Synthesis of Thiazole, Oxazole and Heterocyclic Ring-Substituted 1,2-Dioxanes

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The reactions of 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane with thioureas or thioamides gave 3-methoxy-3-methyl-6,6-diphenyl-4-(4-thiazolyl)-1,2-dioxanes in 63-90% yields. The similar reaction of 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane with acetamide gave 3-methoxy-3-methyl-4-(2-methyl-4-oxazolyl)-6,6-diphenyl-1,2-dioxane in 39% yields. The reactions of 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane with 3-alkyl-4-amino-5-mercapto[1,2,4]triazoles yielded 3-methoxy-3-methyl-6,6-diphenyl-4-[3-(5-alkyl[1,2,4]triazolo[3,4-*b*]-2,3-dihydro-6*H*-[1,3,4]thiadiazinyl)]-1,2-dioxanes in moderate yields (43-46%).

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Introduction.

We have reported that the manganese(II) or manganese(III) acetate-mediated free-radical cyclization of alkenes with 1,3-diones and oxygen gave 1,2-dioxan-3-ols in good yields [1-3]. We are interested in the formation of O-, N- and S-atom containing heterocycles bearing a 1,2-dioxane ring in view of the facts that naturally occurring 1,2-dioxanes have some effect on the inhibition of root formation [4], and that thiazole and oxazole rings are a partial structure of the potent antibiotics, Althiomycin [5] and Phorboxazoles A and B [6], respectively. It should also be interesting to form 1,2-dioxanes bearing [1,3,4]thiadiazine and [1,2,4]triazole rings because they have various biological activities [7] and antidepressant properties [8], respectively. It seems reasonable that the combination of 1,2-dioxanes, and N- and S-atom containing heterocycles can provide various kinds of new heterocyclic compounds.

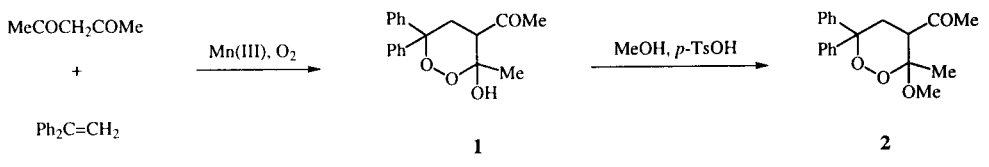
4-Acetyl-3-methyl-6,6-diphenyl-1,2-dioxan-3-ol (**1**) was fairly easy to prepare by the reaction of 1,1-diphenylethene with 2,4-pentanedione in the presence of manganese(III) acetate under air [2], and the treatment of **1** with anhydrous methanol gave 4-acetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**2**) (Scheme 1). It seems that the bromination at the acetyl group in **2** could result in a bromoacetyl group which would then form heterocyclic rings. Therein we describe the reactions of 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxanes with thioureas, thioamides, amides, and 3-alkyl-4-amino-5-mercapto[1,2,4]triazoles in this paper.

Results and Discussion.

Methylation of 4-Acetyl-3-methyl-6,6-diphenyl-1,2-dioxan-3-ol (**1**) and Bromination of 4-acetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**2**).

For the methylation of ethyl *cis*-3-hydroxy-3-methyl-6,6-diphenyl-1,2-dioxane-4-carboxylate, a large excess of

Scheme 1



1 **2**

Table 1

Reaction of 4-Acetyl-3-methyl-6,6-diphenyl-1,2-dioxan-3-ol (**1**) with Methanol in the Presence of CSA or TsOH•H_2O [a]

Entry	Acid	Molar Ratio [b]	Temperature °C	Yield % [c]
1	CSA	1:4	50	48
2	CSA	1:6	50	61
3	CSA	1:8	50	69
4	TsOH•H_2O	1:1	23	76
5	TsOH•H_2O	1:2	23	71
6	TsOH•H_2O	1:3	23	71
7	TsOH•H_2O	1:4	23	70
8	TsOH•H_2O	1:0.2	23	90
9	TsOH•H_2O	1:0.1	23	77
10	TsOH•H_2O	1:0.1	50	95

[a] The reactions were carried out in anhydrous methanol under argon for 18 hours; [b] Molar ratio of **1**: acid; [c] Isolated yields of a mixture of **2** and **2'** based on the amount of **1** used.

(+)-10-camphorsulfonic acid (CSA) was used for the reaction [9]. However, we found that a catalytic amount of *p*-toluenesulfonic acid was enough to complete the methylation of 4-acetyl-3-methyl-6,6-diphenyl-1,2-dioxan-3-ol (**1**), and it also gave a crystalline product which consisted of two stereoisomers. Fractional recrystallization from ethanol yielded the major isomer **2** and the minor isomer **2'**. Optimization of the reaction conditions and the yields are shown in Table 1. Compound **2** yielded a crystalline monobromoacetyl derivative **3** on bromination with trimethylphenylammonium tribromide ($PhMe_3NBr_3$) when a molar ratio of **2** and the reagent was 1:1. This monobromoacetyl derivative **3** was obtained as a single stereoisomer that was confirmed by the ^1H and ^{13}C nmr spectra. When the reaction was carried out at a molar ratio of 1:2, dibromoacetyl derivative **4** was the major product (Scheme 2).

Formation of Heterocyclic Rings by the Reactions of 4-Bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) with Various Reagents.

When 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) was heated with thiourea in a solvent under reflux, it gave 4-(2-amino-4-thiazolyl)-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**5a**) (Scheme 3). The reaction was examined under several reaction conditions (Table 2). The best yield was attained when compound **3** and thiourea (1:2 mole ratio) were reacted in methanol at reflux (entry 2). Similarly, the reactions of **3** with other thioureas or thioamides gave 4-(2-substituted 4-thiazolyl)-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxanes **5b-5e** (entries 5-8). The ^{13}C nmr spectrum in deuteriochloroform of **5a** showed peaks due to carbons bearing no hydrogen at δ 107.9 and 86.9 characteristic to the 1,2-dioxane ring and no peak for a carbonyl group. The presence of a peak for the methine carbon at δ 104.3 due to C-5' of a thiazole ring also indicates the structure of **5a** as shown.

When 4-dibromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**4**) was heated with thiourea in ethanol under reflux, it also gave 4-(2-amino-4-thiazolyl)-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**5a**), showing that the reductive debromination occurred in the reaction (entry 9).

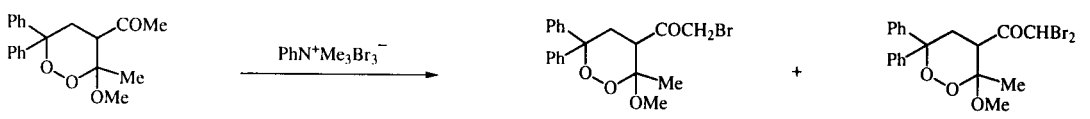
The reaction of **3** with acetamide in ethanol gave a mixture of various products, but the desired oxazole derivative was not formed. When the reaction was carried out without solvent, it gave 3-methoxy-3-methyl-4-(2-methyl-4-oxazolyl)-6,6-diphenyl-1,2-dioxane (**6**) (entry 10). However, another structural possibility for the oxazolyl moiety of **6** is 2-methyl-5-oxazolyl-1,2-dioxanes (**6'**) (Figure 1). The calculated chemical shifts of δ_H 7.69 and δ_C 138.1 for H-5' and C-5' of 2-methyl-4-oxazolyl structure (**6**) are quite close to the observed values, δ_H 7.36 and δ_C 135.4.

6 **6'**

Figure 1. Possible partial structures for **6** and **6'**.

When 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) was heated with 4-amino-5-mercapto-3-methyl[1,2,4]triazole in refluxing ethanol, it gave 3-methoxy-3-methyl-4-[3-(5-methyl[1,2,4]triazolo-[3,4-*b*]-2,3-dihydro-6*H*-[1,3,4]thiadiazinyl)]-6,6-diphenyl-1,2-dioxane (**7a**) (entry 11). The reactions of 3-alkyl-substituted [1,2,4]triazoles were examined and we obtained the corresponding [1,2,4]triazolo[3,4-*b*]-2,3-dihydro-6*H*-[1,3,4]thiadiazinyl)]-1,2-dioxanes **7b** and **7c** in moderate yields (entries 12 and13). The structures were

Scheme 2



2 **3** **4**

Scheme 3

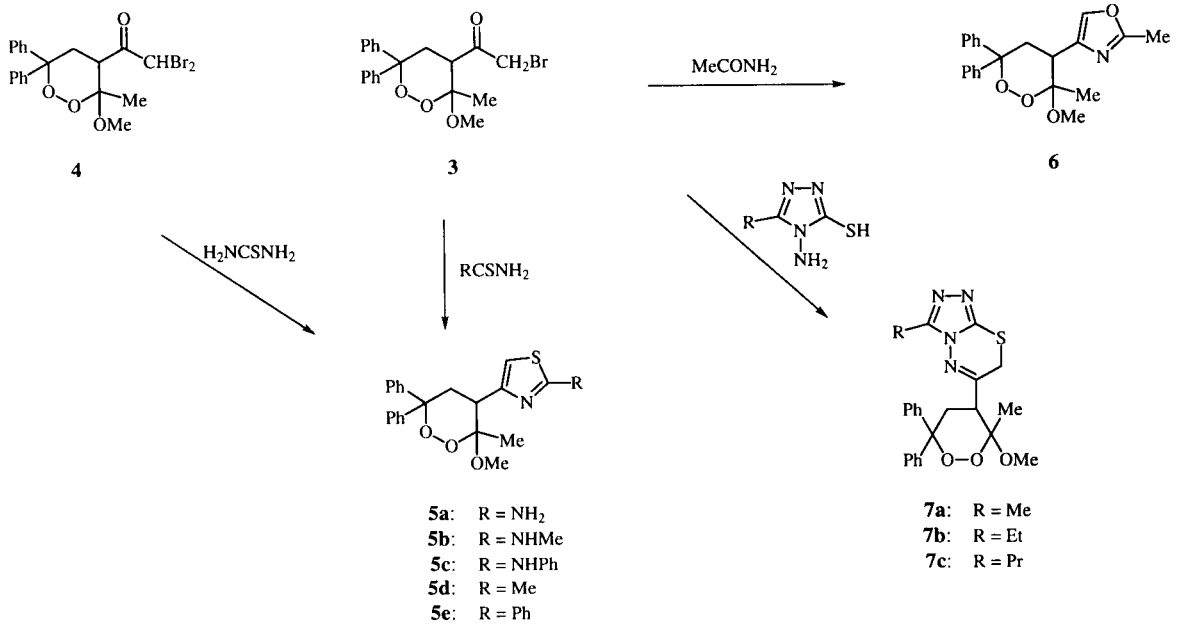


Table 2

Reactions of 4-Bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) and 4-Dibromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**4**) [a]

Entry	Substrate	Reagent	Solvent	Molar Ratio [b]	Time Hours	Product (Yield %) [c]	
1	**3**	H_2NCSNH_2	MeOH	1:1	1.5	**5a**	(76) [d]
2	**3**	H_2NCSNH_2	MeOH	1:2	1.5	**5a**	(90)
3	**3**	H_2NCSNH_2	Et_2O	1:2	1.5	**5a**	(68)
4	**3**	H_2NCSNH_2	MeCN	1:2	1.5	**5a**	(77)
5	**3**	$MeNHCSNH_2$	MeOH	1:2	1.5	**5b**	(63)
6	**3**	$PhNHCSNH_2$	MeOH	1:2	1.5	**5c**	(77)
7	**3**	$MeCSNH_2$	MeOH	1:2	1.5	**5d**	(65)
8	**3**	$PhCSNH_2$	MeOH	1:2	1.5	**5e**	(74)
9	**4**	H_2NCSNH_2	MeOH	1:2	2	**5a**	(78)
10	**3**	$MeCONH_2$	[e]	1:20	2	**6**	(39)
11	**3**	3-Me-AMT [f]	ETOH	1:2	1	**7a**	(46)
12	**3**	3-Et-AMT	ETOH	1:2	1	**7b**	(43)
13	**3**	3-Pr-AMT	ETOH	1:2	1	**7c**	(46)

[a] The reactions were carried out at the reflux temperature; [b] Substrate:reagent; [c] Isolated yields based on the amount of the dioxane used; [d] The substrate was recovered (6%); [e] Heated at 80° C without solvent; [f] AMT: 4-Amino-5-mercapto[1,2,4]triazole.

again confirmed by the presence of two methylene groups in both nmr spectra, and the absence of a peak for the carbonyl group in the ^{13}C nmr spectrum.

Reaction Pathways for the Formation of Heterocyclic Rings.

It was found that acetamide was less reactive than thioamides and thioureas in the reaction of 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**). This could be ascribed to the weaker nucleophilicity of the amino group in the amide than those in thioamides and thioureas presumably due to the resonance contribution of the dipolar structure in the former. The reaction can be initiated by the attack on the carbonyl group in the bromoketone by the amino group and successive ring closure, followed by dehydration to form the heterocyclic rings depicted in Figure 2.

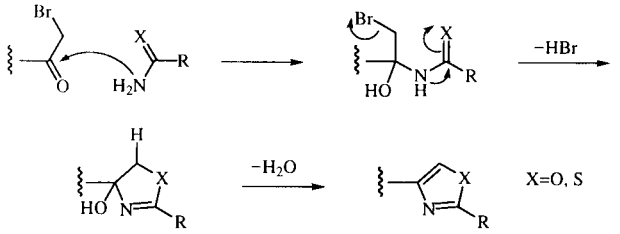


Figure 2. Reaction pathway for the formation of heterocyclic rings.

In conclusion, convenient preparations of compounds bearing a 1,2-dioxane ring and O-, N- and S-atom containing heterocycles were demonstrated. This should be applicable to the synthesis of other 1,2-dioxanes bearing other types of heterocycles.

EXPERIMENTAL

Measurements.

All of the ^1H and ^{13}C nmr spectra were taken with a JNM AL-300FT nmr (300 MHz for ^1H and 75 MHz for ^{13}C) spectrometer with tetramethylsilane being used as the internal standard. Chemical shifts are shown in δ values (ppm) and the coupling constants are expressed in J values (Hz). The ir spectra were measured on a Perkin Elmer Paragon 1000 FT ir spectrometer and expressed in ν values (cm^{-1}). All of the melting points were determined with a Yanagimoto micromelting-point apparatus MP-J3. Elemental analyses were performed by the Instrumental Analysis Center, Kumamoto University and the Microanalytical Center, Kyushu University, Fukuoka, Japan. Calculation of chemical shifts for the ^1H and ^{13}C nmr were performed by CS ChemDraw Pro Version 4.5.

Materials.

4-Acetyl-3-methyl-6,6-diphenyl-1,2-dioxan-3-ol (**1**) was prepared by the method described in the previous papers [1-3]. 3-Alkyl-4-amino-5-mercapto[1,2,4]triazoles were prepared according to the literature [10]. Thioureas and thioamides were commercially available and used as they were received (Wako).

Preparation of 4-Acetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane.

A solution of 4-acetyl-3-methyl-6,6-diphenyl-1,2-dioxan-3-ol (**1**) (1mmole) and (+)-10-camphorsulfonic acid or *p*-toluenesulfonic acid in absolute methanol (30 ml) was stirred at room temperature for 18 hours (Table 1). After the removal of the methanol, water (30 ml) was added. The reaction mixture was then extracted with benzene (2 x 30 ml) and the combined extract was washed with a saturated solution of sodium hydrogencarbonate (10 ml), and dried over sodium sulfate. After removing the benzene, the resulting product solidified and was fractionally recrystallized from ethanol.

Minor Diastereomer of 4-Acetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**2'**).

This compound was obtained as colorless cubes, mp 85-90° (from ethanol) in 35% yield; ir (potassium bromide): ν_{max} = 1710 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ = 7.22 (10H, m, 2 x Ph), 3.46 (3H, s, OMe), 2.99 (1H, m, CH), 2.69 (2H, m, CH_2), 2.25 (3H, s, Ac), 1.24 (3H, s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 207.7 (>C=O), 145.9 (>C=), 141.8 (>C=), 128.5 (2C), 128.3 (2C), 127.6, 127.3, 126.0 (2C), 125.8 (2C) (arom -CH=), 105.7 (>C<), 86.7 (>C<), 53.5 (>CH-), 49.9 (OMe), 33.0 (CH_2), 30.6 (Me), 15.0 (Me).

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.80; H, 6.73.

Major Diastereomer of 4-Acetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**2**).

This compound was obtained as colorless microcrystals, mp 97-98° (from ethanol) in 49% yield; ir (potassium bromide): ν_{max} = 1694 (>C=O) cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ = 7.48-7.22 (10H, m, 2 x Ph), 3.46 (3H, s, OMe), 3.23 (1H, dd, J = 2.7, 13.7 Hz, H-4), 3.22 (1H, dd, J = 2.7, 14.3 Hz, H_{eq}-5), 2.73 (1H, t, J = 13.5 Hz, H_{ax}-5), 2.26 (3H, s, Ac), 1.17 (3H, s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 207.8 (>C=O), 145.9 (>C=), 141.8 (>C=), 128.5 (2C), 128.3 (2C), 127.6, 127.3, 126.0 (2C), 125.8 (2C) (arom -CH=), 105.7 (>C<), 86.7 (>C<), 53.5 (>CH-), 49.9 (OMe), 33.0 (CH_2), 30.6 (Me), 15.0 (Me).

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.64; H, 6.79.

Preparations of 4-Bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) and 4-Dibromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**4**).

A mixture of 4-acetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**2**) (1.5 mmole), trimethylphenylammonium tribromide (1.5 mmole for **3** and 3 mmole for **4**) in tetrahydrofuran (10 ml) was stirred at room temperature for 1.5 hours for **3** and 24 hours for **4**, and then poured into ice water (10 ml). The reaction mixture was extracted with benzene (3 x 20 ml). The combined extract was washed with a saturated solution of sodium hydrogencarbonate (10 ml) and dried over anhydrous sodium sulfate. After removal of the benzene, the crystallized products were purified by recrystallization from ethanol.

4-Bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**).

This compound was obtained as colorless microcrystals, mp 119-120° (from ethanol) in 52% yield; ir (chloroform): ν_{max} = 1717 (>C=O) cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ = 7.44-7.23 (10H, m, 2 x Ph), 4.17 (1H, d, J = 14.6 Hz, *H*CHBr), 4.12 (1H, d, J = 14.6 Hz, HC*H*Br), 3.50 (1H, dd, J = 3.0, 10.8 Hz, H-4), 3.44 (3H, s, OMe), 2.78 (1H, dd, J = 3.0, 14.1 Hz, H_{eq}-5), 2.56 (1H, t, J = 13.8 Hz, H_{ax}-5), 1.19 (3H, s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 200.3 (>C=O), 141.2 (2 x >C=), 128.5 (2C), 128.3 (2C), 127.8, 127.4, 126.1 (2C), 125.7 (2C) (arom -CH=), 105.4 (>C<), 86.7 (>C<), 51.2 (>CH-), 50.1 (OMe), 35.1, 33.2 (CH_2), 15.4 (Me).

Anal. Calcd. for $C_{20}H_{21}BrO_4$: C, 59.27; H, 5.22. Found: C, 59.00; H, 5.20.

4-Dibromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**4**).

This compound was obtained as colorless microcrystals, mp 159-160° (from ethanol) in 85% yield; ir (chloroform): ν_{max} = 1721 (>C=O) cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ = 7.56-7.19 (10H, m, 2 x Ph), 6.32 (1H, s, $CHBr_2$), 3.49 (3H, s, OMe), 3.21 (1H, dd, J = 3.9, 12.6 Hz, H-4), 3.92 (1H, t, J = 13.2 Hz,

H_{ax}-5), 2.88 (1H, dd, J = 3.9, 13.5 Hz, H_{eq}-5), 1.24 (3H, s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 194.7 (>C=O), 143.0, 140.1 (>C=), 128.6 (2C), 128.4 (2C), 128.3, 127.7, 127.0 (2C), 126.2 (2C) (arom -CH=), 100.2 (>C<), 85.3 (>C<), 51.5 (>CH-), 49.5 (OMe), 40.9 (>CH-), 32.7 (CH_2), 19.3 (Me).

Anal. Calcd. for $C_{20}H_{20}Br_2O_4$: C, 49.61; H, 4.16. Found: C, 50.03; H, 4.21.

Reactions of 4-Bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) and 4-Dibromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**4**) with Thiourea or Thioamide.

A typical procedure for the reactions of 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) and 4-dibromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**4**) with thiourea or thioamide is as follows. A solution of **3** (1 mmole) and a reagent (2 mmole) in a solvent (15 ml) was heated under reflux for the time shown in Table 2. After the removal of the solvent, water (15 ml) was added and then the mixture was extracted with chloroform (2 x 15 ml). The chloroform layer was separated, washed with aqueous sodium hydrogencarbonate solution and dried over anhydrous sodium sulfate. After removing the chloroform, the resulting products were purified by tlc (Wakogel B10) while eluting with a mixture of hexane-ethyl acetate (4:6 v/v) and/or recrystallization. The yields are listed in Table 2. Specific details are given below.

Products.

4-(2-Amino-4-thiazolyl)-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**5a**).

This compound was obtained as colorless needles, mp 173-174° (decomp) (from ethanol); ir (potassium bromide): ν_{max} = 3424 (NH_2) cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ = 7.50-7.20 (10H, m, 2 x Ph), 6.24 (1H, s, =CH-), 5.35 (2H, br s, NH_2), 3.40 (3H, s, OMe), 3.38 (1H, m, H-4), 2.90 (1H, dd, J = 3.0, 13.5 Hz, H_{eq}-5), 2.65 (1H, t, J = 13.5, H_{ax}-5), 1.08 (3H, s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 167.3 (C-2'), 150.6 (C-4'), 146.5, 141.7 (arom >C=), 128.4 (2C), 128.2 (2C), 127.6, 127.1, 126.5 (2C), 125.8 (2C) (arom =CH-), 107.9 (>C<), 104.3 (C-5'), 86.9 (>C<), 49.8 (OMe), 42.6 (>CH-), 36.2 (CH_2), 15.4 (Me).

Anal. Calcd. for $C_{21}H_{22}N_2O_3S$: C, 65.95; H, 5.79; N, 7.32. Found: C, 65.91; H, 5.97; N, 7.10.

3-Methoxy-3-methyl-4-[(2-methylamino)-4-thiazolyl]-6,6-diphenyl-1,2-dioxane (**5b**).

This compound had mp 156-158° (from ethanol); ir (potassium bromide): ν_{max} = 3386 (NH) cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ = 7.51-7.18 (10H, m, 2 x Ph), 6.26 (1H, s, =CH-), 5.66 (1H, q, J = 5.0 Hz, NHMe), 3.41 (1H, dd, J = 2.9, 13.4 Hz, H-4), 3.40 (3H, s, OMe), 2.89 (3H, d, J = 5.0 Hz, NMe), 2.89 (1H, dd, J = 2.9, 13.6 Hz, H_{eq}-5), 6.29 (H, dd, J = 13.4, 13.6 Hz, H_{ax}-5), 1.10 (3H, br s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 170.7 (C-2'), 151.1 (C-4'), 141.8 (2 x =C<), 128.3 (2C), 128.2 (2C), 127.5, 127.1, 126.5 (2C), 125.9 (2C) (arom =CH-), 108.0 (>C<), 102.4 (C-5'), 86.9 (>C<), 49.8 (OMe), 42.7 (>CH-), 36.4 (CH_2), 32.3 (NMe), 15.5 (Me).

Anal. Calcd. for $C_{22}H_{24}N_2O_3S$: C, 66.65; H, 6.10; N, 7.07. Found: C, 66.50; H, 6.13; N, 6.88.

3-Methoxy-3-methyl-4-[(2-phenylamino)-4-thiazolyl]-6,6-diphenyl-1,2-dioxane (**5c**).

This compound had mp 70-75° (from light petroleum, bp 40-70°); ir (potassium bromide): ν_{max} = 3370 (NH) cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ = 7.65 (1H, br s, NH), 6.91-7.40 (15H, m, arom H), 6.29 (1H, s, H-5'), 3.40 (1H, dd, J = 2.7, 13.5 Hz, H-4), 3.30 (3H, s, OMe), 2.86 (1H, dd, J = 2.7, 13.6 Hz, H_{eq}-5), 2.68 (1H, dd, J = 13.5, 13.6 Hz, H_{ax}-5), 1.05 (3H, br s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 164.0 (C-2'), 150.4 (C-4'), 141.8 (=C<), 140.4 (2 x =C<), 129.4 (2C), 128.4 (2C), 128.2 (2C), 127.5, 127.1, 126.5 (2C), 125.8 (2C), 122.7, 117.7 (2C) (arom =CH-), 107.9 (>C<), 104.0 (C-5'), 86.9 (>C<), 49.8 (OMe), 42.6 (-CH<), 36.3 (CH_2), 15.5 (Me).

Anal. Calcd. for $C_{27}H_{26}N_2O_3S \cdot 1/4H_2O$: C, 70.04; H, 5.77; N, 6.04. Found: C, 69.87; H, 5.96; N, 5.59.

3-Methoxy-3-methyl-4-(2-methyl-4-thiazolyl)-6,6-diphenyl-1,2-dioxane (**5d**).

This compound had mp 103-104° (from ethanol); ^1H nmr (300 MHz, deuteriochloroform): δ = 7.52-7.18 (10H, m, 2 x Ph), 6.90 (1H, s, H-5'), 3.58 (1H, dd, J = 3.4, 13.1 Hz, H-4), 3.40 (3H, s, OMe), 2.97 (1H, dd, J = 3.4, 13.7 Hz, H_{eq}-5), 2.87 (1H, dd, J = 13.1, 13.7 Hz, H_{ax}-5), 2.69 (3H, s, Me), 1.06 (3H, br s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 164.9 (C-2'), 154.2 (C-4'), 141.9 (2 x =C<), 128.4 (2C), 128.2 (2C), 127.5, 127.1, 126.5 (2C), 125.9 (2C) (arom =CH-), 114.9 (C-5'), 107.9 (>C<), 87.0 (>C<), 49.8 (OMe), 42.4 (CH), 35.5 (CH_2), 19.3 (Me), 15.5 (Me).

Anal. Calcd. for $C_{22}H_{23}NO_3S$: C, 69.26; H, 6.08; N, 3.67. Found: C, 69.06; H, 6.25; N, 3.63.

3-Methoxy-3-methyl-4-(2-phenyl-4-thiazolyl)-6,6-diphenyl-1,2-dioxane (**5e**).

This compound had mp 115-117° (from ethanol); ^1H nmr (300 MHz, deuteriochloroform): δ = 7.96-7.99 (2H, m, arom H), 7.93-7.19 (13H, m, arom H), 7.07 (1H, s, H-5'), 3.63 (1H, dd, J = 3.3, 12.1 Hz, H-4), 3.41 (3H, s, OMe), 3.09-2.95 (2H, m, CH_2), 1.14 (3H, br s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 167.1 (C-2'), 155.4 (C-4'), 141.8 (2C), 133.8 (=C<), 129.9, 128.9 (2C), 128.4 (2C), 128.2 (2C), 127.5, 127.1, 126.5 (2C), 126.48 (2C), 125.9 (2C) (arom =CH-), 115.7 (C-5'), 107.9 (>C<), 87.0 (>C<), 49.8 (OMe), 42.7 (-CH<), 36.6 (CH_2), 15.7 (Me).

Anal. Calcd. for $C_{27}H_{25}NO_3S$: C, 73.12; H, 5.68; N, 3.16. Found: C, 73.28; H, 5.63; N, 3.28.

Reaction of 4-Bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) with Acetamide.

A mixture of 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) (1 mmole) and acetamide (20 mmoles) was heated at 80° for 2 hours. Water (15 ml) was added to the reaction mixture and then the mixture was extracted with benzene (2 x 15 ml). The benzene layer was separated and washed with sodium hydrogencarbonate solution. After removing the chloroform, the resulting product was purified by tlc (Wakogel B10) while eluting with a mixture of hexane-ethyl acetate (4:6 v/v) followed by recrystallization. The yield is listed in Table 2.

3-Methoxy-3-methyl-4-(2-methyl-4-oxazolyl)-6,6-diphenyl-1,2-dioxane (**6**).

This compound had mp 118-120° (from ethanol); ^1H nmr (300 MHz, deuteriochloroform): δ = 7.48-7.19 (10H, m, arom H),

7.36 (1H, s, H-5'), 3.39 (3H, s, OMe), 3.38 (1H, dd, J = 3.0, 13.5 Hz, H-4), 2.89 (1H, dd, J = 3.0, 13.5 Hz, H_{eq}-5), 2.73 (1H, t, J = 13.5 Hz, H_{ax}-5), 2.43 (3H, s, Me), 1.17 (3H, br s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 161.2 (C-2'), 141.8, 138.7 (arom =C<), 135.4 (C-5'), 128.4 (2C), 128.2 (2C), 127.6, 127.2, 126.5 (3C), 125.9 (2C) (arom =CH- and C-4'), 107.5 (>C<), 86.8 (>C<), 49.8 (OMe), 38.1 (C-4), 35.8 (CH_2), 15.6 (Me), 14.0 (Me).

Anal. Calcd. for $C_{22}H_{23}NO_4$: C, 72.31; H, 6.34; N, 3.83. Found: C, 72.13; H, 6.40; N, 3.88.

Reactions of 4-Bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) with 3-Alkyl-4-amino-5-mercapto[1,2,4]triazoles.

The general procedure for the reactions of 4-bromoacetyl-3-methoxy-3methyl-6,6-diphenyl-1,2-dioxanes (**3**) with 3-alkyl-4-amino-5-mercapto[1,2,4]triazoles was as follows. A solution of 4-bromoacetyl-3-methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**3**) (1 mmole) and a 3-alkyl-4-amino-5-mercapto[1,2,4]triazole (2 mmole) in absolute ethanol (15 ml) was stirred at reflux temperature for one hour. The reaction was quenched by adding water (15 ml) and the mixture was then extracted with benzene. After removing the benzene, the resulting product was separated on tlc (Wakogel B 10) while eluting with a mixture of hexane-ethyl acetate (4:6 v/v). The product was further purified by recrystallization from appropriate solvent for an analytical sample. The yields are listed in Table 2.

Products.

3-Methoxy-3-methyl-4-[3-(5-methyl[1,2,4]triazolo[3,4-*b*]-2,3-dihydro-6*H*-[1,3,4]thiadiazinyl)]-6,6-diphenyl-1,2-dioxane (**7a**).

This compound was obtained as colorless needles, mp 219-221° (from ethanol); ^{1}H nmr (300 MHz, deuteriochloroform): δ = 7.50-7.23 (10H, m, 2 x Ph), 3.81 (1H, d, J = 15.9 Hz, C*H*H), 3.68 (1H, d, J = 15.9 Hz, CH*H*), 3.47 (3H, s, OMe), 3.30 (1H, dd, J = 2.0, 13.0 Hz, H-4), 2.99 (1H, dd, J = 2.0, 14.1 Hz, H_{eq}-5), 2.70 (1H, dd, J = 13.0, 14.0 Hz, H_{ax}-5), 2.54 (3H, s, Me-7'), 1.22 (3H, br s, Me-3); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 157.6, 151.0, 141.3 (2C), 140.3 (>C=), 128.6 (2C), 128.4 (2C), 127.9, 127.5, 126.1 (2C), 125.8 (2C) (arom =CH-), 106.9 (>C<), 87.0 (>C<), 50.1 (OMe), 48.4 (>CH-), 33.6 (CH_2), 25.2 (CH_2), 16.1 (Me), 10.4 (Me).

Anal. Calcd. for $C_{23}H_{24}N_4O_3S$: C, 63.28; H, 5.54; N, 12.83. Found: C, 63.22; H, 5.40; N, 12.72.

4-[3-(5-Ethyl[1,2,4]triazolo[3,4-*b*]-2,3-dihydro-6*H*-[1,3,4]thiadiazinyl)]-3methoxy-3-methyl-6,6-diphenyl-1,2-dioxane (**7b**).

This compound was obtained as colorless needles, mp 225-226° (from ethanol); ^{1}H nmr (300 MHz, deuteriochloroform): δ = 7.50-7.23 (10H, m, 2 x Ph), 3.79 (1H, d, J = 15.9 Hz, C*H*H), 3.52 (1H, d, J = 15.9 Hz, CH*H*), 3.47 (3H, s, OMe), 3.30 (1H, dd, J = 1.8, 12.9 Hz, H_{eq}-4), 3.00 (1H, dd, J = 2.7, 14.3 Hz, H_{eq}-5), 2.96-2.88 (2H, m, CH_2), 2.64 (1H, t, J = 13.5 Hz, H_{ax}-5), 1.39 (3H, t, J = 7.5 Hz, Me), 1.28 (3H, br s, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 157.4, 155.2, 141.3 (2C), 140.3 (>C=), 128.6 (2C), 128.4 (2C), 127.9, 127.5, 126.1 (2C), 125.7 (2C) (arom =CH-), 196.9 (>C), 87.0 (>C<), 50.1 (OMe), 48.4 (C-4), 33.6 (CH_2), 25.3 (CH_2), 18.4 (CH_2), 16.1 (Me), 11.2 (Me).

Anal. Calcd. for $C_{24}H_{26}N_4O_3S$: C, 63.98; H, 5.82; N, 12.44. Found: C, 63.84; H, 5.71; N, 12.26.

3-Methoxy-3-methyl-6,6-diphenyl-4-[3-(5-propyl[1,2,4]triazolo[3,4-*b*]-2,3-dihydro-6*H*-[1,3,4]thiadiazinyl)]-1,2-dioxane (**7c**).

This compound was obtained as colorless needles, mp 182-184° (from ethanol); ^{1}H nmr (300 MHz, deuteriochloroform): δ = 7.50-7.22 (10H, m, 2 x Ph), 3.78 (1H, d, J = 15.9 Hz, C*H*H), 3.52 (1H, d, J = 15.9 Hz, CH*H*), 3.47 (3H, s, OMe), 3.30 (1H, dd, J = 0.9, 12.3 Hz, H-4), 2.98 (1H, dd, J = 2.7, 14.1 Hz, H_{eq}-5), 2.88 (2H, dt, J = 1.8, 7.5 Hz, CH_2), 2.64 (1H, t, J = 13.3 Hz, H_{ax}-5), 1.84 (2H, sextet, J = 7.3 Hz, CH_2), 1.28 (3H, s, Me), 1.04 (3H, t, J = 7.3 Hz, Me); ^{13}C nmr (75 MHz, deuteriochloroform): δ = 157.3, 154.2, 141.3 (2C), 140.2 (>C=), 128.6 (2C), 128.4 (2C), 127.9, 127.5, 126.1 (2C), 125.7 (2C) (arom =CH-), 106.9 (>C<), 87.0 (>C<), 50.1 (OMe), 48.5 (>CH-), 33.6 (CH_2), 26.5 (CH_2), 25.3 (CH_2), 20.4 (CH_2), 16.1 (Me), 13.9 (Me).

Anal. Calcd. for $C_{25}H_{28}N_4O_3S$: C, 64.63; H, 6.07; N, 12.06. Found: C, 64.69; H, 6.28; N, 12.10.

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