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Bromomethyl-1,2,5-thiadiazoles **2a-c** were prepared by bromination of methyl-1,2,5-thiadiazoles **1a-c** by NBS in refluxing carbon tetrachloride. When bromination of **1a** and **1b** was carried out under irradiation of tungsten lamp, mixtures of *cis*-**5a** and **b** and *trans*-1,2-dibromo-1,2-bis(1,2,5-thiadiazol-3-yl)ethylene (**6a** and **b**) were obtained.

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Some stable heterocycles are considered to be masked forms of functionalized acyclic systems; therefore functional heterocycles are important synthons in organic synthesis.

Aiming at the functionalization of the methyl group on the 1,2,5-thiadiazole ring, we investigated the bromination reaction of 3-methyl- (**1a**) [1], 3-methyl-4-phenyl- (**1b**) [2] and 3,4-dimethyl-1,2,5-thiadiazole (**1c**) [1] with *N*-bromosuccinimide (NBS).

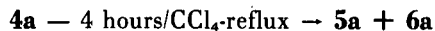
Results and Discussion.

Bromination of **1a** and **1b** was carried out under various conditions and the results are summarized in Scheme 1 and the Table.

3-Bromomethyl-1,2,5-thiadiazole (**2a**) was obtained in 22% yield with a recovery of **1a** in 27% yield when **1a** was treated with 1.1 equivalents of NBS in refluxing carbon tetrachloride for 4 hours. In the reaction with prolonged reaction time, 3-dibromomethyl- (**3a**) and 3-tribromomethyl-1,2,5-thiadiazole (**4a**) were formed and the isolation of **2a** was difficult.

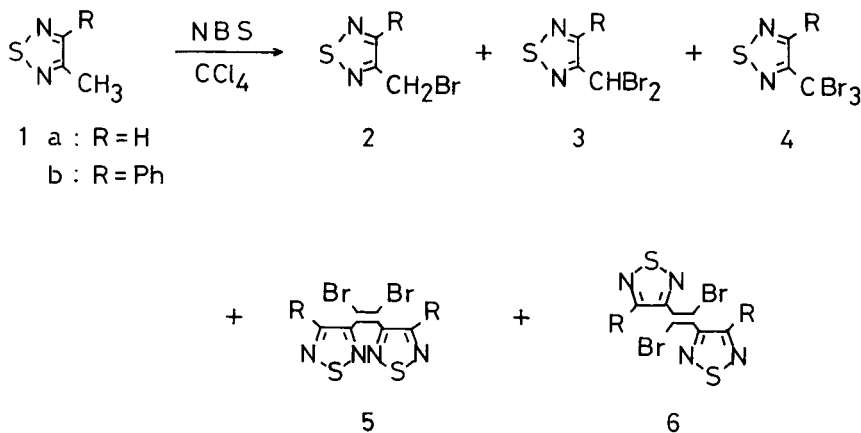
In the reaction of **1a** with 3.1 equivalents of NBS under the above conditions for 10 hours, unchanged **1a** was detected. Irradiation of tungsten lamp accelerated the reaction and **1a** was consumed in 1 hour, giving also a mixture of **2a**, **3a** and **4a**. With reaction time, compounds **2a** and **3a** gradually disappeared and after 7 hours, **4a**, *cis*- (**5a**) and *trans*-1,2-dibromo-1,2-bis(1,2,5-thiadiazol-3-yl)ethylene (**6a**) were obtained in 38, 7 and 19% yields, respectively. Further irradiation caused the conversion of **4a** and, after 32 hours, **5a** and **6a** were obtained in 18 and 49% yields, respectively. Irradiation of **4a** for 4 hours gave a 4:6 mixture of **5a** and **6a** in 49% yield.

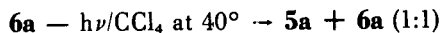
It is noted that the above reaction presents a novel example of C=C bond formation by photolysis of organic halides, which has not been well known.



Interconversion between **5a** and **6a** was studied; **5a** gave a 7:3 mixture of **5a** and **6a** on being heated in carbon tetrachloride at reflux for 65 hours while **6a** afforded a 1:1 mixture of **5a** and **6a** on irradiation at 40° for 25 hours.

Scheme 1

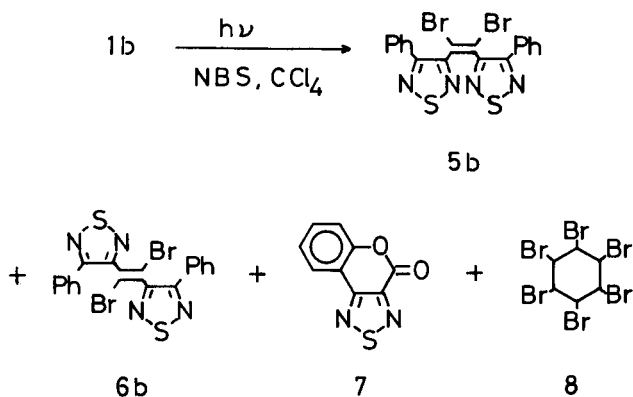




On the other hand, bromination of **1b** under thermal conditions proceeded slowly but selectively. Compounds **2b** and **3b** were obtained in 76 and 100% yields, respectively, however, tribromide **4b** could not be prepared.

Under irradiation, the bromination of **1b** proceeded smoothly but afforded a mixture of the corresponding bromides in a short time.

When irradiation of **1b** with 6.1 equivalents of *N*-bromosuccinimide was carried out for 80 hours, *cis*- (**5b**) and *trans*-1,2-dibromo-1,2-(4-phenyl-1,2,5-thiadiazol-3-yl)-ethylene (**6b**) were obtained in 15 and 20% yields, respectively, together with 4-oxo-2*H*-chromeno[3,4-*c*]1,2,5-thiadiazole (**7**) [3] and *trans*-benzene hexabromide (**8**) [4] in 2 and 3% yields, respectively.



Electronic spectra of **5** and **6** are shown in Figure 1.

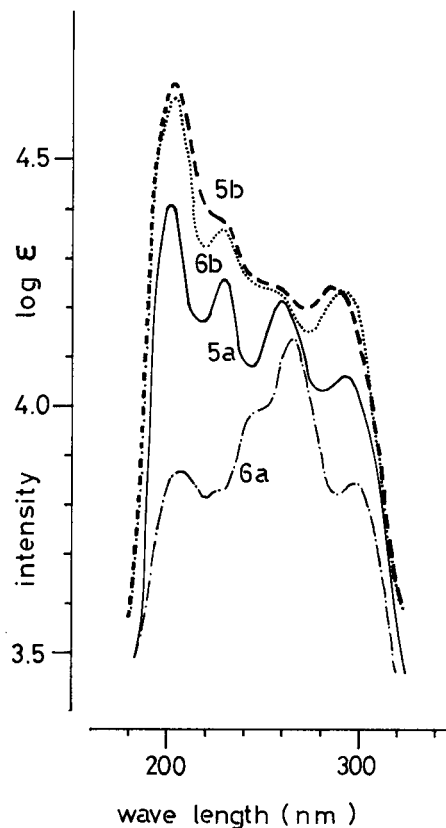


Figure 1. Electronic spectra of **5a**, **5b**, **6a** and **6b**.

3-Bromomethyl-4-methyl-1,2,5-thiadiazole (**2c**) was obtained in 46% yield with a recovery of **1c** in 14% yield when the bromination was conducted for 4 hours with 1.1 equivalents of *N*-bromosuccinimide without irradiation.

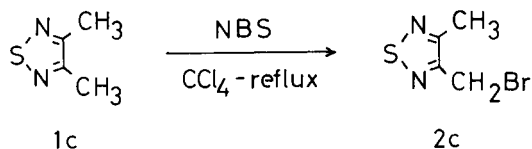
Table

Bromination of Methyl Substituted 1,2,5-Thiadiazoles **1a** and **b**

Run	I	NBS/I [a]	time (hours)	2	3	Products, Yield (%) [b]			recovered I
						4	5	6	
1 [c]	A	1.2	4	22	—	—	—	—	27
2 [c]	A	3.1	10	(57)	(29)	(12)	—	—	(2)
3 [d]	A	2.1	2	(28)	(45)	(24)	—	—	(3)
4 [d]	A	3.1	1	(23)	(38)	(36)	—	(3)	—
5 [d]	A	3.1	2	(8)	(29)	(48)	(7)	—	—
6 [d]	A	3.1	4	(5)	(21)	(53)	(8)	(13)	—
7 [d]	A	3.1	10	—	(9)	(34)	(14)	(44)	—
8 [d]	A	4.0	7	—	—	38	7	19	—
9 [d]	A	3.1	24	—	—	(3)	(25)	(72)	—
10 [d]	A	3.1	32	—	—	—	18	49	—
11 [c]	B	1.1	24	76	—	—	—	—	—
12 [c]	B	2.1	24	—	100	—	—	—	—
13 [d,e]	B	6.1	17	—	—	—	15	20	—

[a] Molar ratio. [b] Yields in parenthesis are relative yields determined by pmr. [c] Without irradiation in the presence of benzoyl peroxide or 2,2'-azobisisobutyronitrile. Both catalysts gave almost same results. [d] With irradiation. [e] Compounds **7** and **8** were obtained in 2 and 3% yields, respectively.

Prolonged reaction time or the use of more *N*-bromosuccinimide caused the formation of a mixture of bromides and isolation of the specialized bromide became difficult.



EXPERIMENTAL

All melting points are uncorrected. The ir spectra were measured on a Nippon Bunko A-102 spectrophotometer as potassium bromide pellets or as liquid films on sodium chloride discs. The ¹H-nmr spectra were determined at 100 MHz on a Nippon Denshi JEOL FT-100 in deuteriochloroform or carbon tetrachloride using TMS as an internal standard. Mass spectra were obtained on a Nippon Denshi JMS-01SG-2 mass spectrometer at 75 eV using a direct inlet system. Electronic spectra were measured on a Hitachi 220 A spectrometer in cyclohexane.

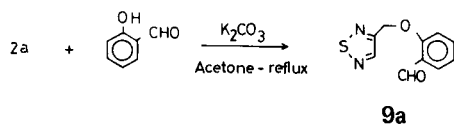
Preparation of 3-Bromomethyl-1,2,5-thiadiazole (2a).

After a mixture of 50 g (0.5 mole) of **1a**, 99 g (0.55 mole) of *N*-bromosuccinimide and 0.5 g of benzoyl peroxide in 500 ml of dry carbon tetrachloride was refluxed for 4 hours, precipitates were removed by filtration and the filtrate was evaporated *in vacuo* to leave a red oil, which was distilled *in vacuo* to give 20 g (22%) of **2a** (bp 25-31°/21 mm Hg).

3-Bromomethyl-1,2,5-thiadiazole (2a).

This compound was obtained as a colorless oil, ¹H-nmr (deuteriochloroform): δ 4.70 (s, 2H), 8.60 (s, 1H). Because **2a** is strongly lachrymatory, other spectra were not measured and **2a** was identified by the reaction with salicylaldehyde.

Reaction of 2a with Salicylaldehyde.



A mixture of 2.1 g (12 mmoles) of **2a**, 1.4 g (12 mmoles) of salicylaldehyde and 2.4 g (17 mmoles) of potassium carbonate in 10 ml of acetone was refluxed for 1 hour. Inorganics were filtered and the filtrate was evaporated *in vacuo* to leave a colorless solid, which, on recrystallization from hexane, gave 1.42 g (55%) of **12a**.

3-(*o*-Formylphenoxy)methyl-1,2,5-thiadiazole (9a).

This compound was obtained as colorless needles, mp 91-93°; ir: ν CO 1675 cm⁻¹; ms: m/e (relative intensity) 220 (M⁺, 71), 121 (100), 99 (72); ¹H-nmr (deuteriochloroform): δ 5.45 (s, 2H), 6.96-7.86 (m, 4H), 8.65 (s, 1H), 10.46 (s, 1H).

Anal. Calcd. for C₁₀H₈N₂O₂S: C, 54.55; H, 3.64; N, 12.73. Found: C, 54.42; H, 3.77; N, 12.31.

Preparation of 3-Dibromomethyl-1,2,5-thiadiazole (3a).

After a mixture of 5.0 g (50 mmoles) of **1a**, 19.0 g (107 mmoles) of *N*-bromosuccinimide and 0.2 g of 2,2'-azobisisobutyronitrile in 50 ml of carbon tetrachloride was refluxed for 2 hours with irradiation of tungsten lamp, it was treated as described above to leave a red oil. It was column chromatographed on silica gel (Wako gel, C-300) using benzene as an eluent to give 5.3 g (41%) of **3a** (bp 80°/4 mm Hg), then 2.4 g (14%) of **4a**, 2.0 g (22%) of **2a**, and finally, a trace of ethylene (**5a** and **6a**).

3-Dibromomethyl-1,2,5-thiadiazole (3a).

This compound was obtained as a colorless oil; ms: m/e (relative intensity) 259 (52), 257 (100), 255 (40), 179 (53), 177 (56); ¹H-nmr (deuteriochloroform): δ 6.84 (s, 1H), 8.88 (s, 1H).

Anal. Calcd. for C₃H₂Br₂N₂S: C, 13.97; H, 0.78; N, 10.86. Found: C, 14.24; H, 0.85; N, 10.93.

Preparation of 5a and 6a.

After a mixture of 5.0 g (50 mmoles) of **1a**, 28.0 g (155 mmoles) of *N*-bromosuccinimide and 0.2 g of 2,2'-azobisisobutyronitrile in 100 ml of carbon tetrachloride was refluxed with irradiation of tungsten lamp for 32 hours, it was treated as described above to give a colorless oil, which was extracted with hexane and hexane-extract was evaporated *in vacuo* to give a colorless solid. Recrystallization from hexane afforded 6.0 g (67%) of a 18:49-mixture of **5a** and **6a**. Pure samples of **5a** and **6a** were obtained through column chromatography on silica gel (Wako C-300) using hexane as an eluent.

cis-1,2-Dibromo-1,2-bis(1,2,5-thiadiazol-3-yl)ethylene (5a).

This compound was obtained as pale yellow prisms, mp 150-151°; ms: m/e (relative intensity) 355 (53), 354 (60), 353 (100), 352 (84), 351 (49), 350 (41), 274 (75), 272 (83), 194 (70), 167 (80); ¹H-nmr (carbon tetrachloride): δ 8.94 (s, 2H); uv: λ max nm (log ε) 295 (4.11), 261 (4.20), 230 (4.27), 200 (4.32).

Anal. Calcd. for C₆H₂Br₂N₄S₂: C, 20.36; H, 0.57; N, 15.83. Found: C, 20.42; H, 0.83; N, 15.81.

trans-1,2-Dibromo-1,2-bis(1,2,5-thiadiazol-3-yl)ethylene (6a).

This compound was obtained as yellow prisms, mp 59-60°; ms: m/e (relative intensity) 356 (46), 355 (48), 354 (83), 353 (78), 352 (40), 351 (38), 275 (63), 273 (60), 194 (64), 167 (100); ¹H-nmr (deuteriochloroform): δ 8.48 (s, 2H); uv: λ max nm (log ε) 300 (3.95), 267 (4.12), 246 (4.01), 226 (3.94), 206 (3.96).

Anal. Calcd. for C₆H₂Br₂N₄S₂: C, 20.36; H, 0.57; N, 15.83. Found: C, 20.29; H, 0.85; N, 15.98.

Preparation of 3-Tribromomethyl-1,2,5-thiadiazole (4a).

After a mixture of 5.0 g (50 mmoles) of **1a**, 36.0 g (200 mmoles) of *N*-bromosuccinimide and 0.2 g of 2,2'-azobisisobutyronitrile in 100 ml of carbon tetrachloride was refluxed with irradiation of tungsten lamp for 7 hours, it was treated as described above to leave a red oil. It was column chromatographed on silica gel (Wako C-300) using benzene as an eluent to afford colorless oil, which, on distillation *in vacuo*, gave 6.3 g (38%) of **4a** (bp 123°/7 mm Hg). Recrystallization of the residue from hexane afforded 2.3 g (26%) of a mixture of **5a** and **6a**.

3-Tribromomethyl-1,2,5-thiadiazole (4a).

This compound was obtained as colorless prisms, mp 44-46°; ms: m/e (relative intensity) 259 (53), 257 (100), 255 (50), 230 (19), 70 (14); ¹H-nmr (deuteriochloroform): δ 8.98 (s, 1H).

Anal. Calcd. for C₃HBr₃N₂S: C, 10.70; H, 0.30; N, 8.32. Found: C, 10.78; H, 0.75; N, 8.19.

Photolysis of 4a.

After a solution of 1.00 g (3 mmoles) of **4a** in 30 ml of carbon tetrachloride was refluxed with irradiation of tungsten lamp for 4 hours, it was treated as described above to afford a colorless solid, which, on recrystallization from hexane gave 0.26 g (49%) of a 2:3 mixture of **5a** and **6a**.

Preparation of 3-Bromomethyl-4-phenyl-1,2,5-thiadiazole (2b).

After a mixture of 0.90 g (5.2 mmoles) of **1b**, 0.94 g (5.2 mmole) of *N*-bromosuccinimide and a catalytic amount of benzoyl peroxide in 20 ml of dry carbon tetrachloride was refluxed for 24 hours, succinimide was filtered off and the solvent was evaporated *in vacuo* to leave a red oil, which, on distillation *in vacuo*, afforded 1.0 g (76%) of **2b** (bp 150°/2 mm Hg).

3-Bromomethyl-4-phenyl-1,2,5-thiadiazole (2b).

This compound was obtained as colorless prisms, mp 47-49°; ms: m/e (relative intensity) 256 (24), 254 (24), 175 (100); ¹H-nmr (deuteriochloroform): δ 4.70 (s, 2H), 7.20-8.09 (m, 5H).

Anal. Calcd. for C₉H₇Br₂N₂S: C, 42.37; H, 2.77; N, 10.98. Found: C, 42.66; H, 2.91; N, 10.51.

Preparation of 3-Dibromomethyl-4-phenyl-1,2,5-thiadiazole (3b).

After a mixture of 7.1 g (40 mmoles) of **1b**, 16 g (84 mmoles) of *N*-bromosuccinimide and a catalytic amount of benzoyl peroxide in 70 ml of dry carbon tetrachloride was refluxed for 24 hours, it was treated as described above to give 13.4 g (100%) of **3b** (bp 177-179°/2 mm Hg).

3-Dibromomethyl-4-phenyl-1,2,5-thiadiazole (3b).

This compound was obtained as colorless prisms, mp 64-66°; ms: m/e (relative intensity) 335 (9), 333 (17), 331 (9), 255 (42), 253 (40), 173 (100); ¹H-nmr (deuteriochloroform): δ 6.76 (s, 1H), 7.44-7.68 (m, 5H).

Anal. Calcd. for C₉H₆Br₂N₂S: C, 32.36; H, 1.81; N, 8.39. Found: C, 32.31; H, 1.80; N, 8.27.

Bromination of **1b**.

After a mixture of 3.0 g (17 mmoles) of **1b**, 18.0 g (103 mmoles) of *N*-bromosuccinimide and 0.2 g of 2,2'-azobisisobutyronitrile in 50 ml of carbon tetrachloride was refluxed with irradiation of tungsten lamp for 80 hours, it was treated as described above to leave a red oil, which was extracted with hot hexane. The extract was column chromatographed on silica gel (Wako C-300) using hexane as an eluent to give 0.66 g (15%) of **5b**, 0.08 g (2%) of **7** and 0.30 g (3%) of **8**. The hexane insoluble was washed with hot-ethanol to give yellow solid, which was recrystallized from hexane to give 0.88 g (20%) of **6b**.

cis-1,2-Dibromo-1,2-bis(4-phenyl-1,2,5-thiadiazol-3-yl)ethylene (5b).

This compound was obtained as colorless prisms (hexane), mp 139-141°; ms: m/e (relative intensity) 508 (20), 506 (35), 504 (16), 427 (72), 425 (70), 345 (100); ¹H-nmr (carbon tetrachloride): δ 7.70-7.80 (m, 5H), 7.96-8.08 (m, 4H); uv: λ max nm (log ε) 285 (4.27), 250 (4.28), 225 (4.36), 205 (4.54).

Anal. Calcd. for C₁₈H₁₀Br₂N₄S₂: C, 42.71; H, 1.99; N, 11.07. Found: C, 42.52; H, 2.24; N, 10.88.

trans-1,2-Dibromo-1,2-bis(4-phenyl-1,2,5-thiadiazol-3-yl)ethylene (6b).

This compound was obtained as colorless prisms (hexane), mp 195-200°; ms: m/e (relative intensity) 507 (2), 505 (3), 503 (1), 426 (77), 424 (78), 345 (100); ¹H-nmr (carbon tetrachloride): δ 7.40-7.68 (m, 6H), 7.85-7.96 (m, 4H); uv: λ max nm (log ε) 290 (4.26), 250 (4.27), 230 (4.33), 205 (4.52).

Anal. Calcd. for C₁₈H₁₀Br₂N₄S₂: C, 42.71; H, 1.99; N, 11.07. Found: C, 42.40; H, 2.13; N, 10.87.

4-Oxo-2H-chromeno[3,4-c]-1,2,5-thiadiazole (7).

This compound was obtained as pale yellow prisms (hexane), mp

155-157°; lit [3], mp 157-159°; ir: ν CO 1750 cm⁻¹; ms: m/e (relative intensity) 204 (M⁺, 100), 176 (12), 148 (5); ¹H-nmr (deuteriochloroform): δ 7.32-7.72 (m, 3H), 8.16-8.26 (m, 1H).

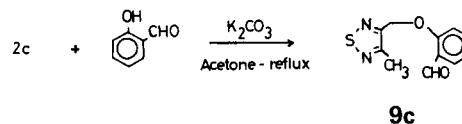
Anal. Calcd. for C₉H₄N₂SO₂: C, 52.94; H, 1.97; N, 13.72. Found: C, 52.95; H, 2.22; N, 13.46.

Preparation of 3-Bromomethyl-4-methyl-1,2,5-thiadiazole (2c).

After a mixture of 50 g (0.44 mole) of **1c**, 86 g (0.48 mmole) of *N*-bromosuccinimide and 0.5 g of benzoyl peroxide in 500 ml of dry carbon tetrachloride was refluxed for 4 hours, the precipitate was filtered and the filtrate was evaporated *in vacuo* to leave a red oil, which was distilled *in vacuo* to give 39 g (46%) of **2c** (bp 30-35°/7 mm Hg).

3-Bromomethyl-4-methyl-1,2,5-thiadiazole (2c).

This compound was obtained as a colorless oil, ¹H-nmr (deuteriochloroform): δ 2.60 (s, 3H), 4.60 (s, 2H). As **2c** is strongly lachrymatory, it was identified by the reaction with salicylaldehyde.



3-Methyl-4-(o-formylphenoxy)methyl-1,2,5-thiadiazole (9c).

This compound was obtained as pale yellow needles (hexane), mp 92-94°; ir: ν CO 1680 cm⁻¹; ms: m/e (relative intensity): 234 (M⁺, 81), 121 (100), 113 (91); ¹H-nmr (deuteriochloroform): δ 2.63 (s, 3H), 5.38 (s, 2H), 6.96-7.83 (m, 4H), 10.40 (s, 1H).

Anal. Calcd. for C₁₁H₁₀N₂O₂S: C, 56.41; H, 4.27; N, 11.97. Found: C, 56.07; N, 4.38; N, 11.49.

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