) were prepared from a mixture of salt **5** and aromatic amines in presence of triethylamine (in 64-82% yield) by heating (at 90°C) and stirring (about 4-8 h) in acetonitrile. In microwave-assisted synthesis conditions, the yields of the new compounds were better than conventional method (78-95% yield) and the reaction time in 8-12 minutes (Table 1).

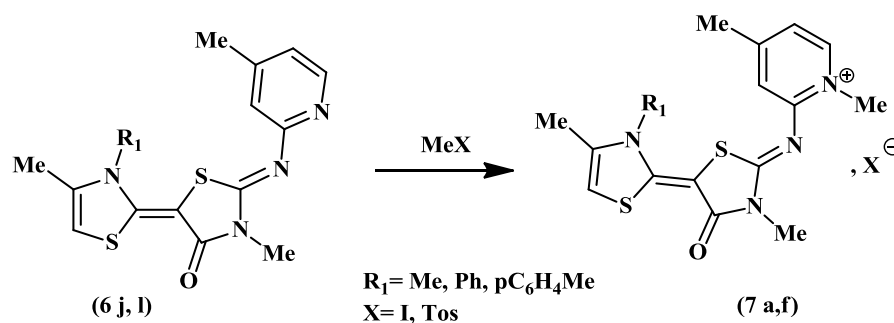
Table1. Results for (**6a,l**) syntheses under conventional method and under MW irradiation

Entry	6	R ₁	Ar	Classical heating		MW ^b	
				Method A		Method B	
				Time (min)	Yield ^a (%)	Time (min)	Yield ^a (%)
1	6a	Me	Ph	360	82	10	92
2	6b	Ph	Ph	360	64	8	78
3	6c	pMeC ₆ H ₄	Ph	300	79	10	90
4	6d	Me	pMeC ₆ H ₄	240	71	10	94
5	6e	Ph	pMeC ₆ H ₄	240	73	8	92
6	6f	pMeC ₆ H ₄	pMeC ₆ H ₄	360	80	10	91
7	6g	Me	2-Pyridyl	300	75	8	90
8	6h	Ph	2-Pyridyl	300	72	10	93
9	6i	pMeC ₆ H ₄	2-Pyridyl	300	73	10	95
10	6j	Me	4-Me-2-Pyridyl	480	78	10	88
11	6k	Ph	4-Me-2-Pyridyl	480	80	12	90
12	6l	pMeC ₆ H ₄	4-Me-2-Pyridyl	480	78	10	86

^a Isolated yields

^b P = 90W, T = 90°C

Alkylation of aryliminothiazolidene-2-thiazolidin-4-ones (**6j,l**) via quaternization of the pyridine nitrogen atom with methyl iodide or methyl *p*-toluenesulfonate, gave the corresponding azarhodacyanines (**7a,f**) in 43-70% yield under classical heating, during 6-8 h, at 90°C in refluxing acetonitrile, and in 64-85% yield, during 8-15 min, at 120°C under microwave irradiation. The reaction is depicted in scheme 1 and the results are summarized in Table 2.



Scheme 3. Synthesis of azarhodacyanines (**7a,f**)

Reagents and conditions: **6** (1 equiv), MPTS (7 equiv) or MeI (10 equiv), MeCN, reflux; 6-8 h or MW, 10-15 min at 120°C for MPTS and at 60°C for MeI.

Table 2. Results for Azarhodacyanines (**7a,f**)

Entry	7	R ₁	X	Classical heating Method C		MW Method D	
				Time (min)	Yield ^a (%)	Time (min)	Yield ^a (%)
1	7a	Me	pTos	420	55	10	75
2	7b	Me	I	360	43	8	64
3	7c	Ph	pTos	420	44	10	77
4	7e	Ph	I	480	45	13	70
5	7f	pMeC ₆ H ₄	pTos	420	70	15	85
6	7f	pMeC ₆ H ₄	I	420	57	8	69

^a Isolated yield

The results summarized in table 1 and 2 show that in microwave-assisted synthesis conditions, the yields of the new compounds **6** and **7** were better than conventional method. The difference in reaction time between these two condensation conditions methods procedure was evident.

The structural elucidation of compounds (**6** and **7**) is based on spectroscopic data (¹H and ¹³C NMR) and mass spectrometry HRMS. The attribution for (2*Z*, 5*E*)-stereochemistry of compounds (**6** and **7**) was based on the literature data^{19,27}.

The ¹H NMR of compounds (**6** and **7**) exhibit a typical signal for the H-5 proton of the thiazolic ring around 5.98-6.63 ppm for (**6**) and 6.45-6.85 ppm for (**7**), while the ¹H NMR spectra of **6** showed N-CH₃ as a singlet at 3.53-4.10 ppm. The ¹³C NMR spectra of (**6** and **7**) were characterized by the presence of C-2 rhodanine C=N at 153.5-159.7 ppm for (**6**) and 157.6-160.1 ppm for (**7**); and C=O the C-4 rhodanine at 163.2-166.6 ppm for (**6**) and 162.8-163.2 ppm for (**7**).

Conclusion

The microwave-assisted condensation reaction of 2'-(methylthio)-4'-oxo-3*H*,4'*H*-[2,5-bithiazolylidene]-3'-ium tosylates (**5a,c**) with aromatic amines, is a technique which gives satisfactory experimental results, affording good to high yields of new aryliminothiazolylidene-2-thiazolidin-4-ones (**6a,l**) and their azarhodocyanines derivatives (**7a,f**), in significantly shorter reaction times compared to classical conditions. Up to now, this new approach has never been reported and may be a complement to those existing in the literature. This class of compound will be soon tested for biological activities.

Acknowledgments

We are grateful to the group of the CRMPO (Rennes I) for mass spectrometry.

Experimental Section

Melting points were determined on a Kofler apparatus. ¹H NMR spectra were recorded on Bruker ARX 200 (200 MHz), Bruker 250 MHz and Bruker AC 300P (300 MHz) spectrometers and ¹³C NMR spectra on Bruker AC 300P (75 MHz) spectrometer in CDCl₃ or DMSO-d₆. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. The mass spectra (MS) on a VARIANT MAT 311 at a ionizing potential of 70 eV in the Centre de Mesures Physiques de l'Ouest (CRMPO, Rennes). Reactions under microwave were performed in a PROLABO Synthwave^(R) 402 (2.45 GHz) microwave reactor with a single focused system. All solvents and reagents were purchased from Acros Organics and Aldrich Chemic and used without further purification unless otherwise stated.

Preparation of the compounds 1, 2, 3,4 and 5

Compounds (1a,c)

The preparation of the compounds **1** was obtained according to the literature^{22,26} from disulfide carbon, amine in aqueous ammonia, and chloroacetone by Hantzsch's cyclization.

3,4-Dimethyl-1,3-thiazole-2(3*H*)-thione (1a). Beige crystals; yield = 85%; mp 116°C.

4-Methyl-3-phenyl-1,3-thiazole-2(3*H*)-thione (1b). White crystals; yield = 82%; mp = 151°C.

4-Methyl-3-(4-methylphenyl)-1,3-thiazole-2-(3*H*)-thione (1c). Beige crystals; yield = 97%; mp = 112°C.

Compounds (2a,c)

The alkylation of **1** (30 mmol, 1equiv) with iodomethane (60 mmol, 2equiv) gave (**2a-c**).²²

3,4-Dimethyl-2-(methylthio)-1,3-thiazol-3-ium iodide (2a): pale yellow needles; yield: 74%; mp = 163°C.

4-Methyl-3phenyl-2-(methylthio)-1,3-thiazol-3-ium iodide (2b): pink needles; yield: 70%; mp = 194°C.

4-Methyl-3-(4-methylphenyl)-2-(methylthio)-1,3-thiazol-3-ium iodide (2c): orange crystals; yield: 80%; mp = 162°C.

Compound 3

The preparation of the compounds **3** was obtained according to the literature,²² from disulfide carbon, amine in aqueous ammonia and chloroacetic acid and was purified by recrystallisation from aqueous ethanol.

3-Methyl-2-thioxo-1,3-thiazolidin-4-one (3): Yellow crystals; yield = 75%; mp = 69- 71°C (lit. 71°C²⁸).

Compounds (4a,c)²²

In a 250 mL round-bottomed flask, 10 mmol of salt **2**, 10 mmol of *N*-methylrhodanine **3**, 20 mL of acetone, and 2 mL of triethylamine are placed. After stirring at room temperature during 4 h, a yellow-green solid is formed. It is filtered off and washed several time with acetone.

(5E)-3-Methyl-5-(3,4-dimethylthiazol-2(3H)-ylidene)-2-thioxothiazolidin-4-one

(4a): yellow-green powder; yield = 95%; mp > 260°C.

(5E)-3-Methyl-5-(4-methyl-3-phenylthiazol-2(3H)-ylidene)-2-thioxothiazolidin-4-one

(4b): yellow powder; yield = 82% mp > 260°C.

(5E)-3-Methyl-5-(4-methyl-3-*p*-tolylthiazol-2(3H)-ylidene)-2-thioxothiazolidin-4-one

(4c): brown yellow powder; yield = 94%; mp >260°C

General Procedure for Salts Tosylates (5a,c)²²

A mixture of **4** (5 mmol), 15 mmol of MPTS (methyl *p*-toluenesulfonate), and 3 mL of DMF is stirred at 110–120°C during 4 h. The reaction mixture is cooled and 50 mL of acetone is added. After completion, the mixture is cooled down to refrigerated for one night. The resulting salt **5** is filtered off and dried under vacuum.

(5E)-3-Methyl-5-(3,4-dimethyl-1,3-thiazol-2-ylidene)-2-(methylthio)-4-oxo-1,3thiazolium *p*-toluenesulfonate (5a):

Yellow-green powder; yield = 70%; mp= 253°C. ¹H NMR (300 MHz, CDCl₃):

7.90 (d, 2H, *J* = 8.0 Hz); 7.18 (d, 2H, *J* = 8.0 Hz); 7.02 (s, 1H, H-5); 4.12 (s, 3H, CH₃N-thiazol); 3.73 (s, 3H, CH₃N⁺); 2.99 (s, 3H, CH₃-S); 2.50 (s, 3H, CH₃-tosyl); 2.11 (s, 3H, CH₃-thiazol).

(5E)-3-Methyl-5-(4-methyl-3-phenyl-1,3-thiazol-2-ylidene)-2-(methylthio)-4-oxo-1,3 thiazolium *p*-toluenesulfonate (5b):

Deep green crystals; yield = 80%; mp = 206°C. ¹H NMR (300 MHz, CDCl₃):

7.79–7.74 (m, 5H, Ar); 7.72 (d, 2H, *J* = 8.0 Hz); 7.69 (d, 2H, *J* = 8.0 Hz); 7.12 (s, 1H, H-5); 3.50 (s, 3H, CH₃N⁺); 2.60 (s, 3H, CH₃-S); 2.29 (s, 3H, CH₃-tosyl); 2.08 (s, 3H, CH₃-thiazol).

(5E)-3-Methyl-5[4-methyl-3-(4-methylphenyl)-1,3-thiazol-2-ylidene]-2-(methylthio)-4-oxo-1,3-thiazolium *p*-toluenesulfonate (5c):

Deep green crystals; yield =68%; mp = 198°C. ¹H NMR (300 MHz, CDCl₃) δ:

7.76 (d, 2H, *J* = 8.0 Hz); 7.57 (d, 2H, *J* = 8.1 Hz); 7.32 (d, 2H, *J* = 8.2 Hz); 7.11 (d, 2H, *J* = 8.0 Hz); 7.05 (s, 1H, H₅); 3.56 (s, 3H, CH₃N⁺); 2.73 (s, 3H, CH₃S); 2.48 (s, 3H, *p*-CH₃-thiazol); 2.32 (s, 3H,CH₃-tosyl); 2.11 (s, 3H,CH₃-thiazol).

The spectral data of the compounds **1**, **2**, **3**, **4** and **5** were identical with reported ones²².

II-General procedure for the preparation of aryliminothiazolylidene-2-thiazolidin-2-ones (6a,l)

(a)Classical heating: Method A

To a solution of the appropriate amines (2.5 mmol) in 20mL of anhydrous acetonitrile, the salts tosylates **5** (3mmol) and triethylamine (0.4ml, 3mmol, 0.30g) were added and reaction mixture was refluxed for 4-8h. Evaporation of the solvent was followed by purification of the residue by recrystallization from ethanol.

(b)Microwave-irradiation (MW): Method B

In an open cylinder quartz reactor ($\phi = 1.5\text{cm}$) are placed (1.8 mmol) the appropriate salt **5**, aromatic amine (1.5 mmol), acetonitrile (2mL) and triethylamine (0.20 mL, 0.152g, 1.5 mmol). The stirred mixture was irradiated at 90°C (90W, Synthewave^(R) 402) with an appropriate reaction time from 8 to 12min. The crude reaction mixture was cooled at room temperature; the residue was recrystallized from ethanol.

(2Z,5E)-3-Methyl-5-(3,4-dimethylthiazol-2(3H)-ylidene)-2-(phenylimino)thiazolidin-4-one(6a):

Green dark crystal; mp = 203°C. ¹H NMR (CDCl₃) δ : 7.20 (m, 5H, Ar); 6.02 (s, 1H, H-5); 3.50 (s, 3H, CH₃N rod); 3.41 (s, 3H, CH₃N thiazol); 2.11 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ : 165.3 (C=O); 155.4 (C=N); 152.8 (C-2 thiazol); 149.6; 136.1 (C-4 thiazol); 129.2, 123.7, 121.8; 102.5 (dq, $J = 190.1$ and 5.4 Hz, C-5 thiazol); 78.8 (C-5 rod); 34.2 (q, $J = 140.2$ Hz, CH₃-N thiazol); 29.0 (q, $J = 140.1$ Hz, CH₃-N rod); 14.5 (qd, $J = 129.5$ and 2.5 Hz, CH₃-thiazol). HRMS (m/z): found 157.0020 (calc. for C₁₅H₁₅N₃OS₂, M⁺ requires: 157.0099).

(2Z,5E)-3-Methyl-5-(4-methyl-3-phenylthiazol-2(3H)-ylidene)-2-(phenylimino)thiazolidin-4-one (6b):

Braun dark crystal; mp = 240°C. ¹H NMR (CDCl₃) δ : 7.40-6.70 (m, 10H); 6.04 (s, 1H, H-5); 3.20 (s, 3H, CH₃-N rod); 1.71 (s, 3H, CH₃ thiazol). ¹³C NMR (CDCl₃) δ : 165.6 (C=O); 153.5 (C=N); 152.8 (C-2 thiazol); 148.9; 136.0 (C-4 thiazol); 131.1; 130.4; 129.9; 129.8; 129.5; 129.2; 128.7; 123.4; 121.7; 101.7 (dq, $J = 190.1$ and 5.2Hz, C-5 thiazol); 80.0 (C-5 rod); 28.7 (q, $J = 140.8$ Hz, CH₃-N rod); 14.5 (qd, $J = 129.8$ and 2.4 Hz, CH₃-thiazol). HRMS (m/z): found 379.0826 (calc. for C₂₀H₁₇N₃OS₂, M⁺ requires: 379.0813).

(2Z,5E)-3-Methyl-5-[4-methyl-3-[4-methylphenyl]thiazol-2(3H)-ylidene)-2-(phenylimino)thiazolidin-4-one (6c):

Braun crystal; mp >260°C. ¹H NMR (CDCl₃) δ : 7.30 (m, 5H); 6.80 (d, 2H, $J = 7.1$ Hz); 6.3 (d, 2H, $J = 7.0$ Hz); 6.10 (s, 1H, H-5); 3.31 (s, 3H, CH₃N rod); 2.30 (s, 3H, CH₃-*p*-tolyl); 1.82 (s, 3H, CH₃-thiazol). ¹³C (CDCl₃) δ : 165.9 (C=O); 154.3 (C=N); 152.0 (C=N pyridine); 151.6 (C₂ thiazol); 141.0; 136.1 (C₄ thiazol); 132.7; 130.1; 129.8; 128.7; 123.5; 121.9; 101.6 (dq, $J = 190.1$ and 5.2 Hz, C-5 thiazol); 80.0 (C-5 rod); 28.7 (q, $J = 140.1$ Hz, CH₃-N rod); 21.1 (q, $J = 126.8$ and 4.4 Hz, CH₃-*p*-tolyl); 14.5 (qd, $J = 129.0$ and 2.5 Hz, CH₃-thiazol). HRMS (m/z): found 393.0966 (calc. for C₂₁H₁₉N₃OS₂, M⁺ requires: 393.0970).

(2Z,5E)-2-[4-(Methylphenyl)imino]-3-methyl-5-(3,4-dimethylthiazol-2(3H)-ylidene)thiazolidin-4-one (6d):

Yellow crystal; mp = 203°C. ¹H NMR (CDCl₃) δ : 7.11 (d, 2H, $J = 7.6$ Hz); 6.90 (d, 2H, $J = 7.7$ Hz); 5.58 (s, 1H, H-5); 3.48 (s, 3H, CH₃N rod); 3.34 (s, 3H, CH₃N thiazol); 2.30 (s, 3H, CH₃-*p*-tolyl); 2.08 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ : 165.4 (C=O); 155.3 (C=N); 152.7 (C-2 thiazol); 147.0; 136.1 (C-4 thiazol); 133.1; 129.9, 121.5, 102.4 (qd, $J = 190.1$ and 5.3 Hz, C-5 thiazol); 77.6 (C-5 rod); 34.1 (q, $J = 140.1$ Hz, CH₃-N thiazol); 29.0 (q, $J = 140.0$

Hz, CH₃-N rod); 20.9 (qt, $J = 126.9$ and 4.3 Hz, CH₃-*p*-tolyl); 14.5 (qd, $J = 129.3$ and 2.5 Hz, CH₃-thiazol). HRMS (m/z): found 331.0802 (calc. for C₁₆H₁₇N₃OS₂, M⁺ requires: 331.0813).

(2Z,5E)-2-[(4-Methylphenyl)imino]-3-methyl-5-(4-methyl-3-phenylthiazol-2(3H)-ylidene)thiazolidin-4-one (6e).

Green crystal; mp >260°C. ¹H NMR (CDCl₃) δ: 7.4 (m, 5H); 7.1 (d, 2H, $J = 8.2$ Hz); 7.0 (d, 2H, $J = 8.8$ Hz); 6.8 (s, 1H, H-5); 3.50 (s, 3H, CH₃-N rod); 2.30 (s, 3H, CH₃-*p*-tolyl); 1.90 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 163.2 (C=O); 157.9 (C=N); 152.0 (C-2 thiazol); 137.5; 137.5; 136.1 (C-4 thiazol); 134.6; 131.5; 130.5; 129.4; 123.7; 104.6 (dq, $J = 190.2$ and 5.4 Hz, C-2 thiazol); 78.0 (C-5 rod); 30.0 (q, $J = 141$ Hz, CH₃-N rod); 21.1 (qt, $J = 126.4$ and 4.4 Hz, CH₃-*p*-tolyl); 14.29 (qd, $J = 129$ and 2.4 Hz, CH₃-thiazol). HRMS (m/z): found 393.0966 (calc. for C₂₁H₁₉N₃OS₂, M⁺ requires: 393.0970).

(2Z,5E)-2-[(4-Methylphenyl)imino]-3-methyl-5-[4-methyl-3-(4-methylphenyl)thiazol-2(3H)-ylidene]thiazolidin-4-one (6f):

Green powder; mp >260°C. ¹H NMR (CDCl₃/CF₃COOH) δ: 7.30 (d, 2H, $J = 9$ Hz); 7.20 (d, 2H, $J = 9.0$ Hz); 7.00 (d, 2H, $J = 8.2$ Hz); 7.00 (d, 2H, $J = 8.2$ Hz); 6.60 (s, 1H, H-5); 3.60 (s, 3H, CH₃-N rod); 2.30 (s, 3H, CH₃-*p*-tolyl); 2.10 (s, 3H, CH₃-*p*-tolylimino); 2.01 (s, 3H, Me-thiazol). ¹³C NMR (CDCl₃/CF₃COOH) δ: 166.6 (C=O); 159.7 (C=N); 152.9(C-2 thiazol); 143.2; 139.7; 138.7 (C-4 thiazol); 132.5; 131.3; 130.5; 129.0; 124.8; 117.2; 113.3; 106.0 (dq, $J = 190.1$ and 5.2 Hz, C-5 thiazol); 78.3 (C-5 rod); 29.9 (q, $J = 140.1$ Hz, CH₃-N rod); 21.0 (q, $J = 127.1$ and 4.2 Hz, CH₃-*p*-tolyl); 20.9 (qt, $J = 126.8$ and 4.4 Hz, CH₃-*p*-tolyl); 14.1 (qd, $J = 129.2$ and 2.5 Hz, CH₃-thiazol). HRMS (m/z): found 407.1114 (calc. for C₂₂H₂₁N₃OS₂, M⁺ requires: 407.2610).

(2Z,5E)-3-Methyl-5-(3,4-dimethylthiazol-2(3H)-ylidene)-2-(pyridin-2-ylimino)thiazolidin-4-one(6g):

Green dark powder; mp = 219°C. ¹H NMR (CDCl₃) δ:8.40 (d, 1H, $J = 5.1$ Hz);7.60 (t, 1H, $J = 4.5$ Hz); 7.20 (d, 1H, $J = 5.0$ Hz); 6.90 (t, 1H, $J = 5.1$ Hz); 6.10 (s, 1H, H-5); 3.80 (s, 3H, CH₃-N rod); 3.50 (s, 3H, CH₃-N thiazol); 2.20 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 165.0 (C=O); 159.1 (C=N); 157.4 (C=N pyridine); 155.0 (C-2 thiazol); 146.3; 137.7 (C-4 thiazol); 120.8; 117.9; 103.6 (C-5 thiazol); 82.6 (C-5 rod); 35.4 (CH₃-N thiazol); 30.1 (CH₃-N rod); 15.0 (CH₃-thiazol). HRMS(m/z): found 318.0596 (calc. for C₁₄H₁₄N₄OS₂, M⁺ requires: 318.0609).

(2Z,5E)-3-Methyl-5-(4-methyl-3-phenylthiazol-2(3H)-ylidene)-2-(pyridin-2-ylimino)thiazolidin-4-one (6h):

Green dark crystals; mp = 209°C. ¹H NMR (CDCl₃) δ: 8.20 (d, 1H, $J = 6.0$ Hz);7.40 (m, 5H); 7.10 (t, 1H, $J = 4.5$ Hz); 7.10 (d, 1H, $J = 5.1$ Hz); 6.80 (t, 1H, $J = 5$ Hz); 6.20 (s, 1H, H-5); 3.40 (s, 3H, CH₃-N rod); 1.90 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 165.7 (C=O); 158.9 (C=N); 156.5 (C=N pyridine); 155.2 (C-2 thiazol); 145.5; 137.8; 136.7; 130.8; 130.6; 130.4; 129.6; 120.4; 117.7; 102.8 (C-5 thiazol); 84.7 (C-5 rod); 29.7 (CH₃-N rod); 15.0 (CH₃-thiazol). HRMS (m/z): found 380.0799 (calc. for C₁₉H₁₆N₄OS₂, M⁺ requires: 380.0766).

(2Z,5E)-3-Methyl-5-[4-methyl-3-(4-methylphenyl)thiazol-2(3H)-ylidene]-2-(pyridin-2-ylimino)thiazolidin-4-one (6i):

Braun powder; mp = 236°C. ¹H NMR (CDCl₃) δ:8.10 (d, 1H, $J = 6.0$ Hz);7.50 (t, 1H, $J = 4.5$ Hz); 7.40 (d, 2H, $J = 8.1$ Hz); 7.20 (d, 2H, $J = 8.1$ Hz); 7.01 (d, 1H, $J = 5.0$ Hz); 6.8 (t, 1H, $J = 5.0$ Hz); 6.10 (s, 1H, H-5); 3.40 (s, 3H, CH₃-N rod); 2.60 (s, 3H, CH₃-*p*-tolyl); 1.90 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 165.7 (C=O); 159.1 (C=N); 156.6 (C=N pyridine); 152.2 (C-2 thiazol); 145.6; 141.34 (C-4 thiazol); 138.2; 137.5; 130.3; 129.9; 117.7; 116.8; 104.3 (C-

5 thiazol); 88.0 (C-5 rod); 29.7 (CH₃-N rod); 21.9 (CH₃-*p*-tolyl); 15.0 (CH₃-thiazol). HRMS (*m/z*): found 394.0912 (calc. for C₂₀H₁₈N₄OS₂, M⁺ requires: 394.0922).

(2Z,5E)-2-(4-Methylpyridin-2-ylimino)-3-methyl-5-(3,4-dimethylthiazol-2(3H)-ylidene)thiazolidin-4-one (6j):

Green crystals; mp = 215°C. ¹H NMR (CDCl₃) δ: 8.20 (d, 1H, *J* = 5.1 Hz); 6.90 (s, 1H); 6.60 (d, 1H, *J* = 5.0 Hz); 6.00 (s, 1H, H-5); 3.70 (s, 3H, CH₃-N rod); 3.40 (s, 3H, CH₃-thiazol); 2.30 (s, 3H, CH₃-pyridine); 2.03 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 164.6 (C=O); 158.8 (C=N); 156.8 (C=N pyridine); 154.5 (C-2 thiazol); 148.4 (C-Me pyridine); 145.6; 136.4; 120.9; 103.1 (dq, *J* = 190.3 and 5.4 Hz, C-5 thiazol); 82.1 (C-5 rod); 35.0 (q, *J* = 140.8 Hz, CH₃-N thiazol); 29.5 (q, *J* = 141.1 Hz, CH₃-rod); 20.9 (qt, *J* = 126.0 and 4.3 Hz, CH₃-pyridine); 14.8 (qd, *J* = 129.5 and 2.5 Hz, CH₃-thiazol). HRMS (*m/z*): found 332.6771 (calc. for C₁₅H₁₆N₄OS₂, M⁺ requires 332.0766).

(2Z,5E)-2-(4-Methylpyridin-2-ylimino)-3-methyl-5-(4-methyl-3-phenylthiazol-2(3H)-ylidene)thiazolidin-4-one (6k):

Yellow-green crystal; mp 235°C. ¹H NMR (CDCl₃) δ: 7.90 (d, 1H, *J* = 5.1 Hz); 7.40 (m, 5H); 6.90 (s, 1H); 6.60 (d, 1H, *J* = 5.0 Hz); 6.20 (s, 1H, H-5); 3.40 (s, 3H, CH₃-N rod); 2.3 (s, 3H, CH₃-pyridine); 1.90 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 165.4 (C=O); 158.7 (C=N); 155.9 (C=N pyridine); 154.5 (C-2 thiazol); 148.2; 144.8; 136.3 (C-4 thiazol); 130.3; 130.2; 129.9; 120.4; 118.7; 102.3 (dq, *J* = 190.0 and 5.0 Hz, C-5 thiazol); 84.4 (C-5 rod); 29.2 (q, *J* = 140.0 Hz, CH₃-N rod); 20.9 (qt, *J* = 127.7 and 5.1 Hz, CH₃-pyridine); 14.6 (qd, *J* = 129.7 and 3 Hz). HRMS (*m/z*): found 394.0930 (calc. for C₂₀H₁₈N₄OS₂, M⁺ requires: 394.0992).

(2Z,5E)-2-(4-Methylpyridin-2-ylimino)-3-methyl-5-[4-methyl-3-(4-methylphenyl)thiazol-2(3H)-ylidene]thiazolidin-4-one (6l):

Braun crystal; mp = 238°C. ¹H NMR (CDCl₃) δ: 7.80 (d, 1H, *J* = 5.1 Hz); 7.30 (d, 2H, *J* = 8.1 Hz); 7.20 (d, 2H, *J* = 8.2 Hz); 6.80 (s, 1H); 6.10 (s, 1H, H-5); 3.30 (s, 3H, CH₃-N rod); 2.49 (s, 3H, CH₃-pyridine); 2.20 (s, 3H, CH₃-*p*-tolyl); 1.20 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 165.3 (C=O); 158.8 (C=N); 156.1 (C=N pyridine); 148.2; 144.9; 140.9; 136.4; 133.6; 130.0; 129.9; 120.5; 118.8; 102.1 (dq, *J* = 190.1 and 5.3 Hz, C-5 thiazol); 84.2 (C-5 rod); 29.2 (q, *J* = 140.9 Hz, CH₃-N rod); 21.4 (qt, *J* = 126.9 and 4.3 Hz, CH₃-*p*-tolyl); 20.9 (qt, *J* = 127.0 and 4.4 Hz, CH₃-pyridine); 14.5 (qd, *J* = 129.8 and 2.3 Hz, CH₃-thiazol). HRMS (*m/z*): found 408.1065 (calc. for C₂₁H₂₀N₄OS₂, M⁺ requires 408.1079).

IV-General Procedure for the preparation of azarhodacyanines (7a,f) by quarternization of (6j,l)

(a) Classical heating: Method C

In a 250 mL round bottom flask are placed 1mmol of (6j,l), 7 mmol of MPTS (methyl *p*-toluenesulfonate) or 10 mmol of MeI, 20 mL of acetonitrile. The reaction mixture was refluxed during 6-8 h. After cooling to room temperature and solvent evaporation, the residue was washed with acetone.

(b) Microwave-irradiation: Method D

In an open quartz reactor are added 1mmol of imine (6j,l), 7 mmol of MPTS (methyl *p*-toluenesulfonate) or 10 mmol of MeI. The mixture was exposed to microwave at 120°C (90 W, Synthrowave^(R), 402), for MPTS or 60°C (90 W, Synthrowave^(R), 402) for MeI during 10-15 min. The residue was washed with acetone.

4-Methyl-2-[3-methyl-5-(3,4-dimethylthiazol-2(3H)-2-ylidene)-4-oxothiazolidin-2-ylidene amino]-1-methylpyridinium *p*-toluenesulfonate (7a):

Red crystals; mp = 122°C. ¹H NMR (CDCl₃) δ: 8.40 (d, 1H, *J* = 5.9 Hz); 7.62 (d, 2H, *J* = 8.0 Hz); 7.30 (d, 2H, *J* = 7.9 Hz); 7.03 (d, 1H, *J* = 5.7 Hz); 6.91 (s, 1H); 6.5 (s, 1H, H-5); 3.89 (s, 3H, CH₃-N⁺); 3.56 (s, 3H, CH₃-N thiazol); 3.20 (s, 3H, CH₃-N rod); 2.45 (s, 3H, CH₃-pyridine); 2.37 (s, 3H, CH₃-tosyl); 2.32 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 162.8 (C=O); 160.1 (C=N); 158.8 (C=N pyridine); 152.2 (C-2 thiazol); 145.1; 143.5; 142.6; 139.5 (C-4 thiazol); 131.2; 129.6; 120.5; 117.7; 110.6; 104.9 (C-5 thiazol); 88.7 (C-5 rod); 42.5 (CH₃-N⁺); 35.7 (CH₃-N rod); 30.3 (CH₃-N thiazol); 22.0 (CH₃-*p*-tolyl); 21.1 (CH₃-tosyl); 14.7 (CH₃-thiazol). HRMS (*m/z*): found 347.1000 (calc. for C₁₆H₁₉N₄OS₂, M⁺ requires: 347.1003).

4-Methyl-2-[3-methyl-5-(3,4-dimethylthiazol-2(3H)-2-ylidene)-4-oxo-thiazolidin-2-ylideneamino]-1-methylpyridinium iodide (7b):

Green powder; mp >260°C. ¹H NMR (DMSO) δ: 8.60 (d, 1H, *J* = 6.6Hz); 7.60 (s, 1H); 7.3 (d, 1H, *J* = 6.5 Hz); 6.80 (s, 1H, H-5); 4.00 (s, 3H, CH₃-N⁺); 3.80 (s, 3H, CH₃-N rod); 3.40 (s, 3H, CH₃-N thiazol); 2.50 (s, 3H, CH₃-pyridine); 2.30 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 163.2 (C=O); 161.1 (C=N⁺); 159.9 (C=N); 152.3 (C-2thiazol); 140.2; 139.6 (C-4 thiazol); 120.6; 117.2; 110.1; 105.1 (C-5 thiazol); 79.7 (C-5 rod); 42.9 (CH₃-N⁺); 36.2 (CH₃-N rod); 30.6 (CH₃-N thiazol); 22.4 (CH₃-pyridine); 14.8 (CH₃-thiazol). HRMS (*m/z*): found 347.1000 (calc. for: C₁₆H₁₉N₄OS₂, M⁺ requires: 347.1003).

4-Methyl-2-[3-methyl-5-(3-phenyl-4-methylthiazol-2(3H)-2-ylidene)-4-oxo-thiazolidin-2-ylideneamino]-1-methylpyridinium *p*-toluenesulfonate (7c):

Orange crystal; mp = 207°C. ¹H NMR (CDCl₃)δ: 9.04 (d, 1H, *J* = 6.0Hz); 7.83 (d, 2H, *J* = 7.9 Hz); 7.70 (m, 5H); 7.20 (d, 1H, *J* = 5.3 Hz); 7.10 (d, 2H, *J* = 7.8 Hz); 6.90 (s, 1H); 6.50 (s, 1H, H-5); 4.00 (s, 3H, CH₃-N⁺); 3.50 (s, 3H, CH₃-N rod); 2.40 (s, 3H, CH₃-tosyl); 2.20 (s, 3H, Me-pyridine); 2.00 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 163.0 (C=O); 160.3 (C=N⁺); 157.5 (C=N); 157.3 (C-2); 153.6; 144.8; 143.6; 138.6 (C-4); 137.6; 134.9; 131.5; 130.6; 129.8; 128.2; 120.5; 116.8; 104.8 (C-5 thiazol); 79.7 (C-5 rod); 42.9 (CH₃-N⁺); 29.7 (CH₃N rod); 22.3 (CH₃-pyridine); 21.3 (CH₃-tosyl); 14.9 (CH₃-thiazol). HRMS (*m/z*): found 409.1153 (calc. for C₂₁H₂₁N₄OS₂, M⁺ requires: 409.1568).

4-Methyl-2-[3-methyl-5-(3-phenyl-4-methylthiazol-2(3H)-ylidene)-4-oxo-thiazolidin-2-ylideneamino]-1-methylpyridinium iodide (7d):

Red crystals; mp >260°C. ¹H NMR (CDCl₃) δ: 8.96 (d, 1H, *J* = 6.3 Hz); 7.60 (m, 5H); 7.20 (d, 1H, *J* = 6.1Hz); 7.00 (s, 1H); 6.56 (s, 1H, H-5); 4.10 (s, 3H, CH₃-N⁺); 3.20 (s, 3H, CH₃-N rod); 2.50 (s, 3H, Me-pyridine); 2.00 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 162.9 (C=O); 159.5 (C=N⁺); 158.7 (C=N); 157.2 (C-2 thiazol); 146.8; 143.3; 141.3; 139.9; 129.9; 127.5; 123.5; 118.1; 116.3; 105.1; 77.8; 44.8 (CH₃-N⁺); 29.8 (CH₃-N rod); 22.6 (CH₃-pyridine); 14.9 (CH₃-thiazol). HRMS (*m/z*): found 409.1153 (calc. for C₂₁H₂₁N₄OS₂, M⁺ requires: 409.1157).

4-Methyl-2-[3-methyl-5-[3-(4-methylphenyl)]-4-methylthiazol-2(3H)-2-ylidene)-4-oxo-thiazolidin-2-ylideneamino]-1-methylpyridinium *p*-toluenesulfonate (7e):

Braun crystal; mp = 134°C. ¹H NMR (CDCl₃) δ: 8.70 (d, 1H, *J* = 6.6 Hz); 7.70 (d, 2H, *J* = 8.1 Hz); 7.40 (d, 2H, *J* = 8.1Hz); 7.1 (d, 2H, *J* = 8.2Hz); **7.25** (d, 1H, *J* = 6.6 Hz); **7.01** (d, 2H, *J* = 8.0 Hz); 6.86 (s, 1H); 6.50 (s, 1H, H-5); 3.90 (s, 3H, CH₃-N⁺); 3.30 (s, 3H, CH₃-N-rod); 2.40 (s, 3H, CH₃-pyridine); 2.30 (s, 3H, CH₃-tosyl); 2.20 (s, 3H, CH₃-*p*-tolyl-Nthiazol); 1.90 (s, 3H, CH₃-thiazol). ¹³C NMR (CDCl₃) δ: 162.9 (C=O); 160.2 (C=N⁺); 157.6 (C=N); 157.1 (C-2 thiazol); 153.6; 144.6; 143.9; 142.0; 138.9; 137.8; 132.1; 130.9; 129.4; 128.4; 126.0; 120.3; 115.9; 104.7 (C-5 thiazol); 78.7 (C-5 rod); 42.3 (CH₃-N⁺); 29.6 (CH₃-rod);

21.9 (CH₃-*p*-tolyl); 21.4 (CH₃-pyridine); 21.1 (CH₃-tosyl), 14.3 (CH₃-thiazol). HRMS (*m/z*): found 423.1315 (calc. for C₂₂H₂₃N₄OS₂, M⁺requires: 423.1313).

4-Methyl-2-[3-methyl-5-[3-(4-methylphenyl)]-4-methylthiazol-2(3*H*)-2-ylidene]-4-oxo-thiazolidin-2-ylideneamino]-1-methylpyridinium iodide (7f).

Braun powder; mp = 260°C. ¹H NMR (DMSO) δ: 9.04 (d, 1H, *J* = 6.6 Hz); 7.50 (d, 2H, *J* = 7.8 Hz); 7.32 (d, 2H, *J* = 7.8 Hz); 7.20 (d, 1H, *J* = 6.6 Hz); 7.03 (s, 1H); 6.53 (s, 1H, H-5); 4.10 (s, 3H, CH₃-N⁺); 3.30 (s, 3H, CH₃-N rod); 2.50 (s, 3H, CH₃-*p*-tolyl); 2.50 (s, 3H, CH₃-pyridine); 2.00 (s, 3H, CH₃-thiazol). ¹³C NMR (DMSO) δ: 163.2 (C=O); 161.2 (C=N⁺); 158.2 (C=N); 157.6 (C-2-thiazol); 154.2; 144.3; 142.6; 138.4; 132.5; 131.5; 129.8; 120.4; 116.6; 105.3 (C-5-thiazol); 79.6 (C-5 rod); 43.2 (CH₃-N⁺); 30.2 (CH₃-rod); 22.6 (CH₃-*p*-tolyl); 21.9 (CH₃-pyridine); 14.9 (CH₃-thiazol). HRMS (*m/z*): found 423.1315 (calc. for C₂₂H₂₃N₄OS₂, M⁺requires: 423.1313).

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