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Oxazepines and Thiazepines XXXVII [1]. A Simple and Convenient Procedure for the Preparation of 3-Acyl-2,3-dihydrobenzothiazoles by Ring Contraction of 2,4-Diaryl-2,3-dihydro-1,5-benzothiazepines under Acylating Conditions[a]

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Summary. 3-Acyl-2,3-dihydrobenzothiazoles **13–30** were prepared by ring contraction of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines **1–12** under acylating conditions. This procedure provides a general and efficient access to these benzothiazole derivatives.

Keywords. Acylation; Ring contraction; Benzothiazoles; 1,5-Benzothiazepines.

Oxazepine und Thiazepine, 37. Mitt. [1]**. Ein einfaches und bequemes Verfahren zur Darstellung von 3-Acyl-2,3-dihydrobenzothiazolen durch Ringverengung von 2,4-Diaryl-2,3-dihydro-1,5-benzothiazepinen unter acylierenden Bedingungen**

Zusammenfassung. Die 3-Acyl-2,3-dihydrobenzothiazole **13–30** wurden durch Ringverengung der 2,4-Diaryl-2,3-dihydro-1,5-benzothiazepine **1–12** unter acylierenden Bedingungen dargestellt. Das Verfahren stellt einen allgemeinen und ergiebigen Zugang zur Gewinnung dieser Benzothiazolderivate dar.

Introduction

3-Acyl-2,3-dihydrobenzothiazoles have generally been prepared by acylation of appropriate 2,3-dihydrobenzothiazoles either with acid anhydrides or with acyl halides in the presence of an inorganic or an organic base [2–6]. Recently we have demonstrated that the ring contraction of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines under acetylating conditions is an efficient procedure for the preparation of 3-acetyl-2,3-dihydrobenzothiazoles [7]. One of the benefits of this method is that the readily available 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines [8–15] are used as starting materials. It is worth mentioning that 2-styrylbenzothiazoles have also

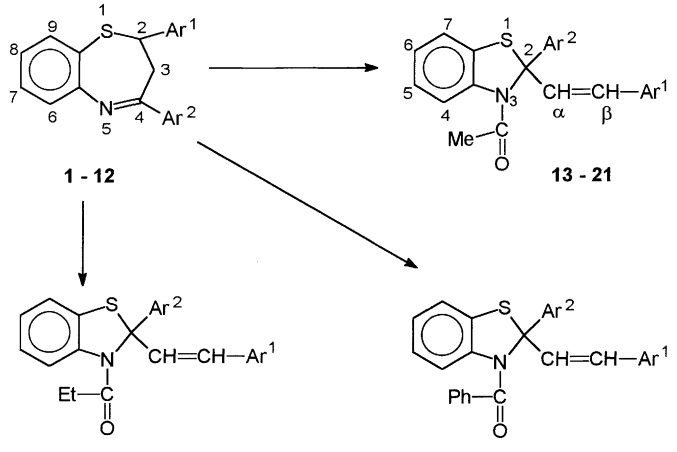
[a] Dedicated to the late Prof. Dr. Dr. h.c. *Günther Snatzke* on the occasion of his 70th birthday

been prepared either by a thermally mediated or an acid catalyzed ring contraction of 2,3-dihydro-1,5-benzothiazepines [16–19]. However, such conversions are not suitable for the preparation of 2,2-disubstituted benzothiazoles. As a continuation, in this paper we report on the generalization of this convenient procedure for the synthesis of 2,2-disubstituted 3-acyl-2,3-dihydrobenzothiazoles.

Results and Discussion

Recently, ring contraction of 2,3-dihydro-1,5-benzothiazepines bearing an unsubstituted or a substituted phenyl ring at positions 2 and 4 of the 1,5-benzothiazepine skeleton have been investigated [7]. It has turned out that both the substitution pattern of these phenyl rings and the electronic character of their substituents are almost without influence on the course and the outcome of the ring contraction of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines *via* a bond scission between S-1 and C-2 followed by a ring closure to afford 3-acetyl-2-aryl-2,3-dihydro-2-styrylbenzothiazoles under acetylating conditions [7].

In our present study, 2,3-dihydro-1,5-benzothiazepines bearing a bulky aryl moiety (1-naphthyl, 2-naphthyl, or 9-phenanthryl group either at position 2 or 4) were also included (Scheme 1, compounds **5**–**12**). It was found that these benzothiazepines gave 3-acetyl-2-aryl-2-(β-arylvinyl)-2,3-dihydrobenzothiazoles **15**–**21** under acetylating conditions (*cf.* Experimental, *Method i*) similarly to the previously investigated compounds [7]. Our experimental results reveal that such ring contractions of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines under acetylating



	Ar^1	Ar^2		Ar^1	Ar^2
1, **22**, **27**	C_6H_5	C_6H_5	**7**, **16**, **25**	2-naphthyl	C_6H_5
2, **28**	2-Cl-C_6H_4	C_6H_5	**8**, **17**, **26**	2-naphthyl	4-Cl-C_6H_4
3, **13**, **23**	C_6H_5	4-MeO-C_6H_4	**9**, **18**	2-naphthyl	3,4-OCH_2O-C_6H_3
4, **24**	C_6H_5	4-Cl-C_6H_4	**10**, **19**	C_6H_5	2-naphthyl
5, **14**, **29**	C_6H_5	4-Br-C_6H_4	**11**, **20**	9-phenanthryl	C_6H_5
6, **15**, **30**	1-naphthyl	C_6H_5	**12**, **21**	C_6H_5	9-phenanthryl

Scheme 1

conditions are almost independent of the spatial demand and electronic distribution of the aryl groups at position 2 and 4. Therefore, this simple and convenient method can be utilized for the preparation of a wide variety of 2,2-disubstituted 3-acetyl-2,3-dihydrobenzothiazoles.

Since we planned to generalize this method for the preparation of 2,2-disubstituted 3-acyl-2,3-dihydrobenzothiazoles, a similar ring contraction reaction of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines was performed using propionic anhydride and benzoic anhydride as acylating agents. However, it turned out that the reaction conditions used for the synthesis of 3-acetyl-2,3-dihydrobenzothiazoles could not be applied without modification to the preparation of 3-benzoyl or 3-propionyl derivatives of 2,3-dihydrobenzothiazoles. For this reason, 4-dimethylaminopyridine was used as the catalyst [20] together with triethylamine in the case of compounds **22–26** or pyridine for substances **27–30**. This modification proved to be beneficial in each case.

Structure elucidation of the new compounds **13–30** was performed by means of elemental analysis, as well as IR and ^{1}H NMR spectroscopic measurements. In their IR spectra, a characteristic amide C=O band was observed between 1657 and 1672 cm^{-1} proving the presence of an N-acyl moiety in the molecule. In the ^{1}H NMR spectra of compounds **13–21** both the N-acetyl signal at *ca.* 2.0 ppm and the signal of the 4-H proton at around 7.9–8.0 ppm were broad singlets in each case, indicating a hindered rotation of the N-acetyl group. Splitting of the ^{1}H signal of the 4-H proton into a doublet with coupling constant of 7.8–7.9 Hz in the case of the 3-propionyl derivatives **22–26** and a considerable broadening of the signal of this aromatic proton in the N-benzoyl derivatives **27–30** refer to the hindered rotation of the N-acyl moiety in these 2,3-dihydrobenzothiazoles. The ^{1}H NMR signal of the β-H proton is a well separated doublet between 6.0–7.0 ppm with a coupling constant of *ca.* 16 Hz, indicating the presence of an α,β-disubstituted ethylene moiety in the molecule. The ^{1}H signal of the α-H proton is overlapped by the aromatic signals.

In summary, a simple and convenient procedure for the preparation of hitherto unknown 3-acyl-2,3-dihydrobenzothiazoles was developed using the ring contraction of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines under acylating conditions. The addition of 4-dimethylaminopyridine as catalyst seems to be especially beneficial.

Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker WP 200 SY spectrometer at 200 MHz in $CDCl_3$ (internal standard *TMS*, $\delta = 0.0$ ppm) at room temperature. The IR spectra (KBr discs) were measured with a Perkin-Elmer 16 PC instrument. TLC was performed on Kieselgel 60 F_{254} (Merck) layer using hexane:acetone (7:3 v/v) or toluene:ethyl acetate (4:1 v/v) as eluents. Starting materials **1–12** were synthesized according to Refs. [10–12, 14]. Elemental analysis (C, H, N) was in good agreement with the calculated values.

General procedures for the synthesis of 3-acetyl-2-aryl-2-(β-arylvinyl)-2,3-dihydrobenzothiazoles **13–21**

Method i. A mixture of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepine **3**, **5–12** (5.0 mmol), acetic anhydride (15.0 ml), and anhydrous pyridine (8.0 ml) was maintained at 80°C for 7 h and then poured

into water. The precipitate was filtered off, washed with water, and purified by column chromatography using silica gel (Merck) and hexane:acetone (7:3 v/v) as eluent to afford compounds **13**–**21**.

Method ii. 2,4-Diaryl-2,3-dihydro-1,5-benzothiazepine **6**–**12** (5.0 mmol) was refluxed in a mixture of acetic anhydride (10.0 ml), triethylamine (5.0 ml), and 4-dimethylaminopyridine (0.5 g) for 3 h and then poured into water. The crude product was extracted with chloroform (3×50 ml), the separated organic phase was washed with brine and dried over $CaCl_2$, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography as described for *Method i* to obtain compounds **15**–**21**.

3-Acetyl-2,3-dihydro-2-(4-methoxyphenyl)-2-styrylbenzothiazole (**13**; $C_{24}H_{21}NO_2S$)

Yield (*Method i*): 62.5%;m.p.: 112–113°C; IR (KBr): $\nu = 1667$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.87 (s, 3H), 3.71 (s, 3H), 6.51 (d, 1H), 6.89–7.96 (m, lH+13 arom. H) ppm.

3-Acetyl-2-(4-bromophenyl)-2,3-dihydro-2-styrylbenzothiazole (**14**; $C_{23}H_{18}BrNOS$)

Yield (*Method i*): 66.3%; m.p.: 78–79°C; IR (KBr): $\nu = 1670$ (C=O) cm^{-1}; ^1H NMR (200 MHZ, δ, $CDCl_3$): 2.08 (s, 3H), 6.56 (d, 1H), 6.89 (d, 1H), 7.08–7.95 (m, 13 arom. H) ppm.

3-Acetyl-2,3-dihydro-2-(β-(1-naphthyl)vinyl)-2-phenylbenzothiazole (**15**; $C_{27}H_{21}NOS$)

Yield (*Method ii*): 71.8%; m.p.: 95–96°C; IR (KBr): $\nu = 1671$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 2.01 (s, 3H), 6.93 (d, 1H), 7.04–7.96 (m, 1H+16 arom. H) ppm.

3-Acetyl-2,3-dihydro-2-(β-(2-naphthyl)vinyl)-2-phenylbenzothiazole (**16**; $C_{27}H_{21}NOS$)

Yield (*Method ii*): 63.0%; m.p.: 83–84°C; IR (KBr): $\nu = 1660$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 2.00 (s, 3H), 6.75 (d, 1H), 7.03–7.97 (m, 1H+16 arom. H) ppm.

3-Acetyl-2-(4-chlorophenyl)-2,3-dihydro-2-(β-(2-naphthyl)vinyl)benzothiazole (**17**; $C_{27}H_{20}ClNOS$)

Yield (*Method ii*): 63.6%; m.p. 111–112°C; IR (KBr): $\nu = 1662$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 2.02 (s, 3H), 6.60 (d, 1H), 7.02 (d, 1H), 7.04–7.87 (m, 15 arom. H) ppm.

3-Acetyl-2,3-dihydro-2-(3,4-methylenedioxyphenyl)-2-(β-2-naphthyl)vinyl) benzothiazole (**18**; $C_{28}H_{21}NO_3S$)

Yield (*Method ii*): 63.7%; m.p.: 185–186°C; IR (KBr): $\nu = 1671$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.99 (s, 3H), 5.99 (s, 2H), 6.56 (d, 1H), 6.74–7.99 (m, 1H+14 arom. H) ppm.

3-Acetyl-2,3-dihydro-2-(β-(2-naphthyl)vinyl)-2-phenylbenzothiazole (**19**; $C_{27}H_{21}NOS$)

Yield (*Method ii*): 62.7%; m.p.: 97–98°C; IR (KBr): $\nu = 1671$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.97 (s, 3H), 6.63 (d, 1H), 7.02–8.03 (m, 1H+16 arom. H) ppm.

3-Acetyl-2,3-dihydro-2-(β-(9-phenanthryl)vinyl)-2-phenylbenzothiazole (**20**; $C_{31}H_{23}NOS$)

Yield (*Method ii*): 90.9%; m.p.: 107–108°C; IR (KBr): $\nu = 1672$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 2.03 (s, 3H), 7.01 (d, 1H), 7.07–8.64 (m, 1H+18 arom. H) ppm.

3-Acetyl-2,3-dihydro-2-(9-phenanthryl)-2-styrylbenzothiazole (**21**; $C_{31}H_{23}NOS$)

Yield (*Method ii*): 66.6%; m.p.: 177–178°C; IR (KBr): $\nu = 1672$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 2.01 (s, 3H), 7.02 (d, 1H), 7.04–8.60 (m, 1H+18 arom. H) ppm.

General procedure for the preparation of 2-aryl-2-(β-arylvinyl)-2,3-dihydro-3-propionylbenzothiazoles **22–26**

A mixture of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepine **1**, **3**, **4**, **7**, or **8** (5.0 mmol), propionic anhydride (10.0 ml), triethylamine (5.0 ml), and 4-dimethylaminopyridine (0.5 g) was refluxed for 4 h and then poured into water. The reaction mixture was worked up as described in *Method ii* for compounds **15–21** to yield **22–26**.

2,3-Dihydro-2-phenyl-3-propionyl-2-styrylbenzothiazole (**22**; $C_{24}H_{21}NOS$)

Yield: 70.3%; m.p.: 74–75°C; IR (KBr): $\nu = 1663$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.00 (t, 3H), 1.99 (m, 1H), 2.31 (m, 1H), 6.59 (d, 1H), 6.96 (d, 1H), 7.06–7.92 (m, 14 arom. H) ppm.

2,3-Dihydro-2-(4-methoxyphenyl)-3-propionyl-2-styrylbenzothiazole (**23**; $C_{25}H_{23}NO_2S$)

Yield: 60.9%; m.p.: 77–78°C; IR (KBr): $\nu = 1670$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.01 (t, 3H), 1.97 (m, 1H), 2.27 (m, 1H), 3.85 (s, 3H), 6.51 (d, 1H), 6.89–7.92 (m, 1H+13 arom. H) ppm.

2-(4-Chlorophenyl)-2,3-dihydro-3-propionyl-2-styrylbenzothiazole (**24**; $C_{24}H_{20}ClNOS$)

Yield: 70.0%; IR (KBr): $\nu = 1665$ (C=O) cm^{-1}; ^1H NMR (200 Mz, δ, $CDCl_3$): 1.09 (t, 3H), 2.18 (m, 1H), 2.41 (m, 1H), 6.59 (d, 1H), 6.90 (d, 1H), 7.02–7.71 (m, 13 arom. H) ppm.

2,3-Dihydro-2-(β-(2-naphthyl)vinyl)-2-phenyl-3-propionylbenzothiazole (**25**; $C_{28}H_{23}NOS$)

Yield: 57.1%; m.p.: 121–122°C; IR (KBr): $\nu = 1670$ (C=O) cm^{-1}; ^1H NMR (200 Mz, δ, $CDCl_3$): 1.00 (t, 3H), 2.01 (m, 1H), 2.36 (m, 1H) 6.63 (d, 1H), 7.03–8.01 (m, 1H+16 arom. H) ppm.

2-(4-Chlorophenyl)-2,3-dihydro–2-(β-(2-naphthyl)vinyl)-3-propionylbenzothiazole (**26**; $C_{28}H_{22}ClNOS$)

Yield: 63.6%; m.p.: 92–93°C; IR (KBr): $\nu = 1670$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.00 (t, 3H), 2.10 (m, 1H), 2.38 (m, 1H), 6.57 (d, 1H), 7.01–7.89 (m, 1H+15 arom. H) ppm.

General procedure for the synthesis of 2-aryl-2-(β-arylvinyl)-3-benzoyl-2,3-dihydrobenzothiazoles **27–30**

A mixture of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepine **1**, **2**, **5**, or **6** (5.0 mmol), anhydrous pyridine (20.0 ml), benzoic anhydride (15.0 mmol), and 4-dimethylaminopyridine (0.5 g) was refluxed for 6 h and then poured into water. The precipitated material was extracted with chloroform (3×50.0 ml), and the solution was worked up as described in *Method ii* for compounds **15–21** to afford **27–30**.

3-Benzoyl-2,3-dihydro-2-phenyl-2-styrylbenzothiazole (**27**; $C_{28}H_{21}NOS$)

Yield: 54.3%; m.p.: 76–77°C; IR (KBr): $\nu = 1661$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 6.27 (d, 1H), 6.67–8.10 (m, 1H+19 arom H) ppm.

3-Benzoyl-2-(2-chlorostyryl)-2,3-dihydro-2-phenylbenzothiazole (**28**; $C_{28}H_{20}ClNOS$)

Yield: 66.1%; m.p.: 94–95°C; IR (KBr): $\nu = 1657$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 6.30 (d, 1H), 6.74–8.08 (m, 1H+18 arom. H) ppm.

3-Benzoyl-2-(4-bromophenyl)-2,3-dihydro-2-styrylbenzothiazole (**29**; $C_{28}H_{20}BrNOS$)

Yield: 55.6%; m.p.: 188–189°C; IR (KBr): $\nu = 1659$ (C=O) cm^{-1}, ^1H NMR (200 MHz, δ, $CDCl_3$): 6.07 (d, 1H), 6.75–7.72 (m, 1H+18 arom. H) ppm.

3-Benzoyl-2,3-dihydro-2-(β-(1-naphthyl)vinyl)-2-phenylbenzothiazole (**30**; $C_{32}H_{23}NOS$)

Yield: 59.0%; m.p.: 138–139°C; IR (KBr): $\nu = 1660$ (C=O) cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 6.29 (d, 1H), 6.79–8.12 (m, 1H+21 arom. H) ppm.

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