[Chem. Pharm. Bull. 18(8)1576—1588(1970)]

UDC 547.341.04 : 547.781.4.04 : 547.785.5.04

Studies on Pyrimidine Derivatives and Related Compounds. LXVIII.[1] Reactions of Dialkyl Acylphosphonates with 1,3-Disubstituted Benzimidazolium Halides

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(Received February 18, 1970)

The reaction of 1,3-disubstituted benzimidazolium halides (**1a—d, 16**) with diethyl- and dimethyl acylphosphonates (**2a—b, 12a—b**) were investigated. 1:1 adducts (**3a—b**) were obtained from the reactions of **1a** and **2a—b**. From the reactions of **1a** with **12a—b**, **1b—d** with **2a**, and **1b—d** with **12a—b** were obtained betaines (**13a—b, 3c—e, 13c—f**), respectively. The adduct **3a** was synthesized by an alternative method. Alkaline treatment of both **3a** and **3b** afforded 1,3-dimethyl-2-(1-hydroxy)benzyl- and ethylbenzimidazolium iodides (**8a—b**) as major products. Alkaline treatment of betaines (**13a—d, 3c—e**) gave only corresponding 2-imidazolinones and/or ring-opened N-formates. Neither of the adducts gave corresponding quinoxaline derivatives. In the case of the reactions of 1,3-dimethyl-5-nitrobenzimidazolium iodide (**16**) with **2a—b** were obtained 1:1 adducts (**17a—b**) accompanied by ring-opened phosphates (**18a—b**). The reactions of **16** with **12a—b** gave betaines (**23a—b**). Neither of **17a—b, 18a—b**, or **23a—b** gave corresponding quinoxaline derivatives. Treatment of **17a** with dimethylsulfoxide afforded 1,4-dimethyl-3-hydroxy-3-phenyl-7-nitro-1,2,3,4-tetrahydro-2-quinoxalinone (**25**) in moderate yield. The mechanisms of these reactions are discussed briefly.

A novel reaction of thiamine and other thiazolium salts with dialkyl acylphosphonates to give 1,4-thiazine derivatives has been reported.[3a-c] In the course of investigating this reaction it has been possible to elucidate the mechanism of the reactions of thiazolium salts with dialkyl acylphosphonates.[3a] The reaction of azolium salts with dialkyl acylphosphonates was expected to be analogous to that of thiazolium salts. In this paper we wish to describe the reaction of benzimidazolium salts with dialkyl acylphosphonates.

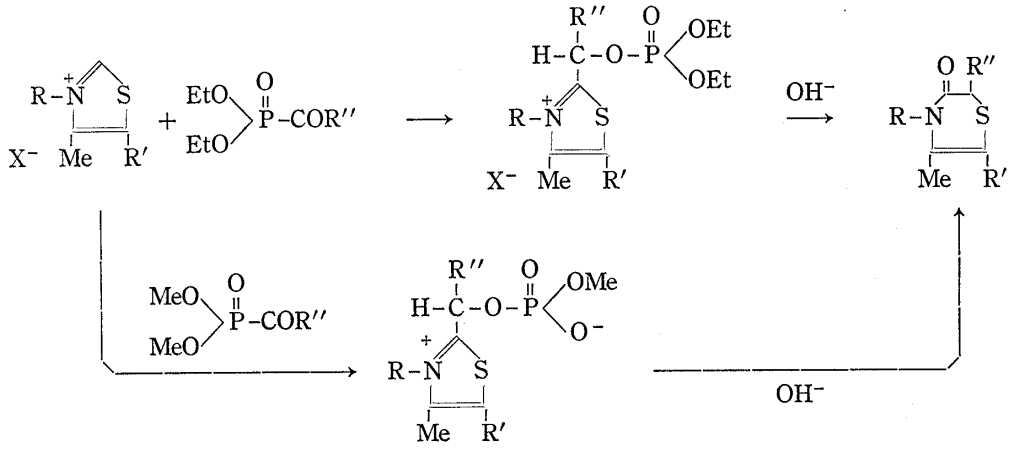


Chart 1

1) Part LXVII: A. Takamizawa and H. Harada, *Chem. Pharm. Bull.* (Tokyo), **18**, 1402 (1970).
2) Location: *Fukushima-ku, Osaka.*
3) *a*) A. Takamizawa, Y. Hamashima, and H. Sato, *J. Org. Chem.*, 33, 4038 (1968); *b*) A. Takamizawa and Y. Sato, *Chem. Pharm. Bull.* (Tokyo), **14**, 742 (1966); *c*) A. Takamizawa, Y. Hamashima, Y. Sato, and H. Sato, *ibid.*, **15**, 1178 (1967).

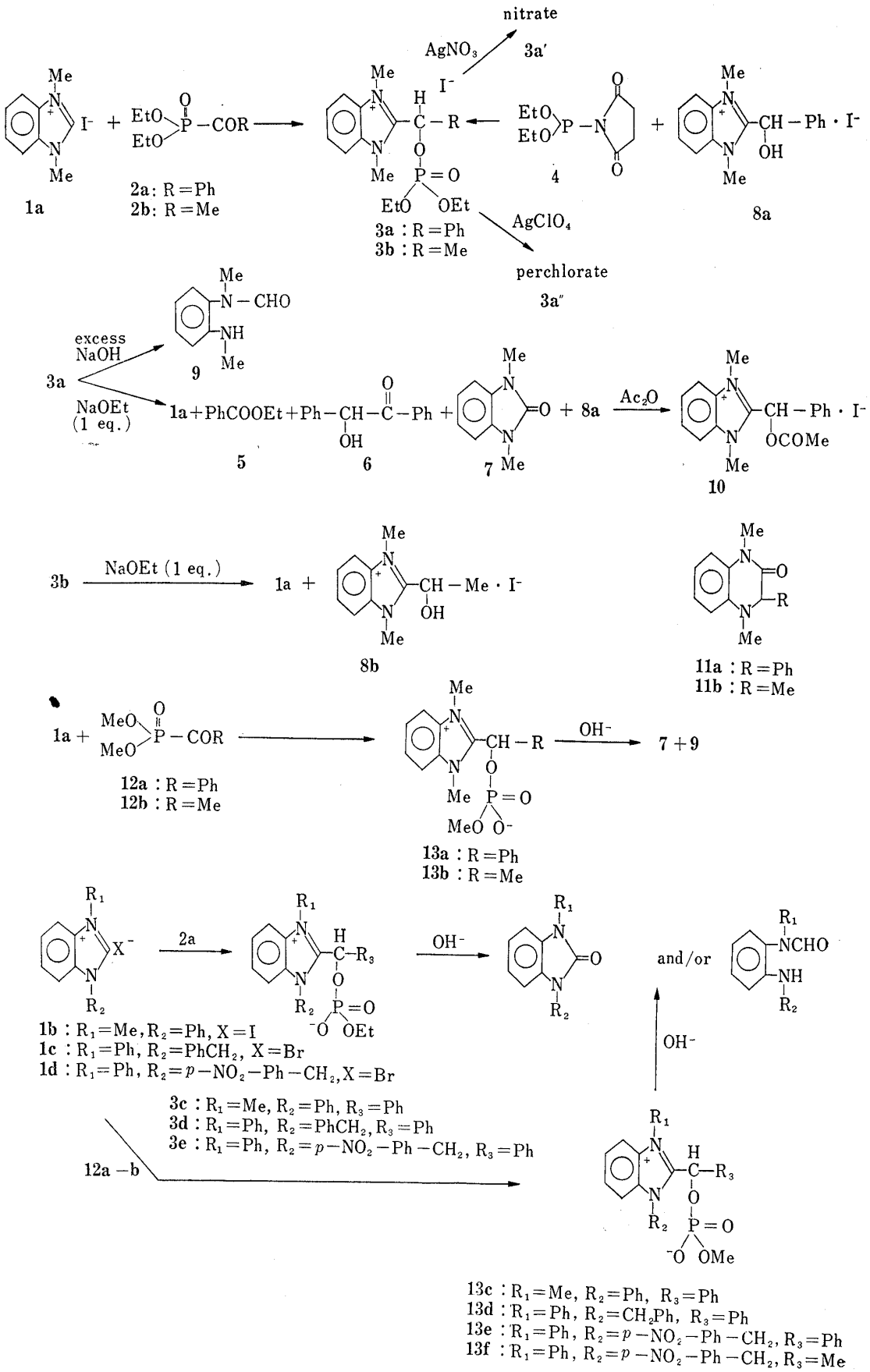


Chart 2

Reactions of 1,3-Dimethylbenzimidazolium Iodide (1a) and Some Other 1,3-Disubstituted-benzimidazolium Halides (1b—d) with Dialkyl Acylphosphonates

In a previous paper[4] we reported that thiazolium salts reacted with diethyl acylphosphonates to give 1:1 adducts in good yields whereas reactions with dimethyl acylphosphonates produced betaines of O-methyl-O-1-(2-thiazolium)alkylphosphoric acids with the loss of methyl halides.

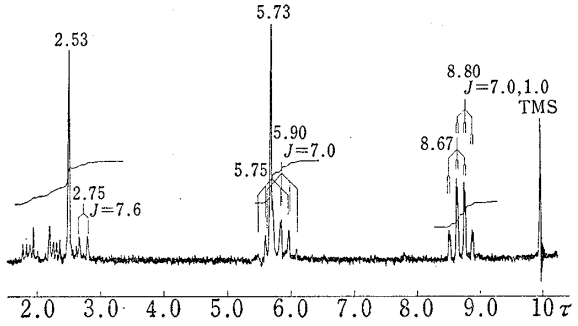


Fig. 1. PMR Spectrum of 3a in $CDCl_3$

The corresponding 1:1 benzimidazolium adduct (**3a**) was obtained in good yield by the reaction of 1,3-dimethylbenzimidazolium iodide (**1a**) with diethyl benzoylphosphonate (**2a**) in N,N-dimethylformamide(DMF)solution in the presence of triethylamine. The elemental analysis for **3a** corresponded to $C_{20}H_{26}O_4N_2IP$, and the PMR spectrum (Fig. 1) exhibited a singlet at 5.73 τ for six protons (two $>N-CH_3$ groups, suggesting that the 1,3-dimethylbenzimidazolium moiety was intact), and doublet at 2.75τ for one proton indicating the presence of a group such as $C_6H_5-C\underline{H}(R)-O-P$. These data are in accord with the structure of **3a** being 1,3-dimethyl-2-(diethylphosphoroyl)benzylbenzimidazolium iodide. Moreover, **3a** was identified with the compound synthesized by an alternative route using 1,3-dimethyl-2-benzhydrylbenzimidazolium iodide (**8a**) and O,O-diethyl-N-succinyl-phosphoramide[5] (**4**).

The adduct (**3a**) was somewhat unstable, decomposing on standing to a brown resin, however, the nitrate (**3a'**) and perchlorate (**3a''**) salts were obtained as stable oils. When **3a** was treated with an exactly equimolar amount of sodium ethoxide, ethyl benzoate (**5**), benzoin (**6**), 1,3-dimethyl-2-benzimidazolinone (**7**),[6] alcohol (**8a**), and **1a** were produced, whereas on treatment with an excess of sodium hydroxide, cleavage occurred to give a single product (**9**).

The analogous diethylphosphoroyl derivative (**3b**), obtained by the reaction of **1a** with diethyl acetylphosphonate (**2b**), was cleaved by sodium ethoxide to give the alcohol (**8b**) in good yield. The salts (**8a—b**) were synthesized directly by the reaction of **1a** with benzaldehyde and acetaldehyde respectively in DMF solution in the presence of triethylamine. O'Sullivan, *et al.*,[7] have previously synthesized **8a** by another route. Contrary to our expectations, cleavage of **3a** and **3b** under basic conditions did not produce any ring-expanded products, *e.g.*, 1,4-dimethyl-3-phenyl (or methyl)-1,2,3,4-tetrahydro-2-quinoxalinone (**11a** or **11b**).

Both the betaines (**13a—b**), which were prepared in good yields by the reaction of **1a** with dimethyl benzoylphosphonate (**12a**) and dimethyl acetylphosphonate (**12b**) respectively, were relatively stable toward alkali, but under forcing conditions were cleaved to give **7** and **9** without giving ring-expanded tetrahydroquinoxaline derivatives respectively. Compounds **13a** and **13b** as well as **3a** and **3b** were all stable to hydrogen chloride in methanol and could be recovered unchanged.

The effects of substituents at N_1 and N_3 of the benzimidazolium nucleus on the overall course of the reaction was investigated. The reactions of several 1,3-disubstituted benzimidazolium salts [1-methyl-3-phenyl-(**1b**), 1-phenyl-3-benzyl (**1c**), and 1-phenyl-3-*p*-nitrobenzylbenzimidazolium halides (**1d**)] with **2a** were carried out and produced the expected 1:1 oily adducts which were purified by column chromatography and isolated as the betaines (**3c—e**). Similarly reactions of **1b** and **1c** with **12a—b** produced the betaines (**13c—f**) directly,

4) A. Takamizawa, Y. Hamashima, H. Sato, and S. Sakai, *Chem. Pharm. Bull.* (Tokyo), **17**, 1356 (1969).
5) T. Mukaiyama, T. Obata, and O. Mitsunobu, *Bull. Chem. Soc. Japan*, **38**, 1091 (1965).
6) J.K. Landquist, *J. Chem. Soc.*, **1953**, 2830.
7) D.G. O'Sullivan and A.K. Wallis, *J. Chem. Soc.*, **1965**, 2331.

however, the transformation of these products into the desired quinoxaline derivatives was not successful.

Reactions of 1,3-Dimethyl-5-nitrobenzimidazolium Iodide (16) with Dialkyl Acylphosphonates

Since the anticipated ring-expanded quinoxaline derivatives could not be obtained directly by alkaline treatment of the benzimidazolium salts (**3a—e**, and **13a—f**), an indirect synthesis *via* ring-opened intermediates was attempted. An electron-withdrawing group at C_5 in the benzimidazole nucleus was expected to deactivate the nitrogen atom at position **1** and to stabilize the open chain form of such compounds as **18**.

Reaction of the appropriate nitro derivative, 1,3-dimethyl-5-nitrobenzimidazolium iodide (**16**), with **2a** in DMF solution in the presence of triethylamine afforded three products (Chart 3). The structure of the benzimidazolium adduct (**17a**) was confirmed by PMR and infrared spectral data, and elemental analysis. Elemental analysis of the second reaction product corresponded to the formula $C_{20}H_{26}O_7N_3P$ and the infrared spectrum showed absorption bands at 3230 (NH), 1677 (CO), 1605 and 1589 (NH or phenyl), 1499 and 1316 (NO_2), 1259 (P=O) and 1030 cm^{-1} (P–O–C). The PMR spectrum (Fig. 2) exhibited a doublet at 4.83 τ (one proton) indicating the group (C_6H_5–CH–O–P), a singlet at 6.85 τ (three protons), >N–CH_3 coupled with a hydrogen resonating at 6.99 τ.

Based on these data, the structure of the ring-opened adduct was elucidated as O,O-diethyl-O-[N-methyl-N-(2-methylamino-5-nitro)phenylcarbamoyl)]benzylphosphate (**18a**). Evidence that the anticipated N_1–C_2 bond fission of **17a** did in fact occur, as opposed to C_2–N_3 fission, comes from the PMR spectrum; the signal for the aromatic proton at C_6 occurs at a relatively high field (3.32 τ) which is compatible with the proximity of an acyclic amino group. The third product was identified as 1,3-dimethyl-5-nitro-2-benzimidazolinone (**19**)[8] which could be also obtained from **18a** directly by treatment with sodium hydroxide. The ring-opened adduct (**18a**) accompanied by **19** was also obtained from treatment of **17a** with aqueous triethylamine. When an acetone solution of **17a** was allowed to stand, elimination of ethyl iodide occurred, and the product (**20a**) precipitated from the solution. The structure of **20a** was deduced from the elemental analysis, infrared and PMR spectral data as the betaine of O-ethyl-O-1-(1,3-dimethyl-5-nitro-2-benzimidazolyl)benzylphosphoric acid. When **20a** was heated with aqueous triethylamine, the ring-opened triethylammonium salt (**21**) was obtained. Thus attempts to obtain the desired products **22a** *via* **17a** isolated from the reaction mixture or the ring-expanded **18a** under alkaline conditions failed. Acidic treatment of **18a** did effect ring closure, but only provided the benzimidazolium hydrochloride salt (**20′**), corresponding to **20a**. Comparable results were obtained in the reaction of **16** with **2b**, but the desired product (**22b**) was not obtained. Reactions of **16** with **12a** and **12b** produced the corresponding betaines (**23a—b**) as expected. The ring-opened triethylammonium salt (**24**) could

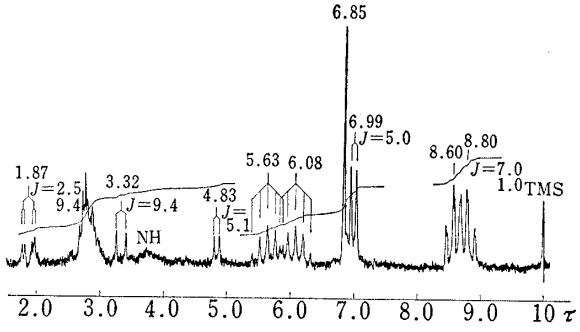


Fig. 2. PMR Spectrum of **18a** in $CDCl_3$

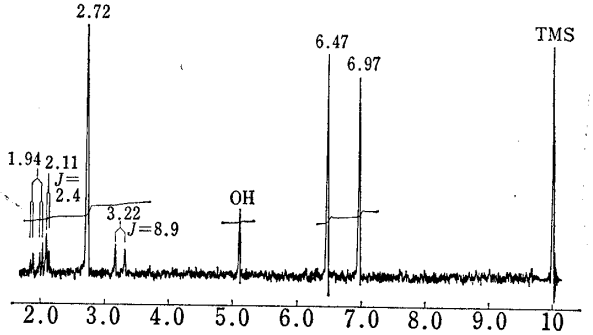


Fig. 3. PMR Spectrum of **25** in $CDCl_3$

8) L.S. Efros and A.V. El'tsov, *Obshch. Khim.*, **27**, 127 (1957).

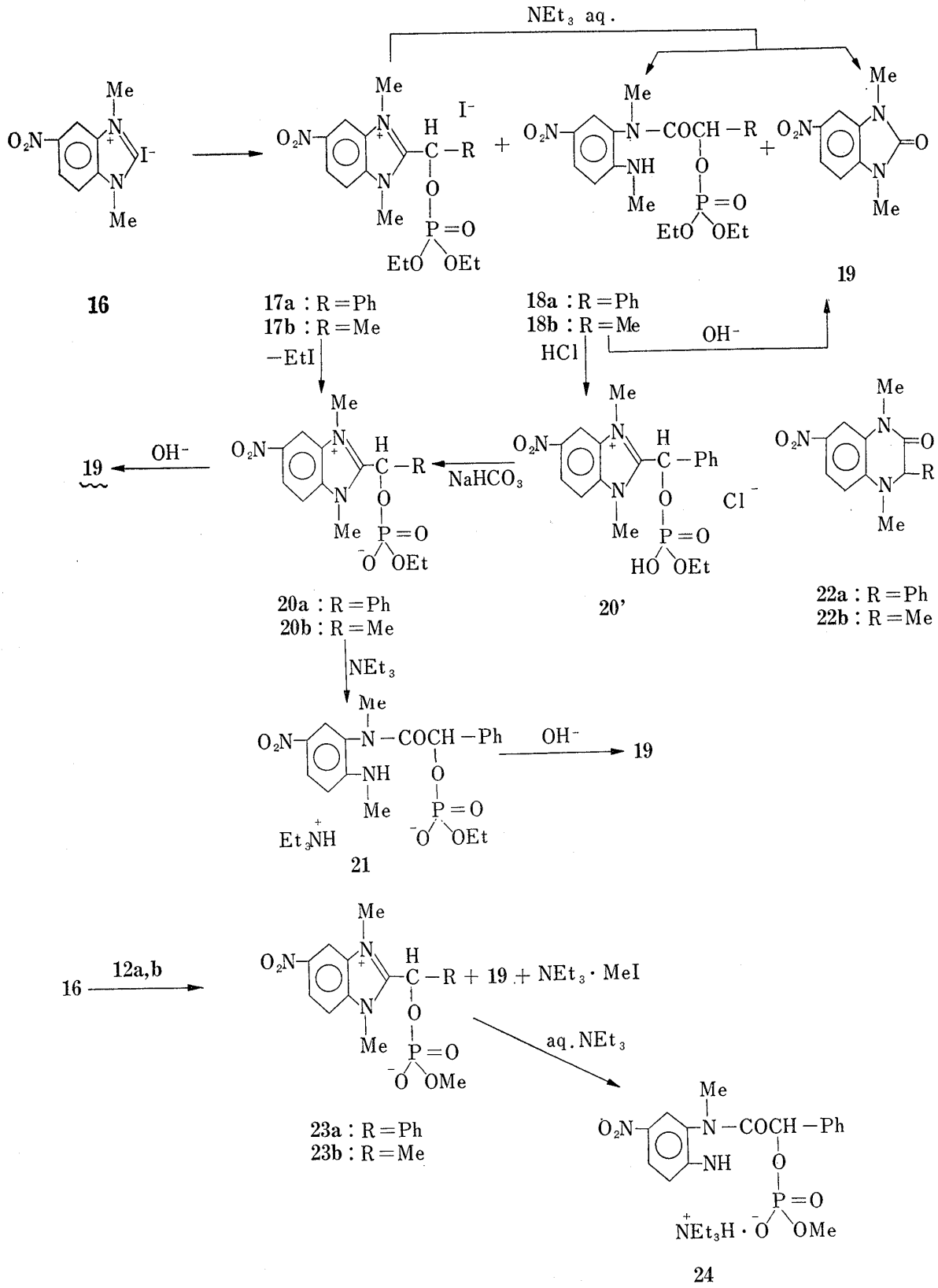


Chart 3

be obtained by treating of **23a** with aqueous triethylamine, but ring expansion of these compounds (**23a—b**, **24**) to the desired quinoxaline derivatives (**22a—b**) was not effected.

Treatment of **17a** with triethylamine in dimethylsulfoxide solution resulted in the same products (**18a** and **19**) as obtained in aqueous solution. A quinoxaline derivative (**25**), however, was produced in moderate yield, accompanied by **18a** and **19**, when **17a** was treated with dimethylsulfoxide in the absence of triethylamine or in less than one mole of triethylamine. The elemental analysis of the product corresponded to the formula $C_{15}H_{15}O_4N_3$. The infrared spectrum showed absorption bands at 3400 (OH), 1667 (CO), 1507 and 1320 cm^{-1} (NO_2), and the PMR spectrum (Fig. 3) exhibited a doublet signal at 3.22 τ for one proton (assigned to the aromatic proton meta to the nitro group), and other signals which were consistent with the assignment of the structure of 1,4-dimethyl-3-hydroxy-3-phenyl-7-nitro-1,2,3,4-tetrahydro-2-quinoxalinone (**25**).

When **25** was treated with ethanol, the ethyl ether (**26**) was obtained, determined by elemental analysis and spectroscopy. Mixtures of **25** and **26** were also obtained from **17a** by treatment with dimethylsulfoxide, though the product ratio was variable. The reaction mechanism is still unresolved, however, it is sure that the ethoxyl group in the acylphosphonate participates in the formation of **26**, and further investigation on this point is now being made. When **18a** was treated with dimethylsulfoxide, it was recovered unchanged, precluding its intermediacy in the formation of **25** from **17a**. Treatment of **17b** with dimethylsulfoxide gave only **18a** and **19**.

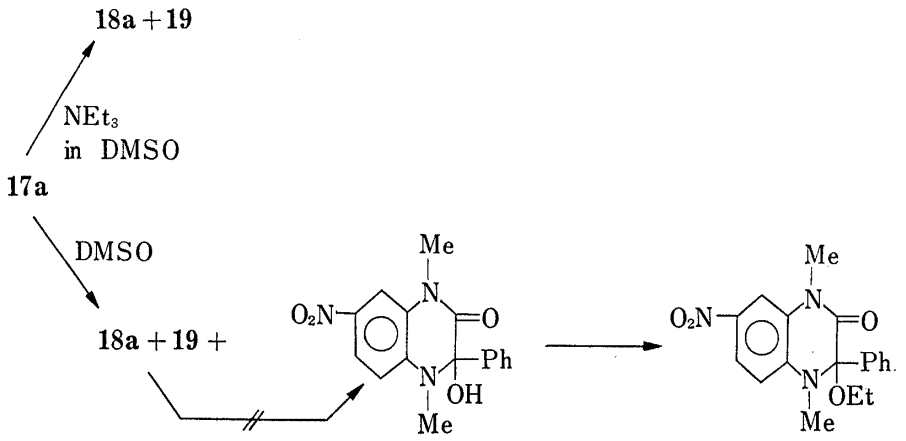


Chart 4

Discussion

N,N-Disubstituted benzimidazolium salts reacted with dialkylacylphosphonates to produce adducts in good yield, however, the anticipated quinoxaline derivatives could not be obtained by treatment of the benzimidazolium adducts (**3a—b** and **13a—b**) with alkali, in contrast with the results obtained with thiazolium salts. Changes in the substituent groups on the nitrogen atoms at positions 1 and 3 in the benzimidazolium salts (**3c—e**, and **13c—f**) failed to affect the course of the reactions and did not result in quinoxaline derivative formation.

An indirect synthesis *via* ring-openedi ntermediates was attempted. An electron-withdrawing group at C_5 in the benzimidazole nucleus would be expected to deactivate the nitrogen atom at position 1 and stabilize the open chain form of such compounds as **18**. In the case of 1,3-dimethyl-5-nitrobenzimidazolium iodide (**16**) (Chart 3), ring-opened products were readily obtained upon alkaline treatment. However, ring closure to a quinoxaline derivative could not be effected, and the product was 1,3-dimethyl-5-nitro-2-benzimidazolinone.

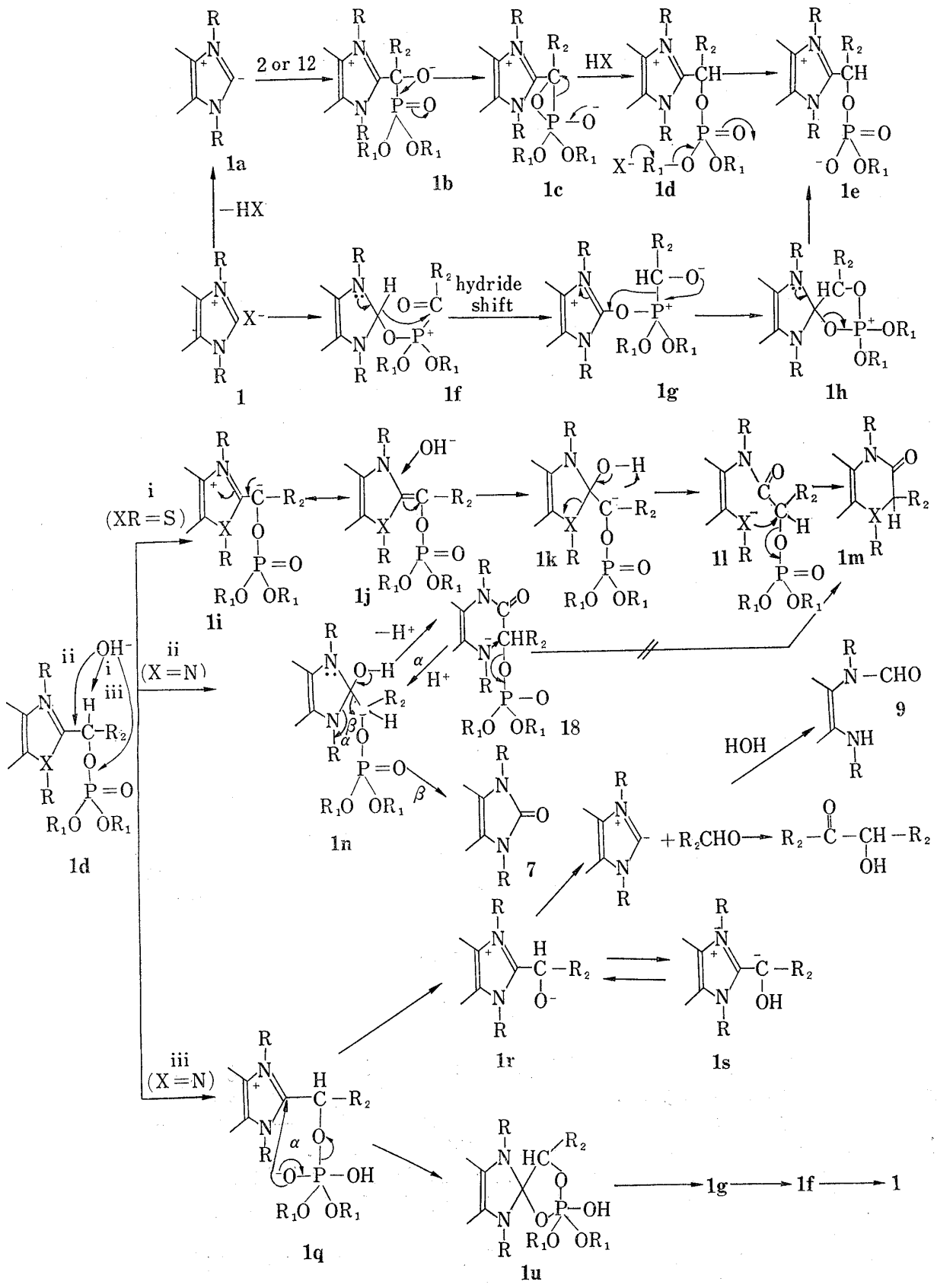


Chart 5

It is not certain which is the main pathway. The C_2-proton is completely exchange in a few minutes upon addition of D_2O in d_7-DMF in the presence of triethylamine, but this does not confirm the reaction of the ylid.

In the case of compound **17a**, however, quinoxaline derivatives (**25** and **26**) were obtained by treatment with dimethylsulfoxide under neutral conditions.

The difference in the behavior of thiazolium and benzimidazolium adducts noted above is attributed to the enhanced stability of the benzimidazolium ring system toward alkali and lower nucleophilicity of nitrogen compared to sulfur.

Possible reaction mechanisms for the reactions described above are shown in chart 5. The mechanism of adduct formation (**1a**—**d**) is not established, however, the ylid structure (**1a**) may stabilize the carbanion considerably and thus be a more plausible intermediate than those shown in the alternate mechanizm (**1**→**f**→**g**→**h**→**d**). Possible mechanisms for the formation of the main alkaline hydrolysis products are also shown (X=N). Compound **7** may be derived as shown (**d**→**n**→**7**). If no ring opening occurs as in **d**→**n**→**18**, this may account for the absence of ring-expanded products. Ring-opened products (**18**) have only been isolated for 5-nitro derivatives (Chart 3), and these products result from deactivation of the nitrogen atom at position 1 (X=N). Hence the failure of ring closure to produce the quinoxaline derivative (**m**, X=N) is explicable. The formation of **8** may proceed as in **d**→**q**→**r**⇄**8**. The formation of **9** may arise either by the reversal of adduct formation in the presence of an excess of hydroxide ion (**d**→**1a**) or decomposition of **8** to **1**. It is perhaps significant that under milder conditions (*e.g.* aqueous triethylamine Chart 3) no such product is observed.

It is of interest that oxidation occurred and changed the course of the reaction entirely in the successful formation of a quinoxaline derivatives from the benzimidazolium acylphosphonate adducts. Chart 6 outlines a possible mechanism for this reaction in dimethylsulfoxide. The effect of dimethylsulfoxide on this reaction is at present under active investigation.

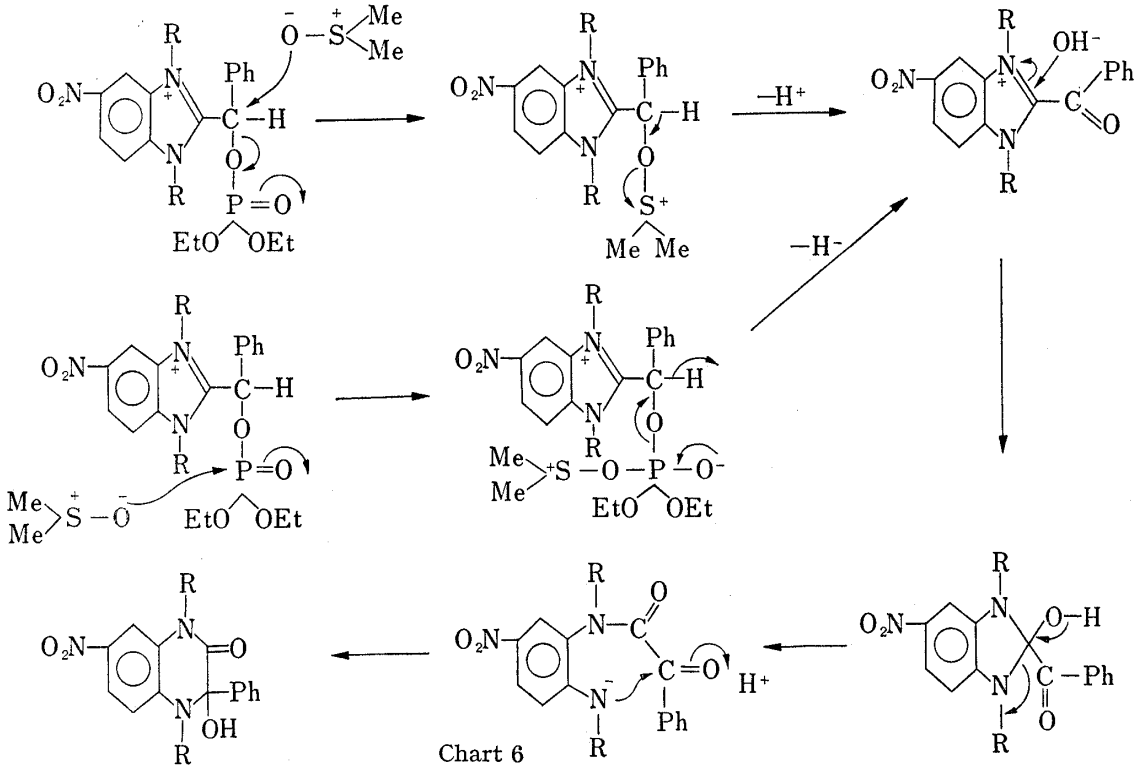


Chart 6

Experimental[9]

1,3-Dimethyl-2-(diethylphosphoroyl)benzylbenzimidazolium Iodide (3a)——To an ice-cooled mixture of **1a** (2.74 g) and triethylamine (2.53 g) in DMF (20 ml) was added **2a** (2.42 g) in nitrogen atmosphere, and

9) All melting points were obtained using a stirred Yamato Kagaku silicon oil bath. Infrared spectra were measured using a JASCO DS-201B recording spectrophotometer, and proton magnetic resonance spectra were obtained using Varian A-60 Mc apparatus with tetramethylsilane as internal standard.

the mixture was stirred at 2—5° for 30 min, then the mixture reacted at room temperature for 4 hr resulting in a dark blue solution. The solution was concentrated *in vacuo* leaving a brown crystalline residue, which was washed with ether and ethyl acetate. The light brown residue was recrystallized from acetone affording **3a** as colorless rhombics (4.8 g): mp 107—108°: IR ν_{max}^{Nujol} cm^{-1}: 1264 (P=O), 1019 and 958 (P–O–C). *Anal.* Calcd. for $C_{20}H_{26}O_4N_2IP$: C, 46.12; H, 4.97; O, 12.55; N, 5.51; I, 24.67; C_2H_5O, 17.45. Found: C, 46.53; H, 5.08; O, 12.39; N, 5.43; I, 24.63; C_2H_5O, 17.26.

3a was obtained by the reaction of **8a** with **4** in the presence of boron trifluoride as catalyst. To a mixture of **8a** (0.38 g), and **4** (0.235 g) was added one drop of boron trifluoride etherate; then the mixture was heated at 100—110° for 2 hr. After cooled the reaction mixture was extracted with acetone [residue: **8a** (0.045 g)] and the extract was column chromatographed over silica gel and eluted with acetone and methanol gave **3a** (0.01 g), which was identical with the compound **3a** described above.

1,3-Dimethyl-2-(1-diethylphosphoroyl)ethylbenzimidazolium Iodide (3b)——The adduct **3b** was obtained by a method similar to that for **3a** using 2.74 g of **1a**, 1.52 g of triethylamine and 1.80 g of **2b** in DMF (20 ml). Recrystallization of the residue from acetone gave colorless needles (2.0 g): mp 128—129° (decomp.); IR ν_{max}^{Nujol} cm^{-1}: 1254 (P=O), 1056—972 (P–O–C); PMR ($CDCl_3$) τ: 1.98—2.48 (m, 4H, C_4H_4-), 3.77 (qui, 1H, –CH(O–P)–CH_3, $J_{HH}=J_{HP}=7.0$), 5.68 (s, 6H, N–$CH_3\times2$), 5.95 (qui, 4H, O–$C\underline{H}_2$–$CH_3\times2$, $J_{HH}=J_{HP}=7.0$), 7.85 (dd, 3H, CH(O–P)–$C\underline{H}_3$, $J_{HH}=7.0$, $J_{HP}=1.0$), 8.70 (triplet of doublets, 3H, O–$C\underline{H}_2$–$C\underline{H}_3$, $J_{HH}=7.0$, $J_{HP}=1.0$), 8.82 (triplet of doublets, 3H, O–CH_2–$C\underline{H}_3$, $J_{HH}=7.0$, $J_{HP}=1.0$). *Anal.* Calcd. for $C_{15}H_{24}O_4N_2IP$: C, 39.66; H, 5.33; N, 6.17; I, 27.94. Found: C, 40.10; H, 5.46; N, 5.77; I, 28.55.

Treatment of 3a with an Equimolar Amount of Sodium Ethoxide——To a cooled solution of 1.87 g of **3b** in 20 ml of ethanol was added dropwise 0.083 g of sodium in 2 ml of ethanol, and the mixture was stirred at −50° for 30 min, after which the mixture was allowed to warm to room temperature and stirred for 5 hr. On cooling in dry-ice acetone, colorless solid was precipitated, which was filtered (**1a**; 0.575 g) and the filtrate was concentrated. The residue was extracted with ether and then acetone. The remained solid was identical with authentic **1a** (0.67 g). Ether extract was submitted to silica gel chromatography. Elution with ether gave 0.18 g of benzoin (**6**), 0.108 g of ethyl benzoate (**5**), and 0.01 g of colorless crystals, mp 107—108°, which was proved to be identical with **7** by the elemental analysis, mixture melting point, IR, and PMR spectral comparison. Acetone extract was chromatographed over silica gel. Elution with acetone gave 0.25 g of colorless thin plates, mp 190—192°, which was proved to be identical with **8a** by mixture melting point, IR, and PMR spectroscopic consideration. From the second fraction was obtained **3a** (0.1 g, recovered).

Treatment of 3b with an Equimolar Amount of Sodium Ethoxide——To a cooled suspension of **3b** (0.454 g) in ethanol (12 ml) was added dropwise 0.023 g of sodium in ethanol (2 ml), and the mixture was stirred at −50° for 1.5 hr, after which the mixture was allowed to stand at room temperature affording clear solution, which gradually became cloudy and precipitated, then the mixture left overnight. Filtration of the mixture gave **8b** as colorless rhombics (0.2 g, from ethanol), mp 196—198° (decomp.); PMR ($CDCl_3$) τ: 1.87—2.4 (m, 4H, aromatic protons), 3.58 (b, OH), 4.34 (q, 1H, CH_3–C$\underline{H}$–O, $J=7.0$), 6.87 (s, 6H, N–$CH_3\times2$), 8.38 (d, 3H, $C\underline{H}_3$–CH–O, $J=7.0$). *Anal.* Calcd. for $C_{11}H_{15}ON_2I$: C, 41.52; H, 4.75; N, 8.80; I, 39.89. Found: C, 41.76; H, 4.76; N, 8.56; I, 40.08.

From the filtrate were obtained 0.02 g of **8b** and 0.08 g of **1a**.

Treatment of Benzaldehyde with 1a——A mixture of **1a** (1.37 g), triethylamine (0.76 g) and benzaldehyde (1.6 g) in DMF (10 ml) was stirred at room temperature for 8 hr, and left overnight. The residue after concentrated *in vacuo* was washed several times with ether, and the residue was chromatographed over silica gel. Elution with acetone gave **8a** as light yellow prisms, mp 190—191°.

A mixture of **8a** (0.1 g) and acetic anhydride (2 ml) in acetic acid (5 ml) was heated on steam bath for 3 hr to afford a clear solution, which was concentrated to dryness. Addition of acetone gave crystals. Recrystallization from acetone afforded **10** as colorless sticks (0.06 g), mp 105—110° (decomp.); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1755 (CO), 1702 (acetone), and 1213; PMR ($CDCl_3$) τ: 1.86—2.38 (m, 4H, C_6H_4-), 2.45 (s, 1H, C_6H_5–C$\underline{H}$–O), 2.57 (s, 5H, C_6H_5), 5.76 (s, 6H, N–$CH_3\times2$), 7.63 (s, 3H, CH_3CO), 7.73 (s, 3H, acetone). *Anal.* Calcd. for $C_{18}H_{19}O_2N_2I\cdot1/2C_3H_6O$: C, 51.90; H, 4.91; N, 6.03; I, 28.12. Found: C, 51.98; H, 4.84; N, 6.06; I, 28.28.

1,3-Dimethyl-2-(1-hydroxyethyl)benzimidazolium Iodide (8b)——To an ice-cooled solution of **1a** (1.37 g) and triethylamine (0.76 g) in DMF (10 ml) was added 80% acetaldehyde (2.5 g), and the mixture was stirred at 5—10° for 30 min, after which the mixture reacted at room temperature for 8 hr. Concentration of the mixture *in vacuo* gave light brown solid, which was washed and recrystallized from ethanol giving **8b** as colorless rhombics (1.5 g), mp 196—198° (decomp.).

O-Methyl-O-1-(1,3-dimethyl-2-benzimidazolium)benzylphosphoric Acid Betaine (13a)——To an ice-cooled solution of **1a** (2.74 g) and triethylamine (2.5 g) in DMF (20 ml) was added dropwise **12a** (2.14 g), after which the mixture was stirred at 2—5° for 30 min, then the mixture reacted at room temperature for 4 hr affording light green solution. Concentration of the solution *in vacuo* left oily residue, which was washed with ether. Addition of acetone precipitated crystals, which were washed several times with hot acetone to give colorless solid. Recrystallization of the residue from chloroform gave **13a** as colorless needles (3.2 g), mp 243—244° (decomp.); IR ν_{max}^{Nujol} cm^{-1}: 1540, 1260 (P=O), 1082, 1049, and 1028 (P–O–C); PMR ($CDCl_3$) τ: 1.85—2.40 (m, 4H, C_6H_4), 2.56 (s, 5H, C_6H_5), 3.13 (d, 1H, C_6H_5–C$\underline{H}$–O–P, $J=7.6$), 5.82 (s, 6H, CH_3), 6.62

(d, 3H, CH_3O, J=10.7). *Anal.* Calcd. for $C_{17}H_{21}O_5N_2P \cdot 4H_2O$: C, 46.70; H, 6.69; P, 7.09; N, 6.42; CH_3O, 7.11. Found: C, 46.95; H, 6.91; N, 6.78; P, 7.55; CH_3O, 7.63.

O-Methyl-O-1-(1,3-dimethyl-2-benzimidazolium)ethylphosphoric Acid Betaine (13b)——Betaine (**13b**) was obtained by a method similar to that for **13a** using 2.74 g of **1a**, 2.53 g of triethylamine and 1.52 g of **12b** in DMF (20 ml). Recrystallization of the solid from acetonitrile gave colorless rhombics (3.1 g), mp 239—240° (decomp.); IR ν_{max}^{Nujol} cm^{-1}: 1540, 1252 (P=O), 1081, 1040, and 956 (P–O–C); PMR (d_6-DMSO) τ: 1.80—2.50 (m, 4H, C_6H_4), 4.30 (quint, 1H, CH_3–C<u>H</u>–O–P, $J_{HH}=J_{HP}$=6.7), 5.86 (s, 6H, N–$CH_3\times2$), 6.67 (d, 3H, OCH_3, J=11.0), 8.33 (d, 3H, C<u>H</u>$_3$–CH–O–P, J=6.7). *Anal.* Calcd. for $C_{12}H_{17}O_4N_2P$: C, 50.70; H, 5.99; N, 9.85; P, 10.90; CH_3O, 10.92. Found: C, 50.06; H, 6.23; N, 9.67; P, 11.18; CH_3O, 10.25.

Alkaline Treatment of 13a——To an ethanol solution (10 ml) containing 5% of sodium was added 0.5 g of **13a**, and the mixture reacted at 50° for 5 hr. The residue after concentrated was extracted with chloroform, and the chloroform extract was washed, dried, and concentrated to leave brown residue, which was column chromatographed over silica gel. Elution with acetone gave **7** as colorless crystals (0.07 g), the following fraction afforded **9** as light brown solid, which was recrystallized from *n*-hexane giving colorless sticks (0.04 g), mp 68—69°.

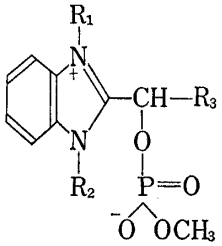
O-Ethyl-O-1-(1-methyl-3-phenyl-2-benzimidazolium)benzylphosphoric Acid Betaine (3c)——To a mixture of 1.68 g of **1b** and 1.3 g of triethylamine in DMF (10 ml) was added 1.21 g of **2a**, the mixture was stirred at room temperature for 15 hr resulting brown solution, after which the mixture was concentrated and the residue was washed with ether, then the residue was submitted to silica gel chromatography. Elution with acetone gave pale yellow oil, after that elution was treated with methanol to give solid, which was recrystallized from acetone affording colorless needles, mp 206° (decomp.); IR ν_{max}^{Nujol} cm^{-1}: 1268 (P=O), 1042, and 978 (P–O–C); PMR ($CDCl_3$) τ: 1.7 (b, 1H, P–OH ?), 2.17—2.87 (m, 14H, C_6H_4, $C_6H_5\times2$), 3.36 (d, 1H, C_6H_5–C<u>H</u>–O–P, J=6.4), 5.73 (s, 3H, N–CH_3), 5.98 (quin, 2H, CH_3–C<u>H</u>$_2$–O, $J_{HH}=J_{HP}$=7.0), 8.83 (t, 3H, C<u>H</u>$_3$–CH_2–O, J=7.0). *Anal.* Calcd. for $C_{23}H_{23}O_4N_2P \cdot H_2O$: C, 62.72; H, 5.72; N, 6.36; P, 7.02. Found: C, 62.32; H, 5.96; N, 6.13; P, 6.58.

O-Ethyl-O-1-(1-phenyl-3-benzyl-2-benzimidazolium)benzylphosphoric Acid Betaine (3d)——Betaine **3d** was obtained by a method similar to that for **3c** using **1c** (1.83 g), triethylamine (1.3 g), and **2a** (1.21 g), in DMF (10 ml). Recrystallization of the solid from acetone after washed with ether gave **3d** as colorless sticks, mp 230—231°; IR ν_{max}^{Nujol} cm^{-1}: 1282 (P=O), 1086, and 1065 (P–O–C); PMR ($CDCl_3$) τ: 1.68—2.78) (m, 19H, C_6H_4, $C_6H_5\times3$), 3.22 (d, 1H, C_6H_5–C<u>H</u>–O–P, J=6.2), 3.85 (s, 2H, C_6H_5–C<u>H</u>$_2$–), 5.95 (quin, 2H, CH_3–C<u>H</u>$_2$–O, $J_{HH}=J_{HP}$=6.7), 8.83 (t, 3H, C<u>H</u>$_3$–CH_2–O, J=6.7). *Anal.* Calcd. for $C_{29}H_{27}O_4N_2P$: C, 69.86; H, 5.46; N, 5.62; P, 6.21; C_2H_5O, 9.03. Found: C, 70.15; H, 5.95; N, 5.87; P, 5.84; C_2H_5O, 9.37.

O-Ethyl-O-1-(1-phenyl-3-*p*-nitrobenzyl-2-benzimidazolium)benzylphosphoric Acid Betaine (3e)——Betaine **3e** was obtained by a method similar to that for **3c** using **1d** (2.05 g), triethylamine (1.3 g), and **2a** (1.21 g) in DMF (10 ml). The residue after washed with ether was submitted to alumina column chromatography. Elution with methanol was obtained solid, which was recrystallized from acetone gave **3e** as colorless sticks, mp 143—145° (0.58 g); IR ν_{max}^{Nujol} cm^{-1}: 3410 (OH), 1516, 1350 (NO_2), 1258 (P=O), 1052, and 1040 (P–O–C); PMR ($CDCl_3$) τ 3.29 (d, 1H, C_6H_5–C<u>H</u>–O–P, J=6.2), 3.70 (s, 2H, CH_2), 6.02 and 6.11 (quint of each, 2H, CH_3–C<u>H</u>$_2$–O, $J_{HH}=J_{HP}$=6.7), 8.85 (t, 3H, C<u>H</u>$_3$–CH_2–O, J=6.7). *Anal.* Calcd. for $C_{29}H_{26}O_6N_3P \cdot 3H_2O$: C, 58.29; H, 5.40; N, 7.04; P, 5.18; C_2H_5O, 7.53. Found: C, 58.60; H, 5.85; N, 7.32; P, 4.53; C_2H_5O, 7.71.

O-Methyl-O-1-(1,3-Disubstituted-3-benzimidazolium)benzyl(or ethyl)phosphoric Acid Betaines (13c—f)

TABLE. Physical Data of the Betaines (13c-f)



Compd. No.	R_1	R_2	R_3	mp (°C)	Formula		*Anal.* C	H	N	P	OCH_3
13c	CH_3	Ph	Ph	99—103	$C_{22}H_{21}O_4N_2P \cdot 2H_2O$	Calcd.	59.46	5.67	6.30	6.97	6.98
						Found	59.62	5.94	6.15	6.92	6.70
13b	Ph	CH_2Ph	Ph	237—239	$C_{28}H_{25}O_4N_2P$	Calcd.	69.41	5.21	5.79	6.39	6.41
						Found	69.34	5.42	5.78	6.48	6.31

13e	Ph	CH_2Ph NO_2-*p*	Ph	203—204	$C_{28}H_{24}O_6N_3P$	Calcd.	63.51	4.57	7.94	5.85	5.86
						Found	63.76	4.91	7.63	5.48	6.12
13f	Ph	CH_2Ph- NO_2-*p*	CH_3	230	$C_{23}H_{22}O_6N_3P$	Calcd.	59.10	4.74	8.99	6.63	6.64
						Found	58.92	4.99	8.72	6.25	6.40

Compd. No.	Infrared spectra (Nujol mull, cm^{-1}) NO_2	P=O	P-O-C	PMR spectra ($CDCl_3$) $CH-R_3$	OCH_3
13c		1267	1042	3.38^d (J=6.7)	6.37^d (J=11.0)
13d		1270	1043	2.98^d (J=9.0)	6.28^d (J=11.1)
13e	1520, 1343	1273	1054	3.28^d (J=6.0)$^{a)}$	6.34^d (J=10.8)$^{a)}$
13f	1519, 1361	1271	1080, 1051		

a) solvent: D_2O

Reaction of 1,3-Dimethyl-5-nitrobenzimidazolium Iodide (16) with 2a——To an ice-cooled solution of **16** (3.19 g), and triethylamine (2.53 g) in DMF (20 ml) was added dropwise **2a** (2.42 g) in nitrogen atmosphere to give violet solution immediately. The mixture was stirred at 2—5° for 2 hr, then the mixture reacted at room temperature for 3 hr resulting in a dark violet solution. The solution was concentrated *in vacuo* leaving a brown residue, which was washed with ether. The crystalline residue was recrystallized from ethanol to give **17a** as yellow needles, mp 147—148° (3.2 g); IR ν_{max}^{Nujol} cm^{-1}: 1530, 1350 (NO_2), 1286 (P=O), and 1020 (P-O-C); PMR (d_6-DMSO) τ 0.85 (d, 1H, C_4-H, J=2.0), 1.37 (doublet of doublets, 1H, C_6-H, J_o=9.0, J_m=2.0), 1.62 (d, C_7-H, J=9.0), 2.47 (s, 5H, C_6H_5), 2.45 (d, 1H, C_6H_5-C<u>H</u>-O-P, J=7.8), 5.77 (s, 3H, N-CH_3), 5.82 (s, 3H, N-CH_3), 5.57—6.15 (m, 4H, CH_3-C<u>H_2</u>-O×2), 8.78 (triplet of doublets, 3H, CH_3-CH_2-O, J_{HH}=6.8, J_{HP}=1.1), 8.83 (triplet of doublets, 3H, C<u>H_3</u>-CH_2-O, J_{HH}=6.8, J_{HP}=1.1). *Anal.* Calcd. for $C_{20}H_{25}O_6N_3IP$: C, 42.79; H, 4.49; N, 7.49; I, 22.61; P, 5.52; C_2H_5O, 16.05. Found: C, 42.85; H, 4.73; N, 7.36; I, 22.78; P, 5.27; C_2H_5O, 16.12.

Ether solution was concentrated to leave light brown oil, which was chromatographed over alumina and eluted with ethyl acetate affording two compounds. 1,3-Dimethyl-5-nitro-2-benzimidazolinone (**19**), mp 210—211° (0.25%), was obtained first, which was proved to be identical with authentic **19** by the comparison of their infrared spectra. Yellow crystals were obtained as the second eluent, which was recrystallized from ether to give **18a** as yellow sticks (0.33 g), mp 103—104° (decomp.). *Anal.* Calcd. for $C_{20}H_{26}O_7N_3P$: C, 53.22; H, 5.81; N, 9.31; P, 6.86; C_2H_5O, 19.93. Found: C, 53.25; H, 5.95; N, 9.56; P, 6.24; C_2H_5O, 19.81.

Treatment of 17a with Aqueous Triethylamine——A mixture of **17a** (0.5 g), triethylamine (1.0 g), H_2O (1.5 ml) in ethanol (10 ml) was heated to reflux for 5 hr, the mixture was concentrated and the residue was extracted with chloroform. The chloroform extract was washed, dried and chromatographed over alumina. Elution with ethyl acetate afforded **19** (0.15 g) as the first fraction. Yellow crystals (0.21 g) were obtained as the following fraction, which was proved to be identical with **18a** obtained above.

Treatment of 17a with Aqueous Sodium Hydroxide——To 20 ml of 80% ethanol containing 5% of sodium hydroxide was added 0.28 g of **17a**, and the mixture was stirred at room temperature for 2 hr. After worked up as usual the crystalline residue was recrystallized from ether to give **19** as yellow needles (0.086 g), mp 210—211°.

O-Ethyl-O-(1,3-Dimethyl-5-nitro-2-benzimidazolyl)benzylphosphoric Acid Betaine (20a)——i) When the solution of **17a** in acetone was allowed to stand for several months, a yellow crystals were precipitated, which was recrystallized from ethanol–ether to give **20a** as yellow needles, mp 226—229° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3380 (NH or OH), 1351 (NO_2), 1256 (P=O), 1059 and 1041 (P-O-C); PMR (D_2O) τ 1.00 (d, 1H, C_4-H, J=2.2), 1.37 (dd, 1H, C_6-H, J_o=9.6, J_m=2.2), 1.80 (d, 1H, C_7-H, J=9.6), 2.43 (s, 5H, C_6H_5), 2.83 (d, 1H, C_6<u>H</u>$_5$-C<u>H</u>-O-P, J=8.3), 5.67 (s, 3H, N-CH_3), 6.00 (quintet, 2H, CH_3-C<u>H_2</u>-O, J_{HH}=J_{HP}=7.2), 8.83 (t, 3H, C<u>H_3</u>-CH_2-O), J=7.2). *Anal.* Calcd. for $C_{18}H_{20}O_6N_3P\cdot H_2O$: C, 51.11; H, 5.23; N, 9.94; P, 7.32. Found: C, 51.58; H, 5.46; N, 9.68; P, 7.29.

ii) The solution of **17a** (0.1 g) in 10% alcoholic HCl (10 ml) was stirred at room temperature untill the yellow color became colorless. To the residue after concentrated was added acetone to give **20′** as colorless hydroscopic cubics. *Anal.* Calcd. for $C_{18}H_{21}O_6N_3Cl\cdot H_2O$: C, 62.60; H, 6.09; N, 12.27; Cl, 10.26. Found: C, 63.02; H, 6.38; N, 11.56; Cl, 9.07.

The salt obtained above was dissolved in water and was carefully neutralized with sodium bicarbonate. The residue after concentrated was extracted with ethanol. The extract was concentrated leaving light yellow solid, which was recrystallized to give **20a** as light yellow needles, mp 223—226° (decomp.), which was proved to be identical with the sample obtained above.

Treatment of 20a with Triethylamine——A mixture of **20a** (0.1 g), triethylamine (1.5 ml) in ethanol (5 ml) was refluxed on the water bath for 2 hr. The residue after concentrated was chromatographed over silica gel by using methanol and gave **21** as yellow amorphous powder (0.015 g), mp 203—205°, which could not be

further purified; IR ν_{max}^{film} cm^{-1}: 2620—2450 (⟩N–$^+$), 1675 (CO), 1521, 1310 (NO_2), 1235 (P=O), and 1050 (P–O–C).

Treatment of 16 with Diethyl Acethylphosphonate (2b)——The oily residue obtained after usual working up as above using **16** (1.6 g), triethylamine (1.2 g), and **2b** (0.9 g) in DMF (15 ml)was washed with ether. The residue solidified on standing at room temperature for several weeks. Recrystallization of the solid from methanol–ether gave **20b** as light brown rhombics, mp 210—152° (decomp.) (0.76 g); IRν_{max}^{Nujol} cm^{-1}: 3320 (OH), 1518, 1346 (NO_2), 1245 (P=O), 1066, 1055 and 935 (P–O–C); PMR (d_6–DMSO) τ: 0.90 (d, 1, C_4–H, J=2.2), 1.47 (dd, 1, C_6–H, J_{46}=2.2, J_{67}=9.0), 1.67 (d, 1, C_7–H, J=9.0), 4,28 (quintet, 1, –CH(O–P)–CH_3, $J_{HH}=J_{HP}$=7.0), 5.73 (s, 3, N–CH_3), 5.78 (s, 3, N–CH_3), 6.29 (quintet, 2, O–CH_2–CH_3, $J_{HH}=J_{HP}$=7.0), 8.31 (d, 3, –CH–CH_3, J=7.0), 8.93 (t, 3, O–CH_2–CH_3, J=7.0). *Anal.* Calcd. for $C_{13}H_{18}O_6N_3P\cdot H_2O$: C, 43.22; H, 5.55; N, 11.65; P, 9.88; OC_2H_5, 12.48. Found: C, 43.03; H, 5.64; N, 11.74; P, 9.11; OC_2H_5, 12.08.

Ether extract was concentrated to leave light brown oil, which was chromatographed over alumina and eluted with chloroform. The compound **19** was obtained as the first fraction (0.015 g), which was proved to be identical with an authentic **19** by their spectral compairson. From the second fraction was obtained **18b** as yellow oil (0.063 g); IRν_{max}^{film} cm^{-1}: 3356 (NH), 1669 (CO), 1587, 1330 (NH_2), 1265 (P=O), 1092, 1040, and 988 (P–O–C): PMR ($CDCl_3$) τ 1.83 (dd. 1, C_5–H, J_0=10.5, J_m=2.6), 2.09 (d, 1, C_3–H, J =2.6), 3.33 (d, 1, C_6–H, J=10.5), *ca.* 3.45 (b, 1, NH), 5.25—6.13 (m, 5, –CH(O–P)–CH_3, 2×O–CH_2–CH_3), 6.82 (s, 3, N–CH_3), 7.06 (d, 3, $NHCH_3$, J=5.1), 8.48—8.86 (m, 9, CH_3–CH–O–P, 2×O–CH_2–CH_3). *Anal.* Calcd. for $C_{15}H_{24}O_7N_3P$: C, 46.27; H, 6.21; N, 10.79. Found: C46.38; H, 6,50; N, 10.51.

Reaction of 16 with Dimethyl Benzoylphosphonate (12a)——To an ice-cooled solution of 16 (3.19 g), and triethylamine (2.53 g) in DMF (20 ml) was added dropwise **12a** (2.2 g) in nitrogen atomosphere to give violet solution immediately. The mixture was stirred at 20° for 10 hr; then the mixture was concentrated *in vacuo* leaving a brown semisolid, which was washed successively with ether and acetone. The crystalline residue was resrystalized from ethanol–acetone give **23a** as yellow sands. mp 243° (decomp.) (3.6 g); IR ν_{max}^{Nujol} cm^{-1}: 1350, 1271, and 1039: PMR (D_2O) τ: 1.01 (d, 1, C_4–H, J=2.0), 1.38 (dd. 1, C_6–H, J_0=9.2, J_m=2.0), 1.83 (d, 1, C_7–H, J=9.2,), 2.44 (s, 5, C_6H_5), 2.83 (d, 1, CH(O–P)–C_6H_5, J=8.8), 5.67 (s, 3, N–CH_3), 5,72 (s, 3, N–CH_3), 6.35 (d,3, OCH_3, J=11.0). *Anal.* Calcd. for $C_{17}H_{18}O_6N_3P$: C, 52.18; H, 4.64; N, 10.75; OCH_3 7.94. Found: C, 51.72; H, 4.91; N, 10.72; OCH_3, 7.95.

Methyl triethylammonium iodide (1.3 g) was obtained from the acetone extract. The compound **19** (0.088 g) was obtained from ether extract as yellow needles, mp 208—209°.

Reaction of 16 with Dimethyl Acethylphosphonate (12b)——Betaine **23b** was obtained by a method similar to that for **23a** using **16** (1.69 g), triethylamine (1.2 g), and **12b** (1.09 g) in DMF (10 ml). Recrystallization of the solid from acetone–ethyl acetate after washed with ether gave **23b** as yellow prisms (0.8 g), mp 228° (decomp.); IR $\nu_{max}^{Nujol}$$cm^{-1}$: 3250 (OH), 1525, 1343 (NO_2), 1260 (P=O), 1076, 1050 and 949 (P–O–C): PMR (d_6-DMSO) τ: 0.95 (d, 1H, C_4-H, J=2.0), 1.54 (dd, 1H, C_6-H, J_0=9.2, J_m=2.0), 1.70 (d, 1H, C_7-H, J=9.2), 4.30 (quint, 1H, CH_3–CH–O–P, $J_{HH}=J_{HP}$=7.0), 5.75 (s, 3H, N–CH_3), 5.80 (s, 3H, N–CH_3), 6.65 (d, 3H, OCH_3, J=10.1), 8.32 (d, 3H, CH_3–CH–O–P, J=10.1). *Anal.* Calcd. for $C_{12}H_{16}O_6N_3P\cdot 2H_2O$: C, 39.48; H, 5.52; N, 11.51. Found: C, 40.08; H, 5.13; N, 11.34.

Treatment of 23a with Aqueous Triethylamine——A mixture of **23a** (0.5 g), triethylamine (1.0 g) and H_2O (2.0 ml) in methanol (10 ml) was warmed at 50° for 5 hr, the reaction mixture was concentrated to leave yellow oil, which was chromatographed over alumina affording **24** as yellow oil (0.28 g); IR ν_{max}^{film} cm^{-1}: 2580—2480 (⟩N–$^+$), 1668 (CO), 1493, 1307 (NO_2), 1233 (P=O), and 1115—1018 (P–O–C); PMR ($CDCl_3$) τ: 1.88 (dd, 1H, C_5-H, J_0=9.5, J_m=2.8), 3.35 (d, 1H, C_6-H, J=9.5), 4.90 (d, 1H, C_6H_5–CH–O–P, J=6.5), 5.73 (b, 1H, NH), 6.55 (d, 3H, OCH_3, J=11.0), 6.92 (s, 3H, N–CH_3), 6.93 (q, 6H, N–CH_2–CH_3×3, J=7.0), 7.03 (d, 3H, $NHCH_3$, J=4.5), 8.73 (t, 9H, N–CH_2–CH_3×3).

Treatment of 17a with Dimethylsulfoxide——i) Without Base: A solution of **17a** (2.7 g) in dimethylsulfoxide (90 ml) was stirred at room temperature for 48 hr to give dark green solution, to which was added 0.5 g of triethylamine and was poured into ice-cooled water. The mixture was extracted with chloroform, and the chloroform solution was washed thoroughly and dried over sodium sulfate. The brown residue after removal of the solvent was submitted over silica gel chromatography. Elution with ethyl acetate were obtained yellow crystals (0.25 g) as a first fraction, and light yellow crystals (0.42 g) were obtained as the following fraction, which were identified as **18a** by mixture melting point, and infrared spectra comparison. Rechromatography of the former fraction over alumina using ethyl acetate gave **19** (0.01 g) as yellow crystals. From the second fraction were obtained yellow crystals, which were recrystallized from ether to give **26** as yellow sticks (0.08 g), mp 190—191°. IR ν_{max}^{Nujol} cm^{-1}: 1687 (C=O), 1530, and 1324 (NO_2). PMR ($CDCl_3$) τ: 1.96 (dd, 1H, C_7-H, J_0=2.2, J_m=9.0), 2.13 (d, 1H, C_5-H, J=2.2), 2.63 (m, 5H, C_6H_5), 3.24 (d, 1H, C_8-H, J=9.0), 6.50 (s, 3H, N_4-CH_3), 6.53 (q, 2H, O–CH_2–CH_3, J=7.0), 7.16 (s, 3H, N_1-CH_3), 8.67 (t, 3H, O–CH_2–CH_3, J=7.0). *Anal.* Calcd. for $C_{18}H_{19}O_4N_3$: C, 63.33; H, 5.61; N, 12.31. Found: C, 63.33; H, 5.61; N, 12.03; MS: *m/e* 341 (parent peak).

From the following fraction (methanol) was obtained yellow crystals (0.12 g), which were recrystallized from ether giving **25** as yellow granuals, mp 187—188°. *Anal.* Calcd. for $C_{16}H_{15}O_4N_3$: C, 61.33; H, 4.83; O, 20.43; N, 13.41; mol. wt. 313.3. Found: C, 61.13; H, 4.85; O, 19.03; N, 13.22; MS: *m/e* 313 (parent peak).

ii) With an Equimolar Amount of Triethylamine: To a solution of **17a** (0.112 g) in dimethylsulfoxide

(4 ml) was added triethylamine (0.02 g) showing dark violet immediately. More 0.02 g of triethylamine was added after 3 hr and the mixture was allowed to stand for overnight at room temperature. Treatment of the reaction mixture with similar method mentioned above gave **25** (20.3%), **18a** (trace), and **19** (48%).

iii) With Two Equimolar Amounts of Triethylamine: Similar treatment of **17a** with two equimolar amounts of triethylamine in dimethylsulfoxide gave **25** (9.6%), **18a** (1.8%), and **19** (36.4%).

iv) With an Excess of Triethylamine: Similar treatment of **17a** with excess amount of triethylamine in dimethylsulfoxide gave **25** (trace), **18a** (28%), and **19** (44.9%).

Treatment of 18a with Triethylamine in Dimethylsulfoxide——To a solution of **18a** (0.165 g) in dimethylsulfoxide (7.5 ml) was added triethylamine (0.2 g), and the mixture was stirred at room temperature for a week. Usual working up of the reaction mixture gave **25** (trace), **19** (24%), and **18a** (32%, recovered).

1,4-Dimethyl-3-phenyl-3-ethoxy-7-nitro-1,2,3,4-tetrahydro-2-quinoxalinone (**26**)——To a solution of **25** (0.1 g) in ethanol (10 ml) was added 2 drops of 10% ethanolic HCl and the mixture was stirred at room temperature for 24 hr. Evaporation and column chromatography (alumina-ethyl acetate) of the reaction mixture gave yellow sticks (**26**) as first fraction, mp 190—191° (ether), yielded 0.053 g. From the second fraction was recovered 0.023 g of **25**.

Treatment of 17b with Dimethylsulfoxide——To an ice-cooled and stirred solution of **16** (3.1 g) and triethylamine (2.5 g) in DMF (30 ml) was added **2b** (1.8 g) in nitrogen atomosphere and the mixture was stirred at 0—5° for 1 hr, then the mixture reacted at room temperature for 5 hr resulting dark brown solution. The solution was concentrated *in vacuo* leaving dark brown oily residue, which was dissolved in dimethylsulfoxide (70 ml) and stirred for 3 days. Then the mixture was poured into ice-cooled water and extracted with chloroform. The chloroform extract was washed, dried and concentrated to leave yellow oil, which was submitted to silica gel column chromatography. Elution with ethyl acetate gave yellow oil, which crystallized on standing. Recrystallization from ether gave **18b** as yellow needles, mp 82—84°, which was proved to be identical with authentic **18b** obtained above by their infrared spectra comparison. Yield, 1.7 g. From the following fraction was obtained **19** (0.015 g).