Reactions of *cis*- and *trans*-6,6a,7,8,9,10,10a,11-Octahydro-11-oxodibenzo[*b,e*]thiepins and -Oxepins

Mikio Kurokawa*, Hitoshi Uno, Akira Itogawa, Fuminori Sato, Shunsuke Naruto and Jun-ichi Matsumoto

Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Enoki 33-94, Suita, Osaka 564, Japan

Received July 15, 1991

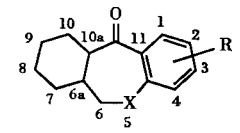
Several reactions of 6,6a,7,8,9,10,10a,11-octahydro-11-oxodibenzo[*b,e*]thiepins and -oxepins were studied, which included reduction, oxidation, the Grignard reaction, thiation, and the Wittig reaction. Stereochemistry of the reaction products was confirmed on the basis of proton nuclear magnetic resonance analysis.

J. Heterocyclic Chem., **28**, 1891 (1991).

In the previous papers [1] [2], we reported the synthesis and stereochemistry of new tricyclic compounds, *trans*- and *cis*-6,6a,7,8,9,10,10a,11-octahydro-11-oxodibenzo-[*b,e*]thiepins **1** and **2** and -oxepins **3** and **4**, as well as their acetic acid derivatives **5** which possessed potent antiinflammatory activity. However, their chemical and biological properties have not extensively been studied thus far in contrast to the corresponding dibenzo derivatives [3] [4]. It became interest to us to study chemical properties of the octahydro derivatives **1-4** in order to develop biologically-active compounds with a new tricyclic nucleus. Hence we chose to investigate several fundamental reactions of **1-4**, which reactions included reduction, oxidation, the Grignard reaction, thiation and the Wittig reaction; this is the primary subject of the present paper.

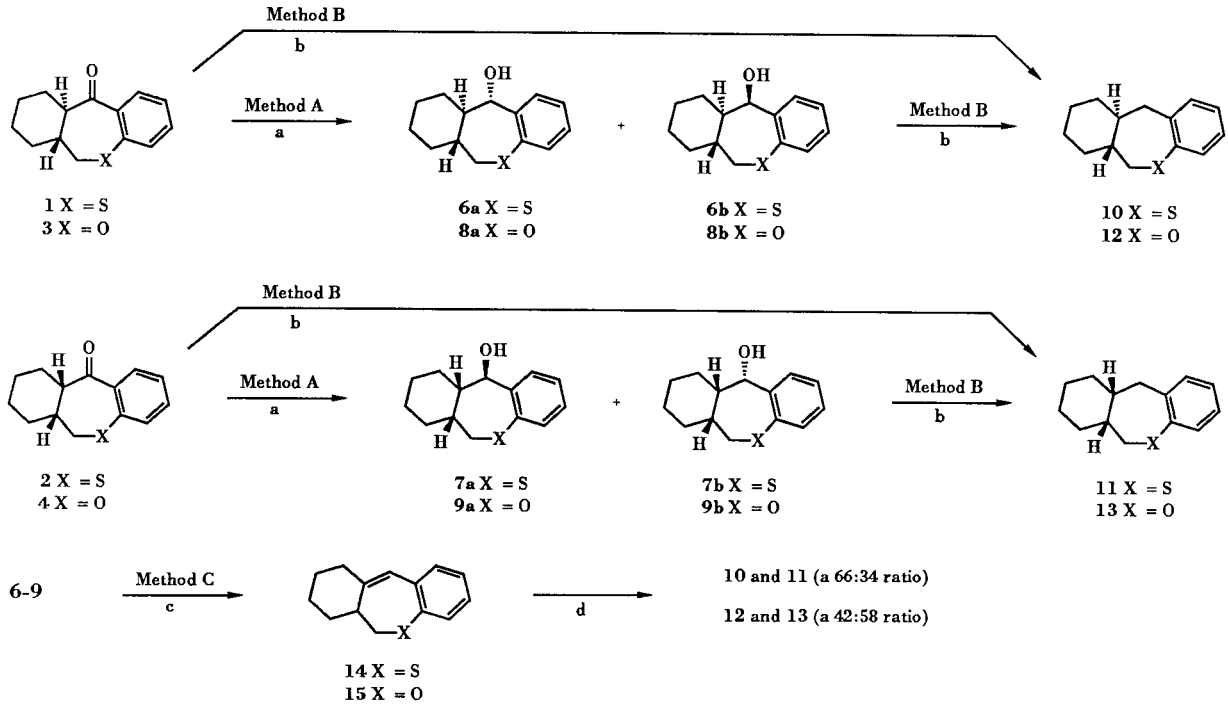
Reductions.

Reductions of *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-oxodibenzo[*b,e*]thiepin **1** and -oxepin **3** with sodium borohydride in methanol at 5° gave *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-hydroxydi-



1 X = S, R = H, 6a, 10a-trans
2 X = S, R = H, 6a, 10a-cis
3 X = O, R = H, 6a, 10a-trans
4 X = O, R = H, 6a, 10a-cis
5 X = S,O, R = CH(Me)COOH

Chart 1

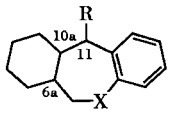


a: $NaBH_4$/MeOH b: $NaBH_4$/CF_3COOH c: HCl/EtOH d: H_2, Pd-C/EtOH

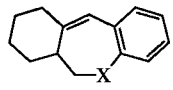
Chart 2

Table I

Physical Properties of the Reduction Products 6-15



6-13



14, 15

Compound No.	X	R	Stereochemistry 6a-*H*/10a-*H*	Stereochemistry 10a-*H*/11-*H*	Method [a]	Yield (%)	Mp (°C)	Recrystallization Solvent	t_R [b] (minutes)	Formula	Analysis (%) Calcd. (Found) C	H	S
6a	S	OH	*trans*	*trans*	A	5	[c]		28.9	$C_{14}H_{18}OS$	71.75 (71.78	7.74 8.04	13.68 13.79)
6b	S	OH	*trans*	*cis*	A	88	[c]		25.9	$C_{14}H_{18}OS$	71.75 (71.77	7.74 7.70	13.68 13.66)
7a	S	OH	*cis*	*trans*	A	71	[c]		20.5	$C_{14}H_{18}OS$	71.75 (71.68	7.74 7.86	13.68 13.46)
7b	S	OH	*cis*	*cis*	A	20	73	ether	19.9	$C_{14}H_{18}OS$	71.75 (71.75	7.74 7.98	13.68 13.75)
8a	O	OH	*trans*	*trans*	A	35	154	AcOEt	16.1	$C_{14}H_{18}O_2$	77.03 (77.13	8.31 8.23)	
8b	O	OH	*trans*	*cis*	A	60	[c]		16.6	$C_{14}H_{18}O_2$	77.03 (77.02	8.31 8.29)	
9a	O	OH	*cis*	*trans*	A	10	111	ether	12.7	$C_{14}H_{18}O_2$	77.03 (76.89	8.31 8.27)	
9b	O	OH	*cis*	*cis*	A	84	110	ether	14.3	$C_{14}H_{18}O_2$	77.03 (77.23	8.31 8.44)	
10	S	H	*trans*		B	74	[c]		6.0 [d]	$C_{14}H_{18}S$	77.01 (76.88	8.31 8.51	14.68 14.46)
11	S	H	*cis*		B	68	[c]		7.1 [d]	$C_{14}H_{18}S$	77.01 (77.26	8.31 8.11	14.68 14.53)
12	O	H	*trans*		B	73	71	hexane	2.9 [d]	$C_{14}H_{18}O$	83.12 (83.36	8.97 9.05)	
13	O	H	*cis*		B	70	[c]		3.3 [d]	$C_{14}H_{18}O$	83.12 (82.96	8.97 8.86)	
14	S				C	62	[c]		11.7 [e]	$C_{14}H_{16}S$	77.72 (77.56	7.45 7.46	14.82 14.75)
15	O				C	58	[c]		5.5 [e]	$C_{14}H_{16}O$	83.96 (83.99	8.05 7.96)	

[a] See Experimental. [b] Hplc: Shimadzu STR ODS-M column, 4.6 x 150 mn i.d. at 35°, mobil phase, 1% acetic acid/acetonitrile (60/40), flow rate, 1.0 ml/minute, detection, 254 nm. [c] Oil. [d] Capillary glc: PEG 20M column, 12.5 m x 0.25 mn i.d. at 180°. [e] Capillary glc: PEG 20M column, 12.5 m x 0.25 mm i.d. at 190°.

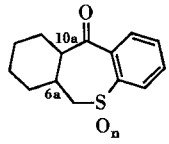
benzo[*b,e*]thiepin **6** and -oxepin **8**, respectively (Method A) (Chart 2). Analogous reduction of the *cis*-6a-*H*,10a-*H*-ketones **2** and **4** afforded the *cis*-6a-*H*,10a-*H*-alcohols **7** and **9**, respectively. Each alcohol **6-9** was separated by preparative high-performance liquid chromatography (hplc) into two enantiomers **A**, **6a-9a**, and **B**, **6b-9b**, concerning the C-11 configuration (Table I).

The alcohols **6a,b**, **7a**, **8a,b** and **9a** showed broad peaks in their ^1H and ^{13}C nmr spectra in deuteriochloroform at room temperature. In particular, the signals for 6a-*H*, 10a-*H* and 11-*H* were so broad that no J values were obtainable; however the spectra at 100-120° in nitrobenzene-d_5 showed sharp signals. This observation implies that the conformations of these compounds are very flexible. The 10a-*H* and 11-*H* configurations of the isomers **6a,b-9a,b** were assigned on the basis of the ^1H nmr spectra measured at 120° in nitrobenzene-d_5, particularly coupling constants between 10a-*H* and 11-*H* (Table III). Thus, $J_{10a,11}$ values of the enantiomer **A**, **6a-9a** were in a range of 6.5-8.6 Hz, which permitted the assignment of **6a-9a** as the *trans*-10a-*H*,11-*H*-isomers. The 10a-*H* and 11-*H* of the enantiomer **B** **6b-9b**, have rather small coupling constants of J = 0.9-2.1 Hz, therefore strongly indicative of the *cis*-10a-*H*,11-*H*-isomers.

Reductions of the *trans*-6a-*H*,10a-*H*-ketones **1** and **3** with sodium borohydride in cold (−10°) trifluoroacetic acid (Method B) [5] gave the *trans*-6a-*H*,10a-*H*-deoxo compounds **10** and **12**, respectively. On the same treatment,

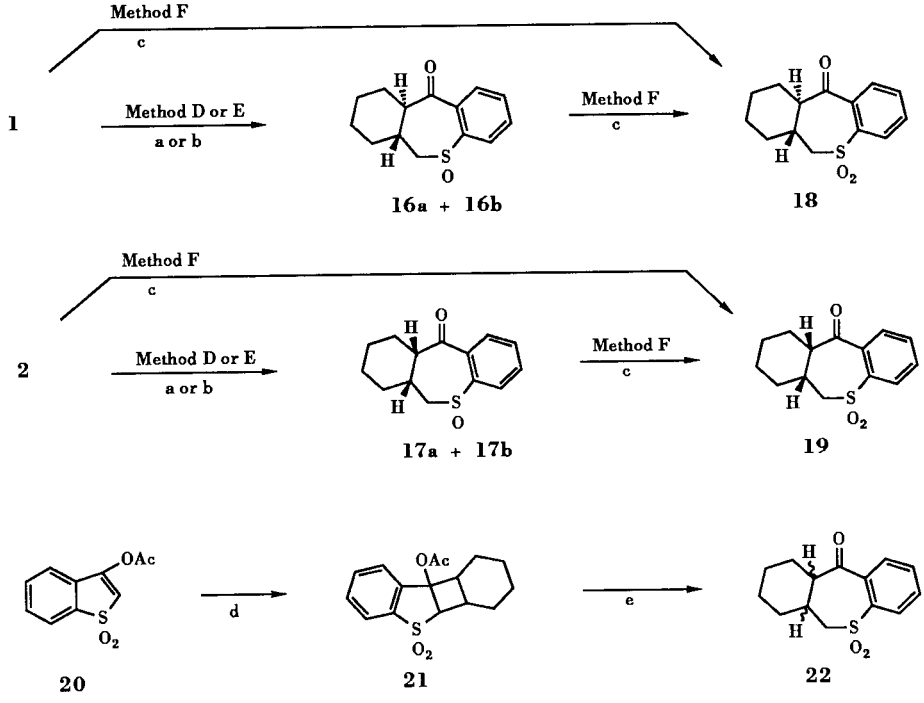
Table II

Physical Properties of the Oxidation Products **16-19**



Compound No.	n	Stereochemistry 6a-*H*/10a-*H*	Method [a]	Yield (%)	Mp (°C)	Recrystallization Solvent	t_R [b] (minutes)	Formula	Analysis (%) Calcd. (Found) C	H	S
16a	1	*trans*	D	2	138	AcOEt	4.5	$C_{14}H_{16}O_2S$	67.71	6.49	12.91
			E	0.2					(67.55	6.66	13.12)
16b	1	*trans*	D	92	136	MeOH	6.3	$C_{14}H_{16}O_2S$	67.71	6.49	12.91
			E	91					(67.44	6.47	12.75)
17a	1	*cis*	D	30	[c]		4.9	$C_{14}H_{16}O_2S$	67.71	6.49	12.91
			E	12					(67.57	6.67	12.81)
17b	1	*cis*	D	59	90	ether	6.7	$C_{14}H_{16}O_2S$	67.71	6.49	12.91
			E	81					(67.98	6.55	12.92)
18	2	*trans*	F	95	154	MeOH	4.5	$C_{14}H_{16}O_3S$	63.61	6.10	12.13
									(63.38	6.13	11.91
19	2	*cis*	F	97	123	MeOH	4.5	$C_{14}H_{16}O_3S$	63.61	6.10	12.13
									(63.45	6.15	12.01)

[a] See the Experimental. [b] Hplc: YMC-Pack A-312 column, 6 x 150 mm i.d. at 35°, mobil phase, 1% acetic acid/methanol (30/70), flow rate 1.0 ml/minute, detection 254 nm. [c] Oil.



a: $NaIO_4/H_2O$, MeOH at 20° b: MCPBA/$CHCl_3$ at 5° c: MCPBA/$CHCl_3$ at 60° d: hv/cyclohexene e: NaOH/MeOH

Chart 3

Table III

NMR Spectral Data for the Reduction and Oxidation Products **6-19**

Compound No.	^{1}H NMR [a] 6-*H*	Chemical Shifts (δ), Coupling Constants (J, Hz) 6a-*H*	10a-*H*	11-*H*	J_{10a-11}	J_{6a-10a}	^{13}C NMR [b] Chemical Shifts (δ) *C*-6	*C*-6a	*C*-10a	*C*-11
6a	2.58 (dd, J = 13.6, 2.8) 2.23 (dd, J = 13.6, 11.0)	1.49 (m)	1.26 (m)	5.02 (d)	7.4	[c]	40.09	46.35	50.12	76.02
6b	2.65 (dd, J = 13.1, 2.6) 2.44 (dd, J = 13.1, 10.2)	1.60 (m)	1.47 (m)	4.86 (d)	2.1	[c]	39.21	41.69	48.72	79.52
7a	2.94 (t, J = 12.2) 2.46 (dd, J = 12.2, 2.8)	1.92 (m)	1.72 (m)	4.91 (d)	7.8	[c]	31.86	35.94	45.86	77.16
7b	2.68 (dd, J = 14.7, 13.0) 2.23 (dd, J = 14.7, 2.9)	2.13 (m)	2.33 (m)	5.41 (d)	<1	[c]	33.58	46.57	42.39	75.12
8a	4.14 (dd, J = 12.0, 3.8) 3.37 (dd, J = 12.0, 9.6)	2.12 (m)	1.36 (m)	4.68 (dd)	8.6	[c]	79.36	39.92	47.75	80.39
8b	4.05 (dd, J = 11.9, 3.8) 3.25 (dd, J = 11.9, 10.5)	1.63 (m)	1.26 (m)	4.41 (dd)	0.9	[c]	78.22	44.87	49.29	74.37
9a	4.01 (dd, J = 11.9, 10.3) 3.93 (dd, J = 11.9, 4.4)	2.47 (m)	2.03 (m)	4.66 (dd)	6.5	[c]	74.06	36.19	43.80	76.66
9b	4.06 (dd, J = 12.1, 4.4) 3.76 (t, J = 12.1)	2.31 (m)	2.13 (m)	5.14 (dd)	2.0	[c]	72.43	39.60	45.60	73.85
10	2.58 (dd, J = 13.9, 2.7) 2.22 (dd, J = 13.9, 10.8)	1.38 (m)	1.02 (m)	3.04 (dd) 2.58 (dd)	8.7 1.6	[c]	40.36	48.56	43.91	44.80
11	2.79 (dd, J = 13.5, 9.2) 2.49 (dd, J = 13.5, 2.4)	1.98 (m)	1.81 (m)	3.04 (dd) 2.79 (dd)	9.5 3.0	[c]	36.23	41.21	37.94	40.84
12	4.07 (dd, J = 12.0, 3.5) 3.14 (dd, J = 12.0, 10.4)	1.51 (m)	1.01 (m)	2.74 (dd) 2.36 (dd)	10.5 1.8	[c]	78.45	47.75	43.11	42.33
13	3.90 (dd, J = 12.1, 7.5) 3.84 (dd, J = 12.1, 4.0)	1.97 (m)	1.90 (m)	2.93 (dd) 2.58 (dd)	8.8 2.4	[c]	75.46	41.77	36.89	37.62
14 [d]	2.99 (dd, J = 14.0, 4.1) 2.77 (dd, J = 14.0, 7.5)	2.67 (m)		6.39 (s)			40.70	46.91	148.11	123.89
15 [d]	4.20 (dd, J = 12.1, 3.9) 3.93 (dd, J = 12.1, 7.0)	2.57 (m)		6.12 (s)			75.87	45.37	146.02	121.45
16a [d]	3.23 (dd, J = 14.1, 9.0) 3.08 (dd, J = 14.1, 4.5)	2.05 (m)	3.06 (m)			11.0	57.57	37.37	54.29	206.63
16b [d]	3.42 (dd, J = 13.1 6.1) 3.13 (dd, J = 13.1, 1.1)	2.55 (m)	1.79 (m)			10.5	62.85	34.89	54.06	199.97
17a [d]	3.36 (dd, J = 13.8, 5.4) 3.05 (dd, J = 13.8, 11.0)	2.76 (m)	3.60 (m)			5.4	52.11	30.71	50.45	204.95
17b [d]	3.45 (dd, J = 12.8, 6.8) 2.94 (t, J = 12.8)	2.58 (m)	3.03 (m)			5.9	61.41	33.19	48.79	199.87
18 [d]	3.48 (dd, J = 15.1, 5.1) 3.36 (dd, J = 15.1 8.6)	2.02 (m)	2.94 (m)			11.0	61.22	36.71	54.20	204.86
19 [d]	3.54 (dd, J = 15.2, 12.0) 3.40 (dd, J = 15.2, 5.2)	2.69 (m)	3.27 (m)			4.4	56.49	32.26	51.77	203.87

[a] In nitrobenzene-d_5 at 120°. [b] In nitrobenzene-d_5 at 100°. [c] J values could not be determined. [d] In deuteriochloroform at 25°.

the *cis*-6a-*H*,10a-*H*-analogues **2** and **4** afforded the *cis*-6a-*H*,10a-*H*-deoxo compounds **11** and **13**, respectively. Compounds **10-13** were alternatively obtained from the corresponding alcohols **6a,b-9a,b** under the same reduction conditions. Although the configurations of 6a-*H* and 10a-*H* of the ketones **1-4** remained unchanged under such conditions, the reduction at the elevated temperature (30°) caused the enolization, thereby giving a mixture of the *cis*-6a-*H*,10a-*H* and *trans*-6a-*H*,10a-*H*-derivatives.

Treatment of the *trans*-6a-*H*,10a-*H*-alcohols **6a,b** and **8a,b** with dilute sulfuric acid in ethanol (Method C) gave the dehydro compounds **14** and **15**, respectively, which were also obtained from the *cis*-6a-*H*,10a-*H*-analogues **7a,b** and **9a,b**.

Catalytic hydrogenation of **14** in the presence of 5% palladium-on-carbon gave a mixture of **10** and **11** in a 2:1 ratio (Chart 2). Similarly, the oxepin analogue **15** afforded a 2:3 mixture of **12** and **13**. The purity and ratio of these stereoisomers were determined by capillary gas-liquid chromatography (glc).

Oxidations.

Oxidations of the *trans*-6a-*H*,10a-*H*-ketone **1** with sodium metaperiodate in aqueous methanol gave the *trans*-6a-*H*,10a-*H*-sulfoxide **16** (Method D) (Chart 3). The *cis*-6a-*H*, 10a-*H*-analogue **2** gave the *cis*-6a-*H*,10a-*H*-sulfoxide **17** under the same reaction conditions. The sulfoxides **16** and **17** consist of two enantiomers, **16a/16b** and **17a/17b**, respectively, concerning the *S*-oxide moiety. Each enantiomer was isolated by preparative hplc (Table II). Compounds **16a,b** and **17a,b** were alternatively obtained by oxidation of the corresponding ketones **1** and **2** with an equimolar amount of *m*-chloroperbenzoic acid (MCPBA) in chloroform at 5° (Method E).

Oxidation of **1** and **2** with two molar MCPBA at 60° gave the sulfones **18** and **19**, respectively (Method F), which were identical with samples obtained from the sulfoxides **16** and **17** under the same reaction conditions.

In the ^{1}H nmr spectroscopy of the sulfoxides **16a,b** and **17a,b** and the sulfones **18** and **19**, there were observed typical *trans* and *cis* coupling constants (10.5-11.0 and 4.4-5.9, respectively) [1] [2] between the angular protons

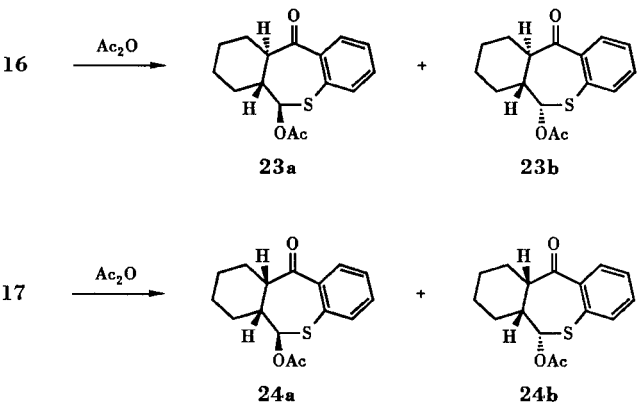


Chart 4

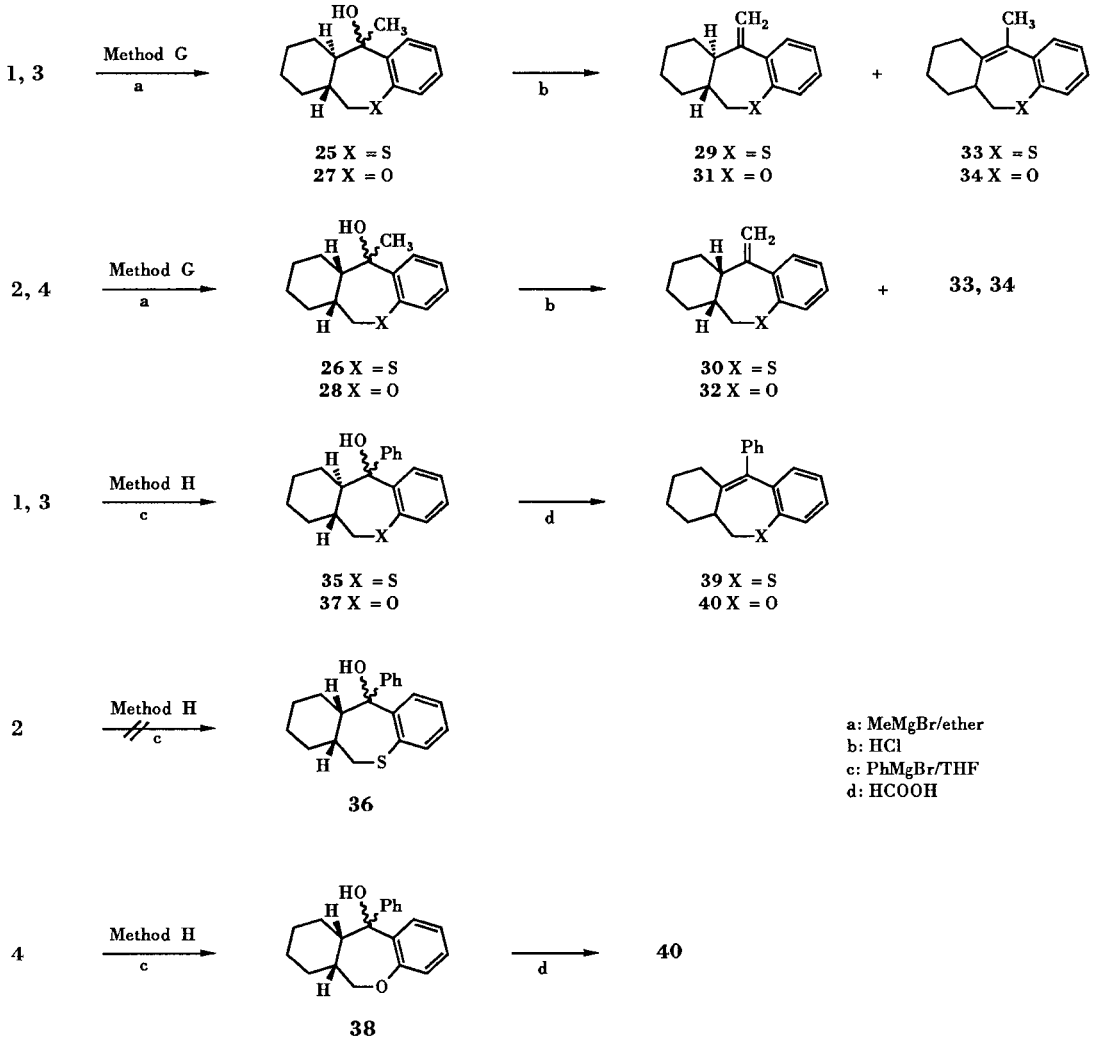


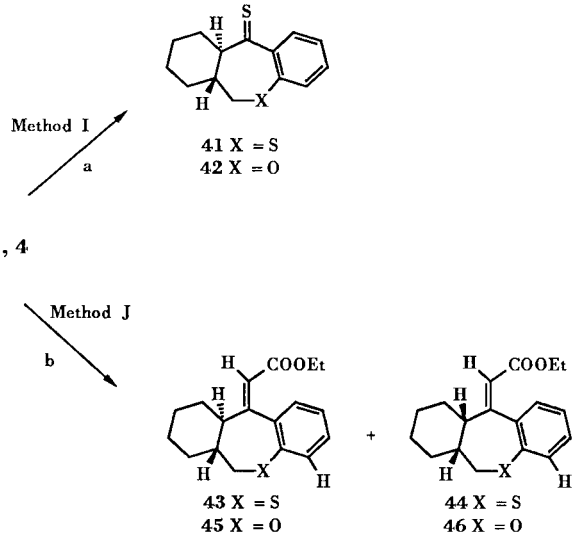
Chart 5

6a-*H* and 10a-*H* (Table III). The coupling constants thus indicated **16a,b** and **18** to be *trans*-6a-*H*,10a-*H* and **17a,b** and **19** to be *cis*-6a-*H*,10a-*H*. The relative stereochemistry of the sulfoxide moiety in **16a,b**, and **17a,b**, however, could not determined by the ^{1}H nmr analysis.

Kirby *et al.* [6] reported that the photoirradiation of 3-acetoxybenzo[*b*]thiophen 1,1-dioxide **20** in the presence of cyclohexene gave the adduct **21**, which on treatment with sodium hydroxide in aqueous methanol was transformed into the tricyclic sulfone **22**, of which relative stereochemistry between 6a-*H* and 10a-*H* had remained indefinite. Compound **22**, however, was identical with the *trans*-6a-*H*, 10a-*H*-sulfone **18** by comparison between the reported and our data for ^{1}H nmr, ^{13}C nmr spectra and melting points.

The Pummerer rearrangement of the *trans*-6a-*H*,10a-*H*-sulfoxide **16** with acetic anhydride gave *trans*-6-*H*,6a-*H*, *trans*-6a-*H*,10a-*H*-6-acetate **23a** and *cis*-6-*H*,6a-*H*, *trans*-6a-*H*,10a-*H*-6-acetate **23b** in 51 and 9% yields, respectively (Chart 4). The same reaction of the *cis*-6a-H,10a-*H*-sulfoxide **17** gave *trans*-6-*H*,6a-*H*, *cis*-6a-*H*,10a-*H*-6-acetate **24a** and *cis*-6-*H*,6a-*H*, *cis*-6a-*H*,10a-*H*-6-acetate **24b** in 20 and 40% yields, respectively.

The 6-*H*,6a-*H* configuration of the isomeric acetates **23a,b** and **24a,b** was assigned on the basis of the coupling constants between 6-*H* and 6a-*H*. The isomers **23a** and **24a** showed a doublet for 6-*H* at δ 5.87 and 5.64 with the coupling constants between 6-*H* and 6a-*H* of 4.7 and 10.6 Hz, respectively; hence **23a** and **24a** were assigned as *trans*-6-*H*,6a-*H*-isomers. Similarly, the other isomers **23b** and **24b** were assigned as *cis*-6-*H*,6a-*H* on the basis of their coupling constants between 6-*H* and 6a-*H* showing J = 2.0 and 5.2 Hz, respectively.



a: Lawesson's reagent/toluene b: $(EtO)_2P(O)CH_2COOEt$, NaH/THF

Chart 6

Reactions of the Carbonyl Group.

The Grignard reactions of the *trans*-6a-*H*,10a-*H*-ketones **1** and **3** with methylmagnesium bromide gave the *trans*-6a-*H*,10a-*H*-alcohols **25** and **27**, respectively (Method G) (Chart 5). Analogously, the *cis*-6a-*H*,10a-*H*-ketones **2** and **4** afforded the corresponding *cis*-6a-*H*,10a-*H*-alcohols **26** and **28**. Dehydration of **25** and **27** with hydrochloric acid in ethanol gave *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-methylenes **29** and **31** along with the 6,6a,7,8,9,10-hexahydro-11-methyl derivatives **33** and **34**, respectively. A similar acid-treatment of the *cis*-6a-*H*,10a-*H*-analogues **26** and **28** gave the *cis*-6a-*H*,10a-*H*-11-methylenes **30** and **32** along with the 11-methyl derivatives **33** and **34** respectively.

Every thiepin derivative **29**, **30** and **33** showed the molecular formula $C_{15}H_{18}S$ and the molecular ion peak (M^+) at m/z 230 in its ms spectrum. The oxepin analogues **31**, **32** and **34** were all analyzed to $C_{15}H_{18}O$. The ^{1}H nmr spectra of **29-32** exhibited signals of two protons for a methylene group at δ 4.91-5.14 (1H, doublet, J = 0.9-2.1 Hz) and δ 5.19-5.28 (1H, doublet, J = 0.9-2.1 Hz), while the spectra of **33** and **34** showed three protons for a methyl group at δ 2.03-2.08 (3H, doublet, $J_{CH_3,10_{eq}}$ = 1.8-2.0 Hz) (Tables IV and V). These data are consistent with the assigned structure of **29-34**.

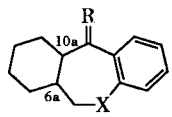
Treatment of the *trans*-6a-*H*,10a-*H*-thiepin **1** and oxepin **3** with phenylmagnesium bromide, followed by dehydration, gave the 6,6a,7,8,9,10-hexahydro-11-phenyl derivatives **39** and **40**, respectively, as a sole product (Method H). The *cis*-6a-*H*,10a-*H*-oxepin **4** underwent smoothly the Grignard reaction with the same reagent to give 40. However, the *cis*-6a-*H*,10a-*H*-thiepin **2** failed to react with phenylmagnesium bromide under the same reaction conditions, resulting in a recovery of the starting ketone **2**. The carbonyl group of **2** thus suffers greatly from steric hindrance to the cyclohexyl ring compared with that of the isomers **1**, **3** and **4**.

Thiation of either **1** or **2** with the Lawesson's reagent [7] gave the thioxo derivative **41** (Method I) (Chart 6), which was analyzed to $C_{12}H_{16}S_2$ and showed the molecular ion peak (M^+) at m/z 248 in its ms spectrum and no carbonyl absorption band in its ir spectrum. The ^{1}H nmr spectrum of **41** showed the 10a-*H* signal at δ 3.80 (1H, multiplet, $J_{6a,10a}$ = 11.8 Hz) (Tables IV and V). These results strongly support the assigned *trans*-6a-*H*,10a-*H*-thioxo structure **41**. Similarly, the *trans*-6a-*H*,10a-*H*-thioxo derivative **42** was obtained from both oxepin analogues **3** and **4**. The epimerization at C-10a occurred during the thiation process and produced finally the more thermodynamically-stable trans-6a-*H*,10a-*H*-isomer **41** or **42** as a sole product.

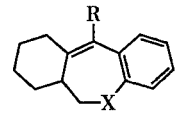
The Wittig reactions of **1** and **2** with triethyl phosphonoacetate and sodium hydride in tetrahydrofurane, ac-

Table IV

Physical Properties of Compounds **29-34** and **39-46**



29-32, 41-46



33, 34, 39, 40

Compound No.	X	Stereochemistry 6a-*H*/10a-*H*	R	Method [a]	Yield (%)	Mp (°C)	Recrystallization Solvent	R_f [b]	Formula	Analysis (%) Calcd. (Found) C	H	N	S
29	S	*trans*	CH_2	G	67	[c]		0.73	$C_{15}H_{18}S$	78.21 (78.20	7.88 7.80	–	13.92 13.71)
30	S	*cis*	CH_2	G	21	[c]		0.66	$C_{15}H_{18}S$	78.21 (77.97	7.88 7.91	–	13.92 13.88)
31	O	*trans*	CH_2	G	38	[c]		0.50	$C_{15}H_{18}O$	84.07 (83.86	8.47 8.66)		
32	O	*cis*	CH_2	G	3	[c]		0.35	$C_{15}H_{18}O$	84.07 (83.95	8.47 8.52)		
33	S		CH_3	G	10 [d] 15 [e]	[c]		0.62	$C_{15}H_{18}S$	78.21 (78.16	7.88 7.92	–	13.92 13.89)
34	O		CH_3	G	36 [d] 43 [e]	[c]		0.23	$C_{15}H_{18}O$	84.07 (83.91	8.47 8.57)		
39	S		C_6H_5	H	72 [d] 0 [e]	91	hexane	0.53	$C_{20}H_{20}S$	82.12 (82.18	6.89 6.99	–	10.96 10.87)
40	O		C_6H_5	H	76 [d] 71 [e]	114	hexane	0.28	$C_{20}H_{20}O$	86.92 (86.95	7.29 7.32)		
41	S	*trans*	S	I	61 [d] 57 [e]	[c]		0.65	$C_{14}H_{16}S_2$	67.67 (67.43	6.49 6.33	–	25.82 25.78)
42	O	*trans*	S	I	56 [d] 58 [e]	[c]		0.28	$C_{14}H_{16}OS$	72.37 (72.61	6.94 7.07	–	13.80 13.62)
43	S	*trans*	CHCOOEt	J	5 [d] 4 [e]	[c]		0.92 [f]	$C_{18}H_{22}O_2S$	71.49 (71.52	7.33 7.24	–	10.60 10.51)
44	S	*cis*	CHCOOEt	J	71 [d] 75 [e]	[c]		0.77 [f]	$C_{18}H_{22}O_2S$	71.49 (71.38	7.33 7.32	–	10.60 10.48)
45	O	*trans*	CHCOOEt	J	13 [d] 12 [e]	[c]		0.71 [f]	$C_{18}H_{22}O_3$	75.50 (75.34	7.74 7.92)		
46	O	*cis*	CHCOOEt	J	71 [d] 73[e]	[c]		0.57 [f]	$C_{18}H_{22}O_3$	75.50 (75.35	7.74 7.84)		

[a] See the Experimental. [b] Tlc: developing solvent, touene/hexane (20/80 v/v). [c] Oil. [d] Yield from the *trans*-ketone **1** or **3**. [e] Yield from the *cis*-ketone **2** or **4**. [f] Tlc: developing solvent, chloroform.

companied by epimerization at 10a-*H*, gave the *trans*-6a-*H*,10a-*H*-adduct **43** and the *cis*-6a-*H*,10a-*H*-adduct **44** in 5:71 and 4:75 ratio, respectively (Method J) (Chart 6) (Table IV). A similar treatment of the oxepin analogues **3** and **4** afforded *trans*-**45** and *cis*-**46** in 13:71 and 12:73 ratios, respectively. The *trans*-6a-*H*,10a-*H* and *cis*-6a-*H*, 10a-*H* relative configurations of the isomers **43-46** were assigned mainly on the basis of the coupling constants between 6a-*H* and 10a-*H* (Table V). The $J_{6a,10a}$ values of compounds **43** and **45** were in a range of 11.1-11.8 Hz, thus permitting the assignment as the *trans*-6a-*H*,10a-*H*-isomers. The two protons, 6a-*H* and 10a-*H*, of compounds **44** and **46** were assigned *cis*-6a-*H*,10a-*H* owing to their small coupling constants (3.7-4.1 Hz). The Wittig reactions of **1** and **2** (also **3** and **4**) caused the epimerization at *C*-10a, always giving the *cis*-6a-*H*,10a-*H*-derivative **44** (**46**) as a major product. This finding interestingly differs from the fact that both the thiation and the epimerization [1] of **1-4** under alkaline conditions yielded the *trans*-6a-*H*,10a-*H*-isomer as a major product. The geometrical configuration of the ethoxycarbonyl methine moieties in **43-46** was determined to be *Z* by the long range coupling constants (J = 0.7-1.0 Hz) between the methine proton and the 4-*H* in their ^1H nmr spectra taken in nitrobenzene-d_5 at 100° (Table V, [c]-[f]).

Table V

^{1}H NMR Spectral Data for Compounds **29-34** and **39-46**

Compound No	Chemical Shifts (δ, in deuteriochloroform), Coupling Constants (J, Hz) 6-*H*	6a-*H*	10a-*H*	J_{6a-10a}	Protons for the *C*-11 Substituent
29	3.37 (dd, J = 14.2, 4.6) 2.48 (dd, J = 14.2, 2.6)	1.69 (m)	2.51 (m)	11.8	5.14 (1H, d, J = 0.9, CH) 5.28 (1H, d, J = 0.9, CH)
30	3.16 (dd, J = 14.4, 12.4) 2.48 (dd, J = 14.4, 3.1)	2.36 (m)	2.73 (m)	4.2	4.91 (1H, d, J = 2.1, CH) 5.27 (1H, d, J = 2.1 CH)
31	4.19 (dd, J = 12.2, 4.1) 3.87 (dd, J = 12.3, 2.6)	1.54 (m)	2.22 (m)	10.7	5.05 (1H, d, J = 1.0, CH) 5.28 (1H, d, J = 1.0, CH)
32	4.12 (dd, J = 12.2, 4.5) 3.98 (dd, J = 12.2, 10.7)	2.35 (m)	2.76 (m)	4.9	5.08 (1H, d, J = 1.8, CH) 5.19 (1H, d, J = 1.8, CH)
33	3.31-3.40 (2H, m)	2.52 (m)			2.03 (3H, d, J = 1.8, CH_3)
34	4.15-4.23 (2H, m)	2.62 (m)			2.08 (3H, d, J = 2.0, CH_3)
39	3.41-3.51 (2H, m)	2.68 (m)			7.08-7.33 (5H, m, Ph)
40	4.30 (dd, J = 11.6, 4.7) 4.05 (dd, J = 11.6, 8.1)	2.76 (m)			7.06-7.39 (5H, m, Ph)
41	3.19 (dd, J = 14.6, 5.1) 2.60 (dd, J = 14.6, 0.5)	2.13 (m)	3.80 (m)	11.8	
42 [a]	4.17 (d, J = 12.3) 3.95 (dd, J = 12.3, 4.3)	2.00 (m)	3.35 (m)	11.6	
43 [b]	2.76 (dd, J = 11.5, 3.1) 2.47 (dd, J = 11.5, 11.1)	1.25 (m)	3.62 (m)	11.1	5.51 [c] (1H, s, CH), 4.21 (2H, q, J = 7.2, CH_2), 1.30 (3H, t J = 7.2, CH_3)
44 [b]	3.06 (dd, J = 14.1, 12.2) 2.41 (dd, J = 14.0, 3.1)	2.34 (m)	2.62 (m)	3.7	6.05 [d] (1H, s, CH), 3.92 (2H, q, J = 7.2, CH_2), 0.99 (3H, t, J = 7.2, CH_3)
45 [b]	4.13 (dd, J = 11.8, 3.9) 3.68 (dd, J = 11.8, 6.5)	1.54 (m)	2.10 (m)	11.8	5.92 [e] (1H, s, CH), 4.06 (2H, q, J = 7.0, CH_2), 1.10 (3H, t, J = 7.0, CH_3)
56 [b]	4.10 (dd, J = 12.3, 4.7) 4.01 (t, J = 12.3)	2.39 (m)	2.61 (m)	4.1	6.00 [f] (1H, s, CH), 4.03 (2H, q, J = 7.1, CH_2), 1.09 (3H, t, J = 7.1, CH_3)

[a] In dichloromethane-d_2 at room temperature. [b] In nitrobenzene-d_5 at room temperature. [c] Observed at δ 5.51 (1H, d, J = 1.0, CH) in nitrobenzene-d_5 at 100°. [d] Observed at δ 6.05 (1H, d, J = 0.9, CH) in nitobenzene-d_5 at 100°. [e] Observed at δ 5.92 (1H, d, J = 1.0, CH) in nitrobvenzene-d_5 at 100°. [f] Observed at δ 6.00 (1H, d, J = 0.7, CH) in nitrobenzene-d_5 at 100°.

EXPERIMENTAL

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. The ^{1}H and ^{13}C nmr spectra were obtained on a Varian XL-300 spectrometer with tetramethylsilane as an internal standard. The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; dd, double doublet; m, multiplet. Ir spectra were recorded on a Hitachi 260-10 grating ir spectrophotometer and ms spectra on a JEOL D-300 ms spectrometer. The hplc was carried out on Shimadazu LC-4A system and capillary glc on a Hewlett Packard 5840A. The tlc were run on pre-coated Silica gel 60F-254 plates (0.2 mm thick, Merck), and spots were detected by uv irradiation on the plate at 254 nm. Column chromatography was carried out on Merck Silica gel 60. Organic extracts were dried over anhydrous sodium sulfate and the solvent was removed with a rotatory evaporator under reduced pressure. Purities of oily compound were examined by tlc, hplc, capillary glc and nmr spectra.

Reduction of **1-4** with Sodium Borohydride in Methanol (Method A).

trans-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-Octahydro-11-oxodibenzo[*b*,*e*]thiepin **1** [1] (2.3 g, 0.010 mole) was dissolved in 20 ml of methanol. Sodium borohydride (1.4 g, 0.037 mole) was added portionwise to the resulting solution below at 5° with stirring. The reaction mixture was stirred for 3 hours at 5° and then poured into water. The product was extracted with toluene. The extract was washed with water, dried and concentrated to give a mixture of *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-hydroxydibenzo[*b*,*e*]thiepins **6a** and **6b** as an oil (2.2 g, 96%). Separation of **6a** and **6b** was achieved by preparative hplc, using a Shimadzu STR PREP-ODS-M column and a mobil phase consisted of a 60:40 mixture of 1% acetic acid and acetonitrile. The first fraction gave **6b** as an oil and the second fraction gave **6a** as an oil. Yield, mp, t_R-value on hplc and analytical data were summarized in Table I; ^{1}H and ^{13}C nmr data were given in Table II.

Reduction of **1-4** with Sodium Borohydride in Trifluoroacetic Acid (Method B).

Compound **1** (2.3 g, 0.010 mole) was dissolved in 10 ml of trifluoroacetic acid. Sodium borohydride (0.4 g, 0.010 mole) was added portionwise to the stirred solution at −10°. The reaction mixture was kept at −10° for 3 hours and poured into water. The product was extracted with hexane. The extract was washed with water, dried and concentrated. The residue was chromatographed on a silica gel column, using hexane as an eluent to give *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydrodibenzo[*b*,*e*]thiepin (**10**) as an oil (Tables I and II).

Dehydration of **6-9** (Method C).

A solution of the *trans*-6a-*H*,10a-*H*-11-hydroxythiepin **6** (0.6 g, 0.0026 mole) in 20 ml of ethanol and 10 ml of 20% sulfuric acid was refluxed for 48 hours and then poured into water. The product was extracted with hexane. The extract was washed with water, dried and concentrated to give the residue, which was chromatographed on a silica gel column, using hexane as an eluent to give 6,6a,7,8,9,10-hexahydrodibenzo[*b*,*e*]thiepin (**14**) as an oil (Tables I and II).

Catalytic Reduction of **14** and **15**.

A mixture of **14** (0.5 g, 0.0023 mole), 5% palladium-on-carbon (0.25 g), and 10 ml of ethanol was stirred at 60° under a hydrogen atmosphere for 4 hours (60 ml of hydrogen was absorbed). The catalyst was filtered off and the filtrate was concentrated to dryness to give a mixture of **10** and **11** as an oil (0.42 g, 84%). Analysis by capillary glc using a PEG 20M column 12.5 m x 0.25 mm i.d., at 190° showed that the mixture consisted of 66% of **10** (t_R 6.0 minutes) and 34% of **11** (t_R 7.1 minutes).

The same treatment of **15** afforded a mixture of **12** and **13** in 80% yield. The capillary glc analysis revealed that the mixture consisted of 42% of **12** (t_R 2.9 minutes) and 58% of **13** (t_R 3.3 minutes).

Oxidation of **1** and **2** with Sodium Mataperiodate (Method D).

A solution of **1** (2.3 g, 0.010 mole) and sodium metaperiodate (4.3 g, 0.040 mole) in 120 ml of 60% methanol was stirred for 72 hours at room temperature and then poured into water. The product was extracted with chloroform and the extract was washed with water, dried and concentrated to give a mixture of *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-oxodibenzo[*b*,*e*]thiepins 5-oxide **16a** and **16b** (2.4 g, 98%). The separation of **16a** and **16b** was achieved by preparative hplc, using YMC-Pack ODS-A column and a mobil phase consisted of 1% acetic acid:methanol (30:70). The first fraction gave **16a** and the second fraction gave **16b** (Tables II and III).

Oxidation of **1** and **2** with *m*-Chloroperbenzoic Acid at 5° (Method E).

A solution of 80% MCPBA (2.2 g, 0.010 mole) in 30 ml of chloroform was added at below 5° to a solution of **1** (2.3 g, 0.010 mole) in 20 ml of chloroform. The solution was kept at the same temperature for 24 hours and then washed successively with 5% potassium carbonate and water, dried and concentrated to give a mixture of **16a** and **16b** (2.4 g, 98%). The separation of **16a** and **16b** was achieved by the preparative hplc. The first fraction gave **16a** and the second fraction gave **16b** (Tables II and III).

Oxidation of **1** and **2** with *m*-Chloroperbenzoic Acid at 60° (Method F).

A solution of **1** (2.3 g, 0.010 mole) and 80% MCPBA (4.8 g, 0.022 mole) in 30 ml of chloroform was refluxed for 4 hours. The mixture was washed successively with 5% potassium carbonate and water, dried and concentrated to yield residue, which was crystallized from methanol to give *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-oxodibenzo[*b*,*e*]thiepin 5,5-dioxide (**18**) (Tables II and III).

The Pummerer Rearrangement of **16** and **17**.

A mixture of **16** (1 g, 0.004 mole) and 30 ml of acetic anhydride was heated at 110° for 18 hours. The acetic anhydride was removed under reduced pressure and the residue was chromatographed on a silica gel column with toluene as an eluent. The first fraction gave *trans*-6-*H*,6a-*H*, *trans*-6a-*H*,10a-*H*-6-acetoxy-6,6a,7,8,9,10,10a,11-octahydro-11-oxodibenzo[*b*,*e*]thiepin (**23a**, 0.6 g, 51%), which was recrystallized from toluene-hexane, mp 130-131°; ir (potassium bromide): 1745 (C=O), 1665 (C=O) cm^{-1}; ms: m/z 290 (M^+); ^1H nmr (deuteriochloroform): δ 2.10 (3H, s, CH_3), 2.25 (1H, m, 6a-*H*), 3.07 (1H, m, 10a-*H*), 5.87 (1H, d, J = 4.7 Hz, 6-*H*), 7.23-7.90 (4H, m, phenyl).

Anal. Calcd. for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25; S, 11.04. Found: C, 66.22; H, 6.27; S, 10.92.

The second fraction gave *cis*-6-*H*,6a-*H*, *trans*-6a-*H*,10a-*H*-6-acetoxy-6,6a,7,8,9,10,10a,11-octahydro-11-oxodibenzo[*b*,*e*]thiepin as an oil (**23b**, 0.1 g, 9%); ir (film): 1745 (C=O), 1670 (C=O) cm^{-1}; ms: m/z 290 (M^+); ^1H nmr (deuteriochloroform): δ 1.79 (3H, s, CH_3), 2.00 (1H, m, 6a-*H*), 3.08 (1H, m, 10a-*H*), 5.72 (1H, d, J = 2.0 Hz, 6-*H*), 7.28-7.80 (4H, m, phenyl).

Anal. Calcd. for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25; S, 11.04. Found: C, 66.35; H, 6.41; S, 11.03.

The same treatment of **17** gave a mixture of **24a** and **24b**, of which separation was achieved by a silica gel column chromatography with toluene as an eluent. The first fraction gave *trans*-6-*H*,6a-*H*, *cis*-6a-*H*,10a-*H*-6-acetoxy-6,6a,7,8,9,10,10a,11-octahydro-11-oxodibenzo[*b*,*e*]thiepin (**24a**) as an oil in 20% yield; ir (film): 1750 (CO), 1670 (CO) cm^{-1}; ms: m/z 290 (M^+); ^1H nmr (deuteriochloroform): δ 2.11 (3H, s, CH_3), 2.44 (1H, m, 6a-*H*), 3.40 (1H, m, 10a-*H*), 5.64 (1H, d, J = 10.6 Hz, 6-*H*), 7.30-7.80 (4H, m, phenyl).

Anal. Calcd. for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25; S, 11.04. Found: C, 66.15; H, 6.31; S, 10.88.

The second fraction gave *cis*-6-*H*,6a-*H*, *cis*-6a-*H*, 10a-*H*-6-acetoxy-6,6a,7,8,9,10,10a,11-octahydro-11-oxodibenzo[*b*,*e*]thiepin (**24b**) as an oil in 40% yield; ir (film): 1745 (CO), 1675 (CO) cm^{-1}; ms: m/z 290 (M^+); ^1H nmr deuteriochloroform): δ 1.71 (3H, s, CH_3), 2.50 (1H, m, 6a-*H*), 3.85 (1H, m, 10a-*H*), 6.18 (1H, d, J = 5.2 Hz, 6-*H*), 7.30-7.91 (4H, m, phenyl).

Anal. Calcd. for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25; S, 11.04. Found: C, 66.41; H, 6.20; S, 11.12.

The Grignard Reaction of **1-4** with Methylmagnesium Bromide (Method G).

A solution of **1** (2.32 g, 0.010 mole) in 10 ml of ether was added at below 5° to a solution of methylmagnesium bromide (available from Nacalai Tesque Inc., 33 ml, 0.10 mole as a 3 mole/ℓ of ether solution). The solution was stirred for 2 hours at room temperature and then poured into cold dilute hydrochloric acid. The product was extracted with toluene and the extract was washed with water, dried and concentrated. The residue was chromatographed on a silica gel column, using toluene as an eluent to give *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-hydroxy-11-methyldibenzo[*b*,*e*]thiepin (**25**) as an oil (2.3 g, 93%); ir (film): 3400 (OH) cm^{-1}; ms: m/z 248 (M^+).

Anal. Calcd. for $C_{15}H_{20}OS$: C, 72.53; H, 8.12; S, 12.91. Found: C, 72.11; H, 8.44; S, 12.89.

A mixture of **25** (2.3 g) and 2 ml of a 35% hydrochloric acid-ethanol solution in 30 ml of ethanol was heated at 85° for 2 hours. The mixture was poured into water and extracted with hexane. The extract was washed with water, dried and concentrated. The residue was chromatographed on a silica gel column with hexane as an eluent. The first fraction gave *trans*-6a-*H*,10a-

H-6,6a,7,8,9,10,10a,11-octahydro-11-methylenedibenzo[*b,e*]thiepin (**29**) as an oil and the second fraction gave 11-methyl-6,6a,7,8,9,10-hexahydrodibenzo[*b,e*]thiepin (**33**) as an oil (Tables IV and V).

The Grignard Reaction of **1-4** with Phenylmagnesium Bromide (Method H).

A solution of **1** (2.32 g, 0.010 mole) in 20 ml of tetrahydrofuran was added at below 5° to a solution of phenylmagnesium bromide (available from Nacalai Tesque Inc., 11.4 ml, 0.10 mole as a 2 mole/227 ml tetrahydrofuran solution). The solution was stirred for 16 hours at room temperature and then poured into cold dilute hydrochloric acid. The product was extracted with toluene and the extract was washed with water, dried and concentrated to give *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-hydroxy-11-phenyldibenzo[*b,e*]thiepin (**35**) (2.8 g, 90%) as an oil; ir (film): 3430 (OH) cm^{-1}; ms: m/z 310 (M^+).

Anal. Calcd. for $C_{20}H_{22}OS$: C, 77.37; H, 7.14; S, 10.33. Found: C, 77.41; H, 7.27; S, 10.56.

A solution of compound **35** (2.8 g) in 150 ml of formic acid was heated at 110° for 1 hour. The formic acid was removed and the residue was chromatographed on a silica gel column with hexane as an eluent to give 6,6a,7,8,9,10-hexahydro-11-phenyldibenzo-[*b,e*]thiepin (**39**) (Tables IV and V).

Thiation of **1-4** with the Lawesson's Reagent (Method I).

A solution of **1** (2.32 g, 0.010 mole) and the Lawesson's reagent [2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide, available from Aldrich Chemical Co., Ltd., 8.2 g, 0.020 mole] in 20 ml of toluene was refluxed for 16 hours. The toluene was removed and the residue was chromatographed on a silica gel column with hexane as an eluent to give *trans*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-thioxodibenzo[*b,e*]thiepin (**41**) as an oil (Tables IV and V).

The Wittig Reaction of **1-4** (Method J).

Sodium hydride (0.86 g, 0.0214 mole as a 60% dispersion in mineral oil) was added to a solution of triethyl phosphonoacetate (4.8 g, 0.0214 mole) in 50 ml of tetrahydrofuran. The mixture was stirred for 1 hour at room temperature until gas evolution stopped, and then **1** (1.5 g, 0.0065 mole) was added at room temperature. The reaction mixture was stirred for 16 hours at 80° and then poured into water. The product was extracted with toluene and the extract was washed with water, dried and concentrated to give a mixture of (*Z*)-*trans*-6a-*H*,10a-*H*- and (*Z*)-*cis*-6a-*H*,10a-*H*-6,6a,7,8,9,10,10a,11-octahydro-11-(ethoxycarbonyl)-methylenedibenzo[*b,e*]thiepins **43** and **44** as an oil. The residue was chromatographed on a silica gel column, using toluene:hexane (1:1) as eluent. The first fraction gave **43** and the second fraction gave **44** (Tables IV and V).

Acknowledgements.

We thank Dr. M. Hashimoto, Director of Research and Development Headquarters for his encouragement throughout this work. We also thank staffs of the analytical section of these laboratories for the elemental analyses and spectral measurements.

REFERENCES AND NOTES

[1] M. Kurokawa, K. Yoshida, Y. Nagai and H. Uno, *Chem. Pharm. Bull.*, **31**, 4312 (1983).

[2] M. Kurokawa, H. Uno, H. Nakamura, F. Sato and S. Naruto, *J. Med. Chem.*, **33**, 504 (1990).

[3] V. Seidova, M. Rajsner, E. Adlerova, M. Protiva, *Monatsh. Chem.*, **96**, 650 (1965); M. Rajsner, V. Bartl, K. Sindelar, E. Svatek, J. Holubek, J. Metys and M. Protiva, *Collect. Czech. Chem. Commun.*, **44**, 2536 (1979); V. Valenta, F. Kvis, J. Nemic and M. Protiva, *ibid.*, **44**, 2689 (1979); V. Valenta, M. Bartosova and M. Protiva, *ibid.*, **45**, 517 (1980); V. Valenta, A. Dlabac, M. Bartosova, E. Svatek and M. Protiva, *ibid.*, **45**, 529 (1980).

[4] M. Gordon, Medicinal Chemistry, Vol. 4-III, Academic Press, New York, 1974, p 101; F. Gadient, E. Jucker, A. Lindemann and M. Taeschler, *Helv. Chim. Acta*, **45**, 1860 (1962); K. Ueno, S. Kubo, H. Tagawa, T. Yoshioka, W. Tsukada, M. Tsubokawa, H. Kojima and A. Kasahara., *J. Med. Chem.*, **19**, 941 (1976); T. Yoshioka, M. Kitagawa, M. Oki, S. Kubo, H. Tagawa, K. Ueno, W. Tsukada, M. Tsubokawa and A. Kasahara, *ibid.*, **21**, 633 (1978); D. E. Aultz, G. C. Helsley, D. Hoffman, A. R. MacFadden, H. B. Lassman and C. Wilker, *ibid.*, **20**, 66 (1977); D. E. Aultz, A. R. MacFadden and H. B. Lassman, *ibid.*, **20**, 1499 (1977); J. Ackrell, Y. Antonio, F. Franco, R. Landeros, A. Leon, J. M. Muchowski, M. L. Maddox, P. H. Nelson, W. H. Rooks, A. Roszkowski and M. B. Wellach, *ibid.*, **21**, 1035 (1978).

[5] G. W. Gribble and R. M. Leese, *Synthesis.*, 172 (1977); G. W. Gribble, W. K. Kelley and S. E. Emery, *ibid.*, 763 (1978).

[6] N. V. Kirby and S. T. Red, *J. Chem. Soc., Chem. Commun.*, 150 (1980).

[7] W. Walter and T. Prooll, *Synthesis*, 941 (1979); S. Raacher and P. Klein, *Tetrahedron Letters*, **21**, 4061 (1980).