SYNTHESIS OF *tert*-BUTYLCYCLOPENTANE-FUSED 1,3-OXAZINES AND 1,3-THIAZINES

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Dedicated to **Professor Alan R. Katritzky** on the occasion of his 65th birthday

Summary - From 2-hydroxymethyl-4-*tert*-butyl-1-cyclopentylamines (**6**) and (**8**), by different ring-closure methods, a number of *tert*-butylcyclopentane-fused 1,3-oxazines and 1,3-thiazines were synthesized.

INTRODUCTION

Although six-membered saturated or partially saturated 1,3-heterocycles and their benzene ring-fused derivatives have been studied thoroughly,[1] considerably less attention has been paid to the bicyclic saturated derivatives and especially the cyclohexane- and cyclopentane-fused homologue structures. For example, the benzoxazinones were synthesized as early as 1909,[2] whereas the synthesis of the corresponding saturated analogues and homologues was first reported[3,4] and patented[5] only some seventy years later. Similarly, quinazolinones were described[6] in 1910, and widespread scientific and industrial research on quinazolinones followed,[7] but the first stereohomogeneous *cis*- and *trans*-tetramethylene-condensed pyrimidinones were described[8] as late as 1970. The first monograph dealing with saturated heterocycles was published only in 1977,[9] and the first book on the conformational analysis of saturated heterocycles even later.[10]

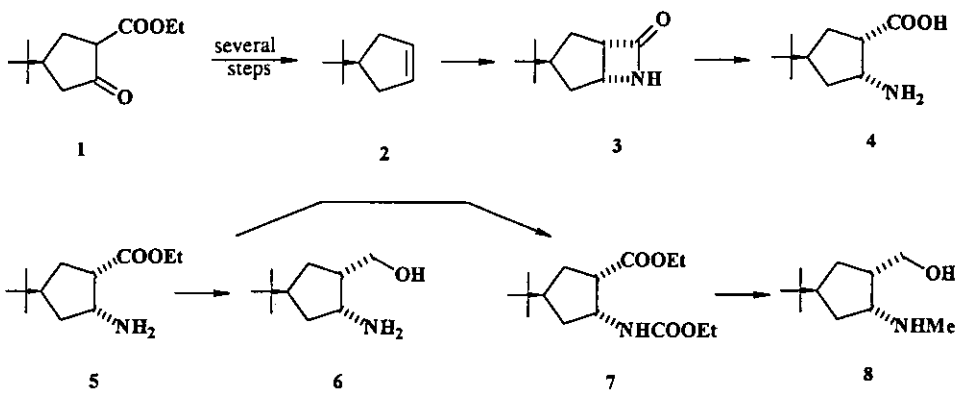
Because of the theoretical and pharmacological importance of the carbocycle-fused saturated heterocycles, the synthesis and conformational study of saturated or partially saturated six-membered 1,3-heterocycles *cis*- or *trans*-fused with 5, 6, 7 or 8-membered alicycles, and with norbornane or norbornene moieties, have been one of our main research topics for many years.[11,12]

A number of cycloalkane *cis*- or *trans*-fused 1,3-oxazines, thiazines and pyrimidinones have been synthesized, and comparative stereochemical and conformational studies have been performed.[11,12] Besides the stereochemical aspects, these types of heterocycles are also of interest as potential drugs.[5,13]

Since the reactivity of 1,2-disubstituted 1,3-difunctional cyclopentane derivatives depends very much on the geometry of the substituents,[14-16] while that of the 1,2-difunctional cyclopentane derivatives dependsdramatically on the presence or absence of a further bulky substituent in position 4, as shown for 1,2-disubstituted 4-*tert*-butyl derivatives,[17] our present aim was the preparation and study of a number of *t*-butylcyclopentane-fused 1,3-heterocycles.

RESULTS

The pathway of the syntheses of the model amino alcohols is shown in Scheme 1. 2-Ethoxycarbonyl-4-*tert*-butylcyclopentanone (**1**) was prepared by an earlier procedure,[18] from 4-*tert*-butylcyclohexanone, and was catalytically reduced to a mixture of hydroxy ester isomers. Hydrolysis and water elimination led to 4-*tert*-butyl-1-cyclopentene-1-carboxylic acid which underwent thermal decarboxylation to 4-*tert*-butyl-1-cyclopentene (**2**). Chlorosulphonyl isocyanate (CSI) addition furnished the azetidinone (**3**), in a stereospecific reaction. Azetidinone **3** was transformed by ring opening with hydrochloric acid to amino acid (**4**), followed by esterification and lithium aluminium hydride (LAH) reduction to the amino alcohol[19] (**6**) (Scheme 1). The relative configuration of the ethyl ester (**5**) derived from **4** was proved by means of X-ray diffraction.



Scheme 1

When amino ester (**5**) was treated with ethyl chloroformate, the *N*-ethoxycarbonyl derivative (**7**) was formed in nearly quantitative yield. LAH reduction of **7** resulted in the *N*-methylamino alcohol (**8**) as a crystalline product. Amino alcohols (**6**) and (**8**) were converted to 1,3-oxazines and 1,3-thiazines by different procedures.[20-22]

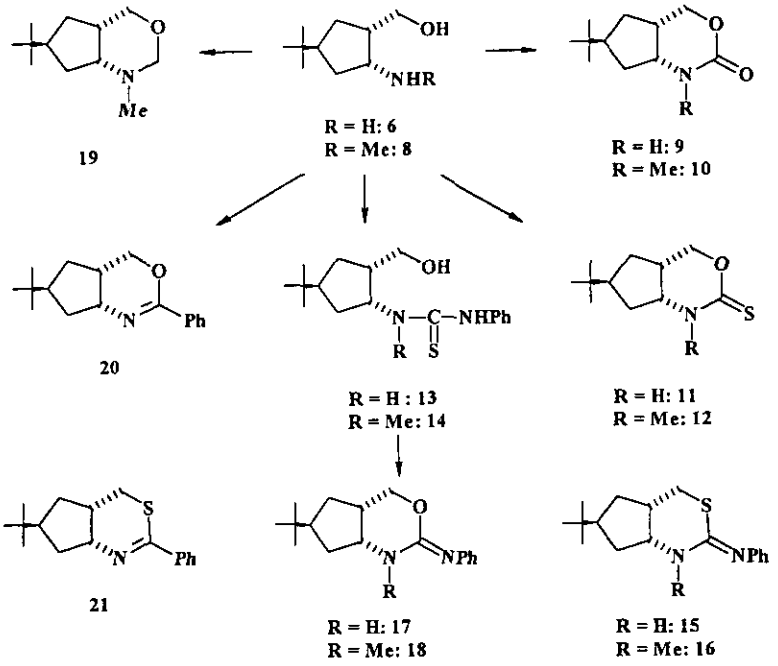
Treatment of **6** and **8** with phosgene in the presence of triethylamine (TEA) furnished 1,3-oxazin-2-ones (**9**) and (**10**) in moderate yields. When **6** was reacted with carbon disulphide in the presence of TEA, triethylammonium dithiocarbamates were formed, which were transformed without isolation to 2-thioxo-1,3-oxazine (**11**) by ethyl chloroformate treatment. The *N*-methyl-substituted 2-thioxo derivative (**12**) was prepared from **8** by reaction with thiophosgene.

With phenyl isothiocyanate, **6** and **8** gave the thiourea derivatives (**13**) and (**14**). Refluxing of **13** and **14** with hydrogen chloride in ethanol yielded 2-phenylimino-1,3-thiazines (**15**) and (**16**). With methyl iodide, **13** and **14** gave thioethers; without isolation, these were transformed in alkaline medium to 2-phenylimino-1,3-oxazines (**17**) and (**18**).

The *N*-methyloxazine (**19**) was prepared in two independent ways: from the *N*-methylamino alcohol (**8**) with aqueous formaldehyde, or from **6** with a formaldehyde/formic acid mixture, when ring closure and *N*-methylation took place.[22]

When **6** was reacted with ethyl benzimidate in ethanol in the presence of an acid catalyst, the dihydrooxazine (**20**) was obtained. This compound can also be prepared from **6**, on melting with triethyl

orthobenzoate. Melting of the dihydrooxazine (**20**) with phosphorus pentasulphide gave the corresponding thiazine (**21**) (Scheme 2).



Scheme 2

Spectroscopic Studies

The ^{1}H- and ^{13}C-nmr data on **9-12** and **15-21** (Tables 1 and 2) are consistent with the expected structures. Determination of the stereostructures is a difficult task; because of the pseudorotation of the cyclopentane and the unsaturated heterorings, the skeleton of these compounds is flexible. The DNOE results reveal that the *cis*-fused heteroring and the *tert*-butyl group in **9** are in the *trans* position.

NOE was not observed between H-8 and the annelated H-4,5, while a weak interaction of the *tert*-butyl hydrogens and H-4,5 was found. Analogous NOE was absent in **16** and **18**, but a control experiment (to prove the expected NOE between H-8 and H-4,5 for the *cis* isomer) was also negative.

The *trans* structure is more probable stereochemically. The vicinal couplings H-5,6 and H-5,6' are small, excluding dihedral angles close to 180°; consequently, the heteroring must have a conformation in which the *O*-3 is *endo* to the skeleton. Such conformers of the *cis* isomer would involve strong steric hindrance between *O*-1 and the *endo*-H-7,9. This is replaced in the *trans* counterpart by a weaker interaction of H-8 and *O*-1. In **15** and **16**, the stronger hindrance of *S*-1 and H-8 results in a change in conformation of the heteroring: this is manifested in significantly enhanced H-5,6 and H-5,6' couplings (the mean value of these couplings is 7.7 Hz for **15**, and 3.6 Hz for **9**).

All compounds investigated afforded very similar nmr data, which indicates analogous stereostructures. Further diastereomers with *trans*-annelated rings are excluded by the nmr data; they are also improbable chemically.

Table 1. Characteristic ir-frequencies (KBr disc, cm^{-1}) and ^1H-nmr data (in $CDCl_3$ solution, chemical shifts in δ, δ_{TMS} = 0 ppm and coupling constants in Hz) for **9-12** and **15-21** at 250 MHz[a].

Compound	C=X band[b]	CH_3 *s*(9H)	CH_2 (Pos. 7, 9) 1 or 2 *m*(4H)	CH-8 *qi*(1H)	CH_2 (6) 2x*dd*(2x1H)[c]	CH-5 *m*[d](1H)	CH-4 *m*(1H)	NH or NMe[f]
9	1713	0.85	~1.7	2.10	4.11 4.28	2.43	3.90	5.73
10	1691	0.86	~1.65 ~1.9[g]	~1.9[g]	4.04 4.16	2.55	3.72	2.91
11	–	0.83	1.5 - 1.9	2.05	4.17 4.30	2.50	3.84	8.32
12	–	0.86	1.75 - 1.9[g]	1.9[g]	4.06 4.19	2.68	3.80	3.34
15	1618	0.82	~1.55	2.06	2.81	2.55	3.85	~5.8
16	1571	0.87	1.6 - 1.9	2.05	~2.75[g]	~2.75[g]	3.70	3.07
17	1686	0.85	~1.6	2.05	3.86 4.18	2.45	3.85	~5.0
18	1643	0.86	~1.55 ~1.9[g]	~1.9[g]	3.90 4.05	2.55	3.70	2.94
19	–	0.84	~1.45 ~1.9[g]	~1.9[g]	3.71	2.15	2.60	2.26
20	1653	0.84	~1.6 ~1.8[g]	~1.8[g]	4.08 4.25	2.35	3.94	–
21	1603	0.87	1.6 - 2.4[g]	~1.9[g]	2.88 3.13	2.25	4.15	–

[a] Assignments were proved by 2D-HSC (**9, 12**) and DNOE measurements (**9, 16, 18**). Further ir bands and nmr signals: υNH, broad or diffuse absorptions: ~3230, ~3200 and 3130 (**9**), 3600-2600 (**11**), 3300-2700 (**15, 17**), $\gamma C_{Ar}H$ and $\gamma C_{Ar}C_{Ar}$ bands: 770 (**15, 18**), 778 (**16, 20**), 791 (**17**), 761 (**21**) and 696 (**15,17, 18, 20**), 700 (**16**), 689 (**21**), ArH nmr signals of the phenyl group: 7.0±0.15 *m* (**16, 17**) of 3H or 2+1H intensity, 7.25 ~*t*(2H): H-3',5' for **15-18**, 7.93 (**20**) and 7.80 (**21**) *dd*(2H): H-2',6'; [b] X = O (**9, 10**) or N (**15-18, 20, 21**); [c] ^2J: 11.2 (**9, 11**), 10.9 (**10, 12**), ~12 (**17**), 10.6 (**18, 20**), 12.6 (**21**), ^3J: 4.0 and 3.3 (**9, 11**), 5.4 and 3.5 (**10**), ~6 and ~4 (**17**), 5.0 and 3.6 (**18**), 4.4 and 3.6 (**20**), 7.3 and 4.1 (**21**); *d* for **15** and **19**, *J*: 7.7 and 4.2; [d] Broad signal, half-width ~30 Hz; [e] Triplet-like multiplet, *J*: 5.7 (**9**), 6.0 (**11**), ~8 (**18**), *dt*, *J*: 6.6, 6.6 and 2.3 (**10**), 5.8, 5.8 and 3.4 (**20**), qa, *J*: ~7 (**16**), 5.8 (**21**), coalesced *m*, half-width ~15 (**12, 15, 17**) ~10 (**19**); [f] NH for **9, 11, 15** and **17**, NMe for **10, 12, 16, 18** and **19**; [g] Overlapping multiplets.

Table 2. ^{13}C-Nmr chemical shifts (δ_{TMS} = 0 ppm) of **9-11** and **15-21** in $CDCl_3$ solution at 63 MHz[a]

Compound	C-2	C-4	C-5	C-6	C-7	C-8	C-9	CH_3 (*t*-Bu)	C_{quat} (*t*-Bu)	NCH_3	C-1'	C-2',6' Ph substituent	C-3',5' Ph substituent	C-4
9	155.8	55.3	35.1	68.2	27.6	47.3	36.4	27.1	31.5	–	–	–	–	–
10	155.3	61.5	36.7	67.2	28.5	47.2	32.7	27.1	31.4	34.1	–	–	–	–
11	187.9	56.1	35.3	69.2	27.5	47.1	34.5	27.0	31.6	–	–	–	–	–
12	188.0	63.0	36.7	68.0	28.8	46.8	33.0	27.0	31.6	41.4	–	–	–	–
15	148.0[b]	56.7	39.0	32.3	30.7	47.4	36.6	27.4	31.3	–	148.0[b]	122.9	128.8	122.1
16	154.2	63.9	38.5[d]	32.1[c]	29.2	47.0	32.8[c]	27.1	31.4	38.3[d]	150.4	122.6	128.5	122.4
17	151.6	54.4	36.2	67.5	28.7	47.5	36.7	27.3	31.4	–	144.7	121.8	128.5	121.5
18	152.1	61.1	35.8[c]	67.3	29.9	48.0	33.1	27.2	31.3	37.4[c]	148.5	123.4	128.1	121.2
19	84.4	65.2	38.4[c]	68.3	28.0	46.5	30.8	27.0	32.3	37.4[c]	–	–	–	–
20	155.1	56.3	35.6	65.7	27.1[b]	47.2	27.9	27.1[b]	31.8	–	134.1	127.0	127.9	130.1
21	156.1	61.1	34.7	32.0	27.7	45.9	30.3	27.1	32.1	–	139.8	126.5	128.2	130.1

[a] Assignments were proved by 2D-HSC (**9, 12**) and DEPT measurements (**10, 12, 16, 18-20**); [b] Two overlapping lines; [c, d] Interchangeable assignments.

EXPERIMENTAL

Ir spectra were run in KBr discs on a Bruker IFS-113v FT-spectrophotometer equipped with an Aspect 2000 computer and a vacuum optical system. ^{1}H- and ^{13}C-Nmr spectra were recorded in $CDCl_3$ solution in 5 or 10 mm tubes at room temperature, on a Bruker WM-250 FT spectrometer controlled by an Aspect 2000 computer at 250.13 (^{1}H) and 62.89 MHz, with the deuterium signal of the solvent as the lock and TMS as internal standard. The most important measuring parameters were as follows: spectral width 5 and 15 kHz, pulse width 1 and 5 μs (20° and 30° flip angle), acquisition time 1.64 and 0.42 s, number of scans 16 or 32 (^{1}H) and 0.2-2.5 K (^{13}C), computer memory 16 and 32 K. Lorentzian exponential multiplication for signal-to-noise enhancement (line broadening 0.7 and 1.0 Hz) and complete proton noise decoupling ($\sim$ 3W) was applied.

The standard Bruker microprogram "DNOEMULT.AU" to generate NOE was used with a selective pre-irradiation time of 5 s and a decoupling power (CW mode) of *ca.* 30-40 mW; number of scans 64-256, dummy scans 4-8, pulse width 5.0 μs (90°) and 16 K data points for ca. 2 kHz spectral width. A line broadening of 1.0 Hz was applied to diminish residual dispersion signals in the difference spectra.

DEPT[23] spectra were run in a standard way,[24] using only the Θ = 135° pulse to separate CH/CH_3 and CH_2 lines phased "up and down", respectively. Typical acquisition data were: number of scans 128-12 K, relaxation delay for protons 3 s, 90° pulse widths 10.8 and 22.8 μs for ^{13}C and ^{1}H, respectively. The estimated value for J (C, H) resulted in a 3.7 ms delay for polarization.

The 2D-HSC spectra were obtained by using the standard BRUKER pulse program "XHCORRD.AU". Data points: 4 K (^{13}C domain), increments: 64-256 digital resolution: better than 5 Hz/points (^{1}H domain), transients: 256, relaxation delay: 3 s. All C-H correlations were found by using a value of J (C, H) = 135 Hz for calculation of the delay.

Melting points were determined on a Kofler apparatus and are uncorrected. Compounds (**3-6**) were prepared as described elsewhere.[19] The physical and analytical data on the compounds prepared are listed in Table 3.

(1*R, 2*S**, 4*S**)-Ethyl 4-*tert*-butyl-2-ethoxycarbonylamino-1-cyclopentanecarboxylate (7)**

Ethyl 4-*etrt*-butyl-2-amino-1-cyclopentanecarboxylate hydrochloride (**5**·HCl) (7.00 g, 28 mmol) was dissolved in 35 ml of water. $NaHCO_3$ (3.53 g, 42 mmol) and ethyl chloroformate (3.34 g, 30.8 mmol) were added to the solution and it was refluxed for 1 h. After standing overnight at room temperature, the white crystals that separated out were filtered off and washed with water.

(1*R, 2*S**, 4*S**)-4-*tert*-Butyl-2-hydroxymethyl-1-methylaminocyclopentane (8)**

To a slurry of LAH (1.56 g, 41.1 mmol) in 100 ml of dry THF, **7** (5.79 g, 20.3 mmol) in 30 ml of THF was added dropwise at 0 °C. After stirring and refluxing for 2 h (the end of the reduction was detected by tlc), the mixture was decomposed with 3 ml of water under ice cooling. The inorganic material was filtered off. After drying and evaporation, the white crystalline product (**8**) was obtained and recrystallized from ethyl acetate.

(4*R, 5*S**, 8*S**)-8-*tert*-Butylcyclopenta[*d*]tetrahydro-1,3-oxazin-2-ones (9 and 10)**

To a solution of amino alcohol (**6**) or (**8**) (4.67 mmol) phosgene (0.465 g; 4.7 mmol) (20% toluene solution was used) and triethylamine (0.99 g, 9.4 mmol) in 20 ml of benzene were added dropwise, with cooling and stirring. The mixture was stirred at room temperature for 1 day, then washed with water (3x15 ml) and with 5% HCl solution. The organic phase was dried (Na_2SO_4), the solvent was evaporated and the residue was recrystallized from diisopropyl ether.

(4*R, 5*S**, 8*S**)-8-*tert*-Butylcyclopenta[*d*]tetrahydro-1,3-oxazin-2-thione (11)**

Triethylamine (0.39 g, 3.85 mmol) dissolved in 5 ml of chloroform was added dropwise to a stirred solution of the amino alcohol (**6**) (0.60 g, 3.5 mmol) in chloroform (15 ml). Carbon disulphide (0.30 g, 3.97 mmol) was then added under ice cooling and the mixture was kept at room temperature for 3 days. The solution was evaporated to dryness, the residual oil was dissolved in 15 ml of chloroform, and triethylamine (0.39 g, 3.85 mmol) and ethyl chloroformate (0.418 g, 3.85 mmol) were added dropwise under ice cooling. The mixture was stirred at room temperature for 10 min, then refluxed for 2 h, and evaporated. The residual oil was dissolved in chloroform and washed with 1% aqueous HCl solution. The organic phase was dried (Na_2SO_4) and evaporated. The yellow product was recrystallized from ethyl acetate.

Table 3. Analytical data on compounds (7-21)

Compound	Yield (%)	mp (°C)	Formula	Analysis C(%) Calcd	C(%) Found	H(%) Calcd	H(%) Found	N(%) Calcd	N(%) Found
7	80	72-74[a]	$C_{15}H_{27}NO_4$	63.13	63.39	9.54	9.26	4.91	4.71
8	86	75-77[a]	$C_{11}H_{23}NO$	71.30	71.48	12.51	12.34	7.56	7.74
9	52	127-130[b]	$C_{11}H_{19}NO_2$	66.97	67.16	9.71	9.85	7.10	6.88
10	35	81-84[b]	$C_{12}H_{21}NO_2$	68.21	68.30	10.02	10.11	6.63	6.70
11	47	136-138[a]	$C_{11}H_{19}NOS$	61.93	61.79	8.98	8.68	6.57	6.43
12	44	133-135[a]	$C_{12}H_{21}NOS$	63.39	63.20	9.31	9.46	6.16	6.09
13	89	178-180[a]	$C_{17}H_{26}N_2OS$	66.63	66.54	8.55	8.68	9.14	9.31
14	98	146-148[a]	$C_{18}H_{28}N_2OS$	67.46	67.64	8.81	8.78	8.74	8.89
15	80	221-223[c]	$C_{17}H_{24}N_2S$	70.79	70.52	8.39	8.25	9.71	10.18
16	80	86-88[c]	$C_{18}H_{26}N_2S$	71.47	71.26	8.66	8.45	9.26	9.48
17	76	177-180[a]	$C_{17}H_{24}N_2O$	74.96	74.78	8.88	8.85	10.28	10.15
18	75	109-110[a]	$C_{18}H_{26}N_2O$	75.48	75.63	9.15	9.38	9.78	9.62
19	81(A) 65(B)	201-202[c]	$C_{12}H_{24}NOCl$	61.65	61.65	10.35	10.34	5.99	5.95
20	78(A) 66(B)	62-64[d]	$C_{17}H_{23}NO$	79.33	79.01	9.01	9.33	5.44	5.53
21	63	54-56[d]	$C_{17}H_{23}NS$	74.67	74.85	8.48	8.23	5.12	5.35

Solvents for recrystallisation: [a]ethyl acetate, [b]diisopropyl ether, [c]ethanol, [d]hexane.

(4*R, 5*S**, 8*S**)-8-*tert*-Butyl-3-methylcyclopenta[*d*]tetrahydro-1,3-oxazin-2-thione (12)**

To a stirred solution of the amino alcohol (**8**) (0.41 g, 2.21 mmol), thiophosgene (0.25 g, 2.21 mmol) in 5 ml of dry benzene, and triethylamine (0.45 g, 4.42 mmol) in 10 ml of benzene, were added dropwise at 0 °C. The mixture was stirred at room temperature for 10 min, then washed with water (2x10 ml) and purified by column chromatography (eluent: benzene, then benzene:EtOAc = 1:4) monitored by tlc. The main fractions were evaporated and the yellow crystalline product was recrystallized from diisopropyl ether.

Thiourea derivatives 13 and 14

Phenyl isothiocyanate (0.695 g, 5.14 mmol) was added to amino alcohols (**6**) or(**8**) (4.67 mmol) dissolved in 80 ml of benzene, and the crystalline product was separated after standing for 1 day at room temperature.

(4*R, 5*S**, 8*S**)-8-*tert*-Butyl-2-phenyliminocyclopenta[*d*]tetrahydro-1,3-thiazines (15 and 16)**

Thiourea (**13**) or (**14**) (1.63 mmol) was refluxed for 1 h in 20 ml of ethanol containing 22% dry hydrogen chloride. After evaporation, the oily residue was neutralized with a 10% aqueous potassium hydroxide and the solution was extracted with chloroform (3x30 ml). Drying (Na_2SO_4) and evaporation of the organic phase resulted in thiazines (**15**) and (**16**) as colourless crystals.

(4*R, 5*S**, 8*S**)-8-*tert*-Butyl-2-phenyliminocyclopenta[*d*]tetrahydro-1,3-oxazines (17 and 18)**

To a solution of thiourea (**13**) or (**14**) (2.77 mmol) in 10 ml of methanol, methyl iodide (0.95 ml, 15 mmol) was added and the solution was stirred for 3 h. After evaporation of the solvent, the residue was stirred in 20 ml of 2.5 N methanolic potassium hydroxide for 4 h. After evaporation, the residue was dissolved in water and extracted with chloroform (3x30 ml). After drying (Na_2SO_4) and evaporation of the organic layer, the oxazines (**17**) and (**18**) were obtained.

(4*R, 5*S**, 8*S**)-8-*tert*-Butyl-3-methylcyclopenta[*d*]tetrahydro-1,3-oxazine (19)**

Method A - Amino alcohol (**8**) (0.39 g, 2.16 mmol) was stirred with 5 ml of 33% aqueous formaldehyde at room temperature for 1 h. The mixture was made alkaline with 10% aqueous potassium hydroxide and extracted with ether. The combined organic phase was dried (Na_2SO_4) and evaporated to give an almost colourless oil which was purified as the hydrochloride. The base liberated for purposes of spectroscopic examination was a colourless, viscous oil.

Method B - Amino alcohol (**6**) (0.20 g, 1.17 mmol) was refluxed with a mixture of 3.5 ml of 33% aqueous formaldehyde and 3.5 ml of 99% formic acid. After 1 h, the mixture was poured onto 20 g of ice, neutralized with 10% aqueous Na_2CO_3 and extracted with chloroform (3x30 ml). The organic layer was dried (Na_2SO_4) and evaporated to afford a colourless oil, which was purified as the hydrochloride.

(4*R, 5*S**, 8*S**)-8-*tert*-Butyl-2-phenylcyclopenta[*d*]-4,5-dihydro-(6*H*)-1,3-oxazine (20)**

Method A - Ethyl benzimidate (0.26 g, 1.75 mmol) and 1 drop of glacial acetic acid were added to a solution of amino alcohol (**6**) (0.30 g, 1.75 mmol) in 10 ml of dry ethanol. The solution was refluxed for 10 h, then evaporated, and the colourless crystals were recrystallized from *n*-hexane.

Method B - An excess of triethyl orthobenzoate (1.48 g, 6.6 mmol) was heated with amino alcohol (**6**) (0.30 g, 1.75 mmol) at 110 °C for 9 h. The light-brown product was dissolved in ether and washed with dilute hydrochloric acid (1%) and water. The aqueous phase was made alkaline with cold, saturated $NaHCO_3$ solution and extracted with chloroform. After drying (Na_2SO_4) and evaporation, a crystalline product was obtained.

(4*R, 5*S**, 8*S**)-8-*tert*-Butyl-2-phenylcyclopenta[*d*]-4,5-dihydro-(6*H*)-1,3-thiazine (21)**

Oxazine (**20**) (0.28 g, 1.1 mmol) was homogenized with P_4S_{10} (0.75 g) and the mixture was heated at 140 °C. After 3 h, the mixture was cooled, made alkaline with NaOH solution (15%) and extracted with ether. The organic layer was dried (Na_2SO_4) and evaporated. The oily product became crystalline after standing for a few days at room temperature.

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