

The Reaction of 2,4,6-Triphenyl-1,3-oxazinylium Perchlorate with Amino Compounds

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(Received October 27, 1980)

The reaction of 2,4,6-triphenyl-1,3-oxazinylium perchlorate with various kinds of amino compounds was studied. Primary amines and semicarbazides gave pyrimidinium perchlorates. *o*-Phenylenediamine, *o*-aminobenzamide, and *o*-aminothiophenol afforded 2,4-diphenyl-1,5-benzodiazepine, 2-phenyl-4-hydroxyquinazoline, and 2-phenyl-1,3-benzothiazole respectively. Benzoylhydrazine, 4-pyridinecarbohydrazide, and 4-phenylthiosemicarbazide all led to pyrazoline derivatives. *N,N*-Dimethylhydrazine yielded two chain products competitively, while *N,N'*-dimethylhydrazine gave 1,2-dimethyl-3,5-diphenyl-1,2,4-triazolylum and 1,2-dimethyl-3,5-diphenylpyrazolylum perchlorate competitively. It was thus shown that 2,4,6-triphenyl-1,3-oxazinylium perchlorate reacts with amino compounds in a complicated fashion to afford various heterocyclic compounds and other derivatives.

It has been reported that pyrylium salts react with various kinds of amino compounds to afford numerous derivatives.¹⁾ 1,3-Oxazinylium salts, the *N*-analogs of pyrylium salts, can also be expected to give many derivatives when treated with amino compounds; however, their behavior has not yet been studied so closely. A 1,3-oxazinylium cation may be supposed to be reactive with nucleophiles at the 2-, 4-, and 6-positions. Since the 1,3-oxazinylium ring is unsymmetrical, its 2- and 6-positions are not equal to each other. This suggests that the cation behaves toward nucleophiles in a more complicated fashion than does a pyrylium cation. On the other hand, it has been known that carbanions derived from active methylenes, enamines, or ethyl diazoacetate always attack at the 6-position of the 2,4,6-triphenyl-1,3-oxazinylium cation to afford pyridine, butadiene, or 1,3-oxazepine derivatives.^{2,3)} In this study, the reaction of 2,4,6-triphenyl-1,3-oxazinylium perchlorate (**1**) with various kinds of amino compounds, such as primary amines, disubstituted hydrazines, hydrazides, and semicarbazides, was attempted; consequently, some interesting results were obtained.

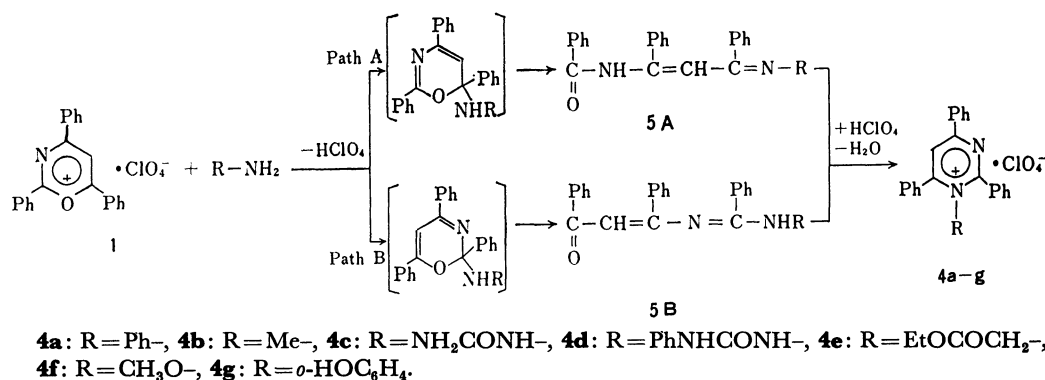
Results and Discussion

The starting material, **1**, was obtained by the reaction of 2,4,6-triphenyl-4*H*-1,3-oxazine with trityl perchlorate.⁴⁾

Primary Amines and Semicarbazides. It has been reported that the reaction of 2,4,6-triphenylpyrylium salt (**2**) with primary amines gives 1-substituted 2,4,6-triphenylpyridinium salt (**3**).⁵⁾ On the other hand, upon refluxing with aniline, methylamine, semicarbazide, 4-phenylsemicarbazide, the glycine ethyl ester, or *O*-methylhydroxylamine in dioxane-triethylamine, **1** afforded 1-substituted 2,4,6-triphenylpyrimidinium perchlorate (**4a–f**), which correspond to **3**. These data are summarized in Table 1. For the formation of **4a–f**, two probable reaction courses were postulated, as is shown in Scheme 1. In order to determine the real reaction course, **1** was treated with aniline under mild conditions to isolate a white powder of **5** (63%). **5** was regarded as the intermediate of the above reaction, because **5** gave **4a** almost quantitatively upon treatment with perchloric acid in acetic anhydride. In its IR spectrum, the presence of the absorption at 1681 cm⁻¹, assigned to C=O stretching, suggested that **5** is

TABLE 1. 1-SUBSTITUTED 2,4,6-TRIPHENYLPYRIMIDINIUM PERCHLORATE (**4a–h**)

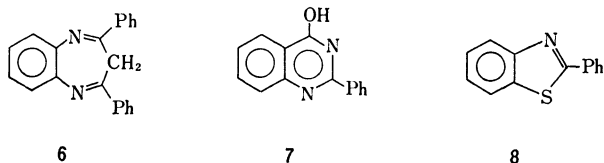
Compd 4	Substituent	Mp(dc) °C	Yield %	Found (Calcd) (%)				$\lambda_{\max}/\text{nm}$ (log ϵ)	IR(KBr) $\bar{\nu}/\text{cm}^{-1}$
				C	H	N	Cl		
a	Ph–	>300	64	69.25 (69.35)	4.33 (4.37)	5.80 (5.78)	7.32 (7.31)	324 (4.51)	1607, 1584, 1527, 1381, 1080.
b	Me–	200.8	21	65.15 (65.33)	4.58 (4.53)	6.65 (6.62)	8.25 (8.38)	319 (4.51)	1607, 1595, 1540, 1391, 1086.
c	NH ₂ CONH–	230.3	37	59.39 (59.17)	4.14 (4.10)	11.95 (12.00)	7.80 (7.59)	323 (4.46)	3400—3200, 1677, 1590, 1539, 1393, 1104.
d	PhNHCONH–	230.1	42	63.89 (64.15)	4.23 (4.27)	10.47 (10.32)	6.46 (6.53)	325 (4.46)	3300, 1719, 1606, 1591, 1536, 1393, 1120.
e	EtOCOCH ₂ –	204.5	43	63.26 (63.10)	4.69 (4.68)	5.75 (5.66)	7.08 (7.16)	327 (4.46)	1743, 1609, 1590, 1543, 1397, 1256, 1085.
f	CH ₃ O–	241.1	35	62.92 (62.95)	4.32 (4.36)	6.46 (6.38)	8.29 (8.08)	320 (4.37)	2960, 1602, 1590, 1543, 1389, 1086.
g	<i>o</i> -HOC ₆ H ₄ –	>300	62	66.91 (67.14)	4.25 (4.23)	5.67 (5.59)	6.84 (7.08)	325 (4.50)	3260, 1603, 1587, 1530, 1390, 1100.
h	(CH ₃) ₂ N–	191.1	46	63.75 (63.51)	4.96 (5.33)	9.38 (9.26)	7.93 (7.81)	320 (4.39)	1606, 1590, 1534, 1390, 1080.



Scheme 1.

one of the two chain compounds (**5A** and **5B**; R=C₆H₅) in Scheme 1. According to ¹³C NMR spectrum, the absorption assigned to a benzoyl carbon (δ ca. 190) was absent, whereas a carbamoyl carbon (δ 166.03 or 165.04) was present. The structure of **5** was thus determined to be **5A**; in addition, it was inferred that the reaction of **1** with these primary amines and semicarbazides takes Path A in Scheme 1 to afford **4a–f**.

***o*-Substituted Anilines.** The reaction of *o*-aminophenol, *o*-phenylenediamine, *o*-aminobenzamide, or *o*-aminothiophenol with **1** under the same conditions as above gave 1-(*o*-hydroxyphenyl)-2,4,6-triphenylpyrimidin-5-yl perchlorate (**4g**, 62%), 2,4-diphenyl-1,5-benzodiazepine (**6**, 80%), 2-phenyl-4-hydroxyquinazoline (**7**, 32%), or 2-phenyl-1,3-benzothiazole (**8**, 68%) respectively. The data of **4g** are also listed in Table 1; **6**, **7**, and **8** were identified by direct comparison with authentic samples.^{6–8} These facts suggest that, in

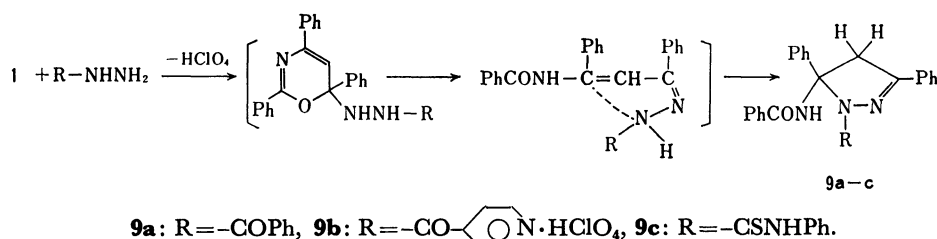


the formation of **6**, the reaction was initiated by the attack of *o*-phenylenediamine at the 6-position of the oxazinylium cation, while *o*-aminobenzamide and *o*-aminothiophenol attacked the 2-position of the cation to produce **7** and **8**. It was thus found that these anilines, which have active hydrogen at their ortho-positions, behave in a complicated fashion toward **1**, and produce derivatives with different structures.

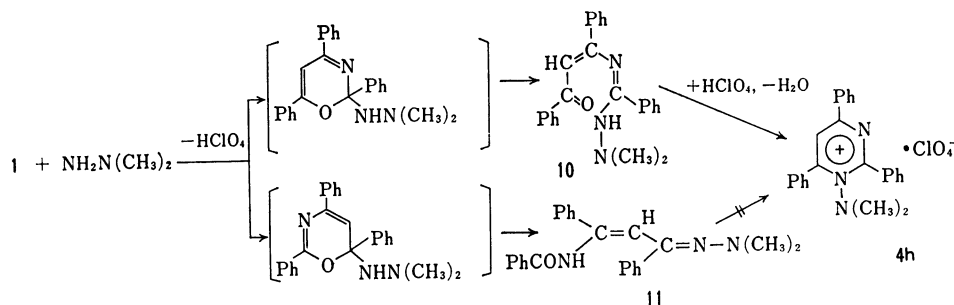
Benzoylhydrazine, 4-Pyridinecarbohydrazide, and 4-Phenylthiosemicarbazide. On treatment with these reagents,

1 gave **9a–c** in 50, 32, and 40% yields respectively. Their ¹H NMR spectra had two characteristic absorptions, at δ 3.61–3.80, and 4.02–4.74, which were assigned to a pyrazolinic methylene with a geminal coupling constant ($J=18$ Hz),⁹ while their IR spectra have three common absorptions, at 3280–3340 (N–H), 1665–1686 (C=O), and 1520–1530 cm^{–1} (C=N). These data suggested that **9a–c** have the same skeletal structure. The ¹³C NMR spectrum of **9a**, as determined by means of the ¹H-off-resonance method, showed the presence of a methylene (δ 48.23), a quaternary (δ 82.26), and two carbamoyl carbons (δ 167.71, 154.17). These spectral results and analytical data confirmed that **9a** is 1-benzoyl-3,5-diphenyl-5-benzoylamino-2-pyrazoline, and that both **9b** and **9c** are also pyrazoline derivatives. The mechanism for the formation of **9a–c** was demonstrated to be as is shown in Scheme 2; this mechanism is similar to that of the reaction of **2** with hydroxylamine or phenylhydrazine which gives oxazoline or pyrazoline compounds.^{9,10}

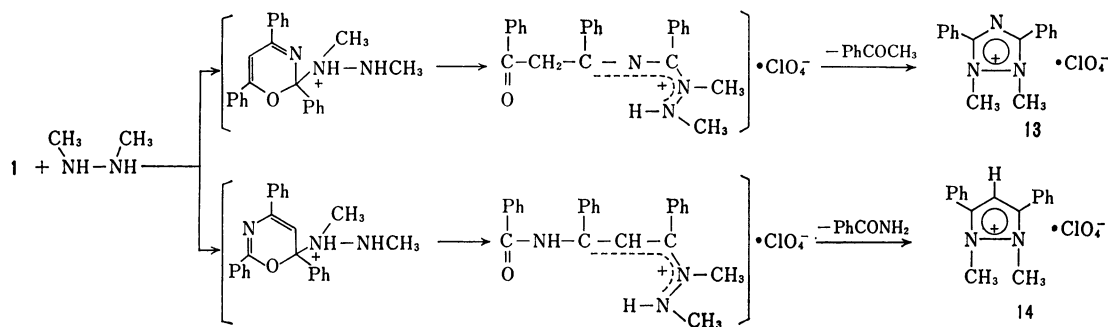
***N,N*-Dimethylhydrazine.** When treated with this reagent under mild conditions, **1** gave a main product, **10** (49%), and also a small amount of **11** (9%) competitively. The analytical data showed that both **10** and **11** are adducts of the anion of this reagent and the oxazinylium cation. The M⁺ value was observed at m/e 369, though their MS spectra were quite different from each other. Their ¹³C NMR spectra showed that **10** has a benzoyl carbon (δ 190.28), whereas **11** has a carbamoyl carbon (δ 165.47). Their IR and UV spectra were also different from each other. When treated with dilute perchloric acid, **10** easily afforded 1-dimethylamino-2,4,6-triphenylpyrimidin-5-yl perchlorate (**4h**); however, **11** afforded no pyrimidin-5-yl salt, even upon treatment with 70% perchloric acid. On



Scheme 2.



Scheme 3.



Scheme 4.

the basis of these results, it seems certain that the reaction course to produce them takes the paths shown in Scheme 3.

N,N'-Dimethylhydrazine. On treatment with this reagent, **1** gave **12** in a good yield. The analytical results of **12** agreed almost entirely with 1,2-dimethyl-3,5-diphenyl-1,2,4-triazolylium perchlorate (**13**), but its IR and ^1H NMR spectra suggested that **12** was a mixture of **13** and 1,2-dimethyl-3,5-diphenylpyrazolylium perchlorate (**14**). Pure samples of **13** and **14** were obtained by the reaction of this reagent with 3,5-diphenyl-1,2,4-dithiazolylium and with 3,5-diphenyl-1,2-dithiolylium salt respectively.^{11,12} The constituent ratio of **13** and **14** in **12** was estimated to be 3 : 1 by the use of the integral ratio of the signals at δ 4.24 (**13**, 18.5) and 4.12 (**14**, 6.0) in the ^1H NMR spectrum of **12**. Therefore, the reaction of **1** with this reagent proceeds as is shown in Scheme 4, and yields **13** and **14** competitively.

Hence, it is proved that 2,4,6-triphenyl-1,3-oxazinylium perchlorate reacts with amino compounds not only at the 6-position, but also at the 2-position, and that the reaction produce various heterocyclic compounds and other derivatives.

Experimental

The melting points of all the products were measured in a capillary tube with a Mettler FPI apparatus at the rate of $2^\circ\text{C}/\text{min}$. The IR spectra were measured in KBr pellets with a JASCO-403G spectrometer. The UV spectra were recorded on a Hitachi 200-10 instrument in an ethanol solution, while the MS spectra were recorded on a Hitachi RMU6E spectrometer with a direct inlet at 70 eV. The ^1H and ^{13}C NMR spectra were obtained with a Varian FT-80 instrument, using tetramethylsilane as the internal standard.

1-Substituted 2,4,6-Triphenylpyrimidinium Perchlorate (4a–g). Into a solution of aniline, methylamine hydrochloride, semicarbazide hydrochloride, 4-phenylsemicarbazide, glycine ethyl ester hydrochloride, *O*-methylhydroxylamine hydrochloride, or *o*-aminophenol (1.5 mmol) and triethylamine (0.3 ml) in dioxane (2 ml), **1** (0.42 g, 1 mmol) was stirred at room temperature for 10 min, after which the mixture was refluxed for 1 h. The solvent was then distilled out under reduced pressure. The resulting residue was washed with 1 mol dm^{-3} perchloric acid (5 ml) and then recrystallized from ethanol to give pyrimidinium perchlorates (**4a–g**). Their data are listed in Table 1.

Reaction of 1 with Aniline under Mild Conditions. Into a solution of aniline (0.14 g, 1.5 mmol) and triethylamine (0.3 ml) in dioxane (2 ml), **1** (0.42 g, 1 mmol) was stirred at room temperature and then the mixture was allowed to stand for 5 d. The mixture was poured into dilute perchloric acid, and the resulting precipitate was recrystallized from methanol to give 0.25 g (63%) of **5**; mp 172.5°C . IR, 1681, 1622, 1544, 1479, and 1296 cm^{-1} ; ^{13}C NMR (HMPA- d_{18}), δ 122.10, 127.15–131.03, 135.07, 138.41, 143.42, 165.04, and 166.03. Found: C, 83.33; H, 5.49; N, 6.83%. Calcd for $\text{C}_{28}\text{H}_{22}\text{N}_2\text{O}$; C, 83.46; H, 5.51; N, 6.69%.

Conversion of 5 to 1,2,4,6-Tetraphenylpyrimidinium Perchlorate (4a). Into a solution of **5** (0.30 g) in acetic anhydride (2 ml), 70% perchloric acid (4 drops) was stirred at room temperature, after which the mixture was allowed to stand overnight. The mixture was poured into ether, and the resulting precipitate was collected by filtration and washed with ether to give a white powder of **4a** (0.34 g, 94%).

Reaction of 1 with *o*-Substituted Anilines. *o*-Phenylenediamine, *o*-aminobenzamide, and *o*-aminothiophenol (1.5 mmol) were treated with **1** (1 mmol) by the same procedure as was used in the preparation of **4a–g**. The resulting residues were washed with dilute perchloric acid and recrystallized from methanol to give **6** (0.24 g, 80%), **7** (0.07 g, 32%), and **8** (0.14 g, 68%) respectively. The IR spectrum of each of them could be completely superimposed on that of the

corresponding authentic samples.⁶⁻⁸⁾

1-Substituted 3,5-Diphenyl-5-benzoylamino-2-pyrazolines (9a—c). Benzoylhydrazine, 4-pyridinecarbohydrazide, and 4-phenylthiosemicarbazide (1.5 mmol) were treated with **1** (1 mmol) by the same procedure as was used in the preparation of **4a—g**. The resulting residues were recrystallized from methanol, ethanol, or acetonitrile to yield **9a** (0.22 g, 50%), **9b** (0.17 g, 32%), or **9c** (0.19 g, 40%) respectively. Their data are shown below.

9a: mp, 165.8 °C; IR, 3280, 1667, 1640, 1530, 1447, 1416, and 1338 cm⁻¹; UV, $\lambda_{\max}$ (ϵ) 293 nm (21400); ¹H NMR (CDCl₃), δ 3.64 (d, $J=18$), 4.74 (d, $J=18$), 7.22—8.40, ¹³C NMR (CDCl₃), δ 48.23 (—CH₂—), 82.26 (—C—), 124.07, 126.89—134.46, 142.39, 154.17, and 167.71. MS, m/e 445 (M⁺), 324 ([M—PhCONH₂]⁺), 295, 220, 121 ([PhCONH₂]⁺), and 105 (PhCO⁺). Found: C, 78.24; H, 5.23; N, 9.53%. Calcd for C₂₉H₂₃N₃O₂; C, 78.24; H, 5.20; N, 9.43%.

9b: mp, 231.2 °C; IR, 3300—3050, 1665, 1651, 1520, 1480, 1432, 1345, and 1100 cm⁻¹; UV, $\lambda_{\max}$ (ϵ) 321 nm (29900); ¹H NMR (C₅D₅N), δ 3.61 (d, $J=18$), and 4.47 (d, $J=18$). Found: C, 61.39; H, 4.23; N, 10.50; Cl, 6.63%. Calcd for C₂₈H₂₃N₄O₆Cl; C, 61.49; H, 4.24; N, 10.24; Cl, 6.48%.

9c: mp, 164.7 °C; IR, 3340, 1686, 1523, 1487, 1450, and 1327 cm⁻¹; UV, $\lambda_{\max}$ (ϵ) 280 nm (21500); ¹H NMR (C₅D₅N), δ 3.80 (d, $J=18$), 3.84 (s), and 4.02 (d, $J=18$); ¹³C NMR (DMF-*d*₇), δ 50.46 (—CH₂—), 83.67 (—C—), 124.93, 127.87—132.46, 139.50, 143.73, 152.58, 167.31, and 173.89; MS, m/e 476 (M⁺), 220, 135, 121, and 105. Found: C, 73.17; H, 5.13; N, 11.68; S, 6.65%. Calcd for C₂₈H₂₄N₄SO; C, 73.08; H, 5.07; N, 11.75; S, 6.72%.

Reaction of *N,N*-Dimethylhydrazine with **1.** Into a solution of *N,N*-dimethylhydrazine (0.10 g, 1.6 mmol) and triethylamine (0.3 ml) in dioxane (2 ml), **1** (1 mmol) was stirred at room temperature. After the mixture had been allowed to stand for 5 d, it was poured into water and the resulting precipitate was purified by preparative thin-layer chromatography (silica gel; benzene—acetic acid, 50 : 1) to give orange-yellow needles of **10** (0.18 g, 49%) and pale yellow granules of **11** (0.03 g, 9%). Their data are shown below.

10: mp, 152.6 °C (ethanol); IR, 3060—2780, 1592, 1560, 1537, 1494, 1325, 1306, and 1295 cm⁻¹; UV, $\lambda_{\max}$ (ϵ) 257 (15900), and 367 nm (14200); ¹H NMR (CDCl₃), δ 2.76 (s, 6H), 6.18 (s, 1H), 6.90—8.14 (m, 16H); ¹³C NMR (CDCl₃), δ 46.74 (—CH₃), 99.31 (=CH—), 127.62—139.56, 153.06, 158.26, and 190.26; MS, m/e 369 (M⁺), 310, 264 ([M—PhCO]⁺), and 105. Found: C, 78.13; H, 6.30; N, 11.37%. Calcd for C₂₄H₂₃N₃O; C, 78.02; H, 6.27; N, 11.37%.

11: mp, 150.1 °C (ethanol); IR, 3060—2780, 1670, 1618, 1498, 1478, 1310, 1298, and 1272 cm⁻¹; UV, $\lambda_{\max}$ (ϵ) 248 (44200), and 299 nm (sh, 28400); ¹H NMR (CDCl₃), δ 2.88 (s, 6H), 6.16 (s, 1H), 7.30—8.12 (m, 15H), and 10.90 (s, 1H); ¹³C NMR (CDCl₃), δ 47.54 (CH₃—), 112.13 (=CH—), and 127.19—138.30, 143.17, 156.69, 165.47; MS, m/e 369 (M⁺), 248 ([M—PhCONH₂]⁺), 105, and 104. Found: C, 77.95; H, 6.27; N, 11.51%. Calcd for C₂₄H₂₃N₃O; C, 78.02; H,

6.27; N, 11.37%.

Conversion of **10 into 1-Dimethylamino-2,4,6-triphenylpyrimidinium Perchlorate (**4h**).** Into a solution of **10** (0.37 g, 1 mmol) in acetonitrile (2 ml), 1 mol dm⁻³ perchloric acid (2 ml) was stirred after which the mixture was allowed to stand at 0—5 °C overnight. The precipitate was collected by filtration and washed with ether to give **4h** (0.43 g) almost quantitatively. The data of **4h** are shown in Table 1.

Reaction of **1 with *N,N*-Dimethylhydrazine.** Into a solution of *N,N*-dimethylhydrazine dihydrochloride (0.20 g, 1.5 mmol) in 2 mol dm⁻³ MeONa—MeOH (2 ml), **1** (1 mmol) was stirred at room temperature for 10 min, and then the mixture was refluxed for 1 h. The reaction mixture was poured into dilute perchloric acid. The resulting precipitate was collected by filtration and recrystallized from methanol to give **12** (0.27 g). IR, 1544, 1487, 1453, 1420, 1111, 1090, 740, 717, and 691 cm⁻¹; ¹H NMR (DMSO-*d*₆), δ 3.36, 4.12, 4.24, 7.32, 7.62—8.02. Found: C, 55.32; H, 4.61; N, 11.86; Cl, 10.13%.

1,2-Dimethyl-3,5-diphenyl-1,2,4-triazolylum Perchlorate (13**) and 1,2-Dimethyl-3,5-diphenylpyrazolylum Perchlorate (**14**).** *N,N*-Dimethylhydrazine dihydrochloride (1.5 mmol) was treated with 1 mmol of 3,5-diphenyl-1,2,4-dithiazolylum salt⁽¹¹⁾ or 3,5-diphenyl-1,2-dithiolylum salt⁽¹²⁾ by the same procedure as above. Their data are shown below.

13: yield 25%, mp 152.0 °C (methanol); IR, 1606, 1544, 1485, 1450, 1418, 1392, 1115, 1087, 742, 718, 693 cm⁻¹; ¹H NMR (DMSO-*d*₆), δ 3.38, 4.24, and 7.62—8.02. Found: C, 54.85; H, 4.59; N, 12.14; Cl, 10.12%. Calcd for C₁₆H₁₆N₃—ClO₄; C, 54.94; H, 4.61; N, 12.01; Cl, 10.12%.

14: yield 46%; mp, 187.4 °C (methanol); IR, 3120, 1565, 1494, 1476, 1434, 1396, 1111, 1092, 766, and 693 cm⁻¹; ¹H NMR (DMSO-*d*₆), δ 3.38, 4.12, 7.34, and 7.72. Found: C, 58.55; H, 4.87; N, 8.17; Cl, 10.14%. Calcd for C₁₇H₁₇—N₂ClO₄; C, 58.55; H, 4.91; N, 8.03; Cl, 10.16%.

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