two 20-mL portions of H_2SO_4 (2 N) and four times with water. After the solution was dried over sodium sulfate and the solvent was evaporated, the Δ^2-isoxazoline (**2c**) was obtained quantitatively, identical with that previously prepared.

Attempted Interconversions of Δ^2-Isoxazolines and Δ^2-Isoxazoline *N*-Oxides. A. Equimolecular amounts of *N*-oxide **4b** (0.024 g) and silver nitrite (0.012 g) in *n*-heptane (5 mL) were heated under reflux for 50 h with stirring. After removal of the insoluble solids and the solvent, the residue was chromatographed (preparative TLC, silica gel, hexane–ethyl acetate (10:1)) to yield 0.021 g of unreacted **4b**.

B. Equimolecular amounts of Δ^2-isoxazoline **2c** (0.06 g) and silver nitrate (0.03 g) in *n*-heptane (5 mL) were heated under reflux for 50 h with stirring. After removal of the insoluble solids and the solvent, the unreacted Δ^2-isoxazoline **2c** was obtained quantitatively.

Registry No. **1a**, 74609-84-0; **1b**, 74609-85-1; **1c**, 74609-86-2; **2a**, 50899-27-9; **2b**, 4894-25-1; **2c**, 5050-64-6; **2d**, 74609-87-3; **2e**, 74609-88-4; **2f**, 74609-89-5; **2g**, 74609-90-8; **2i**, 17669-31-7; **2j**, 17669-33-9; **3j**, 17669-32-8; **4a**, 74609-91-9; **4b**, 19018-61-2; **4c**, 74609-92-0; **4d**, 74609-93-1; **4e**, 74609-94-2; **4f**, 74609-95-3; **4g**, 74609-96-4; **4h**, 74609-97-5; **5c**, 74609-98-6; cyclohexene, 110-83-8; *trans*-stilbene, 103-30-0; 1,1-diphenylethylene, 530-48-3; 1-phenyl-1-(*p*-tolyl)-ethylene, 948-55-0; 1-(*p*-bromophenyl)-1-phenylethylene, 4333-76-0; 1,1-di-(*p*-tolyl)ethylene, 2919-20-2; dimethyl fumarate, 624-49-7; methyl cinnamate, 103-26-4.

Acylphosphonates: P–C Bond Cleavage of Dialkyl Acylphosphonates by Means of Amines. Substituent and Solvent Effects for Acylation of Amines

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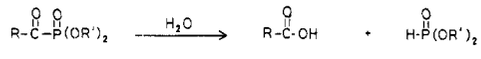
Studies on the benzoylation of amines of dialkyl benzoylphosphonates (**1A–F**) were described in detail. Stoichiometric reactions of diethyl benzoylphosphonate (**1B**) with a variety of amines (**2a–i**) gave amides as the main products along with diethyl phosphonate (**4B**) and α-(phosphoryloxy)benzyl phosphonate (**5B**). The yields of amides increased with the ratio of **1B**/**2a–i**. The use of hindered dialkyl benzoylphosphonates resulted in high yields of amides while the reaction rates decreased markedly. The benzoylations of *n*-propylamine (**2d**) with **1B** in various solvents having dielectric constants of 1.9–36.7 were conducted. The yields of *N*-*n*-propylbenzamide (**3d**) and **5B** were surprisingly almost constant. However, the reaction rates varied as follows. In nonpolar solvents such as *n*-hexane and cyclohexane benzoylation was remarkably rapid while the benzoylation in methylene chloride was much slower than that in other solvents used. Compound **1B** underwent smooth reaction with aliphatic amines but did not react with aromatic amines under the same conditions. Selective N-benzoylation of the bifunctional amine, ethanolamine, was achieved by means of diisopropyl benzoylphosphonate (**1C**) in tetrahydrofuran. The use of the hindered dialkyl benzoylphosphonate **1C** resulted in poorer yields of amides in the case of the reaction with a hindered amine such as diethylamine, but higher yields of amides in the case of primary amines. Addition of triethylamine and 4-(dimethylamino)pyridine (DMAP) slightly accelerated the benzoylation, but yields of amides were similar to those in the absence of the catalysts. Optimum conditions for high yields of amides were proposed for the practical use of dialkyl benzoylphosphonates as the acylating agents in the present reaction.

Acylation of functional groups such as hydroxyl and amino groups is one of the important and fundamental reactions in organic synthesis. Various kinds of acylating agents have been developed and employed, such as acyl halides, anhydrides, mixed anhydrides, active esters, azolides, and ketones.[1] On the other hand, it is generally recognized that phosphorus–carbon (P–C) bonds of organophosphorus compounds are quite stable and are not cleaved easily under the usual conditions.[2] Hence, studies of the cleavage reaction of the P–C bond are lacking and very little data are available for the utilization of organophosphorus compounds as synthetic agents. However, the following character of dialkyl acylphosphonates might provide some information in this direction. Dialkyl acylphosphonates possessing C(O)–P bonds are known to be labile, even toward moisture in air, and decompose into carboxylic acids and dialkyl phosphonates.[3-8]



A few studies on nucleophilic displacement reactions of acylphosphonates have also been reported for reactions with alcohols,[9-11] thiols,[12,13] amines,[11,14] and carbanions.[15-18] In spite of the above features of acylphosphonates, no systematic study on acylphosphonates as acylating agents has appeared.

In this paper, a systematic study on the benzoylation of various amines by use of dialkyl benzoylphosphonates is described in detail.

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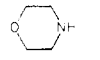
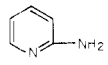
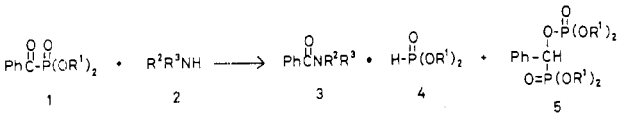
Table I. Stoichiometric Reaction of Diethyl Benzoylphosphonate (1B) with Amines

	amine	pK_b[23]	time[a]	product, % yield 3	4B	5B
2a	Et_2NH	3.1	24 h	47	3	48
b	$C_6H_{11}NH_2$	3.3	50 min	58	2	38
c	n-$BuNH_2$	3.4	20 min	79	42	18
d	n-$PrNH_2$	3.5	20 min	76	46	22
e	i-$BuNH_2$	3.6	1 h	77	40	22
f	$PhCH_2CH_2NH_2$	4.2	1 h	79	43	20
g	$HOCH_2CH_2NH_2$	4.5	2 h	50[b]	46	13
h	$PhCH_2NH_2$	4.6	3 h	82	45	12
i		5.6	6 h	74	34	17
j	$PhNH_2$	9.3	-	no reaction[c]		
k		-	-	no reaction[c]		

[a] Time required for disappearance of 1B. [b] O,N-Dibenzoylated product (6) was obtained in 14% yield. [c] There was no reaction in 24 h.

Results and Discussion

Diethyl benzoylphosphonate (**1B**) was chosen to examine the reactivity of **1**, and its reaction with amines was tested. The reactions were carried out by use of stoichiometric amounts of amines (**2a–k**). For example, **1B** was allowed to react with n-propylamine (**2d**) in dry ether at room temperature. The reaction was monitored by silica gel thin-layer chromatography. After 20 min **1B** had disappeared and the TLC showed three spots. The two major spots were N-propylbenzamide (**3d**) and diethyl phosphonate (**4B**). The minor spot was found to be α-(phosphoryloxy)benzylphosphonate (**5B**).



5B may be formed by the successive reaction of **1B** with **4B**, which accumulates during the formation of **3d**, followed by a C → O rearrangement of the phosphonyl group.[11,19] Similarly, several primary and secondary amines were treated with **1B**. **1B** reacted smoothly with primary aliphatic amines and slowly with secondary amines. On the other hand, **1B** did not react with aromatic amines such as aniline and 2-aminopyridine under these conditions. The distinct difference in reactivity of **1B** between aliphatic and aromatic amines is of interest. This is one of the promising features of benzoylphosphonates as acylating agents and should be emphasized because almost all of the previously known acylating agents react easily with aromatic amines.[1] These results are summarized in Table I. The reactivity of the amines for the benzoylation was found to decrease in the following order: n-$BuNH_2 \simeq n$-$PrNH_2 > C_6H_{11}NH_2 > PhCH_2CH_2NH_2 \simeq (CH_3)_2CHCH_2NH_2 > HOCH_2CH_2NH_2 > PhCH_2NH_2 >$ morpholine $\gg Et_2NH \gg PhNH_2 \simeq$ 2-aminopyridine.

This order almost parallels the basicity of the amines. With an increase of the molar ratio of **1B**/**2d**, the yield of **3B** increased gradually to 94%, the maximum isolated yield, as indicated in Table II. The use of a larger excess of **1B** than 1.4 equiv resulted in a longer period of time for the consumption of **1B** since the remaining **1B** reacted slowly with **4B** with conversion into **5B**. Table III reveals the results of the solvent effect in the benzoylation of **2d** with **1B** and implies that there is no significant difference among solvents possessing dielectric constants in the range of 1.9–36.7. However, a definite solvent effect on the reaction rates was observed. The most remarkable difference was observed between benzene and cyclohexane which have low dielectric constants of 2.0 and 2.3. In the former solvent, benzoylation was complete within 1 min, but in the latter required 30 min. The order of solvent effects for the reaction rates was the following: n-hexane $\simeq$ cyclohexane > ether $\simeq$ DMF > benzene > pyridine > THF > CH_2Cl_2.

Table II. Reaction of Excess Diethyl Benzoylphosphonate (1B) with n-Propylamine (2d) in Dry Ether

1B/2d	time[a]	product, % yield 3d	4B	5B
1.00	20 min	76	46	22
1.20	80 min	88	33	32
1.40	5 h	94	38	45
1.53	20 h	94	33	55
1.20 (1C/2d)	5 days	95	62 (4C)	10 (5C)

[a] Time required for disappearance of 1B or 1C.

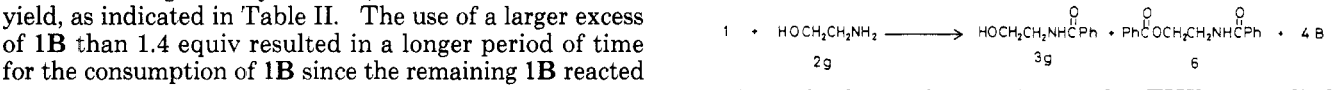
Table III. Solvent Effects for Benzoylation of n-Propylamine (2d) with Diethyl Benzoylphosphonate (1B)

solvent	dielectric constant	time[a]	product, % yield 3d	4B	5B
n-hexane	1.9	1 min	74	29	23
cyclohexane	2.0	1 min	75	48	23
benzene	2.3	30 min	79	55	18
ether	4.2	20 min	76	46	22
tetrahydrofuran	7.4	40 min	78	39	20
CH_2Cl_2	8.9	2 h	79	53	21
pyridine	12.3	30 min	76	34	22
$HC(O)NMe_2$	36.7	20 min	77	6[b]	20

[a] Time required for disappearance of 1B. [b] Almost all of 4B was removed in vacuo with the solvent.

As indicated by this order, there were no regular relationships between the polarity of the solvents and the reaction rate. The benzoylation proceeded quite rapidly in nonpolar solvents such as n-hexane and cyclohexane. The reaction rates were effectively constant in several solvents having higher dielectric constants than that of benzene. Contrary to our expectation, the reaction in dimethylformamide, having the highest dielectric constant among the solvents used, was essentially similar to those in benzene, ether, tetrahydrofuran, and pyridine. On the other hand, it was found that the benzoylation in methylene chloride was remarkably slow.

The reaction of ethanolamine (**2g**) with **1B** was conducted in order to test the selectivity of **1B** in the benzoylation toward amino and hydroxyl groups. The benzoylation of **2g** with **1B** in ether gave **3g** in a relatively low yield (50%) and dibenzoylated product (**6**) was obtained in 14% yield. Mono-O-benzoylated product (**7**) was not formed in this reaction.



A similar benzoylation of **2g** in dry THF gave a little better yield (59%) of **3g** and the yield of **6** decreased to 7%. The mono-N-acylation was improved to a 78% yield by using diisopropyl benzoylphosphonate (**1D**), described

(19) R. D. Moss, U.S. Patent 3012054 (1961); *Chem. Abstr.*, **57**, 4698 (1962); A. N. Pudovik, I. V. Gur'yanova, *Khim. Primen. Forsfororg. Soedin., Tr. Konf., 4th*, 164 (1972); *Chem. Abstr.*, **78**, 136371 (1973).

Table IV. Benzoylation of Ethanolamine (2g) with Dialkyl Benzoylphosphonates (1B and 1C)

benzoylating agent	solvent	time[a]	product, % yield 3g	6	4B
1B	tetrahydrofuran	1 h	59	7	13
	ether	2 h	50	14	13
1C	tetrahydrofuran	3 days	78	9	3

[a] Time required for disappearance of 1B or 1C.

Table V. Substituent Effects of Alkyl Groups of Benzoyl Phosphonates in Benzoylation

	R[1]	Es[c]	time[b]	product, % yield 3d	4	5
1A	Me	0.00	3 min	68	7[c]	27
B	Et	−0.07	20 min	76	46	22
C	*i*-Pr	−0.47	18 h	86	72	13
D	*i*-Bu	−0.93	40 min	78	57	21
E	*s*-Bu	−1.13	40 h	89	76	9
F	Et_2CH	−1.98	4 days	92	86	7

[a] Steric factor reported by Taft et al.[20,21] [b] Time required for disappearance of 1. [c] Almost all of dimethyl phosphonate was removed in vacuo with the solvent.

Table VI. Benzoylation Using Diisopropyl Benzoylphosphonate (1C)

	amine	time[a]	product, % yield 3	4C	5C
2a	Et_2NH	10 days	44	2[b]	49
d	*n*-$PrNH_2$	18 h	86	72	13
h	$PhCH_2NH_2$	20 h	87	74	7

[a] Time required for disappearance of 1C. [b] Almost all of 4C was removed in vacuo along with the solvent in order to make the separation of the products easy.

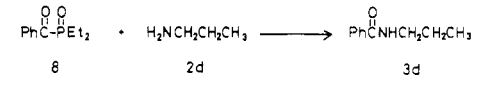
in a later section (see Table IV).

The substituent effect of the alkyl groups of esters (1) was also examined. Table V reveals that an increase in the bulkiness of an alkyl group resulted in an increase in the yield of **3d**. When bis(1-ethylpropyl) benzoylphosphonate (**1F**), containing two bulkyl 1-ethylpropyl groups, was employed in the stoichiometric reaction with **2d**, **3d** was obtained in a higher yield (92%). However, the time taken to reach the complete reaction was 4 days. The order of the bulkiness of alkyl groups based on various physical parameters has been proposed by Taft[20,21] to be as follows: Et_2CH > *sec*-Bu > *i*-Bu > *i*-Pr > Et > Me. Table V indicates that the efficiency of the acylation by use of **1A–F** was consistent with the bulkiness of alkyl groups as given above, except for *i*-Bu. Comparison of the results obtained for **1B** with those for **1C** indicates that the use of more hindered phosphonates enhanced the selectivity of the acylation between primary and secondary amines. The acylation of **2d** with 1.2 equiv of **1C** gave **3d** in maximum yield (95%), where 5 days was taken in order to complete the reaction (see Table II).

In the reaction of **2** with **1**, the side reaction to give **5** seemed to be catalyzed by amines and to depend on their basicities. This is supported by the fact that an independent reaction of **1B** with **4B** in the presence of 0.1 equiv of triethylamine gave **5B** in 86% yield after 1 h without the solvent, but in the absence of triethylamine **5B** was not formed, even after 1 day. When 0.01 equiv of triethylamine was employed in this reaction, only trace amounts of **5B** were formed. The use of enough triethylamine seemed necessary for the detectable acceleration of the side reaction. Therefore, acylation of **2d** with 1 equiv of **1B** in the presence of 1 equiv of triethylamine was conducted. Acylation was complete within 10 min, and **3d** and **5B** were obtained in 75% and 22% yields, respectively. Unexpectedly this result showed no significant effect of the presence of triethylamine on the yields of the products. It was concluded that triethylamine catalyzed both the normal acylation and the side reaction.

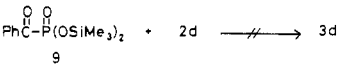
Recently, 4-(dimethylamino)pyridine (DMAP) has been utilized as a promising catalyst for the acetylation of hindered alcohols.[22] Therefore, acylation by **1B** in the presence of DMAP was studied. However, regardless of the addition of DMAP, the yields of **3d**, **4B**, and **5B** were essentially unchanged. Even when a noncatalytic amount of DMAP was employed, the yield of **3d** did not increase but the acylation was slightly (two times) accelerated.

The reaction of diethylbenzoylphosphine oxide (**8**) with **2d** in dry ether was conducted to examine the electrostatic effect of the substituent on the benzoylphosphonates. However, **3d** was obtained in a lower yield of 55%.



8 2d 3d

This result indicates that alkoxy substituents are superior to the alkyl substituent in the present acylation. Next, the reaction of bis(trimethylsilyl) benzoylphosphonate (**9**)[23] with **2d** in ether was examined. In this case, however, a complex reaction occurred and **3d** was not detected among the products.



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In consideration of these facts, suitable conditions for the practical use of benzoylphosphonates as acylating agents can be summarized as follows. It is expected that the use of 2 equiv of the most reactive dialkyl benzoylphosphonate in *n*-hexane or cyclohexane might give the optimum yield of benzamides. However, the most reactive dimethyl benzoylphosphonate, **1A**, was extremely insoluble in both *n*-hexane and cyclohexane. Therefore, satisfactory results were not obtained under these conditions. On the other hand, **1B** can be used in *n*-hexane or cyclohexane because it is partially soluble in *n*-hexane and soluble in cyclohexane. When 2 equiv of **1A** or **1B** was used in any of the solvents studied, a considerable amount of **1A** or **1B** remained after the benzoylation. Decomposition of the remaining dialkyl benzoylphosphonates into benzoic acid and dialkyl phosphonates was necessary before separation of the products by chromatography. Treatment of **1A** or **1B** with aqueous tetrahydrofuran showed that **1A** was much more easily hydrolyzed than **1B** under these neutral conditions. Therefore, it is recommended that the acylation of primary and secondary amines with less steric hindrance should be carried out by using **1A** in solvents such as ether. The conditions for the practical use of **1A** in this direction are listed in Table VII.

The acylation of amines with less than 1.4 equiv of **1B** is also recommended since under these conditions **1B**

(20) R. W. Taft, Jr., "Steric Effects in Organic Chemistry", M. S. Newmann, Ed., Wiley, 1950, p 556.
(21) E. Kutler, C. Hansch, *J. Med. Chem.*, **12**, 647 (1969); M. Charton, *J. Am. Chem. Soc.*, **91**, 615 (1969); "Advances in Linear Free Energy Relationships", J. Shoeter, N. B. Chapmann and J. Shorter, Eds., Plenum, 1972, p 71; S. H. Unger, C. Hansch, *Prog. Phys. Org. Chem.*, **12**, 91 (1976).
(22) H. Vorbrüggen, *Angew. Chem., Int. Ed. Engl.*, **17**, 569 (1978).
(23) M. I. Kabachnik and P. A. Rossiiskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 364 (1945); *Chem. Abstr.*, **40**, 4688 (1946).

Table VII. Benzoylation of Amines with Two Equivalents of Dimethyl Benzoylphosphonate (1A) in Dry Ether[a]

	amine	product, % yield		amine	product, % yield
2b	$C_6H_{11}NH_2$	98	f	$PhCH_2CH_2NH_2$	94
c	*n*-$BuNH_2$	96	h	$PhCH_2NH_2$	99
d	*n*-$PrNH_2$	98	i		94
e	*i*-$BuNH_2$	97			

[a] All of the reactions were carried out at room temperature for 1 day.

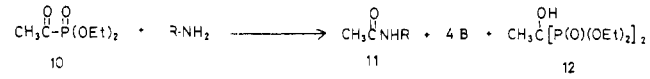
Table VIII. Acetylation of Amines with Diethyl Acetylphosphonate (10)

	amine	solvent	time,[a] h	product, % yield 11	4B	12
2f	$PhCH_2CH_2NH_2$	ether	1	72	50	24
h	$PhCH_2NH_2$	ether	3	64	54	18

[a] Time required for disappearance of 10.

disappears after the reaction and the procedure for the hydrolysis of **1B** can be omitted. For the acylation of relatively less reactive amines such as diethylamine, the use of 2 equiv of **1B** and cyclohexane as the solvent is recommended. Under these conditions, **1B** disappears almost completely after the reaction since the reaction rate is quite fast. Thus, the yield of **3a** increased to 92%. In the case of bifunctional amines such as ethanolamine, sterically hindered benzoylphosphonates such as bis(1-ethylpropyl) benzoylphosphonate (**1F**) are recommended (see Table IV).

For the comparison of benzoylation with acetylation, two reactions of **2f** and **2h** with diethyl acetylphosphonate (**10**) were studied. Table VIII shows that the yields of the



corresponding acetamides (**11f** and **11h**) were a little lower than those of the benzamides. In these reactions, 1,1-bis(diethoxyphosphoryl)ethanol (**12**) was obtained as a byproduct.

Experimental Section

NMR spectra were measured at 60 MHz on a Hitachi R 24-B spectrometer. Infrared spectra were recorded on a Hitachi Model EPI-G3 spectrometer.

All of the amines employed were purified by distillation and stored over calcium hydride except 2-aminopyridine which was recrystallized from benzene.

Benzoylphosphonates **1A–F** were prepared by the Arbuzov reaction of benzoyl chloride with trialkyl phosphites by a modification of the procedure of Kabachnik.[23]

Ether, benzene, *n*-hexane, and cyclohexane were purified by distillation and stored over sodium wire. Tetrahydrofuran was distilled from sodium wire after reflux for 6 h, redistilled over potassium hydroxide after reflux for 6 h, and finally purified by distillation from benzophenone ketyl. Dimethylformamide was purified by distillation and stored over molecular sieves. Pyridine was purified by distillation from *p*-toluenesulfonyl chloride and stored over calcium hydride. Methylene chloride was distilled after drying over P_4O_{10} for 1 day, purified by redistillation from potassium carbonate, and stored over molecular sieves.

General Procedure for the Synthesis of Dialkyl Benzoylphosphonates. Benzoyl chloride (0.15 mol) was put in a two-necked flask with a dropping funnel and an outlet connected to an aspirator. The vessel was kept under slightly reduced pressure (100 mmHg) by the aspirator and then trialkyl phosphite (0.15 mol) was added dropwise, at 0 °C, over a period of 30 min. The mixture was stirred at room temperature for 30 min under the same pressure. Distillation of the resulting oil gave a dialkyl benzoylphosphonate as a slightly yellow oil. **1A**: 83%; bp 130–133 °C (1.1 mm) (lit.[4] bp 146 °C (2.5 mm)). **1B**: 74%; bp 141–147 °C (3 mm) (lit.[10] bp 142 °C (1 mm)). **1C**: 72%; bp 117–120 °C (0.3 mm) (lit.[10] bp 127 °C (0.8 mm)). **1D**: 63%; bp 130–137 °C (0.15 mm); IR (NaCl) 1658 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.97 (d, 6 H, J = 8 Hz, CH_3), 2.00 (m, 2 H, CH), 4.00 (t, 4 H, $J_{H-H} = J_{P-H}$ = 6.5 Hz, CH_2), 7.26–7.80 (m, 3 H, *m*- and *p*-ArH), 8.15–8.45 (m, 2 H, *o*-ArH). Anal. Calcd for $C_{15}H_{23}O_4P$: C, 60.39; H, 7.77. Found: C, 60.54; H, 7.76.

1E: 59%, bp 136–140 °C (0.2 mm); IR (NaCl) 1658 cm^{-1} (C=O); NMR (CCl_4) δ 0.91 (t, 6 H, J = 7 Hz, CH_2CH_3), 1.32 (d, 6 H, J = 6 Hz, $CHCH_3$), 1.55 (m, 4 H, CH_2CH_3), 4.51 (m, 2 H, CH), 7.16–7.73 (m, 3 H, *m*- and *p*-ArH), 8.06–8.40 (m, 2 H, *o*-ArH). Anal. Calcd for $C_{15}H_{23}O_4P$: C, 60.39; H, 7.77. Found: C, 60.42; H, 7.86.

1F: 62%; bp 134–135 °C (0.02 mm); IR (NaCl) 1658 cm^{-1} (C=O); NMR (CCl_4) δ 0.87 (m, 12 H, CH_3), 1.65 (m, 8 H, CH_2), 4.35 (m, 2 H, CH), 7.17–7.66 (m, 3 H, *m*- and *p*-ArH), 8.00–8.43 (m, 2 H, *o*-ArH). Anal. Calcd for $C_{17}H_{27}O_4P$: C, 62.56; H, 8.34. Found: C, 61.68, H, 8.15.

Distillation of **1F** must be done carefully at lower bath temperature than 160 °C, because distillation at higher temperature caused the decomposition of **1F** to form dealkylated products with evolution of 2-pentene gas. The elemental analysis was somewhat poor, indicating decomposition. After careful distillation, the compound was homogeneous by thin-layer chromatography and was used for benzoylation without further purification.

Tris(1-ethylpropyl) Phosphite. A solution of 45.3 g (0.33 mol) of phosphorus trichloride in 200 mL of dry ether was added to a mixture of 88.2 g (1 mol) of 3-pentanol and 121 g (1 mol) of *N,N*-dimethylaniline in 200 mL of dry ether at −20 °C over a period of 3.5 h. After the addition was complete, 200 mL of dry ether was added and the mixture stirred at room temperature overnight. After filtration to remove *N,N*-dimethylaniline hydrochloride, 75 g of crude product, which was contaminated with a small amount of bis(1-ethylpropyl) phosphonate, was distilled. Treatment of the distilled compound with 3 g of sodium metal at 150 °C for 6 h gave 56.4 g (58%) of pure tris(1-ethylpropyl) phosphite, bp 68–73 °C (0.1 mm) (lit.[24] bp 94 °C (0.25 mm)).

General Procedure for Stoichiometric Reaction of Diethyl Benzoylphosphonate (1B) with Amines (2) in Dry Ether. To a solution of 1.21 g (5 mmol) of **1B** in 25 mL of dry ether was added 5 mmol of an appropriate amine. The mixture was stirred at room temperature and the reaction was monitored by TLC. After **1B** had disappeared by TLC, solvent was removed and the residue applied to a silica gel column. Elution was performed with benzene–ethyl acetate. The isolated amides were identified by comparison of their NMR and IR spectra with those of authentic samples. The byproducts of **4A–F** were characterized by their NMR spectra which showed the characteristic long-range couplings between the hydrogen and phosphorus atoms of H–P(O) groups (J_{H-P} = 690–709 Hz).[25] The byproducts of **5A–F** were also characterized by their NMR spectra which showed the distinct double doublets of α-hydrogens (CH–P) at 5.33–5.54 ppm coupled with the different phosphorus atoms (J_{H-P} = 10.5–10.7, J_{H-P} = 13.5–14.0 Hz).[25] Yields of all products are listed in Table I.

Reaction of Excess Diethyl Benzoylphosphonate (1B) or Diisopropyl Benzoylphosphonate (1C) with *n*-Propylamine (2d). To a solution of **1B** (6 mmol, 7 mmol, or 7.7 mmol) or **1C** (6 mmol) in 25 mL of dry ether was added 296 mg (5 mmol) of **2d**. The mixture was kept at room temperature until **1B** had reacted. After the disappearance of **1B**, the solvent was removed and residue applied to a silica gel column. Elution was performed with benzene–ethyl acetate. Yields of the products and times required for the complete reaction are listed in Table II.

Solvent Effects for the Acylation Using Diethyl Benzoylphosphonate (1B). To a solution of 1.21 g (5 mmol) of **1B**

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in 25 mL of an appropriate dry solvent was added 296 mg (5 mmol) of **2d**. The mixture was kept at room temperature with stirring until **1B** had disappeared. Products, isolated according to the procedure described above, are listed in Table III.

Benzoylation of Diisopropyl Benzoylphosphonate (1C) with Ethanolamine (2g). To a solution of 1.41 g (5.22 mmol) of **1C** in 26 mL of tetrahydrofuran was added 319 mg (5.22 mmol) of **2g**. The mixture was kept with stirring at room temperature. After 3 days **1C** disappeared and the solvent was then removed in vacuo. The residue was chromatographed on silica gel and eluted with benzene–ethyl acetate to yield 672 mg (78%) of **3g**, 127 mg (9%) of **6**, and 68 mg (3%) of **4B**. The effects of the use of **1B** in place of **1C** are described in Table IV.

Substituent Effects of Alkyl Groups of Dialkyl Benzoylphosphonates in Benzoylation. To a solution of 5 mmol of an appropriate dialkyl benzoylphosphonate in 25 mL of dry ether was added 296 mg (5 mmol) of **2d**. The mixture was kept at room temperature with stirring until the benzoylphosphonate disappeared by TLC. Complete conversion of the starting material was required for separation of the benzoylated products from the reaction mixture. Products were isolated by column chromatography on silica gel as described above. These results are in Table V.

Benzoylation of Amines by Diisopropyl Benzoylphosphonate (1C). To a solution of 1.35 g (5 mmol) of **1C** in 25 mL of dry ether was added 5 mmol of an appropriate amine. The mixture was kept at room temperature with stirring until **1C** disappeared by TLC. The products obtained after workup are listed in Table VI.

Diethyl α-((Diethylphosphoryl)oxy)benzylphosphonate (5B). To a mixture of 48.4 g (0.2 mol) of **1B** and 27.7 g (0.2 mol) of **4B** was added 2.8 mL (0.02 mol) of triethylamine. The mixture was kept at room temperature with stirring. The NMR spectrum of the mixture after 1 h showed that **5B** was formed in 86% yield. After 16 h, triethylamine was removed in vacuo. Distillation of the oily residue under reduced pressure gave 50 g (66%) of **5B** as a pure material, bp 170–190 °C (0.3 mm) (lit.[26] 183–184 °C (3 mm)).

Benzoylation of Diethylamine (2a) by Diethyl Benzoylphosphonate (1B) in the Presence of 4-(Dimethylamino)pyridine (DMAP). To a solution of 1.21 g (5 mmol) of **1B** and 60 mg (0.5 mmol) of DMAP in 25 mL of dry ether was added 366 mg (5 mmol) of **2a**. After 12 h, solvent and **4B**, formed as byproduct, were removed in vacuo at 40–50 °C. The residue was chromatographed on silica gel and eluted with benzene–ethyl acetate to yield 297 mg (46%) of **3a** and 931 mg (49%) of **5B**.

Benzoylation of *n*-Propylamine (2d) with Diethyl Benzoylphosphonate (1B) in the Presence of Triethylamine. To a solution of 312 mg (5.3 mmol) of **2d** in 26 mL of dry ether was added 1.28 g (5.3 mmol) of **1B** and 0.74 mL (5.3 mmol) of triethylamine. TLC showed that the acylation was complete within 10 min. After 20 min, solvent and **4B** formed were removed in vacuo at 40–50 °C. A workup similar to that described above gave 646 mg (75%) of **3d**, 206 mg (28%) of **4B**, and 444 mg (22%) of **5B**.

Ethyl Diethylphosphinite. To a solution of 23.5 g (160 mmol) of ethyl dichlorophosphite[27] in 200 mL of dry ether was added, dropwise at 0 °C, 160 mmol of the Grignard reagent (Et_2Mg) obtained from ethyl bromide in 160 mL of ether–dioxane. After the mixture was stirred at room temperature for 8 h, distillation gave 11.3 g (53%) of the title compound, bp 61–64 °C (72 mm) (lit.[28] bp 80–85 °C (15 mm)).

Benzoyldiethylphosphine Oxide (8). To 7.3 g (52 mmol) of benzoyl chloride was added dropwise 11 g (82 mmol) of ethyl diethylphosphinite at 0 °C over a period of 10 min. When the addition was complete, the mixture had become red. After the mixture was stirred at room temperature for 30 min, distillation gave 7.9 g of crude **8** (bp 107–109 °C (0.15–0.2 mm)). Redistillation of the crude product gave 4.6 g (42%) of pure **8** as a yellow oil: bp 97–98 °C (0.03 mm); IR (NaCl) 1650 cm^{-1} (C=O). Anal. Calcd for $C_{11}H_{15}O_2P$: C, 62.85; H, 7.19. Found: C, 62.31; H, 7.32.

Bis(trimethylsilyl) Benzoylphosphonate (9). To 21.3 g (87.8 mmol) of **1B** was added 40 mL (311 mmol) of trimethylsilyl bromide.[29] After the mixture was stirred at room temperature for 5 h, distillation gave 30 g (80%) of **9**, bp 113–115 °C (0.5 mm) (lit.[30] bp 140–145 °C (3 mm)).

Reaction of Bis(trimethylsilyl) Benzoylphosphonate (9) with *n*-Propylamine (2d). A. To a solution of 1.65 g (5 mmol) of **9** in 25 mL of dry ether was added 296 mg (5 mmol) of **2d**. A white precipitate appeared gradually. After the mixture was stirred for 4 h, the solvent was removed and the residue was dissolved in dimethyl-d_6 sulfoxide. The NMR spectrum in the solvent indicated that **3d** was not formed.

B. To a solution of 1.63 g (5 mmol) of **9** in 25 mL of dry *n*-hexane was added 591 mg (10 mmol) of **2d**. A white precipitate appeared immediately on addition of **2d**. After the heterogeneous solution was stirred for 12 h, the precipitate was collected by filtration, washed with dry ether, and dried over P_4O_{10} in vacuo. The white powder was extremely hygroscopic and quite unstable on exposure to air. Its NMR spectrum in dimethyl-d_6 sulfoxide showed that ratio of phenyl, *n*-propyl, and trimethylsilyl groups was 2:1:0.3. When the powder was dissolved in aqueous pyridine and chromatographed on "Avicel" plates by development with several solvent systems (for example, *i*-PrOH–concentrated NH_4OH–H_2O, 7:1:2 (v/v); BuOH–H_2O, 84:16 (v/v); EtOH–1 M NH_4OAc, 7:3 (v/v)), it was found to be homogeneous. The Hanes–Isherwood test[31] was positive, indicating that the compound contained phosphorus. The R_f values of the phosphorus-containing spots were consistent with those of unesterified benzoylphosphonic acid. These results indicate the formation of the mono-*n*-propylammonium salt of α-(*n*-propylimino)benzylphosphonic acid which seems to deposit with *n*-propylammonium trimethylsilyl α-(*n*-propylimino)benzylphosphonate although these could not yet be characterized sufficiently.

Practical Methods for the Benzoylation of Amines by Dimethyl Benzoylphosphonate (1A). A. To a solution of 2.14 g (10 mmol) of **1A** in 25 mL of dry ether was added 5 mmol of an appropriate amine. The mixture was kept, with stirring, at room temperature for 24 h. The solvent and **4A** formed were removed in vacuo at 40 °C; the residue was treated with 30 mL of tetrahydrofuran–water (50:1, v/v) at room temperature until excess **1A** was completely hydrolyzed (usually 2–3 h). The aqueous tetrahydrofuran solution was evaporated to dryness. The residue was dissolved in methylene chloride. Benzoic acid was extracted with 5% $NaHCO_3$ (3 × 20 mL) and the organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was dissolved in benzene and applied to a silica gel column. Elution was performed with benzene or toluene–ethyl acetate. The yields of amides are in Table VII.

B. To a solution of 2.42 g (10 mmol) of **1B** in 25 mL of dry cyclohexane was added 366 mg (5 mmol) of **2a**. The homogeneous solution obtained was kept at room temperature with stirring until **1B** disappeared (24 h).

Acetylation of Amines (2) with Diethyl Acetylphosphonate (10). To a solution of 1.2 g (6.67 mmol) of **10** in 33 mL of dry ether was added 809 mg (6.67 mmol) of **2f**. After the mixture was stirred at room temperature for 1 h, the solvent was removed in vacuo and the residue applied to a silica gel column. Elution with benzene–ethyl acetate (1:1, v/v) gave a mixture of **11f** (72%) and **4B** (50%). Further elution with methanol–ethyl acetate (1:9, v/v) gave 514 mg (24%) of crude **12**.[11,32]

Registry No. **1A**, 18106-71-3; **1B**, 3277-27-8; **1C**, 22950-57-8; **1D**, 74449-26-6; **1E**, 74449-27-7; **1F**, 74449-28-8; **2a**, 109-89-7; **2b**, 108-91-8; **2c**, 109-73-9; **2d**, 107-10-8; **2e**, 78-81-9; **2f**, 64-04-0; **2g**, 141-43-5;

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Thermal Rearrangement of 5,6-Benzotricyclo[3.2.0.0^{2,7}]hept-5-ene into 2-Vinylindene via an Intramolecular Retro-Diels–Alder Reaction

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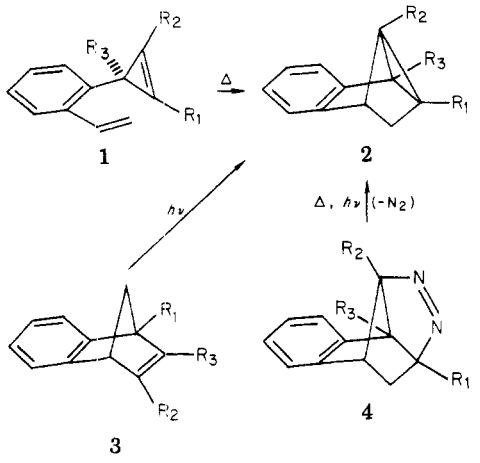
Flash vacuum pyrolysis of the 5,6-benzotricyclo[3.2.0.0^{2,7}]hept-5-ene (**2a**) at ca. 400 °C at 0.7 torr afforded quantitatively 2-vinylindene (**6**). Catalytic hydrogenation of **6** gave 2-ethylindane, thereby unequivocally confirming the proposed 2-vinylindene structure **6**, resulting from intramolecular retrocyclic Diels–Alder reaction of **2a**. Singlet oxygen and PTAD led to the expected cycloadducts, respectively, the endoperoxide **7** and the urazole **8**. It was not possible to trap the postulated isoindene with PTAD.

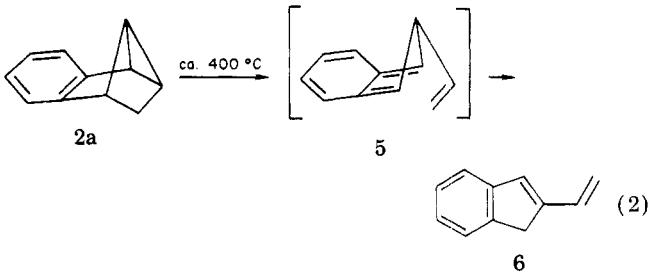
A recent communication[2] reports the synthetically valuable and mechanistically interesting thermal isomerization of 3-(2-styryl)-substituted cyclopropene **1** into benzotricyclo[3.2.0.0^{2,7}]heptene **2**, the di-π-methane rearrangement product[3] of benzonorbornadienes **3** (eq 1). In



(1)

connection with our mechanistic work[4] on the thermal and photochemical denitrogenation of azoalkane **4** as an entry into the diradical intermediates that are postulated in the di-π-methane rearrangement **3** → **2**, we examined the thermal stability and behavior of the tricycloalkene **2**. Presently we report our results of this study.

Preliminary thermolysis attempts on the parent tricycloalkene **2a** in solution at elevated temperatures (>200 °C) led to a complex mixture of products. For this reason we examined the vacuum flash pyrolysis by volatilizing **2** at ca. 60 °C and 0.7 mmHg through a hot Pyrex tube and condensing the effluent in a dry ice cold trap. Exceedingly high temperatures (ca. 400 °C) were necessary under these conditions to effect the thermal decomposition of the tricycloalkene **2**, affording 2-vinylindene (**6**) in quantitative yield (eq 2).



(2)

Confirmation of the indene structure **6** rests on satisfactory elemental composition for $C_{11}H_{10}$ by combustion analysis and ^{1}H NMR, IR, and UV spectral data (cf. Experimental Section). However, since reasonable mechanisms can be envisaged for the production of the isomeric 3-vinylindene, it was essential to conduct chemical transformations for rigorous confirmation of the proposed 2-vinylindene structure **6**. For example, on catalytic hydrogenation (Pd/C) **6** was transformed quantitatively into 2-ethylindane, as confirmed by comparison of the physical constants with the authentic material.[5] Unequivocal assignment of the hydrogenation product as 2-ethyl- rather than 3-ethylindane could be made by ^{13}C NMR. As expected, the more symmetrical 2-ethyl isomer exhibits four

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