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Synthesis of Novel Dihydro-1,2,4-triazoles from Thiosemicarbazones *via* 1,4-Diacetyl-3-methylsulfonyl-4,5-dihydro-1*H*-1,2,4-triazoles as Key Intermediates

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Novel 3,5-disubstituted 4,5-dihydro-1*H*-1,2,4-triazoles were synthesized by nucleophilic substitution of 1,4-diacetyl-3-methylsulfonyl-4,5-dihydro-1*H*-1,2,4-triazoles (**15a—c**), which were obtained by oxidation of 1,4-diacetyl-3-methylthio-4,5-dihydro-1*H*-1,2,4-triazoles (**5a—c**) with 2 mol eq of *m*-chloroperbenzoic acid. Acetylation of aldehyde or ketone *S*-methylisothiosemicarbazones (**3a—c**) with acetic anhydride at room temperature gave aldehyde or ketone 4-acetyl-3-methylisothiosemicarbazones (**4a—c**), which cyclized with acetic anhydride under heating to give **5a—c**. Compounds **5a—c** were also obtained by the reaction of **3a—c** with acetic anhydride under heating.

Keywords——3-methylsulfonyl-4,5-dihydro-1*H*-1,2,4-triazole; nucleophilic substitution; nucleophile; 1,4-diacetyl-3-methylthio-4,5-dihydro-1*H*-1,2,4-triazole; oxidation; *m*-chloroperbenzoic acid; *S*-methylisothiosemicarbazone; acetylation; 4-acetyl-3-methylisothiosemicarbazone; cyclization

Dihydro-1,2,4-triazoles (1,2,4-triazolines) without exocyclic double bonds are not aromatic and are relatively unstable,[1] though a few dihydro-1,2,4-triazoles stabilized by substitution with aromatic rings have been reported.[2] Recently, 4,5-dihydro-1*H*-1,2,4-triazole derivatives have been obtained by the reaction of 1-isopropylidene-3-methylthioisosemicarbazide with isothiocyanates.[3]

Previously, we have reported that the reaction of aldehyde and ketone thiosemicarbazones (**1a—c**) or aldehyde methylthio(thiocarbonyl)hydrazones with acetic anhydride gave 3-acetyl-5-(acetylamino)-2,3-dihydro-1,3,4-thiadiazoles (**2a—c**),[4] or 3-acetyl-5-methylthio-2,3-dihydro-1,3,4-thiadiazoles,[5] respectively. We have also reported that sulfonyl groups at the 2 position of 1,3,4-thiadiazoles can be substituted with nucleophiles.[6]

We now extend these findings to a new approach for convenient synthesis of novel 3-substituted 4,5-dihydro-1*H*-1,2,4-triazole derivatives *via* 1,4-diacetyl-3-methylsulfonyl-4,5-dihydro-1*H*-1,2,4-triazoles (**15a—c**) as key materials. Compounds **15a—c** were prepared by the oxidation of 5-substituted 1,4-diacetyl-3-methylthio-4,5-dihydro-1*H*-1,2,4-triazoles (**5a—c**), which were obtained by the reaction of aldehyde and ketone *S*-methylisothiosemicarbazones[7] (**3a—c**) with acetic anhydride under heating. The reaction of **3a—c**, obtained by *S*-methylation of **1a—c**, with acetic anhydride at room temperature gave aldehyde and ketone 4-acetyl-3-methylisothiosemicarbazones (**4a—c**). Acetylation of **4a—c** with acetic anhydride under heating gave compounds **5a—c**. Therefore, **5a—c** are considered to be produced from **3a—c** by way of **4a—c** as intermediates.

Proof of the structure of the 4,5-dihydro-1*H*-1,2,4-triazole (**5a**) is based upon physical evidence. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **5a** showed a C-5 proton absorption at δ 6.94, and the aromatic proton signals of **5a** appeared as a multiplet centered at δ 7.40 (5H). These chemical shifts are in good agreement with the C-2 and

aromatic proton shifts of 2,3-dihydro-1,3,4-thiadiazoles[4] which have similar structures to 4,5-dihydro-1*H*-1,2,4-triazoles. The carbon-13 nuclear magnetic resonance (^{13}C-NMR) signals of **5a** at δ 76.5 due to sp^3-hybridized C-5 and δ 150.3 due to sp^2-hybridized C-3 also support the 4,5-dihydro-1*H*-1,2,4-triazole structure.

Chemical shift assignment of the protons of the two acetyl groups in **5a** was possible by comparison of the ^{1}H-NMR spectrum of **5a** with that of 4-acetyl-3-methylthio-5-phenyl-1-propionyl-4,5-dihydro-1*H*-1,2,4-triazole (**6**) which was obtained by the reaction of **4a** with propionic anhydride at 90 °C. The signal of the acetyl protons of **6** appeared at δ 1.94, and those of **5a** appeared at δ 1.94 and 2.18. Therefore, the δ 1.94 signal of **5a** was assigned to the N-4 acetyl group, and the δ 2.18 signal to the N-1 acetyl group.

Proofs of the structures of **5b** and **5c** are also based upon physical data. The infrared (IR) absorption maxima at 1690 and 1650 cm^{-1} (C=O) of **5b**, and those at 1685 and 1665 cm^{-1} (C=O) of **5c**, and the ^{1}H-NMR signals at δ 1.74 ($COCH_3$) and 2.12 ($COCH_3$) of **5b**, and those at δ 2.22 ($COCH_3$) and 2.40 ($COCH_3$) of **5c**, and the ^{13}C-NMR signals at δ 84.9 due to sp^3-hybridized C-5 and 148.7 due to sp^2-hybridized C-3 of **5b**, and those at δ 85.7 (C-5) and 146.7 (C-3) of **5c**, suggested the presence of a 1,4-diacetyl-4,5-dihydro-1*H*-1,2,4-triazole ring in **5b** and **5c**.

Treatment of **6** with hydrazine hydrate at room temperature gave 1-propionyl-3-methylthio-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (**7**) in 94% yield. Treatment of **5a** with hydrazine hydrate at room temperature gave 1-acetyl-3-methylthio-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (**8**) in 88% yield, and the reverse reaction was accomplished by treating **8** with acetic anhydride under reflux.

The reaction of **3a** with other acylating agents such as propionic anhydride or benzoyl chloride at 90 °C for 1 h gave 3-methylthio-5-phenyl-1,4-dipropionyl-4,5-dihydro-1*H*-1,2,4-triazole (**9**) (85%) or 1,4-dibenzoyl-3-methylthio-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (**10**)

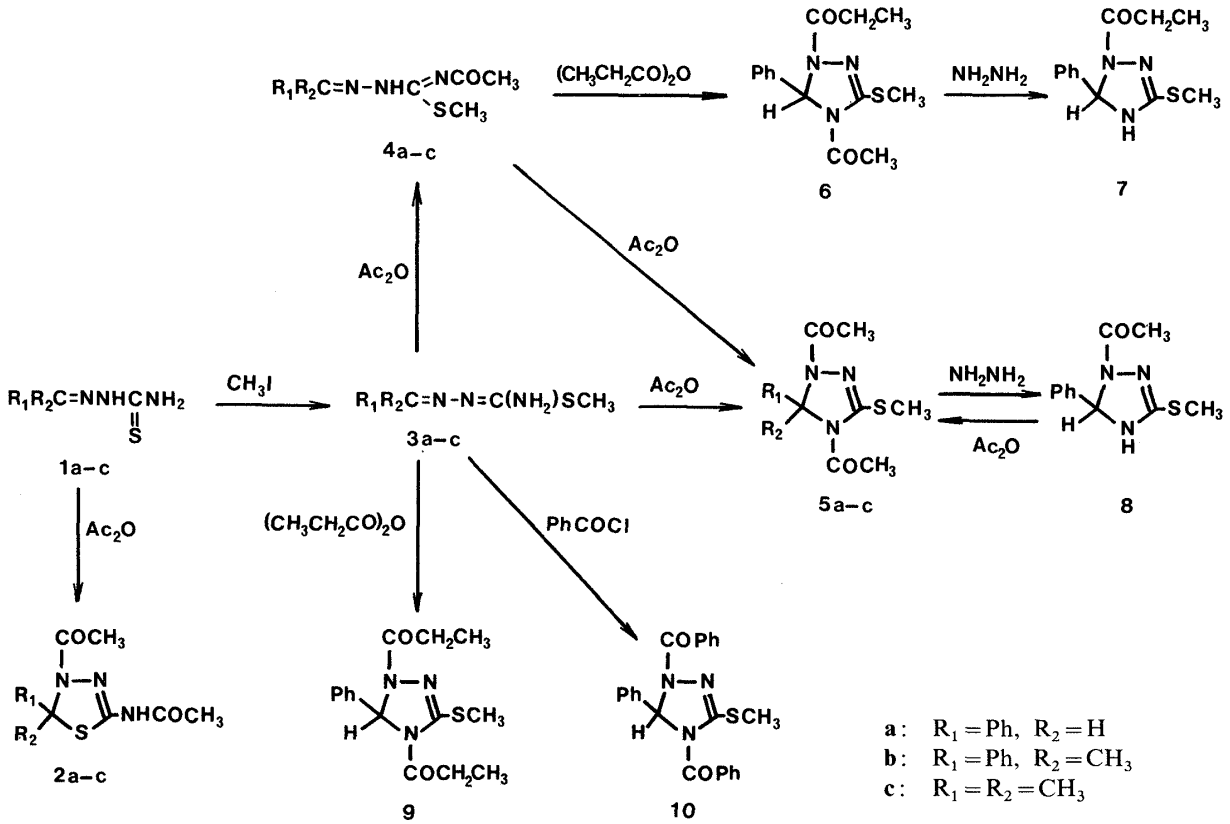

Chart 1

(30%).

In order to obtain **15a—c** from **5a—c** in good yields, the oxidizing agents and reaction conditions were examined. Oxidation of **5a** with potassium permanganate ($KMnO_4$) in acetic acid gave 3-methylsulfonyl-5-phenyl-1*H*-1,2,4-triazole (**11**), which was identical with the compound obtained by oxidation of 3-methylthio-5-phenyl-2*H*-1,2,4-triazole (**12**)[8] with $KMnO_4$.

Oxidation of **5a** with 1 mol eq of *m*-chloroperbenzoic acid (*m*-CPBA) in $CHCl_3$ at room temperature for 1 h gave compound **13** (32%), mp 145—146 °C, and compound **14** (56%), mp 165—168 °C. Both compounds **13** and **14** were determined to be diastereoisomers of 1,4-diacetyl-3-methylsulfinyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole on the basis of their spectral data.[9] The elemental analyses of both compounds were consistent with the molecular formula $C_{13}H_{15}N_3O_3S$. The mass spectra of **13** and **14** showed the same molecular ion peak at *m/z* 293 and fragment ion peaks at *m/z* 277 ($M^+ - O$) and *m/z* 188 [$(M^+ + 1) - COCH_3 - SOCH_3$]. Compounds **13** and **14** showed the IR absorption due to the 3-methylsulfinyl groups at 1080 and 1090 cm^{-1}, and ^{1}H-NMR signals of 3-methylsulfinyl protons at δ 3.06 and 3.00 (singlet) and C-5 protons at δ 7.17 and 7.13, respectively.

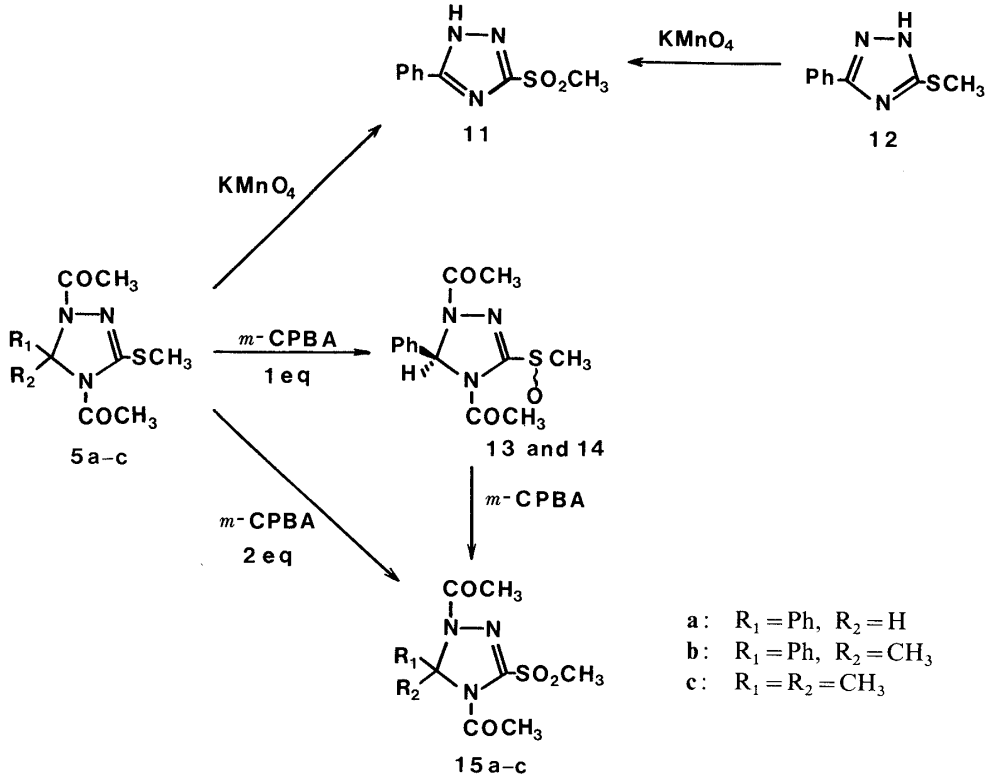

Chart 2

Oxidation of **5a** with 2 mol eq of *m*-CPBA in $CHCl_3$ at room temperature for 24 h gave a single product, 1,4-diacetyl-3-methylsulfonyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (**15a**) (90%) as crystals of mp 158—161 °C; this product was also obtained by oxidation of the diastereoisomers (**13** or **14**) with *m*-CPBA (2.5 mol eq) at room temperature. Oxidation of **5b** and **5c** with 2.1 mol eq of *m*-CPBA at room temperature gave 1,4-diacetyl-5-methyl-3-methylsulfonyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (**15b**) and 1,4-diacetyl-5,5-dimethyl-3-methylsulfonyl-4,5-dihydro-1*H*-1,2,4-triazole (**15c**) in 94 and 80% yields, respectively.

The nucleophilic substitution reactions of **15a—c** with various nucleophiles were examined for the synthesis of 3-substituted 1,4-diacetyl-4,5-dihydro-1*H*-1,2,4-triazoles, since the sulfonyl group is a good leaving group.[10]

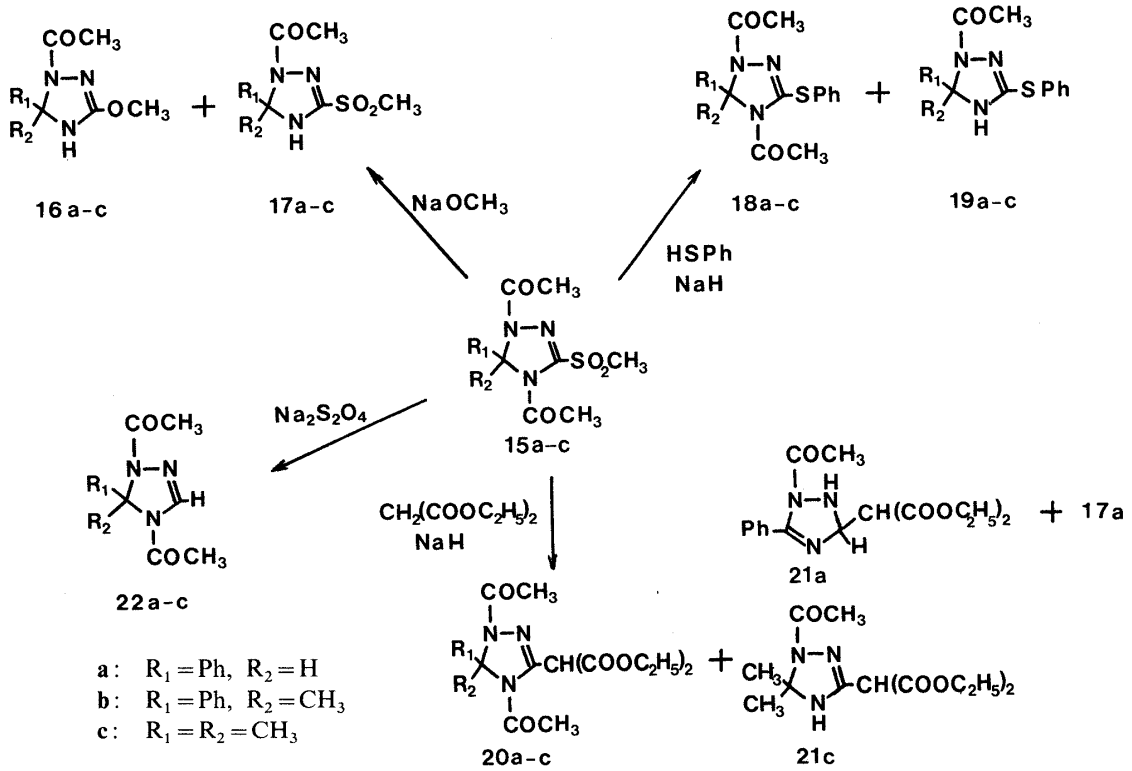

Chart 3

Treatment of **15a—c** with sodium methoxide in methanol at room temperature for 30 min gave 5-substituted 1-acetyl-3-methoxy-4,5-dihydro-1*H*-1,2,4-triazoles (**16a—c**) and 5-substituted 1-acetyl-3-methylsulfonyl-4,5-dihydro-1*H*-1,2,4-triazoles (**17a—c**) (Table I). The result suggests that the hard reagent easily attacks the hard N-4 acetyl group and hence the diacetyl derivative is not obtained. Treatment of **15a—c** with thiophenol in tetrahydrofuran (THF) in the presence of sodium hydride at room temperature for 10 min gave 5-substituted 1,4-diacetyl-3-phenylthio-4,5-dihydro-1*H*-1,2,4-triazoles (**18a—c**) and 5-substituted 1-acetyl-3-phenylthio-4,5-dihydro-1*H*-1,2,4-triazoles (**19a—c**) (Table II). Reaction of **15a** with diethyl malonate in THF in the presence of sodium hydride at room temperature for 1 h afforded diethyl (1,4-diacetyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)malonate (**20a**), diethyl (1-acetyl-5-phenyl-2,3-dihydro-1*H*-1,2,4-triazol-3-yl) malonate (**21a**), and **17a** in 69, 16, and 13% yields, respectively (Table III). The structure of **20a** was confirmed by the following spectral data. The ^{1}H- and ^{13}C-NMR spectra of **20a** showed signals due to the methine of the malonate side chain [δ 5.15 (1H, s), 53.3], C-5 proton [δ 6.90 (1H, s)], C-5 carbon (δ 76.3), and C-3 carbon (δ 143.1) (Table IV).

The ^{1}H- and ^{13}C-NMR spectra of **21a** showed signals due to the methine of the malonate side chain [δ3.94 (1H, d, J=6 Hz), 56.8], C-3 proton [δ5.48 (1H, dd, J=6, 10 Hz)], C-3 carbon

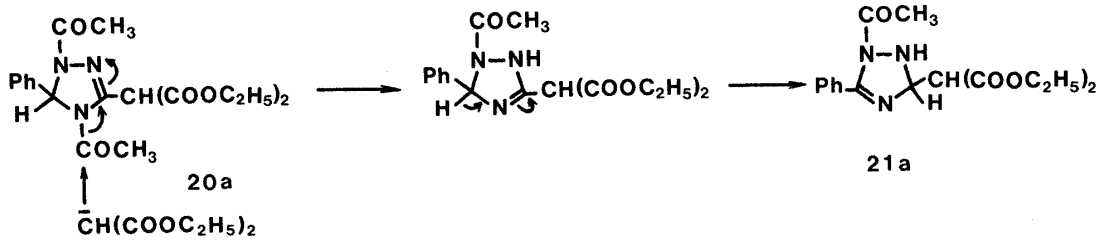

Chart 4

TABLE I. Spectral Data for 5-Substituted 1-Acetyl-3-methoxy-4,5-dihydro-1,2,4-triazoles (**16a—c**) and 5-Substituted 1-Acetyl-3-methylsulfonyl-4,5-dihydro-1,2,4-triazoles (**17a—c**)

Compd. No.	Yield (%)	mp (°C) (Recrystn. solvent)	IR ν_{max}^{KBr} cm^{-1} NH	CO	SO_2	^{1}H-NMR ($CDCl_3$) δ	Formula	Analysis (%) Calcd (Found) C	H	N	MS m/z (M^+)
16a	25	158—160 (EtOH–ether)	3200	1610		2.13 (3H, s, $COCH_3$), 3.92 (3H, s, OCH_3), 5.06 (1H, br s, NH), 6.43 (1H, s, C_5-H), 7.34 (5H, s, ArH)	$C_{11}H_{13}N_3O_2$	60.26 (60.28	5.98 6.04	19.17 19.09)	219
16b	43	155—157 (EtOH–ether)	3280	1615		2.04 (3H, s, CH_3), 2.07 (3H, s, CH_3), 3.84 (3H, s, OCH_3), 5.24 (1H, br s, NH), 7.20—7.50 (5H, m, ArH)	$C_{12}H_{15}N_3O_2$	61.79 (61.71	6.48 6.58	18.01 17.86)	233
16c	73	145—146 (Ether)	3205	1615		1.71 (6H, s, CH_3), 2.10 (3H, s, $COCH_3$), 3.82 (3H, s, OCH_3), 4.95 (1H, br s, NH)	$C_7H_{13}N_3O_2$	49.11 (49.04	7.65 7.91	24.54 24.69)	171
17a	67	134—135 (EtOH)	3340	1665	1330 1145	2.12 (3H, s, $COCH_3$), 3.15 (3H, s, SO_2CH_3), 6.51 (1H, s, C_5-H), 6.63 (1H, br s, NH), 7.30 (5H, s, ArH)	$C_{11}H_{13}N_3O_3S$	49.43 (49.58	4.90 4.89	15.72 15.86)	267
17b	17	185—187 (EtOH)	3110	1635	1325 1155	2.20 (3H, s, CH_3), 2.22 (3H, s, CH_3), 3.25 (3H, s, SO_2CH_3), 5.40 (1H, br s, NH), 7.25—7.55 (5H, m, ArH)	$C_{12}H_{15}N_3O_3S$	51.23 (51.12	5.37 5.30	14.94 14.85)	281
17c	19	167—168 (Ether)	3130	1630	1335 1150	1.79 (6H, s, CH_3), 2.20 (3H, s, $COCH_3$), 3.21 (3H, s, SO_2CH_3), 5.63 (1H, br s, NH)	$C_7H_{13}N_3O_3S$	38.35 (38.24	5.98 6.15	19.16 19.20)	219

(δ 57.1), NH proton [δ6.87 (1H, d, J= 10 Hz)], and C-5 carbon (δ 157.6). These results suggest the presence of a 2,3-dihydro-1*H*-1,2,4-triazole ring with the malonate side chain at C-3. A plausible mechanism for the formation of **21a** is shown in Chart 4.

Reaction of **15b** with the sodium salt of diethyl malonate at room temperature afforded only diethyl (1,4-diacetyl-5-methyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)malonate (**20b**) in 42% yield. Reaction of **15c** with the sodium salt of diethyl malonate under reflux for 30 min afforded diethyl (1,4-diacetyl-5,5-dimethyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)malonate (**20c**) and diethyl (1-acetyl-5,5-dimethyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)malonate (**21c**) in 63 and 13% yields, respectively. The ^{1}H- and ^{13}C-NMR spectra of **21c** showed signals due to the methine of the malonate side chain [δ 4.06 (1H, s), 57.8], C-5 carbon (δ 55.2), and C-3 carbon (δ 157.5). The spectral data of **20a—c** and **21c** in Table IV showed the presence of a 4,5-dihydro-1*H*-1,2,4-triazole ring.

Previously, we have reported that the methylsulfonyl groups of 5-substituted 2-methylsulfonyl-1,3,4-thiadiazoles could be removed by the reaction with $NaBH_4$.[6] Similar reaction of **15a** with $NaBH_4$ gave 1,4-diacetyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (**22a**) in extremely poor yield. However, it was found that reaction of **15a—c** with sodium dithionite

TABLE II. Spectral Data for 5-Substituted 1,4-Diacetyl-3-phenylthio-4,5-dihydro-1,2,4-triazoles (**18a—c**) and 5-Substituted 1-Acetyl-3-phenylthio-4,5-dihydro-1,2,4-triazoles (**19a—c**)

Compd. No.	Yield (%)	mp (°C) (Recrystn. solvent)	IR ν_{max}^{KBr} cm^{-1} NH	IR ν_{max}^{KBr} cm^{-1} CO	^{1}H-NMR ($CDCl_3$) δ	Formula	Analysis (%) Calcd (Found) C	H	N	MS *m/z* (M^+)
18a	83	164—166 (EtOH)		1695 1655	1.90 (3H, s, $COCH_3$), 2.00 (3H, s, $COCH_3$), 6.94 (1H, s, C_5-H), 7.35—7.75 (10H, m, ArH)	$C_{18}H_{17}N_3O_2S$	63.70 (63.61	5.05 4.99	12.38 12.40)	339
18b	73	119—121 (EtOH)		1685 1665	1.76 (3H, s, CH_3), 1.78 (3H, s, CH_3), 2.32 (3H, s, $COCH_3$), 7.18—7.80 (10H, m, ArH)	$C_{19}H_{19}N_3O_2S$	64.57 (64.72	5.42 5.45	11.89 11.93)	353
18c	81	89—91 (EtOH)		1680 1650	1.92 (3H, s, $COCH_3$), 2.02 (6H, s, CH_3), 2.41 (3H, s, $COCH_3$), 7.30—7.66 (5H, m, ArH)	$C_{14}H_{17}N_3O_2S$	57.71 (57.60	5.88 5.82	14.42 14.48)	291
19a	16		3180[a]	1630[a]	2.20 (3H, s, $COCH_3$), 4.92 (1H, br s, NH), 6.43 (1H, s, C_5-H), 7.29 (5H, s, ArH), 7.24—8.05 (5H, m, ArH)	$C_{16}H_{15}N_3OS$	297.0936[b] (297.0965)			297
19b	19	123—125 (EtOH)	3220	1635	2.00 (3H, s, CH_3), 2.09 (3H, s, CH_3), 5.16 (1H, br s, NH), 7.16—7.70 (10H, m, ArH)	$C_{17}H_{17}N_3OS$	65.57 (65.60	5.50 5.53	13.49 13.50)	311
19c	18	88—90 (Ether)	3250	1630	1.66 (6H, s, CH_3), 2.15 (3H, s, $COCH_3$), 4.40 (1H, br s, NH), 7.30—7.66 (5H, m, ArH)	$C_{12}H_{15}N_3OS$	57.81 (57.74	6.06 6.14	16.85 16.69)	249

a) Measured neat. *b*) Determined by high-resolution mass spectrometry. Upper figure, Calcd for M^+; lower figure found.

($Na_2S_2O_4$) in 50% aqueous EtOH under reflux gave 5-substituted 1,4-diacetyl-4,5-dihydro-1*H*-1,2,4-triazoles (**22a—c**) in good yields except for **22b** (Table V).

Experimental

Melting points were determined by the capillary method and are uncorrected. IR spectra were recorded on a Hitachi 215 spectrometer. ^{1}H-NMR spectra were recorded on a JEOL PS-100 spectrometer using tetramethylsilane as an internal standard. Mass spectra (MS) were measured with a JEOL D-300 instrument. For column chromatography, silica gel 60 (230—400 mesh, Nakarai Chemicals, Ltd.) was employed.

Benzaldehyde 4-Acetyl-3-methylisothiosemicarbazone (4a)——A mixture of **3a** (2.5 g, 12.95 mmol) and acetic anhydride (10 ml) was stirred at room temperature for 2 h. The mixture was poured into ice-water, and allowed to stand overnight. The resulting precipitate was collected by filtration and crystallized from EtOH to give **4a** (2.5 g, 82%), mp 86—88 °C. IR ν_{max}^{KBr} cm^{-1}: 3360, 1705. ^{1}H-NMR ($CDCl_3$) δ: 2.16 (3H, s, $COCH_3$), 2.39 (3H, s, SCH_3), 7.30—7.52 (3H, m, ArH), 7.62—7.86 (2H, m, ArH), 8.45 (1H, s, CH), 9.84 (1H, br s, NH). MS *m/z*: 235 (M^+). *Anal.* Calcd for $C_{11}H_{13}N_3OS$: C, 56.15; H, 5.57; N, 17.86. Found: C, 55.99; H, 5.59; N, 17.83.

Acetophenone 4-Acetyl-3-methylisothiosemicarbazone (4b)——Compound **4b** was obtained from **3b** (6.7 g, 32.36 mmol) and acetic anhydride (20 ml) in a similar manner to that described for compound **4a**. Yield, 6.45 g (80%). mp 125—128 °C. IR ν_{max}^{KBr} cm^{-1}: 3320, 1710. ^{1}H-NMR ($CDCl_3$) δ: 2.16 (3H, s, $COCH_3$), 2.44 (3H, s, SCH_3), 2.51 (3H, s, CH_3), 7.32—7.58 (3H, m, ArH), 7.72—7.96 (2H, m, ArH), 9.80 (1H, br s, NH). MS *m/z*: 249 (M^+). *Anal.* Calcd for $C_{12}H_{15}N_3OS$: C, 57.81; H, 6.06; N, 16.85. Found: C, 57.52; H, 5.93; N, 16.76.

Acetone 4-Acetyl-3-methylisothiosemicarbazone (4c)——A solution of acetic anhydride (0.915 g, 8.97 mmol) in $CHCl_3$ (6 ml) was added dropwise to a stirred mixture of **3c** (1 g, 6.89 mmol) and triethylamine (1.05 g, 10.37 mmol) in $CHCl_3$ (9 ml) at 0 °C. After the mixture had been stirred at room temperature for 1 h, the solvent was evaporated off

TABLE III. Spectral Data for Diethyl (5-Substituted 1,4-diacetyl-4,5-dihydro-1,2,4-triazol-3-yl)malonates (**20a**—**c**), Diethyl (1-Acetyl-5-phenyl-2,3-dihydro-1,2,4-triazol-3-yl)malonate (**21a**) and Diethyl (1-Acetyl-5,5-dimethyl-4,5-dihydro-1,2,4-triazol-3-yl)malonate (**21c**)

Compd. No.	Yield (%)	mp (°C) (Recrystn. solvent)	IR ν_{max}^{KBr} cm^{-1}		Formula	Analysis (%) Calcd (Found)			MS *m/z* (M^+)
			NH	CO		C	H	N	
20a	69			1755[a] 1735[a] 1700[a] 1670[a]	$C_{19}H_{23}N_3O_6$	389.1578[b] (389.1590)			389
20b	42			1750[a] 1735[a] 1690[a] 1675[a]	$C_{20}H_{25}N_3O_6$	403.1734[b] (403.1764)			403
20c	63			1755[a] 1740[a] 1685[a] 1675[a]	$C_{15}H_{23}N_3O_6$	341.1587[b] (341.1561)			341
21a	16	159—162 (EtOH)	3210	1750 1635	$C_{17}H_{21}N_3O_5$	58.78 (58.78	6.09 6.14	12.10 12.06)	347
21c	13	76—77 (*n*-Hexane)	3210	1750 1730 1650	$C_{13}H_{21}N_3O_5$	52.16 (52.17	7.07 7.13	14.04 13.89)	299

a) Measured neat. *b*) Determined by high-resolution mass spectrometry. Upper figure, Calcd for M^+; lower figure found.

TABLE IV. ^{1}H-NMR and ^{13}C-NMR Spectral Data for Diethyl (5-Substituted 1,4-diacetyl-4,5-dihydro-1,2,4-triazol-3-yl)malonates (**20a**—**c**), Diethyl (1-Acetyl-5-phenyl-2,3-dihydro-1,2,4-triazol-3-yl)malonate (**21a**) and Diethyl (1-Acetyl-5,5-dimethyl-4,5-dihydro-1,2,4-triazol-3-yl)malonate (**21c**)

Compd. No.	^{1}H-NMR ($CDCl_3$) δ (J=Hz)	^{13}C-NMR ($CDCl_3$) δ
20a	1.33 (6H, t, J=7, $CH_2C\underline{H}_3$), 1.87 (3H, s, $COCH_3$), 2.15 (3H, s, $COC\underline{H}_3$), 4.32 (4H, q, J=7, $C\underline{H}_2CH_3$), 5.15 (1H, s, $C\underline{H}(CO_2CH_2CH_3)_2$), 6.90 (1H, s, C_5-H), 7.32—7.48 (3H, m, ArH), 7.60—7.76 (2H, m, ArH)	14.1 (q), 20.8 (q), 24.2 (q), 53.3 (d), 62.3 (t), 76.3 (d), 127.0 (d), 129.0 (d), 130.0 (d), 136.7 (s), 143.1 (s), 164.6 (s), 164.9 (s), 166.8 (s), 167.0 (s)
20b	1.33 (6H, t, J=7, $CH_2C\underline{H}_3$), 1.64 (3H, s, $COC\underline{H}_3$), 2.09 (3H, s, $COC\underline{H}_3$), 2.34 (3H, s, CH_3), 4.29 (4H, q, J=7, $C\underline{H}_2CH_3$), 5.06 (1H, s, $C\underline{H}(CO_2CH_2CH_3)_2$), 7.32—7.50 (3H, m, ArH), 7.60—7.76 (2H, m, ArH)	14.0 (q), 21.4 (q), 22.3 (q), 23.8 (q), 53.7 (d), 62.2 (t), 84.2 (s), 126.8 (d), 128.6 (d), 129.2 (d), 140.0 (s), 141.9 (s), 164.9 (s), 166.2 (s), 167.1 (s)
20c	1.29 (6H, t, J=7, $CH_2C\underline{H}_3$), 2.05 (6H, s, CH_3), 2.18 (3H, s, $COC\underline{H}_3$), 2.26 (3H, s, $COC\underline{H}_3$), 4.22 (4H, q, J=7, $C\underline{H}_2CH_3$), 4.96 (1H, s, $C\underline{H}(CO_2CH_2CH_3)_2$)	14.0 (q), 22.7 (q), 24.0 (q), 24.6 (q), 53.8 (d), 62.0 (t), 83.3 (s), 142.0 (s), 164.9 (s), 166.4 (s), 167.4 (s)
21a	1.13 (3H, t, J=7, $CH_2C\underline{H}_3$), 1.18 (3H, t, J=7, $CH_2C\underline{H}_3$), 2.33 (3H, s, $COC\underline{H}_3$), 3.94 (1H, d, J=6, $C\underline{H}(CO_2CH_2CH_3)_2$), 4.12 (2H, q, J=7, $C\underline{H}_2CH_3$), 4.14 (2H, q, J=7, $C\underline{H}_2CH_3$), 5.48 (1H, dd, J=6, 10, C_3-H), 6.87 (1H, d, J=10, NH), 7.20—7.60 (5H, m, ArH)	10.9 (q), 13.8 (q), 13.9 (q), 56.8 (d), 57.1 (d), 61.8 (t), 62.0 (t), 126.5 (d), 128.1 (d), 128.7 (d), 138.7 (s), 157.6 (s), 162.7 (s), 166.7 (s), 168.0 (s)
21c	1.24 (6H, t, J=7, $CH_2C\underline{H}_3$), 1.59 (6H, s, CH_3), 2.33 (3H, s, $COC\underline{H}_3$), 4.06 (1H, s, $C\underline{H}(CO_2CH_2CH_3)_2$), 4.16 (4H, q, J=7, $C\underline{H}_2CH_3$), 5.16 (1H, br s, NH)	10.8 (q), 14.0 (q), 25.3 (q), 55.2 (s), 57.8 (d), 61.5 (t), 157.5 (s), 161.6 (s), 167.8 (s)

TABLE V. Spectral Data for 5-Substituted 1,4-Diacetyl-4,5-dihydro-1,2,4-triazoles (**22a**—**c**)

Compd. No.	Yield (%)	mp (°C) (Recrystn. solvent)	IR ν_{max}^{KBr} cm^{-1} CO	^{1}H-NMR δ	Formula	Analysis (%) Calcd (Found) C	H	N	MS *m/z* (M^+)
22a	90	140—141 (EtOH)	1690 1645	[b] 2.10 (3H, s, $COCH_3$), 2.21 (3H, s, $COCH_3$), 6.64 (1H, s, C_5-H), 7.32 (5H, s, ArH), 8.12 (1H, s, C_3-H)	$C_{12}H_{13}N_3O_2$	62.27 (62.50)	5.67 (5.63)	18.17 (18.01)	231
22b	35	157—159 (EtOH)	1680 1660	[b] 2.07 (3H, s, CH_3), 2.17 (3H, s, CH_3), 2.24 (3H, s, CH_3), 7.15—7.55 (5H, m, ArH), 8.00 (1H, s, C_3-H)	$C_{13}H_{15}N_3O_2$	63.66 (63.46)	6.16 (6.29)	17.13 (17.03)	245
22c	88		1700[a] 1650[a]	[c] 1.98 (6H, s, CH_3), 2.21 (3H, s, $COCH_3$), 2.26 (3H, s, $COCH_3$), 7.15 (1H, s, C_3-H)	$C_8H_{13}N_3O_2$	183.1007[d] (183.0998)			183

a) Measured neat. *b*) In DMSO-d_6. *c*) In $CDCl_3$. *d*) Determined by high-resolution mass spectrometry. Upper figure, Calcd for M^+; lower figure found.

under reduced pressure. The residue was chromatographed on a silica gel column ($CHCl_3$–MeOH, 100:1, v/v). Evaporation of the eluates gave a solid, which was crystallized from *n*-hexane to give **4c** (1.04 g, 80%). mp 65—67 °C. IR ν_{max}^{KBr} cm^{-1}: 3130, 1710. ^{1}H-NMR ($CDCl_3$) δ: 2.02 (3H, s, CH_3), 2.06 (3H, s, CH_3), 2.11 (3H, s, $COCH_3$), 2.31 (3H, s, SCH_3), 9.75 (1H, br s, NH). MS *m/z*: 187 (M^+). *Anal.* Calcd for $C_7H_{13}N_3OS$: C, 44.90; H, 7.00; N, 22.44. Found: C, 45.12; H, 7.24; N, 22.18.

1,4-Diacetyl-3-methylthio-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (5a)——i) A mixture of **3a** (2 g, 10.36 mmol) and acetic anhydride (10 ml) was stirred at 90 °C for 1 h. The mixture was poured onto ice, and allowed to stand overnight. The resulting precipitate was collected by filtration and crystallized from EtOH to give **5a** (2.5 g, 87%). mp 150—151 °C. IR ν_{max}^{KBr} cm^{-1}: 1690, 1645. ^{1}H-NMR ($CDCl_3$) δ: 1.94 (3H, s, $COCH_3$), 2.18 (3H, s, $COCH_3$), 2.50 (3H, s, SCH_3), 6.94 (1H, s, C_5-H), 7.30—7.60 (5H, m, ArH). ^{13}C-NMR ($CDCl_3$) δ: 14.8 (q, SCH_3), 20.8 (q, $COCH_3$), 23.8 (q, $COCH_3$), 76.5 (s, C-5), 126.9, 128.9, 129.6 and 136.8 (aromatic C), 150.3 (s, C-3), 165.9 (s, $COCH_3$), 166.4 (s, $COCH_3$). MS *m/z*: 277 (M^+). *Anal.* Calcd for $C_{13}H_{15}N_3O_2S$: C, 56.30; H, 5.45; N, 15.15. Found: C, 56.36; H, 5.38; N, 15.21.

ii) A mixture of **4a** (0.9 g, 3.83 mmol) and acetic anhydride (6 ml) was stirred at 90 °C for 1 h. Work-up as described in i) gave **5a** (1.05 g, 99%). mp 150—151 °C.

1,4-Diacetyl-5-methyl-3-methylthio-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (5b)——i) A mixture of **3b** (0.8 g, 3.86 mmol) and acetic anhydride (6 ml) was stirred under reflux for 1.5 h. The mixture was poured into ice-water, and allowed to stand overnight. The resulting precipitate was collected by filtration and crystallized from EtOH to give **5b** (0.56 g, 50%). mp 159—160 °C. IR ν_{max}^{KBr} cm^{-1}: 1690, 1660. ^{1}H-NMR ($CDCl_3$) δ: 1.74 (3H, s, $COCH_3$), 2.12 (3H, s, $COCH_3$), 2.34 (3H, s, C_5-CH_3), 2.46 (3H, s, SCH_3), 7.28—7.64 (5H, m, ArH). ^{13}C-NMR ($CDCl_3$) δ: 15.2 (q, SCH_3), 21.3 (q, CH_3), 22.3 (q, $COCH_3$), 23.6 (q, $COCH_3$), 84.9 (s, C-5), 126.0, 126.5, 128.5, 129.0, 129.5, 139.7 (aromatic C), 148.7 (s, C-3), 165.2 (s, $COCH_3$), 166.8 (s, $COCH_3$). MS *m/z*: 291 (M^+). *Anal.* Calcd for $C_{14}H_{17}N_3O_2S$: C, 57.71; H, 5.88; N, 14.42. Found: C, 57.60; H, 6.02; N, 14.20.

ii) A mixture of **4b** (3 g, 12.05 mmol) and acetic anhydride (16 ml) was stirred under reflux for 6 h. Work-up as described in i) gave **5b** (1.99 g, 57%). mp 159—160 °C.

1,4-Diacetyl-5,5-dimethyl-3-methylthio-4,5-dihydro-1*H*-1,2,4-triazole (5c)——i) Compound **3c** (0.7 g, 4.82 mmol) was mixed with acetic anhydride (6 ml) at 0 °C. After being stirred at 100 °C for 1.5 h, the mixture was poured into ice-water, and allowed to stand overnight. The resulting precipitate was crystallized from EtOH to give **5c** (0.84 g, 76%), mp 134—136 °C. IR ν_{max}^{KBr} cm^{-1}: 1685, 1665. ^{1}H-NMR ($CDCl_3$) δ: 2.04 (6H, s, C_5-CH_3), 2.22 (3H, s, $COCH_3$), 2.40 (3H, s, $COCH_3$), 2.48 (3H, s, SCH_3). ^{13}C-NMR ($CDCl_3$) δ: 15.4 (q, SCH_3), 22.7 (q, $COCH_3$), 23.5 (q, C(CH_3)$_2$), 24.8 (q, $COCH_3$), 85.7 (s, C-5), 146.7 (s, C-3), 165.8 (s, $COCH_3$), 166.3 (s, $COCH_3$). MS *m/z*: 229 (M^+). *Anal.* Calcd for $C_9H_{15}N_3O_2S$: C, 47.14; H, 6.59; N, 18.33. Found: C, 47.12; H, 6.52; N, 18.31.

ii) A mixture of **4c** (1 g, 5.34 mmol) and acetic anhydride (5 ml) was stirred at 110 °C for 3 h. After the mixture had been concentrated under reduced pressure, the resulting residue was crystallized from EtOH to give **5c** (1.08 g, 88%), mp 134—136 °C.

4-Acetyl-3-methylthio-5-phenyl-1-propionyl-4,5-dihydro-1*H*-1,2,4-triazole (6)——Compound **6** was obtained from **4a** (2.4 g, 10.21 mmol) and propionic anhydride (6 ml) in a similar manner to that described for compound **5a**. Yield 2.67 g (90%). mp 186—189 °C. IR ν_{max}^{KBr} cm^{-1}: 1695, 1640. ^{1}H-NMR ($CDCl_3$) δ: 1.08 (3H, t, J=7 Hz,

$COCH_2C\underline{H}_3$), 1.94 (3H, s, $COCH_3$), 2.48 (3H, s, SCH_3), 2.54 (2H, q, $J=7$ Hz, $COC\underline{H}_2CH_3$), 6.94 (1H, s, C_5-H), 7.30—7.55 (5H, m, ArH). ^{13}C-NMR ($CDCl_3$) δ: 8.4 (q, $COCH_2\underline{C}H_3$), 14.9 (q, SCH_3), 23.9 (q, $CO\underline{C}H_3$), 26.5 (t, $\underline{C}OCH_2CH_3$), 76.7 (d, C-5), 126.9, 129.0, 129.6, 136.9 (aromatic C), 150.2 (s, C-3), 166.4 (s, $\underline{C}OCH_3$), 169.6 (s, $\underline{C}OCH_2CH_3$). MS *m/z*: 291 (M^+). *Anal.* Calcd for $C_{14}H_{17}N_3O_2S$: C, 57.71; H, 5.88; N, 14.42. Found: C, 57.45; H, 5.81; N, 14.41.

3-Methylthio-5-phenyl-1-propionyl-4,5-dihydro-1*H*-1,2,4-triazole (7)——A mixture of **6** (0.75 g, 2.57 mmol) and hydrazine hydrate (10 ml) was stirred at room temperature for 2 h. The resulting precipitate was collected by filtration and crystallized from EtOH to give **7** (0.6 g, 94%). mp 130—132 °C. IR ν_{max}^{KBr} cm^{-1}: 3250, 1640. ^{1}H-NMR (DMSO-d_6) δ: 0.96 (3H, t, $J=7$ Hz, $COCH_2C\underline{H}_3$), 2.43 (3H, s, SCH_3), 2.43 (2H, q, $J=7$ Hz, $COC\underline{H}_2CH_3$), 6.40 (1H, s, C_5-H), 7.32 (5H, s, ArH), 8.23 (1H, br s, NH). MS *m/z*: 249 (M^+). *Anal.* Calcd for $C_{12}H_{15}N_3OS$: C, 57.81; H, 6.06; N, 16.85. Found: C, 57.67; H, 6.13; N, 16.89.

1-Acetyl-3-methylthio-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (8)——Compound **8** was obtained from **5a** (1 g, 3.61 mmol) and hydrazine hydrate (10 ml) in a similar manner to that described for compound **7**. Yield, 0.74 g (87%). mp 120—121 °C. IR ν_{max}^{KBr} cm^{-1}: 3150, 1615. ^{1}H-NMR (DMSO-d_6) δ: 2.04 (3H, s, $COCH_3$), 2.44 (3H, s, SCH_3), 6.40 (1H, s, C_5-H), 7.32 (5H, s, ArH), 8.24 (1H, br s, NH). MS *m/z*: 235 (M^+). *Anal.* Calcd for $C_{11}H_{13}N_3OS$: C, 56.15; H, 5.57; N, 17.86. Found: C, 56.18; H, 5.52; N, 18.06.

Reaction of 8 with Acetic Anhydride——A mixture of **8** (0.5 g, 2.1 mmol) and acetic anhydride (4 ml) was stirred under reflux for 2 h. The mixture was poured into ice-water, and allowed to stand overnight. The resulting precipitate was collected by filtration and crystallized from EtOH to give **5a** (0.29 g, 49%).

3-Methylthio-5-phenyl-1,4-dipropionyl-4,5-dihydro-1*H*-1,2,4-triazole (9)——Compound **9** was obtained from **3a** (0.9 g, 4.7 mmol) and propionic anhydride (3 ml) in a similar manner to that described for compound **5a**. Yield, 1.21 g (85%). mp 144—146 °C. IR ν_{max}^{KBr} cm^{-1}: 1695, 1640. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, t, $J=7$ Hz, $COCH_2C\underline{H}_3$), 1.08 (3H, t, $J=7$ Hz, $COCH_2C\underline{H}_3$), 1.70—2.35 (2H, m, $COC\underline{H}_2CH_3$), 2.48 (3H, s, SCH_3), 2.54 (2H, q, $J=7$ Hz, $COC\underline{H}_2CH_3$), 6.94 (1H, s, C_5-H), 7.30—7.55 (5H, m, ArH). MS *m/z*: 305 (M^+). *Anal.* Calcd for $C_{15}H_{19}N_3O_2S$: C, 59.00; H, 6.27; N, 13.76. Found: C, 59.20; H, 6.33; N, 13.94.

1,4-Dibenzoyl-3-methylthio-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (10)——Compound **10** was obtained from **3a** (0.9 g, 4.66 mmol) and benzoyl chloride (3 ml) in a similar manner to that described for compound **5a**. Yield, 0.55 g (30%). mp 167—169 °C. IR ν_{max}^{KBr} cm^{-1}: 1655, 1620. ^{1}H-NMR ($CDCl_3$) δ: 2.48 (3H, s, SCH_3), 7.10—8.15 (15H, m, ArH). MS *m/z*: 401 (M^+). *Anal.* Calcd for $C_{23}H_{19}N_3O_2S$: C, 68.81; H, 4.77; N, 10.47. Found: C, 68.97; H, 4.67; N, 10.45.

3-Methylsulfonyl-5-phenyl-1*H*-1,2,4-triazole (11)——i) Powdered potassium permanganate (1.88 g, 11.90 mmol) was added portionwise to a stirred solution of **5a** (1.5 g, 5.41 mmol) in acetic acid (10 ml) at 20 °C. After being stirred at room temperature for 2 h, the mixture was decolorized with 30% hydrogen peroxide, and concentrated under reduced pressure. The resulting residue was chromatographed on a silica gel column ($CHCl_3$–MeOH, 1:1, v/v). Evaporation of the eluates gave a solid, which was crystallized from benzene–EtOH to give **11** (0.6 g, 50%). mp 142—144 °C. IR ν_{max}^{KBr} cm^{-1}: 3250, 1320, 1135. ^{1}H-NMR (DMSO-d_6) δ: 3.38 (3H, s, SO_2CH_3), 7.48—7.70 (3H, m, ArH), 7.95—8.16 (2H, m, ArH). MS *m/z*: 223 (M^+). *Anal.* Calcd for $C_9H_9N_3O_2S$: C, 48.42; H, 4.06; N, 18.82. Found: C, 48.63; H, 4.03; N, 18.84.

ii) Powdered potassium permanganate (1.8 g, 11.39 mmol) was added portionwise to a stirred solution of 3-methylthio-5-phenyl-2*H*-1,2,4-triazole (**12**) (1 g, 5.23 mmol) in acetic acid (8 ml) at 20 °C. After the mixture had been stirred at room temperature for 1 h, work-up as described in i) gave **11** (1.05 g, 90%). mp 142—143 °C.

1,4-Diacetyl-3-methylsulfinyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (13 and 14)——A solution of 80% *m*-CPBA (2.52 g, 11.68 mmol) in $CHCl_3$ (70 ml) was added dropwise to a stirred solution of **5a** (3.23 g, 11.66 mmol) in $CHCl_3$ (20 ml) at room temperature. After being stirred at room temperature for 1 h, the mixture was neutralized with 5% aqueous sodium hydrogen carbonate and extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was chromatographed on a silica gel column ($CHCl_3$–acetone, 50:1, v/v) to give two fractions of diastereomeric products. Evaporation of the first fraction gave a solid, which was crystallized from EtOH to give **13** (1.1 g, 32%). mp 145—146 °C. IR ν_{max}^{KBr} cm^{-1}: 1710, 1680, 1080. ^{1}H-NMR (DMSO-d_6) δ: 1.90 (3H, s, $COCH_3$), 2.14 (3H, s, $COCH_3$), 3.06 (3H, s, $SOCH_3$), 7.17 (1H, s, C_5-H), 7.32—7.56 (5H, m, ArH). MS *m/z*: 293 (M^+). *Anal.* Calcd for $C_{13}H_{15}N_3O_3S$: C, 53.23; H, 5.15; N, 14.32. Found: C, 52.93; H, 4.91; N, 14.31. Evaporation of the second fraction gave a solid, which was crystallized from EtOH to give **14** (1.91 g, 56%). mp 165—168 °C. IR ν_{max}^{KBr} cm^{-1}: 1690, 1660, 1090. ^{1}H-NMR (DMSO-d_6) δ: 1.84 (3H, s, $COCH_3$), 2.12 (3H, s, $COCH_3$), 3.00 (3H, s, $SOCH_3$), 7.13 (1H, s, C_5-H), 7.34—7.62 (5H, m, ArH). MS *m/z*: 293 (M^+). *Anal.* Calcd for $C_{13}H_{15}N_3O_3S$: C, 53.23; H, 5.15; N, 14.32. Found: C, 53.14; H, 5.16; N, 14.29.

1,4-Diacetyl-3-methylsulfonyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (15a)——i) A solution of 80% *m*-CPBA (0.623 g, 2.88 mmol) in $CHCl_3$ (12 ml) was added dropwise to a stirred solution of **5a** (0.4 g, 1.44 mmol) in $CHCl_3$ (6 ml) at room temperature. After being stirred at room temperature for 24 h, the mixture was neutralized with 5% aqueous sodium hydrogen carbonate and extracted with $CHCl_3$ (3 × 50 ml). The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was crystallized from EtOH to give **15a** (0.4 g, 90%). mp 161—164 °C. IR ν_{max}^{KBr} cm^{-1}: 1705, 1690, 1325, 1150. ^{1}H-NMR ($CDCl_3$) δ: 2.10 (3H, s, $COCH_3$),

2.24 (3H, s, $COCH_3$), 3.49 (3H, s, SO_2CH_3), 7.04 (1H, s, C_5-H), 7.41 (5H, s, ArH). MS *m/z*: 309 (M^+). *Anal.* Calcd for $C_{13}H_{15}N_3O_4S$: C, 50.48; H, 4.89; N, 13.58. Found: C, 50.22; H, 4.73; N, 13.67.

ii) A solution of 80% *m*-CPBA (26 mg, 0.12 mmol) in $CHCl_3$ (2 ml) was added dropwise to a stirred solution of **13** (15 mg, 0.05 mmol) in $CHCl_3$ (1 ml) at room temperature. After the mixture had been stirred at room temperature for 10 h, work-up as described in i) gave **15a** (12 mg, 76%). mp 161—164 °C.

iii) A solution of 80% *m*-CPBA (23 mg, 0.10 mmol) in $CHCl_3$ (2 ml) was added dropwise to a stirred solution of **14** (13 mg, 0.04 mmol) in $CHCl_3$ (1 ml) at room temperature. After the mixture had been stirred at room temperature for 7 h, work-up as described in i) gave **15a** (10 mg, 73%). mp 161—163 °C.

1,4-Diacetyl-5-methyl-3-methylsulfonyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (15b)——Compound **15b** was obtained from **5b** (2.40 g, 8.24 mmol) and 80% *m*-CPBA (3.74 g, 17.33 mmol) in $CHCl_3$ in a similar manner to that described for compound **15a**. Yield, 2.50 g (94%). mp 193—195 °C (dec.). IR ν_{max}^{KBr} cm^{-1}: 1700, 1675, 1335, 1150. ^{1}H-NMR ($CDCl_3$) δ: 1.85 (3H, s, CH_3), 2.18 (3H, s, $COCH_3$), 2.37 (3H, s, $COCH_3$), 3.47 (3H, s, SO_2CH_3), 7.32—7.60 (5H, m, ArH). MS *m/z*: 323 (M^+). *Anal.* Calcd for $C_{14}H_{17}N_3O_4S$: C, 52.00; H, 5.30; N, 13.00. Found: C, 51.85; H, 5.26; N, 13.03.

1,4-Diacetyl-5,5-dimethyl-3-methylsulfonyl-4,5-dihydro-1*H*-1,2,4-triazole (15c)——A solution of 80% *m*-CPBA (6.5 g, 30.13 mmol) in $CHCl_3$ (80 ml) was added dropwise to a stirred solution of **5c** (3.28 g, 14.32 mmol) in $CHCl_3$ (40 ml) at room temperature. After the mixture had been stirred at room temperature for 3 h, work-up as described for the preparation of **15a** gave **15c** (3.01 g, 80%). mp 138—140 °C. IR ν_{max}^{KBr} cm^{-1}: 1690, 1680, 1310, 1150. ^{1}H-NMR ($CDCl_3$) δ: 2.07 (6H, s, CH_3), 2.24 (3H, s, $COCH_3$), 2.49 (3H, s, $COCH_3$), 3.41 (3H, s, SO_2CH_3). MS *m/z*: 261 (M^+). *Anal.* Calcd for $C_9H_{15}N_3O_4S$: C, 41.37; H, 5.79; N, 16.08. Found: C, 41.40; H, 5.86; N, 16.25.

Reaction of 15a—c with Sodium Methoxide——A solution of sodium methoxide (40 mg, 0.74 mmol) in MeOH (3 ml) was added dropwise to a stirred solution of **15a** (200 mg, 0.65 mmol) in MeOH (3 ml) at room temperature. After being stirred at room temperature for 15 min, the mixture was neutralized with aqueous acetic acid and extracted with $CHCl_3$ (3 × 50 ml). The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was chromatographed on a silica gel column ($CHCl_3$–AcOEt, 2 : 1, v/v) to give two fractions. Evaporation of the first fraction gave a solid, which was crystallized from EtOH–ether to give 1-acetyl-3-methoxy-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (**16a**) (35 mg, 25%). Evaporation of the second fraction gave a solid, which was crystallized from EtOH to give 1-acetyl-3-methylsulfonyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (**17a**) (116 mg, 67%). 5-Substituted 1-acetyl-3-methoxy-4,5-dihydro-1*H*-1,2,4-triazoles (**16b** and **16c**) and 5-substituted 1-acetyl-3-methylsulfonyl-4,5-dihydro-1*H*-1,2,4-triazoles (**17b** and **17c**) were prepared in a similar manner to that described for compounds **16a** and **17a**. Yields, melting points, crystallization solvents, and analytical and spectral data for compounds **16a—c** and **17a—c** are given in Table I.

Reaction of 15a—c with Thiophenol in the Presence of Sodium Hydride——A suspension of sodium hydride (31 mg, 0.78 mmol, 60% dispersion in oil, washed twice with ether) in anhydrous THF (4 ml) was added dropwise to a stirred solution of thiophenol (86 mg, 0.78 mmol) in anhydrous THF (4 ml) at room temperature. After being stirred at room temperature for 1 h, the mixture was treated dropwise with a solution of **15a** (200 mg, 0.65 mmol) in anhydrous THF (10 ml). After 10 min at room temperature, the mixture was neutralized with aqueous acetic acid and extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was chromatographed on a silica gel column ($CHCl_3$–acetone, 20 : 1, v/v) to give two fractions. Evaporation of the first fraction gave a solid, which was crystallized from EtOH to give 1,4-diacetyl-5-phenyl-3-phenylthio-4,5-dihydro-1*H*-1,2,4-triazole (**18a**) (183 mg, 83%). Evaporation of the second fraction gave 1-acetyl-5-phenyl-3-phenylthio-4,5-dihydro-1*H*-1,2,4-triazole (**19a**) (30 mg, 16%). 5-Substituted 1,4-diacetyl-3-phenylthio-4,5-dihydro-1*H*-1,2,4-triazoles (**18b** and **18c**) and 5-substituted 1-acetyl-3-phenylthio-4,5-dihydro-1*H*-1,2,4-triazoles (**19b** and **19c**) were prepared in a similar manner to that described for compounds **18a** and **19a**. Yields, melting points, crystallization solvents, and analytical and spectral data for compounds **18a—c** and **19a—c** are given in Table II.

Reaction of 15a—c with Diethyl Malonate in the Presence of Sodium Hydride——A suspension of sodium hydride (130 mg, 3.25 mmol, 60% dispersion in oil, washed twice with ether) in anhydrous THF (5 ml) was added dropwise to a stirred solution of diethyl malonate (520 mg, 3.25 mmol) in anhydrous THF (5 ml) at room temperature. After being stirred at room temperature, the mixture was treated dropwise with a solution of **15a** (500 mg, 1.62 mmol) in anhydrous THF (12 ml). After 1 h at room temperature, the mixture was neutralized with aqueous acetic acid and was extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was chromatographed on a silica gel column ($CHCl_3$–acetone, 20 : 1, v/v) to give three fractions. Evaporation of the first fraction gave diethyl (1,4-diacetyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)malonate (**20a**) (434 mg, 69%) as an oil. Evaporation of the second fraction gave diethyl (1-acetyl-5-phenyl-2,3-dihydro-1*H*-1,2,4-triazol-3-yl)malonate (**21a**) (90 mg, 16%). Evaporation of the third fraction gave **17a** (56 mg, 13%). Diethyl (5-substituted 1,4-diacetyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)malonates (**20b** and **20c**) and diethyl (1-acetyl-5,5-dimethyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)malonate (**21c**) were prepared in a similar manner to that described for compounds **20a** and **21a**. Yields, melting points, crystallization solvents, and analytical and spectral data for compounds **20a—c**, **21a**, **c** are given in Tables III and IV.

Reaction of 15a with $NaBH_4$——$NaBH_4$ (43 mg, 1.13 mmol) was added portionwise to a stirred solution of **15a** (350 mg, 1.12 mmol) in EtOH (5 ml) at room temperature. After being stirred at room temperature for 1 h, the mixture was neutralized with aqueous acetic acid and concentrated under reduced pressure. The resulting residue was chromatographed on a silica gel column ($CHCl_3$–acetone, 20 : 1, v/v) to give a solid, which was crystallized from EtOH to give 1,4-diacetyl-5-phenyl-4,5-dihydro-1*H*-1,2,4-triazole (**22a**) (60 mg, 23%).

Reaction of 15a—c with $Na_2S_2O_4$——A mixture of **15a** (350 mg, 1.13 mmol) and $Na_2S_2O_4$ (395 mg, 2.27 mmol) in 50% aqueous EtOH (25 ml) was stirred under reflux for 5 h. The mixture was extracted with $CHCl_3$ (3 × 100 ml). The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was crystallized from EtOH to give **22a** (235 mg, 90%). Compounds **22b** and **22c** were obtained by the reaction of **15b** and **15c** with 8 and 5 eq of $Na_2S_2O_4$, respectively, in a similar manner to that described for compound **22a**. Yields, melting points, crystallization solvents, and analytical and spectral data for compounds **22a—c** are given in Table V.

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