

r, r, r-Trichloroethylidene-*m*-nitroacetophenone 과 Hydrazine 들의 반응

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Reactions of *r, r, r*-Trichloroethylidene-*m*-Nitroacetophenone with Hydrazines

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요 약 *r, r, r*-trichloroethylidene-*m*-nitroacetophenone 과 phenylhydrazine 및 치환된 phenylhydrazine 들과의 반응으로 2,6-disubstituted-3-pyridazinone 들을 합성하였으며 2,4-dinitrophenylhydrazine 과의 반응에서는 hydrazone 을 중간체로 분리하였다. hydrazinehydrate 와의 반응에서는 3-(*m*-nitrophenyl)-5-trichloromethyl-2-pyrazoline 이 좋은 수득율로 얻어졌다. 또한 *r, r, r*-trichloroethylidene-*m*-nitroacetophenone 과 치환된 phenylhydrazine 과의 반응에서 phenyl기에 결합된 치환기의 효과를 검토하였다.

Abstract. 2,6-Disubstituted-3-pyridazinones were synthesized by the reactions of *r, r, r*-trichloroethylidene-*m*-nitroacetophenone with phenylhydrazine and substituted phenylhydrazines, and hydrazone was isolated as an intermediate from the reaction with 2,4-dinitrophenylhydrazine. From the reaction with hydrazine hydrate 3-(*m*-nitrophenyl)-5-trichloromethyl-2-pyrazoline was obtained in good yield. The effect of substituents on phenyl group in the reaction of *r, r, r*-trichloroethylidene-*m*-nitroacetophenone with substituted phenylhydrazines was also discussed.

Introduction

In previous papers of this series^{1,2}, we have prepared 2,6-disubstituted-3-pyridazinones by the reaction of *r, r, r*-trichloroethylideneacetophenone with phenylhydrazine and substituted phenylhydrazines, and isolated hydrazone as an intermediate from the reaction with 2,4-dinitrophenylhydrazine. We have also obtained pyrazoline derivative from the reaction with hydrazine hydrate.

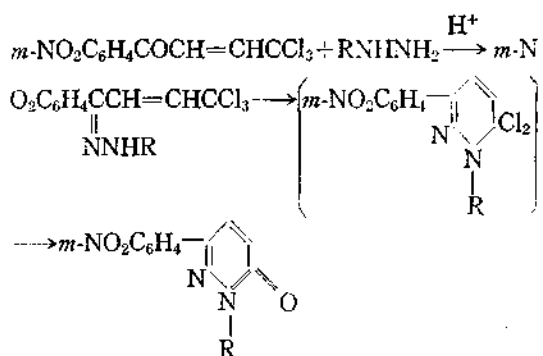
The purpose of this study is the application

of the same reaction to *r, r, r*-trichloroethylidene-*m*-nitroacetophenone as a part of study on the reactions of 3,3,3-trichloro-1-propenyl substituted-phenyl ketones with hydrazines to synthesize pyridazinone or pyrazoline derivatives and to know the effect of substituents on phenyl group.

Results and Discussion

Chloral-*m*-nitroacetophenone and *r, r, r*-trichloroethylidene-*m*-nitroacetophenone were synth-

esized by König method^{3,4}. Chloral-*m*-nitroacetophenone was obtained by acid-catalyzed aldol condensation of chloral and *m*-nitroacetophenone⁵, and converted to *r,r,r*-trichloroethylidene-*m*-nitroacetophenone by dehydration. 2-Phenyl-, 2-(*o*-nitrophenyl)-, 2-(*m*-nitrophenyl)-, 2-(*p*-nitrophenyl)-, 2-(*o*-tolyl)-, 2-(*m*-tolyl)-, 2-(*p*-tolyl)-, 2-(*m*-chlorophenyl) and 2-(*p*-chlorophenyl)-6-(*m*-nitrophenyl)-3-pyridazinone were obtained in good yields from the reaction of *r,r,r*-trichloroethylidene-*m*-nitroacetophenone with phenyl-, *o*-nitrophenyl-, *m*-nitrophenyl-, *p*-nitrophenyl-, *o*-tolyl-, *m*-tolyl-, *p*-tolyl-, *m*-chlorophenyl-* and *p*-chlorophenylhydrazine hydrochloride respectively in ethanol. From the reaction of *r,r,r*-trichloroethylidene-*m*-nitroacetophenone with 2,4-dinitrophenylhydrazine in acetic acid 2-(2,4-dinitrophenyl)-6-(*m*-nitrophenyl)-3-pyridazinone was obtained in 20% yield. Although hydrazones have not been isolated from the reaction of *r,r,r*-trichloroethylidene-*m*-nitroacetophenone with phenylhydrazine or monosubstituted phenylhydrazines, 2,4-dinitro



R = -C₆H₄NO₂ (*o*, *m* & *p*), -C₆H₄CH₃ (*o*, *m* & *p*),
-C₆H₄Cl (*m* & *p*), -C₆H₃(NO₂)₂-2,4

-phenylhydrazone was isolated from the reaction with 2,4-dinitrophenylhydrazine in methanol containing a small amount of hydrochloric acid and it gave 2-(2,4-dinitrophenyl)-6-(*m*-nitrophenyl)-3-pyridazinone on refluxing in acetic acid.

In a series of reaction with monosubstituted phenylhydrazines, phenylhydrazines containing electron-withdrawing group such as nitro and halogen on the phenyl group reacted more readily than those containing electron-releasing group such as methyl on the phenyl group (Table I). This result accords with that obtained from the reaction of *r,r,r*-trichloroethylideneacetophenone with monosubstituted phenylhydrazines, and supports our suggestion that the presence of electron-withdrawing groups on the phenylhydrazine would reduce the basic strength of the hydrazine and increase the concentration of free hydrazine, and accordingly, enhance the nucleophilic attack on the carbonyl group at the slow step for hydrazone formation. The slower rate of 2-(*o*-nitrophenyl)-6-(*m*-nitrophenyl)-3-pyridazinone formation relative to the meta and para compounds is likely due to ortho effect of the nitro group on the *o*-nitrophenylhydrazine as in the case of 2-(*o*-nitrophenyl)-6-phenyl-3-pyridazinone formation². The reaction of *r,r,r*-trichloroethylidene-*m*-nitroacetophenone with phenylhydrazine or substituted phenylhydrazines proceeded at milder condition than the reaction of *r,r,r*-trichloroethylideneacetophenone. It might be expected that the presence of electron-withdrawing nitro group would decrease the electron density on carbonyl carbon and, accordingly, enhance the nucleophilic attack of phenylhydrazines.

From the reaction of *r,r,r*-trichloroethylidene-*m*-nitroacetophenone with hydrazine hydrate 3-(*m*-nitrophenyl)-5-trichloromethyl-2-pyrazoline was obtained in 70% yield.

Experimental

Chloral-*m*-nitroacetophenone (I). A mixture of 52 g of *m*-nitroacetophenone and 48 g of chloral in 48 g of glacial acetic acid was heated under reflux for 40 hrs. The reaction mixture

*Sulfate was used in the case of *m*-chlorophenylhydrazine.

Table 1. Reaction time in the formation of substituted pyridazinones

Compounds	Reaction time
2-phenyl-6-(<i>m</i> -nitrophenyl)-3-pyridazinone	1.5 hrs.
2-(<i>o</i> -nitrophenyl)-6-(<i>m</i> -nitrophenyl)-3-pyridazinone	1.5 hrs.
2,6-di(<i>m</i> -nitrophenyl)-3-pyridazinone	30 min.
2-(<i>p</i> -nitrophenyl)-6-(<i>m</i> -nitrophenyl)-3-pyridazinone	20 min.
2-(<i>o</i> -tolyl)-6-(<i>m</i> -nitrophenyl)-3-pyridazinone	1.5 hrs.
2-(<i>m</i> -tolyl)-6-(<i>m</i> -nitrophenyl)-3-pyridazinone	1 hr.
2-(<i>p</i> -tolyl)-6-(<i>m</i> -nitrophenyl)-3-pyridazinone	2 hrs.
2-(<i>m</i> -chlorophenyl)-6-(<i>m</i> -nitrophenyl)-3-pyridazinone	1 hr.
2-(<i>p</i> -chlorophenyl)-6-(<i>m</i> -nitrophenyl)-3-pyridazinone	40 min.

was washed several times with hot water to remove unreacted chloral and acetic acid. The product was recrystallized from 70 % ethanol. The yield was 49 g (50 %); m. p., 118-120° C.

Anal. Calcd. for $C_{10}H_8O_4NCl_3$: C, 38.40; H, 2.56; N, 4.48. Found: C, 38.6; H, 2.58; N, 4.47.

The IR spectrum for compound I showed OH absorption at 3450 and 3501 cm^{-1} , C=O absorption at 1695 cm^{-1} , aromatic C=C absorption at 1615 cm^{-1} , and NO_2 absorption at 1535 and 1353 cm^{-1} .

***r, r, r*-Trichloroethylidene-*m*-nitroacetophenone (II).** Thirty-four grams of powdered chloral-*m*-nitroacetophenone was dissolved in 280 g of conc. sulfuric acid and the solution was allowed to stand for 40 hrs. at room temperature. Black syrupy solution was poured onto cracked ice with stirring. The crude precipitate was filtered, washed several times with water to remove acid, and recrystallized from 95% ethanol. The yield was 22 g (55 %); m. p., 97-98° C.

Anal. Calcd. for $C_{10}H_8O_3NCl_3$: C, 40.75; H, 2.04; N, 4.75. Found: C, 40.8; H, 2.06; N, 4.70.

The IR spectrum of the II showed C=O absorption at 1680 cm^{-1} , aromatic C=C absorption at 1615 cm^{-1} , and NO_2 absorption at 1530

and 1348 cm^{-1} .

2-Phenyl-6-(*m*-nitrophenyl)-3-pyridazinone (III). A mixture of 0.30 g of the compound II and 0.15 g of phenylhydrazine hydrochloride in 10 ml of ethanol was heated under reflux on the water bath for 1.5 hrs. Water was added until the solution became turbid and it was allowed to cool in the refrigerator. The pale yellow crystals separated were recrystallized from 50 % acetone. The yield was 0.21 g (72 %); m. p., 176-177° C.

Anal. Calcd. for $C_{16}H_{11}O_3N_3$: C, 65.53; H, 3.75; N, 14.33. Found: C, 65.1; H, 3.78; N, 14.3.

The IR spectrum of the compound III showed C=O absorption at 1672 cm^{-1} , aromatic C=C absorption at 1603 cm^{-1} , and NO_2 absorption at 1521 and 1354 cm^{-1} .

2-(*o*-Nitrophenyl)-6-(*m*-nitrophenyl)-3-pyridazinone (IV). A mixture of 0.30 g of the compound II and 0.19 g of *o*-nitrophenylhydrazine hydrochloride in 10 ml of ethanol was heated under reflux on the water bath for 1.5 hrs. Water was added until the solution became turbid and it was allowed to cool in the refrigerator. The product separated was recrystallized from acetone. The yield was 0.30 g (89 %); m. p., 245-247° C.

Anal. Calcd. for $C_{16}H_{10}O_5N_4$: C, 56.80; H, 2.96; N, 16.57. Found: C, 57.1; H, 3.03; N, 16.4.

The IR spectrum of the compound IV showed C=O absorption at 1683 cm^{-1} , aromatic C=C absorption at 1599 cm^{-1} , and NO_2 absorption at 1533 and 1352 cm^{-1} .

2, 6-Di (*m*-nitrophenyl)-3-pyridazinone (V).

A mixture of 0.30 g of the compound II and 0.19 g of *m*-nitrophenylhydrazine hydrochloride in 10 ml of ethanol was heated under reflux on the water bath for 30 min. Water was added until the solution became turbid and it was allowed to cool in refrigerator. The product separated was recrystallized from acetone. The yield was 0.24 g (72 %); m. p., $245\text{--}247^\circ\text{C}$.

Anal. Calcd. for $C_{16}H_{10}O_5N_4$: C, 56.80; H, 2.96; N, 16.57. Found: C, 56.7; H, 2.98; N, 16.5.

The IR spectrum of the compound V showed C=O absorption at 1687 cm^{-1} , aromatic C=C absorption at 1604 cm^{-1} , and NO_2 absorption at 1532 and 1355 cm^{-1} .

2-(*p*-Nitrophenyl)-6-(*m*-nitrophenyl)-3-pyridazinone (VI). A mixture of 0.30 g of the compound II and 0.19 g of *p*-nitrophenylhydrazine hydrochloride in 10 ml of ethanol was heated under reflux on the water bath for 20 min. Black precipitate was obtained after cooling the solution at room temperature. The product was recrystallized from methyl ethyl ketone. The yield was 0.23 g (68 %); m. p., $273\text{--}275^\circ\text{C}$.

Anal. Calcd. for $C_{16}H_{10}O_5N_4$: C, 56.80; H, 2.96; N, 16.57. Found: C, 56.5; H, 3.09; N, 16.4.

The IR spectrum of the compound VI showed C=O absorption at 1687 cm^{-1} , aromatic C=C absorption at 1605 cm^{-1} , and NO_2 absorption at 1520 and 1347 cm^{-1} .

2-(*o*-Tolyl)-6-(*m*-nitrophenyl)-3-pyridazinone (VII). A mixture of 0.30 g of the compound II and 0.16 g of *o*-tolylhydrazine hydrochloride

in 10 ml of ethanol was heated under reflux on the water bath for 1.5 hrs. Water was added until the solution became turbid and it was allowed to cool in the refrigerator. The product separated was recrystallized from 50 % acetone. The yield was 0.19 g (62 %); m. p., $131\text{--}132^\circ\text{C}$.

Anal. Calcd. for $C_{17}H_{13}O_3N_3$: C, 66.45; H, 4.23; N, 13.68. Found: C, 66.3; H, 4.28; N, 13.2.

The IR spectrum of the compound VII showed C=O absorption at 1679 cm^{-1} , aromatic C=C absorption at 1599 cm^{-1} , and NO_2 absorption at 1532 and 1361 cm^{-1} .

2-(*m*-Tolyl)-6-(*m*-nitrophenyl)-3-pyridazinone (VIII). A mixture of 0.30 g of the compound II and 0.16 g of *m*-tolylhydrazine hydrochloride in 10 ml of ethanol was heated under reflux on the water bath for 1 hr. The crude precipitated material was separated after standing the solution at room temperature and recrystallized from 80 % acetic acid. The yield was 0.17 g (55 %); m. p., $170\text{--}171^\circ\text{C}$.

Anal. Calcd. for $C_{17}H_{13}O_3N_3$: C, 66.45; H, 4.23; N, 13.68. Found: C, 65.9; H, 4.19; N, 13.7.

The IR spectrum of the compound VIII showed C=O absorption at 1674 cm^{-1} , aromatic C=C absorption at 1603 cm^{-1} , and NO_2 absorption at 1526 and 1352 cm^{-1} .

2-(*p*-Tolyl)-6-(*m*-nitrophenyl)-3-pyridazinone (IX). A mixture of 0.30 g of the compound II and 0.16 g of *p*-tolylhydrazine hydrochloride in 10 ml of ethanol was heated under reflux on the water bath for 2 hrs. The crude precipitated material was separated after standing the solution at room temperature and recrystallized from 50 % acetone. The yield was 0.15 g (49 %); m. p., $184\text{--}185^\circ\text{C}$.

Anal. Calcd. for $C_{17}H_{13}O_3N_3$: C, 66.45; H, 4.23; N, 13.68. Found: C, 66.5; H, 4.19; N, 13.7.

The IR spectrum of the compound IX showed

C=O absorption at 1673 cm^{-1} , aromatic C=C absorption at 1603 cm^{-1} , and NO_2 absorption at 1513 and 1355 cm^{-1} .

2-(*m*-Chlorophenyl)-6-(*m*-nitrophenyl)-3-pyridazinone (X). A mixture of 0.30 g of the compound II and 0.24 g of *m*-chlorophenylhydrazine sulfate in 10 ml of ethanol was heated under reflux on the water bath for 1 hr. The reaction mixture was allowed to cool in the refrigerator and the precipitated material was recrystallized from 50% acetone. The yield was 0.24 g (74%); m. p., $177\text{--}173^\circ\text{C}$.

Anal. Calcd. for $\text{C}_{16}\text{H}_{10}\text{O}_3\text{N}_3\text{Cl}$: C, 58.63; H, 3.05; N, 12.82. Found: C, 58.6; H, 3.13; N, 12.9.

The IR spectrum of the compound X showed C=O absorption at 1683 cm^{-1} , aromatic C=C absorption at 1605 cm^{-1} , and NO_2 absorption at 1521 and 1357 cm^{-1} .

2-(*p*-Chlorophenyl)-6-(*m*-nitrophenyl)-3-pyridazinone (XI). A mixture of 0.30 g of the compound II and 0.18 g of *p*-chlorophenylhydrazine hydrochloride in 10 ml of ethanol was heated under reflux on the water bath for 40 min. The reaction mixture was allowed to stand at room temperature and the crude material separated was recrystallized from 50% acetone. The yield was 0.15 g (46%); m. p., $238\text{--}239^\circ\text{C}$.

Anal. Calcd. for $\text{C}_{16}\text{H}_{10}\text{O}_3\text{N}_3\text{Cl}$: C, 58.63; H, 3.05; N, 12.82. Found: C, 58.4; H, 3.14; N, 12.9.

The IR spectrum of the compound XI showed C=O absorption at 1684 cm^{-1} , aromatic C=C absorption at 1605 cm^{-1} , and NO_2 absorption at 1519 and 1358 cm^{-1} .

***r, r, r*-Trichloroethylidene-*m*-nitroacetophenone 2,4-dinitrophenylhydrazone (XII).** To a hot solution of 3.23 g of the compound II in 50 ml of methanol was added a hot solution of 2.40 g of 2,4-dinitrophenylhydrazine and 3.0 ml of conc. hydrochloric acid in 60 ml of met-

hanol. The red crystal was obtained after cooling the solution in the refrigerator and recrystallized from acetone. The yield was 3.40 g (65%); m. p., $136\text{--}137^\circ\text{C}$.

Anal. Calcd. for $\text{C}_{16}\text{H}_{10}\text{O}_6\text{N}_5\text{Cl}_3$: C, 40.46; H, 2.12; N, 14.75. Found: C, 40.7; H, 2.08; N, 14.7.

The IR spectrum of the compound XII showed N-H absorption at 3260 cm^{-1} , aromatic C=C absorption at 1617 cm^{-1} , and NO_2 absorption at 1534 and 1337 cm^{-1} .

2-(2,4-Dinitrophenyl)-6-(*m*-nitrophenyl)-3-pyridazinone (XIII). A. **From Compound XII.** 0.40 Grams of the compound XII in 20 ml of glacial acetic acid was heated under reflux on the water bath for 1 hr. Water was added until the solution became turbid and the crude precipitated material was recrystallized from acetone. The yield was 0.37 g (94%); m. p., $218\text{--}220^\circ\text{C}$.

B. From Compound II. A mixture of 0.60g of the compound II and 0.40 g of 2,4-dinitrophenylhydrazine in 20 ml of glacial acetic acid was heated under reflux on the water bath for 1 hr. Water was added until the solution became turbid and the crude precipitated material was recrystallized from acetone. The yield was 0.15 g (20%); m. p., $218\text{--}220^\circ\text{C}$.

Anal. Calcd. for $\text{C}_{16}\text{H}_9\text{O}_7\text{N}_5$: C, 50.13; H, 2.35; N, 18.28. Found: C, 50.3; H, 2.53.

The IR spectrum of the compound XIII showed C=O absorption at 1683 cm^{-1} , aromatic C=C absorption at 1611 cm^{-1} , and NO_2 absorption at 1540 and 1353 cm^{-1} .

3-(*m*-Nitrophenyl)-5-trichloromethyl-2-pyrazoline (XIV). To a solution of 1.0 ml of hydrazine hydrate in 10 ml of ethanol was added a solution of 1.0 g of the compound II in 20 ml of ethanol. The yellow needles were crystallized after cooling the solution in the refrigerator and recrystallized from 50% methanol. The yield was 0.72 g (70%); m. p., $135\text{--}137^\circ\text{C}$.

Anal. Calcd. for $C_{10}H_5O_2N_3Cl_3$: C, 38.90; H, 2.59; N, 13.61. Found: C, 38.9; H, 2.65; N, 13.5.

The IR spectrum of the compound XIV showed N-H absorption at 3340 cm^{-1} , aromatic C=C absorption at 1603 cm^{-1} , and NO_2 absorption at 1528 and 1348 cm^{-1} .

The IR spectra were obtained with Jasco IR-G using KBr disc. Carbon, hydrogen and nitrogen were determined by microanalysis at Korea Institute of Science and Technology.

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References

1. Y. Y. Lee, W. Y. Lee and S. H. Chang; *This Journal*, **14**, 61 (1970).
2. Y. Y. Lee, *This Journal*, **16**, 189 (1972).
3. W. König and E. Wagstaff, *Ber.*, **26**, 554 (1893).
4. W. König, *Ber.*, **25**, 792 (1892).
5. W. Y. Lee, *M.S. Thesis, Graduate School, Seoul National University*, p.13, 1959.