The Reaction of 2,4,6-Triphenyl-1,3,5-thiadiazin-1-ium Salt with Active Methylene Compounds

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The reaction of 2,4,6-triphenyl-1,3,5-thiadiazin-1-ium tetrafluoroborate with several active methylene compounds was studied. Nitromethane and nitroethane gave 2*H*-1,3,5-thiadiazines. The compounds possessing a benzoyl group reacted with this salt to give 5-substituted 2,4,6-triphenylpyrimidines, while those possessing a carbamoyl group afforded 5-substituted 4-hydroxy-2,6-diphenylpyrimidines or 4(3*H*)-pyrimidinone. On the other hand, malononitrile and ethyl cyanoacetate gave 5-substituted 4-mercapto-2,6-diphenylpyrimidines, with the liberation of benzonitrile. It was thus found that 2,4,6-triphenyl-1,3,5-thiadiazin-1-ium tetrafluoroborate reacts with active methylene compounds in fashions similar to that of 2,4,6-triphenyl-1,3-thiazin-1-ium salt.

2,4,6-Triphenylpyrylium salt (**1**) and its *S*-analog (**2**) usually react with active methylenes in a similar way to give 1-substituted 2,4,6-triphenylbenzenes;[1,2] however, 2,4,6-triphenyl-1,3-oxazin-1-ium salt (**3**) and its *S*-analong (**4**) reacted with them in the different manners to afford various pyridines and other derivatives.[3,4] 2,4,6-Triphenyl-1,3,5-oxadiazin-1-ium salt (**5**) reacts with them in ways similar to **3** and produces several pyrimidines.[5,6] The *S*-analog of **5**, 2,4,6-triphenyl-1,3,5-thiadiazin-1-ium salt (**6**), has been synthesized recently,[7] but its behavior toward nucleophiles has not yet been checked. In this report, the reaction of **6** with active methylenes was investigated; the reactivity of these heteroaromatic cation compounds (**1**—**6**) with them was also discussed.

Results and Discussion

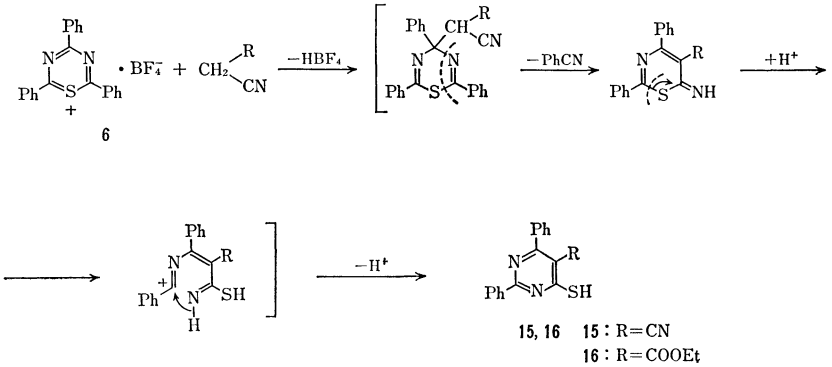
The starting material, 2,4,6-triphenyl-1,3,5-thiadiazin-1-ium tetrafluoroborate (**6**), was obtained by treating 4*H*-1,3,5-thiadiazine with triphenylcarbenium tetrafluoroborate.[7]

When **6** was treated with nitromethane and nitroethane under mild conditions, **7** and **8** were afforded in 62 and 53% yields respectively. The analytical data showed that both the products were adducts of the thiadiazin-1-ium cation and the carbanions given by each active methylene. Their IR spectra closely resembled each other and had no absorption assignable to N–H or S–H stretching. Moreover their UV spectra were almost the same (λ_{max}=252 nm, ε=34000). Therefore, for **7** and **8**, two probable structures, 2*H*- and 4*H*-1,3,5-thiadiazines, can be supposed. According to the MS data, the presence of the fragments at 135 *m/e* of **7** and 149 *m/e* of **8**, assigned to $PhCSCH_2^+$ and $[PhCSCHCH_3]^+$ respectively, strongly suggests that **7** and **8** are 2*H*-1,3,5-thiadiazine derivatives. It was thus confirmed that **7** and **8** are 2-nitromethyl- and 2-(1-nitroethyl)-2,4,6-triphenyl-2*H*-1,3,5-thiadiazine. This reaction mode is found in the reaction of **4** with nitromethane, nitroethane, and diethyl malonate; however, it is not found in that of the corresponding *O*-analogs, **3** and **5**.

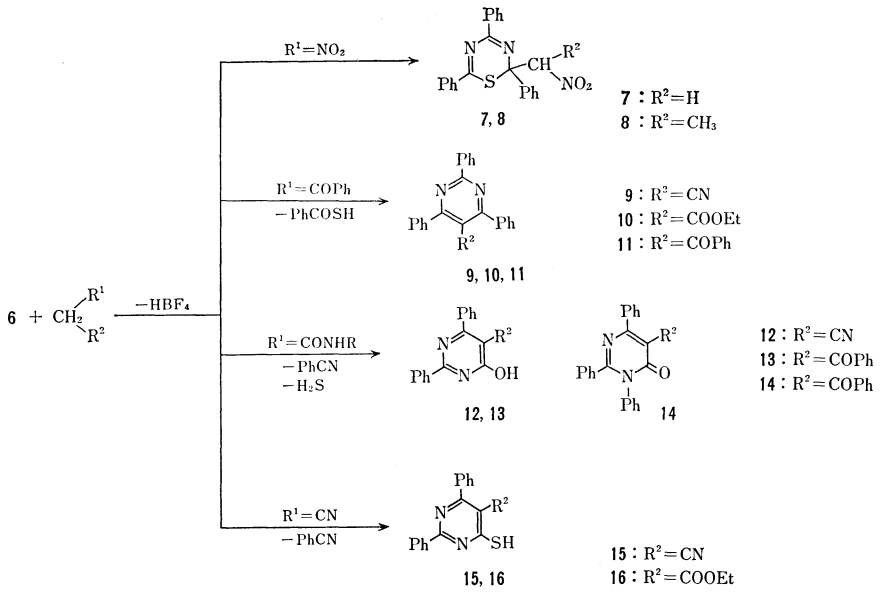
Benzoylacetonitrile, ethyl benzoylacetate, and dibenzoylmethane were treated with **6** to give 5-cyano-, 5-ethoxycarbonyl-, and 5-benzoyl-2,4,6-triphenylpyrimidine (**9**, **10**, and **11**) in 85, 39, and 43% yields respectively. These reagents react also with **5** to give the respective common products; consequently, they appear to behave in the same fashion toward **5** and **6**. This reaction mode can also be found among the reactions of **1**—**6** with active methylenes; especially, the compounds possessing a benzoyl group are apt to obey this mode to afford 1-substituted 2,4,6-triphenylbenzenes, 3-substituted 2,4,6-triphenylpyridines, and 5-substituted 2,4,6-triphenylpyrimidines.[1-4,6]

Cyanoacetamide, benzoylacetamide, and benzoylacetanilide reacted with **6** to give 5-cyano- and 5-benzoyl-4-hydroxy-2,6-diphenylpyrimidines (**12**, **13**), and 5-benzoyl-2,3,6-triphenyl-4(3*H*)-pyrimidinone (**14**) in 73, 46, and 60% yields respectively. This reaction mode is commonly known in the reactions of **3**—**6** with the compounds possessing a carbamoyl group.

Malononitrile reacted with **6** to give a yellow powder,



Scheme 1.



Scheme 2.

15, with the escape of benzonitrile, while ethyl cyanoacetate afforded yellow needles, **16**. Both **15** and **16** were weakly acidic. In their MS spectra the M^+ values were observed at 289 and 336 *m/e*, and a common peak at 264 *m/e*, assignable to $[M+1-CN]^+$ and $[M+1-COOC_2H_5]^+$ respectively, was present. Their UV spectra were similar to one another. Their IR spectra also resembled each other; that of **16** had absorptions assigned to an ester group (1728, 1257 cm^{-1}), but no absorption assigned to a cyano group. These facts suggested that they have the same skeletal structure, and that a cyano group of the reagents participates in this reaction. **15** was obtained by an alternative method as follows: 4-Chloro-5-cyano-2,6-diphenylpyrimidine was treated with hydrogen sulfide in triethylamine–benzene. It was thus concluded that **15** is 5-cyano-4-mercapto-2,6-diphenylpyrimidine; consequently, **16** is 5-ethoxycarbonyl-4-mercapto-2,6-diphenylpyrimidine. For the formation of **15** and **16**, a probable reaction course could be speculated about; it is shown in Scheme 1. This recyclization process into pyrimidine can be regarded as the same as the reaction of *N*-acyl imidoyl chloride with malononitrile.[8]

From all the results described above, the reaction of 2,4,6-triphenyl-1,3,5-thiadiazin-1-ium tetrafluoroborate with active methylenes could be deduced to be as is summarized in Scheme 2.

It is proved that the reaction manner of **6** toward active methylenes is more similar to that of **4** rather than to that of **5**; in addition, these heteroaromatic cations (**1**—**6**), treated with active methylenes, are useful materials for synthesizing benzenes, pyridines, pyrimidines, and other derivatives.

Experimental

2-Nitromethyl- or 2-(1-Nitroethyl)-2H-1,3,5-thiadiazine (7,8). Into a solution of nitromethane or nitroethane (1.5 mmol) and triethylamine (0.3 ml) in chloroform (3 ml), **6** (0.42 g, 1.0 mmol) was stirred at room temperature, after which the mixture was allowed to stand for 5 d. The solvent was distilled out under reduced pressure, and the residue was washed with dilute hydrochloric acid and recrystallized from acetonitrile to give **7** (0.24 g, 62%) or **8** (0.21 g, 53%). Their data are shown below.

7: Mp 166 °C; IR (KBr) 1645, 1555, 1448, 1372, 1224, and 917 cm^{-1}; UV_{max} (EtOH) 252 nm (ε 34000); ^{13}C NMR ($CDCl_3$), δ 82.69 (–C–), 86.02 ($-CH_2NO_2$), 127.21—132.69, 136.66, 137.89, 139.96, and 157.54; ^1H NMR ($CDCl_3$), δ 5.25 (s, $-CH_2NO_2$), 7.24—8.18 (m, arom H); MS, *m/e* (%), 327 (10.4, $[M-CH_2NO_2]^+$), 236 (18.5), 206 (14.6), 135 (36.2 $[PhCSCH_2]^+$), 121 (100, $PhCS^+$), and 103 (63.1, $PhCN^+$). Found: C, 68.41; H, 4.40; N, 10.88; S, 8.39%. Calcd for $C_{22}H_{17}N_3SO_2$; C, 68.20 H, 4.42 N, 10.84; S, 8.28%.

8: Mp 164 °C; IR (KBr), 1651, 1551, 1448, 1382, 1214, and 903 cm^{-1}; UV_{max} (EtOH), 252 nm (ε 34000); ^{13}C NMR ($CDCl_3$) δ 14.47 ($-CH_3$), 84.42 (–C–), 92.15 ($>CHNO_2$), 126.64—132.12, 136.16, 136.41, 139.35, and 156.71; ^1H NMR ($CDCl_3$) δ 1.71 (*d*, $>CH-C\underline{H}_3$), 5.54 (*q*, $>C\underline{H}-CH_3$), 7.24—8.18 (*m*, arom H); MS *m/e* (%), 355 (0.5, $[M-NO_2]^+$), 327 (13.7, $[M-CHNO_2CH_3]^+$), 149 (10.0, $[PhCSCHCH_3]^+$), 121 (100), and 103 (10.3). Found: C, 68.79; H, 4.75; N, 10.51; S, 8.04%. Calcd for $C_{25}H_{19}N_3SO_2$: C, 68.81; H, 4.77; N, 10.47; S, 7.98%.

5-Cyano-, 5-Ethoxycarbonyl-, or 5-Benzoyl-2,4,6-triphenylpyrimidine (9, 10, 11). Into a solution of benzoylacetonitrile, ethyl benzoylacetate, or dibenzoylmethane (1.5 mmol) in 1.0 mol dm^{-3} of MeOH–MeONa (3 ml), **6** (0.42 g, 1.0 mmol) was added; the mixture was stirred at room temperature for 10 min and then refluxed for 1 h. The reaction mixture was poured into dilute hydrochloric acid. The resulting precipitate was collected by filtration and recrystallized from acetonitrile or methanol to give **9** (0.28 g, 84%), **10** (0.15 g, 39%), or **11** (0.18 g, 43%). Their mp and IR spectra agreed with those of authentic samples.[6]

5-Cyano- or 5-Benzoyl-4-hydroxy-2,6-diphenylpyrimidine (12,13), and 5-Benzoyl-2,3,6-triphenyl-4(3H)-pyrimidinone (14). Cyanoacetamide, benzoylacetamide, and benzoylacetanilide (1.5 mmol) were treated with **6** (1.0 mmol), as in the preparation of **9**—**11**. The resulting precipitate was dissolved

in DMF and reprecipitated by the addition of ether to give **12** (0.20 g, 73%), **13** (0.16 g, 46%), and **14** (0.26 g, 60%) respectively. The IR spectra of **12** and **13** were completely superimposed on those of authentic samples.[6] The data of **14** are as below.

14: Mp 243 °C; IR, 1667, 1651, 1535, and 1492 cm^{-1}; UV_{max} (CH_2Cl_2) 252 nm (ε 30900), 315 (sh, ε 9500); ^1H NMR ($CDCl_3$) δ 7.27—8.00 (*m*, arom H); MS *m/e* (%), 428 (28.0, M^+), 400 (15.5, $[M-CO]^+$), 180 (87.6, $[PhC{\equiv}NPh]^+$), 105 (25.7, $PhCO^+$), and 77 (100, Ph^+). Found: C, 81.30; H, 4.67; N, 6.53%. Calcd for $C_{29}H_{20}N_2O_2$: C, 81.29; H, 4.70; N, 6.54%.

*5-Cyano- or 5-Ethoxycarbonyl-4-mercapto-2,6-diphenylpyrimidine (**15**, **16**).* Malononitrile or ethyl cyanoacetate (1.5 mmol) was treated with **6** (1.0 mmol), as in the preparation of **9**—**11**. The resulting precipitation was recrystallized from acetonitrile to give **15** (0.23 g, 80%) or **16** (0.18 g, 54%). Their data are shown below.

15: Mp 250 °C (decomp), IR (KBr), 3176, 3060, 2230, 1545, 1495, and 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45—8.16 (m, arom H), 8.51 (s, SH); UV_{max} (CH_2Cl_2), 283 (ε 26500), 307 (sh, ε 23000), 393 (ε 5000); MS *m/e* (%), 289 (55.6, M^+), 264 (22.8, $[M+1-CN]^+$), 186 (79.0), 153 (44.3), and 135 (100). Found: C, 70.32; H, 3.81; N, 14.47; S, 11.37%. Calcd for $C_{17}H_{11}N_3S$: C, 70.57; H, 3.83; N, 14.52; S, 11.08%.

16: Mp 182 °C; IR (KBr), 2963, 1728, 1546, 1491, 1257, and 1230 cm^{-1}; UV_{max} (CH_2Cl_2), 271 (ε 25200), 303 (sh, ε 17500), 388 (ε 7100); ^1H NMR ($CDCl_3$) δ 7.45—8.16 (m, arom H), 8.51 (s, SH); MS *m/e* (%), 336 (25.2, M^+), 307 (57.0, $[M-C_2H_5]^+$), 292 (20.5, $[M-CO_2]^+$), 290 (30.1, $[M-C_2H_5OH]^+$), 264 (43.3, $[M+1-COOC_2H_5]^+$), 158 (39.3), and 128 (100). Found: C, 67.64; H, 4.70; N, 8.19; S, 9.75%. Calcd for $C_{19}H_{16}N_2SO_2$: C, 67.84; H, 4.79; N, 8.32; S, 9.53%.

*Conversion of 4-Chloro-5-cyano-2,6-diphenylpyrimidine into **15**.* 4-Chloro-5-cyano-2,6-diphenylpyrimidine (0.20 g) was added to a solution saturated with hydrogen sulfide in benzene–triethylamine (2:1, 15 ml), after which the mixture was distilled under reduced pressure, the residue was washed with dilute hydrochloric acid and dissolved with 1 mol dm^{-3} of MeOH–MeONa (5 ml). The solution was filtered to separate an insoluble substance and acidified with hydrochloric acid to produce a yellow powder. The powder was recrystallized from acetonitrile to give **15** (0.15 g, 76%). The mp and the IR spectrum agreed with those of **15** obtained from **6**.

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