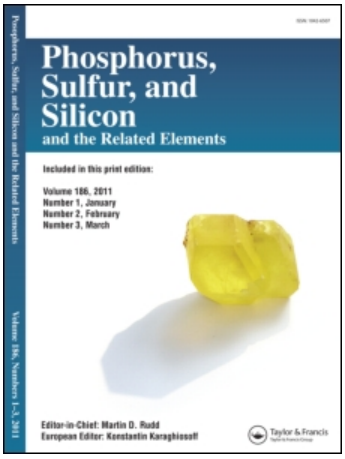

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REACTION BETWEEN 2,2′-DITHIODIANILINE AND FIVE-MEMBERED RING KETONES[1a]

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ABSTRACT

The acid-catalyzed reaction between 2,2′-dithiodianiline (**1**) and various five-membered ring ketones yields, in the absence of oxygen, the expected 1,4-benzothiazines. On exposure to air, the latter undergo an autoxidation process, according to a previously described general pathway. From the autoxidation of **12**, the hemithioketal **16** has been isolated, and its peculiar properties are discussed.

In connection with previous works of this series,[1b] the reaction between 2,2′-dithiodianiline (**1**) and various five-membered ring ketones has been studied.

The reaction of **1** with cyclopentanone (**2**), carried out in the absence of air, yields the expected 1,2,3,9-tetrahydrobenzo[b]cyclopenta[e][1,4]thiazine (**3**), which, on treatment with $NaBH_4$, is reduced to the dihydro derivative **4**. On exposure to air in cyclohexane solution, **3** gives rise to tarry materials, which have not been further investigated.

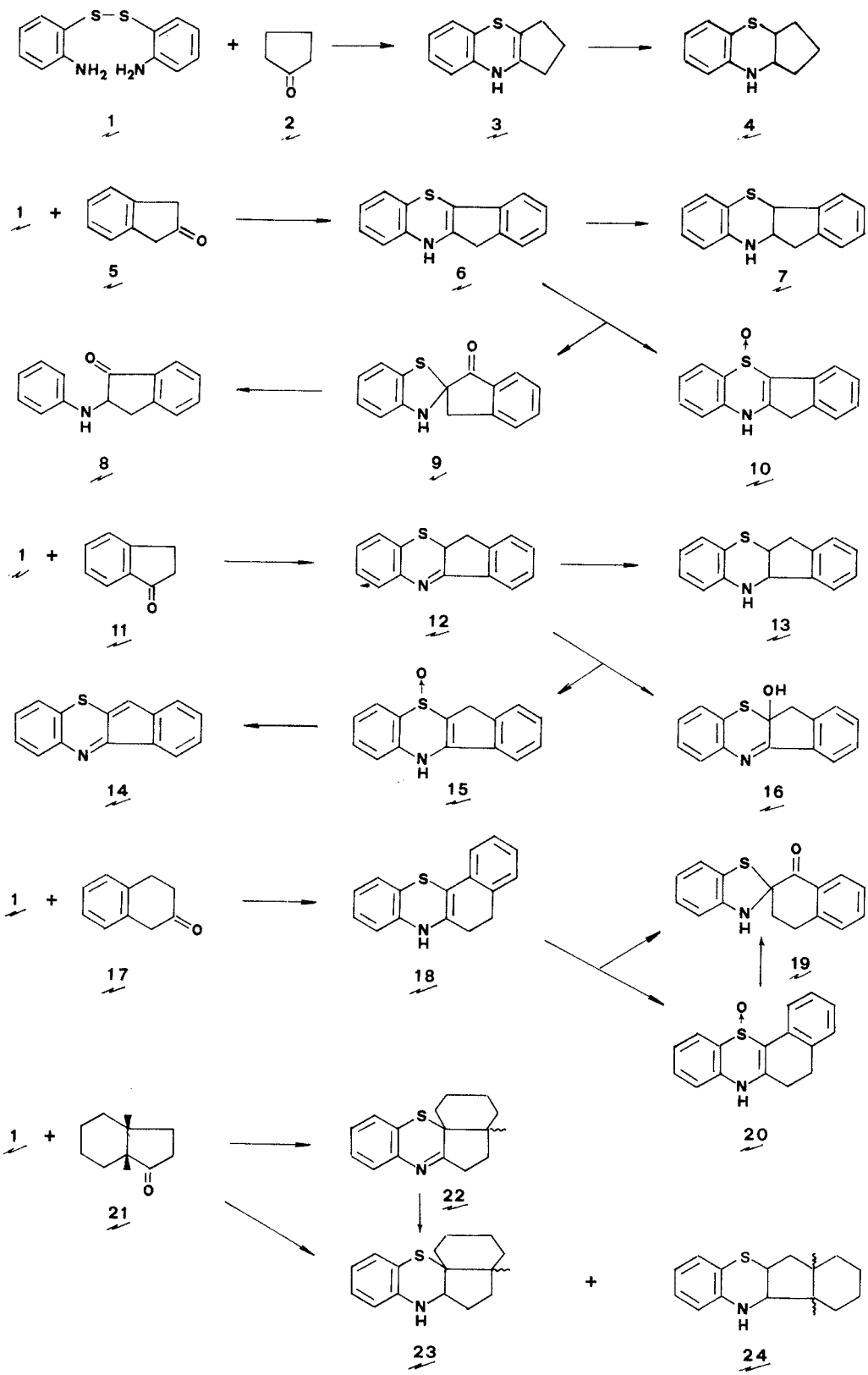
From the reaction of **1** with 2-indanone (**5**), the expected 10,11-dihydrobenz[b]indeno[2,1-e][1,4]-thiazine (**6**) could be isolated. On treatment with $NaBH_4$, **6** yields the dihydro derivative **7**, and on exposure to air it undergoes an autoxidation process,[2] yielding the spiro[benzothiazol-2(3*H*),2′-indan-1′-one] (**9**) and the 10,11-dihydrobenz[b]indeno[2,1-e][1,4]-thiazine-5-oxide (**10**). The structures **9** and **10** are consistent with the spectral data; furthermore, Raney Nickel desulfurization of **9**, gives 2-anilino-1-indanone (**8**), whose structure can be unambiguously deduced from its nmr spectrum. As additional evidence, **9** was prepared following an independent route reacting 2-mercaptoaniline with 1,2-indandione; it should be noted that this reaction was studied by Leaver *et al.*,[3] who surprisingly isolated as the only product the benz[b]indeno[1,2-e][1,4]thiazine-10*a*(11*H*)-ol (**16**) with a yield of *ca.* 50%. In our hands the above reaction, in the reported[3] experimental conditions, gives both **9** and **16**, in the molar ratio of 1 : 3.

Reaction between **1** and 1-indanone (**11**) yields the expected 10*a*,11-dihydrobenz[b]indeno[1,2-e][1,4]-thiazine (**12**), which could be reduced by $NaBH_4$ to the dihydro derivative **13**, and oxidized to 5,11-dihydrobenz-[b]indeno[1,2-e][1,4]thiazine-10-oxide (**15**) and (**16**), on exposure to air. It therefore appears that the reaction of **1** with 2-indanone and 1-indanone follows the general pathway reported by us for the reaction between **1** and ketones.[2]

On the contrary, a peculiar chemical behavior was observed for both autoxidation products **15** and **16**, derived from 1,4-thiazine **12**. In fact, compound **15** can be transformed in the already described[3] benz[b]-indeno[1,2-e][1,4]thiazine (**14**) by treatment with SiO_2. According to our previous reports, sulfoxides similar to **15** can be generally converted, under suitable experimental conditions, either into spiroketones analogous to **29** or in elimination products analogous to **14**, and both of these transformations proceed *via* a common intermediate with hemithioketal structure, analogous to **16**.[2] The transformation of **15** into **14** does not fit in this general scheme, as **16** is stable under the conversion conditions, and can be reasonably ascribed to a direct β-elimination process, promoted by the presence of the two benzylic protons at the β position with respect to the sulfur atom.

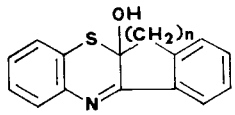
As already mentioned, **16** also displays a peculiar chemical behavior; for example, the conversion of **16** into the corresponding spiroketone **29** could not be observed. While a detailed study of the reactivity of **16** will be published elsewhere, it should be noted that **16** is the second example of a hemithioketal intermediate

SCHEME I



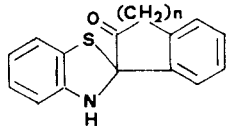
we isolated, and that the first hemithioketal was observed in the course of a similar study on ketone homologs of **11**, namely 1-oxo-1,2,3,4-tetrahydronaphthalene.[2] This observation led us to investigate the reaction between **1** and 2-oxo-1,2,3,4-tetrahydronaphthalene (**17**) as well, yielding 5,6-dihydro-7*H*-benz[c]phenothiazine (**18**), that by exposure to air, gives spiro[benzothiazole-2(3*H*),2′-(1′-oxo-1′,2′,3′,4′-tetrahydronaphthalene)] (**19**) and 5,6-dihydro-7*H*-benzo[c]phenothiazine-12-oxide (**20**). Furthermore, **20** is converted into **19** by treatment with SiO_2. It is evident from the above results that the behavior of **17** is the same as that of **5**: it is therefore possible to state that a uniform behavior does exist for the homologous members of the two series of ketones studied, *i.e.* 1-indanone and 1-tetralone, 2-indanone and 2-tetralone.

As repeatedly mentioned, the hemithioketal intermediates in the autoxidation process of 1,4-thiazines cannot be generally isolated, as they spontaneously evolve to the isomeric spiroketones. On the other hand, the finding that the hemithioketals **16** and **28** were isolated in the place of the corresponding isomeric spiroketones can be rationalized taking into account the stabilizing effect of the delocalized π electrons on the extended conjugated system, typical of these structures.



16) n = 1

28) n = 2



29) n = 1

30) n = 2

It is interesting to point out that, at least in the case of **28**, the hemithioketal structure seems stabilized even when intermolecular interactions, such as hydrogen bond formation, are likely to occur. Such interactions are indeed present in the solid compound, and in its dioxane solution as clearly demonstrated by the corresponding ir spectra, showing OH stretching bands at 3280 and 3330 cm^{-1}, respectively. On the other hand, the OH stretching band falls at 3560 cm^{-1} in the ir spectrum of the chloroform solution of **28**, indicating the absence of hydrogen bonding, and a partial conversion of the hemithioketal **28** into the corresponding spiroketone **30** is observed.[2]

The ir spectra of the solid compound **16** and of its dioxane solution as well show the formation of hydrogen bonds (OH stretching bands at 3050, 2770[4] and 3330 cm^{-1}, respectively), although a full comparison with

TABLE I

1,4-Benzothiazines from the Reaction of 1 with Ketones

Ketone	Time hr	Compd	Yield %	Mp (solvent)	Formula	IR, cm^{-1}	NMR[a]
2	2	**3**	80	120-1° (ligroin/2-propanol)	$C_{11}H_{11}NS$	3320 (NH) 1645 (C=C)	7.5-6.4, 4 H, aromatic H 3.5-1.3, 6 H, methylene H
5	0.5	**6**	95	140-1° (EtOAc)	$C_{15}H_{11}NS$	3360 (NH) 1630 (C=C)	7.48, 8 H, aromatic H[b] 5.49, 1 H, H_b 4.70, 2 H, methylene H
11	10	**12**	70	108-9° (EtOH)	$C_{15}H_{11}NS$	1630 (C=N)	8.1-7.9, 1 H, aromatic H 7.6-6.9, 7 H, aromatic H 3.8-2.7, 3 H, H_b + methylene H
17	4	**18**	70	87-9° (Ligroin/EtOH)	$C_{16}H_{13}NS$	3320 (NH) 1635 (C=C)	7.4-6.2, 8 H, aromatic H 4.21, 1 H, NH 3.0-2.5, 2 H, methylene H 2.4-2.0, 2 H, methylene H
21	12	**22**	70	137-8° (MeOH)	$C_{15}H_{17}NS$	1645 (C=N)	7.5-6.9, 4 H, aromatic H 2.9-2.6, 2 H, allylic H 2.6-2.2, 1 H, methine H 2.2-1.0, 10 H, methylene H

[a] The hydrogen atoms adjacent to the nitrogen and sulfur atoms are indicated as H_a and H_b, respectively.

[b] CF_3COOH was used as solvent.

28 was not possible, owing to the very low solubility of 16 in chloroform.

In connection with the study of the reactivity of five-membered ring ketones, the reaction between 1 and *cis*-perhydro-1-indanone (21) was also explored. In this case, by crystallization of the crude reaction mixture, 2,3,4,4*a*,5,6-hexahydro-1*H*-benz[b]indeno-[3,3*a*-e][1,4]thiazine (22) was isolated. The simultaneous formation of an isomeric 1,4-thiazine was demonstrated by isolating 1,2,3,4,4*a*,4*b*,5,10*a*,11,11*a*-decahydrobenz[b]indeno[1,2-e][1,4]thiazine (24). together with 2,3,4,4*a*,5,6,6*a*,7-octahydro-1*H*-benz[b]-indeno[3,3*a*-e][1,4]thiazine (23), in the molar ratio of 1:3, after reduction with $NaBH_4$ of the crude reaction mixture.

Experimental Section

All melting points were taken on a Kofler apparatus and are uncorrected. Infrared spectra as nujol mulls or liquid films were determined on a Perkin Elmer 257 grating spectrophotometer. Nuclear magnetic resonance spectra, unless otherwise stated, were obtained on a Varian HA-100 spectrometer using $CDCl_3$ as solvent and tetramethylsilane ($\delta = 0$ ppm) as internal standard. Preparative thin-layer chromatography (PLC) was performed on Merck PF_{254} silica gel coated plates using a mixture of light petroleum ether/EtOAc (9:1) as solvent. All compounds were analyzed for C, H, N, S and gave analytical results within ±0.3% of the theoretical values.

Reaction Between 1 and Ketones

1 and the appropriate ketone in the molar ratio 1:1 were refluxed in benzene containing catalytic amounts of *p*-toluene-

TABLE II

Reduction Products of the 1,4-Benzothiazines

Compd	Yield %	Mp (solvent)	Formula	IR: NH, cm^{-1}	NMR[a]
4	60	N–Ac deriv. 102–3° (EtOH)	$C_{11}H_{13}NS$	3390	7.2–6.3, 4 H, aromatic H 3.78, 1 H, NH 3.7–3.4, 1 H, H_a 3.3–3.0, 1 H, H_b 2.2–1.2, 6 H, methylene H
7	85	109–10° (2-propanol)	$C_{15}H_{13}NS$	3350	7.5–6.5, 8 H, aromatic H 4.37, 1 H, H_a 4.18, 1 H, H_b 4.10, 1 H, NH 3.4–2.8, 2 H, methylene H
13	98	102–3° (EtOH)	$C_{15}H_{13}NS$	3400	7.2–6.3, 8 H, aromatic H[b] 4.68, 1 H, H_a 3.88, 1 H, NH 3.72, 1 H, H_b 3.4–2.8, 2 H, methylene H
23		90–1° (EtOH)	$C_{15}H_{19}NS$	3380	7.1–6.4, 4 H, aromatic H 3.92, 1 H, NH 3.7–3.4, 1 H, H_a 2.3–1.0, 13 H, methylene and methine H
24		142–3°(EtOH)	$C_{15}H_{19}NS$	3360	7.2–6.5, 4 H, aromatic H 4.00, 1 H, NH 3.9–3.7, 1 H, H_a 3.28, 1 H, H_b 2.3–0.9, 12 H, methylene and methine H

[a] See corresponding footnote in Table I.

[b] CCl_4 was used as solvent.

sulfonic acid, under N_2, for the indicated time (Table I). Compound **6** precipitates out from the reaction mixture; it was collected by suction and purified by crystallization. In other cases, the benzene solution was cooled at room temperature, 5 *N* KOH added, the organic layer separated, dried (Na_2SO_4), and concentrated. Compounds **12** and **18** were isolated from the residue by crystallization; in the reaction carried out with ketones **2** and **21**, the residue was distilled under vacuum; crystallization of the distillate gave pure **3** and **22**, respectively. All 1,4-benzothiazines, but **22**, undergo autoxidation; they were therefore manipulated in the absence of air.

$NaBH_4$ Reduction of the 1,4-Benzothiazines

An excess of $NaBH_4$ was added portionwise to a stirred solution of the 1,4-benzothiazine in a EtOH/AcOH mixture 2:1, maintained under N_2 at room temperature, the course of the reaction being monitored by tlc. The solvent was evaporated, CH_2Cl_2 and 2 *N* NaOH added, the organic layer was separated, dried (Na_2SO_4), and concentrated. Plc of the residue gave the corresponding dihydro-1,4-benzothiazine, further purified by crystallization (Table II).

Autoxidation of the 1,4-Benzothiazines 6,12,18

A cyclohexane solution of the 1,4-benzothiazine was stirred under air at room temperature for 12 hr. A mixture of the autoxidation products was formed, and resolved by extracting **9** from **10** with Et_2O, **15** from **16** with $CHCl_3$, and **19** from **20** with Me_2CO, respectively. The separated compounds were further purified by crystallization (Table III).

Compound **9** was also obtained by reacting equimolar amounts of 2-mercaptoaniline and 1,2-indandione in EtOH solution, in the presence of piperidine acetate.[3] Both **9** and **16** were formed (approximately in the molar ratio 1:3), and were separated by column chromatography on 70-325 mesh SiO_2 Merck: elution with light petroleum ether/EtOAc 9:1 gave **9**, elution with EtOH gave **16**.

The structure of **9** was proved by Raney Nickel desulfurization (Me_2CO, 10 hr under reflux) to 2-anilino-1-indanone (**8**), mp 91-2° (EtOH); ir 3380 (NH) and 1700 cm^{-1} (C=O); nmr

TABLE III

Autoxidation products of the 1,4-benzothiazines

Compd	Yield %	Mp (solvent)	Formula	IR, cm^{-1}	NMR[a]
9	50	161-2° (EtOAc)	$C_{15}H_{11}NOS$	3360 (NH) 1700 (C=O)	7.9-6.7, 8 H, aromatic H 4.14, 1 H, NH 3.9-3.4, 2 H, methylene H
10	50	198-9°	$C_{15}H_{11}NOS$	3210, 3140 (NH) 1610 (C=C) 970 (S→O)	*b*
15	48	158-9° ($CHCl_3/Et_2O$)	$C_{15}H_{11}NOS$	3210, 3150 (NH) 1620 (C=C) 960 (S → O)	11.25, 1 H, NH 6.9-6.5, 8 H, aromatic H 3.9-3.3, 2 H, methylene H
16	48	208-9° (EtOH)	$C_{15}H_{11}NOS$	3050, 2770 (OH) 1630 (C=N)	8.80, 1 H, OH[c] 8.6-8.3, 1 H, aromatic H 8.0-7.1, 7 H, aromatic H 4.1-3.3, 2 H, methylene H
19	50	126-7° (2-propanol)	$C_{16}H_{13}NOS$	3320 (NH) 1680 (C=O)	8.2-8.0, 1 H, aromatic H 7.6-6.7, 7 H, aromatic H 4.70, 1 H, NH 3.6-2.1, 4 H, methylene H
20	50	162-3° (Me_2CO/MeOH)	$C_{16}H_{13}NOS$	3230, 3140 (NH) 1615 (C=C) 980 (S→O)	10.90, 1 H, NH 8.0-7.8, 2 H, aromatic H 7.4-6.7, 6 H, aromatic H 2.6-1.6, 4 H, methylene H

[a] See corresponding footnote in Table I.

[b] The nmr spectrum of **10** could not be obtained since it is practically insoluble in common organic solvents.

[c] The nmr spectrum of **16** was recorded on a Varian A-60 spectrometer in C_5D_5N.

δ 7.9–7.1 (6 H, aromatic H), 6.9–6.6 (3 H, aromatic H), 4.34 (1 H, NH), 4.16 (1 H, H_a), 3.76 (1 H, benzylic H), and 2.96 ppm (1 H, benzylic H).

Conversion of 20 into 19

A mixture of **20** (0.30 g), 70-325 mesh SiO_2 Merck (0.30 g), and $CHCl_3$ (40 ml) was stirred at room temperature for 6 hr, the solid filtered off, and the filtrate concentrated. Plc of the residue gave **19** (0.25 g).

Conversion of 15 into 14

A mixture of **15** (0.30 g), 70-325 mesh SiO_2 (0.30 g), and $CHCl_3$ (50 ml) was stirred at room temperature for 12 hr, the solid was filtered off, and the filtrate concentrated. Plc of the residue gave **14** (0.20 g), mp 169-70°(EtOH) (Lit.[3] mp 169.5-70°)

Acknowledgment

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References and Notes

1. *a.* Part XI in the series: "A new reaction of bis(*o*-aminophenyl) disulfide with ketones."
   b. Part X: See previous paper.
2. V. Carelli, F. Micheletti Moracci, F. Liberatore, M. Cardellini, M. G. Lucarelli, P. Marchini, G. Liso, and A. Reho, *Int. J. Sulfur Chem.*, 8, 267 (1973), and previous paper in the series.
3. D. Leaver, J. Smolicz, and W. H. Stafford, *J. Chem. Soc.*, 740 (1962).
4. Leaver *et al.*[3] have reported for compound **16** a very weak OH band at 3620 cm^{-1}, which we have consistently failed to observe.