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Carboxylation of Nitromethane by Carbon Dioxide and Potassium Phenoxide Derivatives. Substituent Effect upon the Yield of Carboxylate

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The carboxylation of nitromethane with carbon dioxide proceeded in the presence of potassium phenoxides in DMF, yielding dipotassium nitroacetate as a precipitate. This reaction proceeded well at 0 °C. The substituent effect upon the carboxylation was investigated by using potassium phenoxides with various substituents (p-OCH_3, p-CH_3, H, p-Cl, m-Cl, p-$COCH_3$, and p-NO_2). The reaction was completed in 5 min at 0 °C. The maximum yield of carboxylate was obtained when unsubstituted phenoxide was used; the yield of carboxylate was low when potassium phenoxide with a substituent having a highly negative or highly positive σ value was used.

The mechanism of the carboxylation is discussed. The formation of the carboxylate as a precipitate is considered to be an important factor. Methods for the effective transformation of dipotassium nitroacetate to methyl nitroacetate are briefly surveyed.

Keywords——potassium phenoxide; carbon dioxide; nitromethane; dipotassium nitroacetate; substituent effect; carboxylation

We have investigated the carboxylation of organic compounds containing active hydrogens by carbon dioxide in the presence of potassium phenoxide.[1] Furthermore, in order to clarify the mechanism of this reaction, the effect of using substituted potassium phenoxide derivatives upon the rates and equilibria of the carboxylation was studied with indene or cyclohexanone as a substrate.[2] In the present paper we report the carboxylation of nitromethane, the pK_a of which is much smaller than that of indene or cyclohexanone. Carboxylation was conducted in the presence of potassium phenoxides with various substituents (RPhOK) in N,N-dimethylformamide (DMF). Nitroacetic acid or methyl nitroacetate, the reaction product of carboxylation of nitromethane, is one of the starting materials for the synthesis of glycine, so that it may be useful to know which substituted phenoxide gives the best yield of the carboxylate.

Nitroacetic acid is an unstable compound; acidification of the carboxylation product of nitromethane with dilute hydrochloric acid at room temperature gave nitroacetic acid in a yield of only 25%, as previously reported.[1] Thus, in the present study, we also briefly survey methods by which nitroacetate salt can be converted effectively to methyl ester. Methyl ester can be quantitatively determined by gas chromatography.

Results

The reaction product in the carboxylation of nitromethane by potassium phenoxide in DMF was obtained as a precipitate. The infrared (IR) spectrum of this precipitate coincided with that of authentic dipotassium nitroacetate, synthesized separately.[3] The potassium content of this precipitate also coincided with that of dipotassium nitroacetate. Thus, the reaction product was shown to be dipotassium nitroacetate.

In order to determine the amount of reaction product by gas chromatography, two methods for methylating dipotassium nitroacetate were examined. One method is the methylation with diazomethane of nitroacetic acid, which is formed by the acidification of dipotassium nitroacetate. The other is the direct methylation of dipotassium nitroacetate by HCl–MeOH. The acidification of dipotassium nitroacetate in the former method proceeded well in 50% H_2SO_4 at −20 °C, but the reproducibility in terms of the yield of nitroacetic acid was poor. Moreover the methylation of nitroacetic acid by diazomethane yielded by-products other than methyl nitroacetate, as observed by gas chromatography. In the methylation with HCl–MeOH, the yield of methyl ester was comparatively high and was reproducible. By-products were scarcely formed in this methylation. Thus, the methylation with HCl–MeOH was applied for methylation of the product of the carboxylation reaction (dipotassium nitroacetate), in order to determine the yield of carboxylate by gas chromatography as methyl nitroacetate.

The carboxylation of nitromethane was carried out with a molar ratio of nitromethane to potassium phenoxide of 1 to 2, because the reaction product was the dipotassium salt of nitroacetic acid. The concentrations of the reactants used were higher than in the carboxylation of other substrates[2] so that the ratio of the amount of product precipitated to that in the solution increased.

Figure 1 shows the time course of the carboxylation of nitromethane in the presence of potassium phenoxide at various temperatures. At 0 °C, the reaction took place rapidly and gave carboxylate in high yield. Temperatures above or below 0 °C were less favourable. The carboxylation reactions with potassium phenoxide derivatives were therefore carried out at 0 °C.

Figure 2 shows the time course of carboxylation with *m*-chlorophenoxide. The reaction took place very rapidly and was completed in 5 min, as expected from the high acidity of nitromethane. The carboxylation with other potassium phenoxide derivatives also took place rapidly. Precise measurement of the reaction rate was not attempted because of the rapidity of the reaction and the heterogeneity of the reaction system. Table I lists the yields of carboxylate

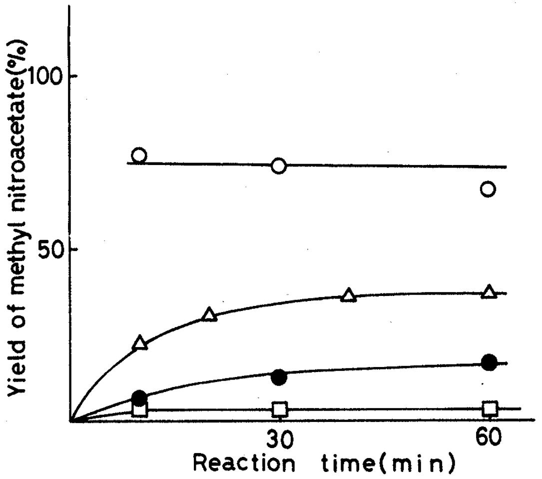

Fig. 1. Carboxylation of Nitromethane in the Presence of Potassium Phenoxide at Various Temperatures

—●—, 80 °C; —△—, room temperature; —○—, 0 °C; —□—, −20 °C.

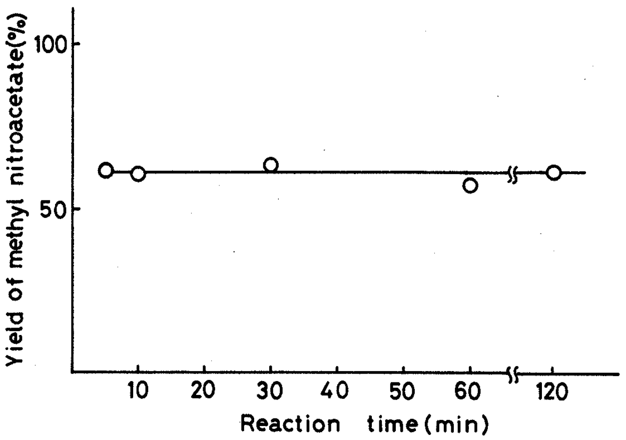

Fig. 2. Carboxylation of Nitromethane in the Presence of *m*-Chloro-substituted Phenoxide at 0 °C

TABLE I. The σ Values of Substituents of RPhOK and the Yields of Methyl Nitroacetate in the Carboxylation Using RPhOK

R	σ Value	Yield[a] (%)
p-OCH_3	-0.27	22
p-CH_3	-0.17	64
H	0	73
p-Cl	0.23	67
m-Cl	0.37	62
p-$COCH_3$	0.50	43
p-NO_2	0.78	14

[a] Each value is the average of 2 runs.

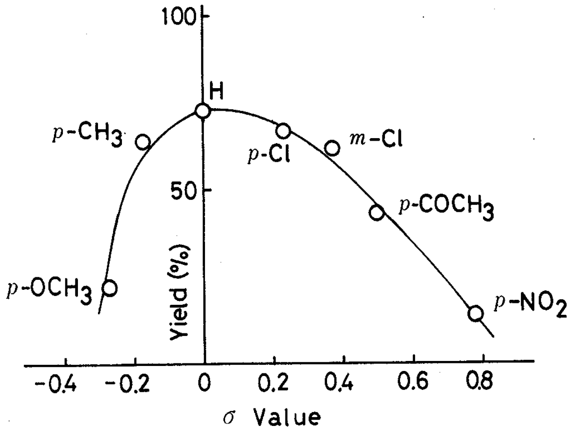

Fig. 3. The Relationship between σ Values of Substituents and the Yields of Methyl Nitroacetate

when potassium phenoxides with various substituents (RPhOK) were used, together with the σ values[4)] of the substituents of RPhOK applied. The relationship between the yields of carboxylates and σ values of the substituents is shown in Fig. 3. In the region of positive σ value, the yield of the carboxylate decreased with increase of σ value. On the other hand, the yield of the carboxylate increased with increment of σ value in the region of negative σ value. The maximum yield was obtained when potassium phenoxide with no substituent was used. The relationship mentioned above is in contrast to that for indene carboxylation;[2)] in the latter case the yields of carboxylates decreased with increase of the σ value of all substituents investigated.

Discussion

For the carboxylation of nitromethane, CO_2 at atmospheric pressure was passed through the DMF solution of RPhOK prior to the addition of nitromethane. It has been shown previously[2)] that RPhOK absorbs CO_2, forming a complex. RPhOK with a substituent of smaller σ

$$\mathrm{RPhOK} + \mathrm{CO_2} = \mathrm{RPhOK \cdot CO_2} \qquad (1)$$

value takes up CO_2 more effectively owing to its higher basicity, and RPhOK with a substituent of negative σ value would bind CO_2 strongly. As we had previously suggested in connection with the carboxylation of indene,[2)] it can be assumed that the carboxylate is formed *via* CO_2 transfer from $\mathrm{RPhOK \cdot CO_2}$ to nitromethane.

$$\mathrm{RPhOK \cdot CO_2} + \mathrm{NO_2CH_3} = \mathrm{NO_2CH_2CO_2K} + \mathrm{RPhOH} \qquad (2)$$

In this reaction, the use of RPhOK with a substituent of large σ value such as a nitro group would result in the formation of a small amount of carboxylate ($NO_2CH_2CO_2K$) because of the small amount of $RPhOK \cdot CO_2$. Similarly, with the use of RPhOK having a substituent with a large negative σ value, reaction (2) may not progress due to the strong binding with CO_2. The carboxylate formed in reaction (2) would be transformed to dipotassium nitroacetate by RPhOK present in the solution.

$$NO_2CH_2CO_2K + RPhOK = KO_2N{=}CHCO_2K + RPhOH \qquad (3)$$

The second ionization constant of nitroacetic acid is 1.25×10^{-9} ($pK_a = 8.90$),[5] which is comparable with the pK_a of phenol, 10.0,[6] or those of phenol derivatives. RPhOK with a substituent of negative σ value seems to shift this reaction to the right owing to its high basicity. However, the amount of RPhOK present in the solution is greatly reduced by its tendency to form a complex with CO_2. Thus, the application of RPhOK with a substituent of negative σ value may mean that reaction (3) does not progress. RPhOK with a substituent having a large positive σ value would also be unfavorable for reaction (3) due to its low basicity in spite of the large amount of RPhOK present in the solution. The yield of methyl nitroacetate when *p*-OCH_3-substituted phenoxide was used was low. This result can be ascribed to the strong binding between CO_2 and RPhOK in reaction (2), and/or, the disadvantage of RPhOK in reaction (3) as described above. Comparison with the results of indene carboxylation suggest that the latter may be the main reason, because, in the indene carboxylation, the yield of carboxylate with *p*-OCH_3-substituted phenoxide was high compared with that in the carboxylation with other substituted phenoxides; and step (3) is absent in the indene carboxylation. The carboxylation of nitromethane with *p*-nitro-substituted phenoxide also gave a low yield of carboxylate, possibly because the complex formation between CO_2 and RPhOK (reaction (2)) and/or reaction (3) is difficult. Thus, the maximum yield of carboxylate was obtained when unsubstituted phenoxide was used.

Another mechanism would also explain the results. The pK_a of nitromethane is 10.2,[7] which is comparable with that of phenol derivatives. Accordingly, the formation of the nitromethane salt[8] can be expected in the reaction between RPhOK and nitromethane.

$$CH_3NO_2 + RPhOK = KCH_2NO_2 + RPhOH \qquad (4)$$

RPhOK with a substituent of negative σ value would not necessarily favor this reaction because RPhOK is very reduced due to its complex formation with CO_2. RPhOK with a substituent having a highly positive σ value would also be unfavorable for this reaction owing to its low basicity. The nitromethane salt would rapidly react with CO_2, forming carboxylate.

$$KCH_2NO_2 + CO_2 = NO_2CH_2CO_2K \qquad (5)$$

This reaction would be followed by reaction (3), yielding dipotassium nitroacetate. The finding, as shown in Fig. 3, that RPhOK with a substituent having a large negative or large positive σ value gave a low yield of the carboxylate could also be explained by the mechanism noted here regarding the substituent effect of RPhOK upon reactions (4) and (3).

Stiles *et al.*[5] considered the formation of the chelate compound shown in Chart 1 to be

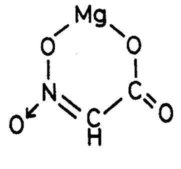

Chart 1

the driving force for the carboxylation of nitromethane with magnesium methoxide and CO_2. The reaction product in the carboxylation of nitromethane by RPhOK was dipotassium nitroacetate, which separated out from the reaction system as a precipitate, and this may be one of the most important factors in shifting the reaction toward the formation of the carboxylate. As shown in Fig. 1, the carboxylation reaction proceeded best at 0 °C, being less efficient above or below this temperature. These observations suggest the importance of this factor in relation to the solubility of the reaction product in the solvent (DMF).

The yield of methyl nitroacetate when unsubstituted phenoxide was used is as high as that reported by Zen *et al.*,[3] who synthesized this product from nitromethane and potassium hydroxide by an improved method. Thus, the reactions described here (carboxylation and methylation with HCl–MeOH) seem to afford an excellent method for the synthesis of methyl nitroacetate.

Experimental

Reaction Product Formed in the Carboxylation of Nitromethane——CO_2 was sufficiently passed through a DMF solution of potassium phenoxide (about 0.9 M) for 30 min at room temperature, then nitromethane (a half equivalent with respect to potassium phenoxide) was added. At 10 min after the start of the reaction, the precipitate formed in the reaction mixture was filtered off, and washed with DMF and benzene. It was dried *in vacuo* to remove residual benzene. The content of potassium was determined by the sodium tetraphenylboron method.[9] *Anal.* Calcd for $C_2HK_2NO_4$: K, 43.09. Found: K, 42.21. The product obtained was acidified with dilute hydrochloric acid at -5 °C and extracted with ether. The ether was evaporated off, chloroform was added to the residue, and nitroacetic acid was obtained as crystals. mp 91—92 °C (lit.,[5] 91—92 °C).

Transformation of Dipotassium Nitroacetate to the Methyl Ester by Acidification Followed by Methylation with Diazomethane——Acidification was done with hydrochloric acid (3.2 and 5.2%) or with sulfuric acid (50%) at various temperatures from -5 to -40 °C. The carboxylate was extracted with ether. The yield of the carboxylate was measured gravimetrically. Acidification with 50% sulfuric acid at -20 °C gave the best yield (60—70%) of nitroacetic acid. However, gas chromatographic analysis showed that methylation of the carboxylate with diazomethane also gave by-products.

Methylation of Dipotassium Nitroacetate by HCl–MeOH——Dipotassium nitroacetate (1 g) was reacted with 10 ml of 7% HCl–MeOH at room temperature. The time course of the reaction was followed by gas chromatography. After about 3 h, the yield of methyl nitroacetate reached a constant value of about 80%. The addition of 7% HCl–MeOH at -50 °C followed by reaction at room temperature gave the same yield of methyl nitroacetate as in the case mentioned above. The product of the methylation of dipotassium nitroacetate with 7% HCl–MeOH gave only one peak in gas chromatographic analysis.

Carboxylation of Nitromethane with RPhOK——A potassium phenoxide derivative (0.1 mol) was dissolved in 100 ml of DMF. CO_2 was sufficiently passed through the solution for 30 min at 0 °C, then nitromethane (0.05 mol) was added. The total volume of the reaction mixture amounted to 114 ml. After an appropriate time interval, 10 ml of the reaction mixture was sampled with a volumetric pipet, and added to ether. This sample was centrifuged and the supernatant was discarded. The precipitate was washed with ether and the ether suspension was again centrifuged. The resulting precipitate was dried *in vacuo*, then 10 ml of 7% HCl–MeOH and β-methylnaphthalene (internal standard for gas chromatographic analysis) were added and the mixture was left for about 3 h at room temperature. The methyl nitroacetate formed was quantitatively analyzed by gas chromatography (DEGA on Uniport B, 150 °C, hydrogen flame ionization detector).

References and Notes

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