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디에틸 α-페닐비닐인산과 아크릴로니트릴 및 말레산무수물의 자유라디칼 혼성중합

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Copolymerization of Diethyl α-Phenylvinyl Phosphate with Acrylonitrile and Maleic Anhydride

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요 약. 자유라디칼 개시제에 의한 디에틸 α-페닐비닐 인산(DEPVP)과 아크릴로니트릴(AN) 및 말레산 무수물(MAnh)의 혼성중합 연구를 행하였다. 개시제로는 과산화벤조일을 사용하였으며 중합온도는 70°C이었다. 단위체 반응성비는 r_1(AN)=0.77, r_2(DEPVP)=0.002 이었으며, 이 값으로 부터 DEPVP의 Alfrey-Price 상수 Q=0.012, e=−1.35를 얻었다. 이와 대조적으로 DEPVP와 MAnh와의 자유라디칼 혼성중합은 과산화 벤조일을 개시제로 사용하여 70°C에서 클로로포름 용액중에서 행한 결과 초기 단위체의 농도비에 무관하게 1 : 1 교대 혼성 중합체를 형성하였으며, 두 단위체의 몰비가 MAnh/DEPVP=7/3 일때 중합속도가 최대였다. 핵자기 공명 분광법으로 구한 DEPVP와 MAnh의 전하이동 착물의 평형상수는 21°C 클로로포름 용액에서 0.085*l*/mol 이었다. 혼성 중합체중 DEPVP의 함량이 증가함에 따라 AN/DEPVP 쌍에서는 환산점성도가 감소함을 보였고 MAnh/DEPVP 쌍에서는 변화가 별로 없었다.

ABSTRACT. Free radical-initiated copolymerizations of diethyl α-phenylvinyl phosphate (DEPVP) with acrylonitrile (AN) and maleic anhydride (MAnh) were studied. The monomer reactivity ratios for AN/DEPVP pair, determined at 70°C in bulk using benzoyl peroxide as an intiator, were; r_1(AN)=0.77, r_2(DEPVP)=0.002. The values of the Alfrey-Price constants, Q and e, for DEPVP were calculated to be 0.012 and −1.35, respectively. Free radical-initiated copolymerization of MAnh/DEPVP pair in chloroform at 70°C produced 1 : 1 alternating copolymers regardless monomer feed composition with the highest copolymerization rate at the molar ratio of MAnh: DEPVP=7 : 3. The equilibrium constant of a charge-transfer complex betweeen DEPVP and MAnh in deuterated chloroform, determined at room temperature by transformed Benesi-Hildebrand NMR method, was 0.085 *l*/mol. The reduced viscosity of copolymers of AN/DEPVP pair decreased as the content of DEPVP units increased, while that of MAnh/DEPVP pair remained more or less constant.

INTRODUCTION

Even though polymers and copoylmers derived from phosphorus containing vinyl monomers are of great interest for various applications, there have not been much systematic copolymerization study of those monomers[1~3]. We recently reported free radical-initiated copolymerizations of diethyl vinyl phosphate (DEVPA) and diethyl isopropenyl phosphate (DEIPA) with AN and vinyl acetate (VAc)[4,5]. The values of Alfrey-Price constants, Q and e, for DEVPA were found to be 0.025 and 0.14, respectively and for DEIPA 0.015 and 0.39, respectively. As a continuing effort to clarify further the structure-reactivity relationship of phosphorus-containing vinyl monomers, we have studied the free radical-initiated copolymerization of DEPVP, which has a phenyl substituent at vinyl functional group, with acrylonitrile and maleic anhydride.

There have been a number of studies on the alternating radical vinyl copolymerization with MAnh in view of both synthetic and mechanistic interest. The formation of alternating copolymers of MAnh with the many different π-electron donating comonomers has been attributed to the presence of a charge-transfer complex. Two different mechanisms have been proposed to explain the 1 : 1 alternating tendency in the resulting copolymers. One is the cross-reaction of free monomers whose transition state is considered to be more stabilized than that of the homo-reaction due to either the difference in polarity between monomer pairs or charge-transfer interactions between a growing polymer radical and a monomer[6,7]. The other is the homopolymerization of a charge-transfer complex formed between monomer pairs which is usually detected spectrophotometrically[8].

Since DEPVP was expected to be a reasonably good electron-donating monomer, we examined its possible 1 : 1 alternating copolymerization with maleic anhydride which is known to be an excellent electron-accepting monomer.

EXPERIMENTAL

Chemicals. The monomer DEPVP was synthesized by refluxing α-chloroacetophenone with triethyl phosphite following the literature method[9]. DEPVP thus prepared was purified by fractional distillation and had a boiling point of 117~121°C at 0.2 torr, in agreement with the literature value[9]. Gas chromatographic analysis of the distilled monomer showed that it was 99.7% pure. AN (Merck A.G.) was purified by standard procedure. Afterwards, gas chromatographic analysis found it to be better than 99.8% pure. MAnh was purified by vacuum distillation. Benzoyl peroxide (Fisher Scientific) used as an initiator throughout the present work was dissolved in chloroform and then precipitated with ethanol. It was dried at room temperature under vacuum. All other chemicals employed in the present investigation were of reagent grade and used as received.

Instruments. Pye Unicam GCD chromatograph, Varian EM 360A NMR spectrophotometer, Jasco DS 701G diffraction grating IR spectrophotometer and Unicam SP 500UV and VIS spectrophotometer were used in the present investigation.

Copolymerization of Diethyl α-Phenylvinyl Phosphate (DEPVP) and Acrylonitrile (AN). Copolymerization of DEPVP and AN was conducted in bulk. Given amounts of two monomers and 0.2 mol % benzoyl peroxide (based on the total monomer mixture) were placed in a polymerization tube. The tube then was connected to a vacuum line and degassed

by the usual freeze and thaw cycles. Next, the tube was filled with predried nitrogen and placed in a water bath at 70.0±0.1°C. Polymerization was stopped by immersing the tube in a dry ice-acetone bath, followed by the transfer of the frozen mixture into 10 m*l* of acetone containing 2 % by weight of hydroquinone. Reaction periods ranged from 6 to 22 hours, depending on the feed composition. The polymers formed were precipitated when the acetone solution was transfered to a large volume of diethyl ether. The precipitated polymers were separated by centrifugation and purified by dissolution-precpitation cycles using acetone and diethyl ether. The polymers obtained were dried under vacuum at 35°C to a constant weight. Conversions ranged from about 0.46 to 5.84 wt. % (*Table* 1).

Copolymerization of Diethyl α-Phenylvinyl Phosphate (DEPVP) and Maleic Anhydride (MAnh). Required amounts of the two monomers and benzoyl peroxide were placed in a volumetric flask and the mixture was diluted to the mark by chlorform. A certain amount of the solution was pipetted and transfered to a polymerization tube, which was immediately stoppered and the mixture was frozen in a dry ice-acetone bath. The tube was then connected to a vacuum line and degassed by the usual freeze and thaw cycles. The polymerization tube filled with nitrogen was placed in a water bath whose temperature was maintained at 70.0±0.1°C. Polymerization was stopped after 26 hrs regardless the feed composition. Copolymers formed were purified by dissolution-precipitation cycles using chloroform and diethyl ether. The polymers obtained were dried under vacuum at 35°C to a constant weight. Conversions ranged from about 4.3 to 43.1 wt. % (*Table* 2).

High Conversion Polymerizations. Copolymerization to high conversions (1.9~57.7 wt. %) were conducted in the same manner, with the exception that larger amount of benzoyl peroxide (0.4 mole %) and longer reaction time (26 hr) were employed.

Characterization of Polymers. Copolymer compositions were determined colorimetrically from their phosphorus contents, indicative of DEPVP units[10]. A small quantity (10~20mg) of copolymer was first oxidized in a hot 1 : 1 mixture of concentrated nitric and sulfuric acids. Further oxidation with perchloric acid and then with hydrogen peroxide resulted in a colorless solution. Reaction with ammonium molybdate and hydrazine sulfate produced a colored solution. Its absorbance was measured at 830 nm using a UV-VIS spectrophotometer. Tri-*para*-cresyl phosphate was used as a standard for the construction of a calibration curve. Blank tests were run side by side with actual experiments.

Reduced viscosities of copolymers were measured at 25.0±0.1°C using an Ubbelohde-type viscometer.

Determination of Equilibrium Constant for the Formation of 1 : 1 Complex between DEPVP and MAnh. The equilibrium constant of a charge transfer complex between DEPVP and MAnh was determined at 21°C by the transformed Benesi-Hildebrand NMR method in deuterated chloroform[11,21]. The concentration of MAnh was maintained constant at 0.10 mole/*l*, while the concentration of electron-donor monomer, DEPVP, varied from 1.02 to 3.65 mole/*l*.

RESULTS AND DISCUSSION

Copolymerization of Diethyl α-Phenylvinyl Phosphate with Acrylonitrile. The results of the copolymerization of DEPVP with AN are summarized in *Table* 1. These data were

Table 1. Copolymerization of acrylonitrile (AN:M_1)and diethyl α-phenylvinyl phosphate (DEPVP:M_2)[a]

Exp. No.	1	2	3	4	5	6	7
M_1/M_2(mole ratio)[b]	0.4167	0.7307	1.050	2.030	3.094	4.8217	6.664
Conversion (wt. %)	0.46	3.05	4.91	5.24	4.96	4.28	5.84
P content (wt. %)	9.45	9.15	8.77	7.92	7.14	6.15	5.32
m_1/m_2 (mole ratio)[b]	1.36	1.63	1.83	2.55	3.36	4.67	6.15

[a] Copolymerized at 70°C using 0.2 mole % benzoyl peroxide as initiator.
[b] M_1/M_2 designates mole ratio of M_1 and M_2 in feed and m_1/m_2 mole ratio of M_1 and M_2 units in the copolymer formed.

analyzed by the Kelen-Tûdos method[12] to determine the monomer reactivity ratios for the monomer pair (*Fig.* 1). Using the method of least squares, well defined values were obtained from this system: r_1(AN) = 0.77 and r_2(DEPVP) = 0.002.

The values of the monomer reactivity ratios for DEPVP lead to Alfrey-Price values[6] of Q = 0.012 and e = −1.35. The magnitude of Q of a monomer expresses the general reactivity or the degree of delocalization of the π electrons in the vinyl group of a monomer. Therefore, the phenyl substituent on α-position of vinyl group was expected to significantly increase the Q value compared with that of 0.025 for diethyl vinyl phosphate (DEVPA). However, the opposite trend was observed in the present study. The lower Q value for DEPVP than for DEVPA can be explained by the fact that the presence of the large phenyl substituent in addition to the bulky phosphate group causes a steric hindrance between propagating radical and approaching monomer. Dilatometric study of free-radical homopolymerization of DEPVP led us to the conclusion that, even though it is an 1,1-disubstituted olefin, this monomer was not able to undergo homopolymerization. This is another indicative of steric effect of the substituents. Many acrylic esters with bulky α-alkyl substituents are known not to be capable of undergoing homopolymerization due to the same reason[13,14]. We earlier reported a similar

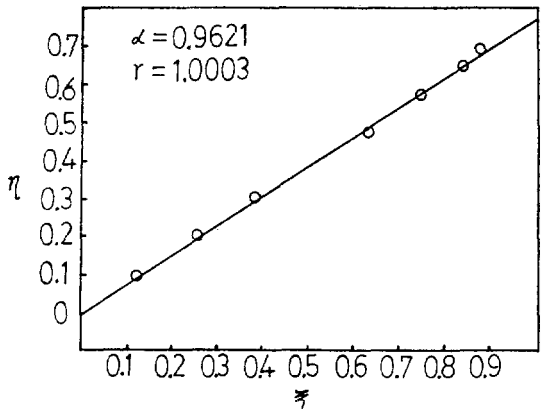

Fig. 1. Kelen-Tûdos plot for copolymerization of AN and DEPVP (r_1=0.77, r_2=0.002). α stands for the constant of Kelen-Tûdos equation and r for the coefficient of correlation.

phenomenon for DEIPA, in which a methyl substituent lowered Q value (0.015) compared with that (0.025) of DEVPA. Of course, there is another important fact that Alfrey-Price's theory does not accomodate the steric effect of substituents.

Contrary to what was observed for the Q value, the phenyl substituent decreased the magnitude of the e value for DEPVP to −1.35 which is much lower than that (0.14) of DEVPA. Such a low e value implies that DEPVP is a very good π-donor monomer. Judged by the values of Q and e, DEPVP appears to have same general character in free-radical vinyl copolymerization as propylvinyl ether (Q=0.014, e=−1.520[15]).

Copolymerization of Diethyl α-Phenylvinyl

Table 2. Copolymerization of MAnh (M_1) and DEPVP(M_2)*

Exp. No.	M_1/M_2, mole ratio	Conversion, wt. %	M_1 content, mole % in copolymer
1	0.1111	4.3	49.5
2	0.4286	14.3	50.8
3	0.9954	24.7	51.0
4	1.497	38.2	50.4
5	2.332	43.1	51.6
6	3.995	32.7	49.3
7	5.660	25.4	50.1
8	9.009	15.8	51.9

*Copolymerized in chloroform at 70°C. Total monomer concentration was 4.0 mole/*l* and the concentration of benzoyl peroxide was 0.2 mole/*l* based on monomer mixture. Reaction time: 26 h.

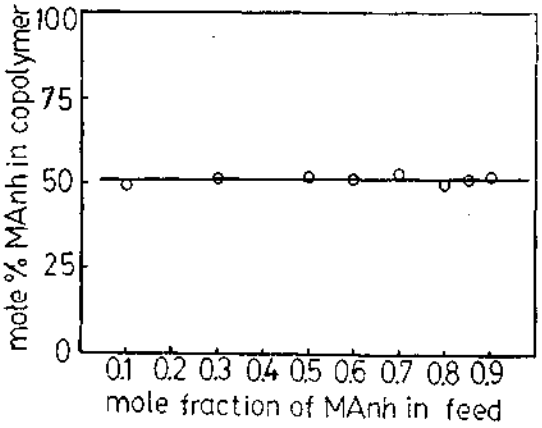

Fig. 2. Monomer-copolymer composition curve for the copolymerization of MAnh with DEPVP at 70°C in chloroform.

Phosphate (DEPVP) and Maleic Anhydride (MAnh). As pointed above, DEPVP is a π-electron rich monomer and it was our interest to study the copolymerization behavior of this monomer with MAnh which is a well-known π-acceptor with e value of 2.25. The results of the copolymerization of DEPVP with MAnh are summarized in *Table* 2. The monomer pair formed 1 : 1 alternating copolymers (*Fig.* 2) regardless monomer feed composition. The profile of copolymerization rate vs. monomer feed ratio was not symmetrical as shown in

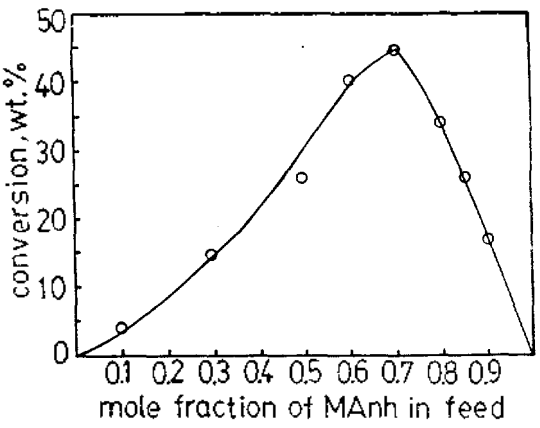

Fig. 3. Dependence of polymer yield on the feed composition in copolymerization of MAnh with DEPVP (M_1 stands for MAnh and M_2 for DEPVP).

Fig. 3 and the maximum copolymerization rate was at the molar ratio of MAnh:DEPVP=7 : 3. Such an asymmetric rate profile suggests that this copolymerization proceeds through a mixed reaction mechanism which involves charge-transfer complex between the two monomers and the free monomers[16,17]. Many π-donor and -acceptor pairs of vinyl monomers are known to form 1 : 1 alternating copolymers by free-radical initiators.

Since many of the monomer pairs form 1 : 1 donor-acceptor, so called, charge-transfer complexes and polymerizations are usually fastest at equimolar feed compositions, participation of the intermolecular donor-acceptor complexes between the two monomers in propagation reactions have been claimed to occur by many authors[18~22]. The other mechanism is based on the assumption that alternating copolymerization results from the resonance stabilization of the transition state between a π-electron donating radical and the π-electron accepting comonomer, or vice versa[23]. However, in reality, especially for the copolymerization systems whose rate profile is not symmetric against the monomer feed composition as was observed for

the present monomer pair, participation of both mechanisms is evident. Shirota *et al.*[24] reported a detailed kinetic analysis of 1 : 1 alternating copolymerizations. They proposed a generalized mechanism involving participation for both the monomer complex and the free monomers.

Formation of the charge-transfer complex between the present monomer pair was confirmed spectroscopically by the transformed Benesi-Hildebrand NMR method in deuterated chloroform (*Fig.* 4)[11,21]. The equilibrium constant thus determined for the monomer pair was 0.085 *l*/mol (*Fig.* 4). This value seems to be rather low compared with those for other monomer pairs such as styrene/maleic anhydride[25], ethylvinyl ether/maleic anhydride[26] and etc.. This can be at least partly explained by the fact that DEPVP monomer has two fairly bulky substituents on the vinyl group which would cause a steric barrier to the present monomer pair from approaching to each other to form a complex. It is not yet clear how much significant role the intermolecular charge-transfer complex plays in the copolymerization of the monomer pair. We are presently conducting a detailed kinetic analysis of this system to obtain further information on copolymerization mechanism.

High Conversion Copolymerization of Diethyl α-Phenylvinyl Phosphate (DEPVP) with Acrylonitrile (AN) and Maleic Anhydride (MAnh).

Finally, the results of high conversion copolymerizations of DEPVP with AN and MAnh are summarized in *Table* 3.

The reduced viscosity of copolymers of AN/DEPVP pair decreased as their content of DEPVP units increased, while that of MAnh/DEPVP pair remained more or less constant. This suggests that the chain-transfer constant of DEPVP is higher than AN or its steric effect hinders propagation reactions or both. But for MAnh/DEPVP pair, which formed 1 : 1 alternating copolymers regardless monomer feed composition, chain-transfer reactions seemed to be much less sensitive to the feed composition, whose reason is not yet clear. Further study is needed to quantify the chain-transfer characteristics of DEPVP in free radical-initiated copolymerizations.

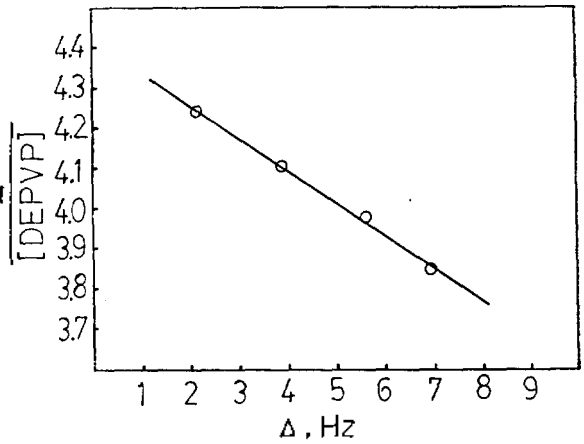

Fig. 4. Determination of K_C^{AD} for the system MAnh-DEPVP (K_C^{AD}=0.085 *l*/mol). $\Delta=\delta^{A}_{obsd}-\delta^{A}_{o}$ is the difference between the chemical shifts of the acceptor protons in complexing media, δ^{A}_{obsd}, and in uncomplexed form, δ^{A}_{o}.

Table 3. Results of high conversion copolymerization of DEPVP (M_2) with AN(M_1) and MAnh(M_1).

Copolymer	AN/DEPVP				MAnh/DEPVP		
M_1/M_2(mole ratio)	0.5191	0.9953	2.076	100/0	0.4281	0.9913	2.300
Conversion(wt. %)	1.9	7.7	22.0	9.5	19.8	39.2	57.7
P content (wt. %)	9.21	8.72	7.78	0	8.75	8.82	8.60
m_1/m_2 (mole ratio)	1.51	1.87	2.69	100/0	1.03	0.974	1.07
Reduced viscosity* (d*l*/*g*)	0.0946[a]	0.179[a]	0.201[a]	0.721[a]	0.452[b]	0.457[b]	0.479[b]

* Determined using (a) DMF or (b) chloroform as a solvent.

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O, O′-Diethyl DL-1-Aminobenzylphosphonate와 그의 유도체들을 포함한 *p*-Acetamidobenzenesulfonamide의 합성

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Synthesis of *p*-Acetamidobenzenesulfonamide Containing O, O′-Diethyl DL-1-Aminobenzylphosphonate and Their Derivatives.

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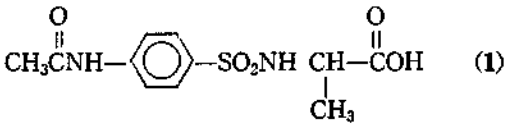
요 약. 새로운 O, O′-diethyl DL-1-aminobenzylphosphonate와 그의 유도체들을 포함한 다음의 6가지의 *p*-acetamidobenzenesulfonamide를 합성하였다. O, O′-Diethyl N-(*p*-acetamidobenzenesulfonyl) aminobenzylphosphonate, N-*p*-acetamidobenzenesulfonyl) aminobenzylphosphonic acid, O, O′-diethyl N-[N-(*p*-acetamidobenzenesulfonyl)glycyl] aminobenzylphosphonate, O, O′-diethyl N-[N-(*p*-acetamidobenzenesulfonyl)-DL-alanyl] aminobenzylphosphonate, O, O′-diethyl N-[N-(*p*-acetamidobenzenesulfonyl)-L-leucyl] aminobenzylphosphonate, O, O′-diethyl N-[N-(*p*-acetamidobenzenesulfonyl)-L-phenylalanyl] aminobenzylphosphonate. 모든 화합물은 흰색 결정으로 얻었으며 적외선 분광법과 원소분석으로 확인되었다.

ABSTRACT Six new compounds of *p*-acetamidobenzenesulfonamides which contain O, O′-diethyl-1-aminobenzylphosphonate and their derivatives were prepared: O, O′-diethyl N-(*p*-acetamidobenzenesulfonyl) aminobenzylphosphonate, N-(*p*-acetamidobenzenesulfonyl) aminobenzylphosphonic acid, O, O′-diethyl N-[N-(*p*-acetamidobenzenesulfonyl) glycyl] aminobenzylphosphonate, O, O′-diethyl N-[N-(*p*-acetamidobenzenesulfonyl)-DL-alanyl] aminobenzylphosphonate, O, O′-diethyl N-[N-(*p*-acetamidobenzenesulfonyl)-L-leucyl] aminobenzylphosphonate, and O, O′-diethyl N-[N-(*p*-acetamidobenzenesulfonyl)-L-phenylalanyl]aminobenzylphosphonate. All the compounds were obtained as white crystals and characterized by means of elemental analysis and infrared spectroscopy.

서 론

Aminophosphonic acid는 구조식으로 아미노산과 비슷하므로 아미노산과 유사한 성질을 갖고 있으리라 생각되어 최근 많은 흥미를 끌게 되었다. Horiguchi 등[1]은 1959년 양의 반추물에서 처음으로 2-aminoethylphosphonic acid (2-AEP)를 발견하였으며, 그 후 Kettredge[2], Quin[3], Hori[4], Kantatsu[5], Cull-Candy[6]는 여러 생물에서 2-AEP 및 2-amino-4-phosphonobutyric acid를 발견하였다. 또 이 aminophosphonic acid는 구조식으로 아미노산과 비슷할 뿐만 아니라 Thayer 등[7]은 생물학적 활성을 갖고 있다고 보고하였다. 실제로 김 등[9]은 1-aminoethylphosphonic acid를 흰쥐에 투여하여 이것이 생체에 해롭지 않을 뿐만 아니라 단백질 및 인 대사에도 관여함을

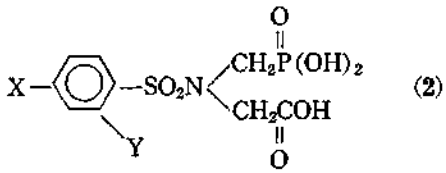
보고하였다. 특히 최근에는 1-aminophosphonic acid의 디펩티드(alaphosphine)가 항박테리아 활성이 있다고 Allen[10]이 발표하면서부터 1-aminophosphonic acid의 생체내에서의 메카니즘과 화학적 합성에 관한 연구가 활발히 진행되고 있다[11~15]. 생물학적 활성이 있다고 보고된 바 있는 아미노산과 aminophosphonic acid의 유도체들 가운데는 sulfonamide 결합을 포함하는 sulfonylamino acid (1)[16~20]가 합성되었다.



(1)

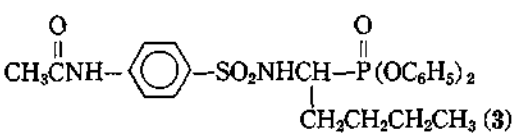
모두 Arylsulfonyl chloride와 아미노산과의 Schotten-Bauman condensation으로 합성되었다. 특히 Frankel 등[21]은 이것들이 미생물의 성장을 억제하는 효과가 있다고 발표하였다. Sulfonylaminophosphonic acid의 유도체로서는 Kirsanov 등[22]이 Arylsulfonamidophosphonamide [$ArSO_2NHP(O)(OH)$]를 합성하였으며, 역시 같은 Kirsanov[23]는 수종의 Arylsulfonamidophosphonic acid [$ArSO_2NHP(O)(OH)_2$]를 합성하였다. Oyamada 등[24]은 항암작용이 있다고 믿어지는 Arylsulfonamidophosphonimide [$ArSO_2NHP(O)(OH)\ N\overline{CH_2CH}$]를 합성하였다.

Franz[25]는 1975년 1-aminophosphonic acid를 포함하는 sulfonamide (2)를 사탕무우에 수확전 5주 동안 처리한 결과 당분이 높아진다고 발표하였다.



(2)

Birum 등[26]은 1977년 sulfonamide (3)를 합성하였다.



(3)

이 화합물은 난연제로서 또는 생물학적 활성을 갖는 물질로서 유용하다고 보고되어 있다.

본 연구에서는 aminophosphonic acid를 포함하는 sulfonamide의 유도체 합성에 관한 연구의 일환으로서 6종의 O,O′-diethyl DL-1-aminobenzylphosphonate를 포함하는 sulfonamide를 합성하였다. 이 화합물들의 사탕무우를 비롯한 다른 작물의 유용한 성분을 증대시키거나 생물의 성장 조절제로서의 역할과 난연제 등의 공업적 응용을 조사할 예정이다.

실 험

1. 시약, 기기 및 분석

실험에 사용한 시약 중 triethyl phosphite는 Mateson Coleman & Bell Co. 제를 사용하였고, dicyclohexylcarbodiimide는 Tokyo Kasei 제를 absolute ethanol, propylene oxide, DL-alanine, L-leucine은 E. Merck제를 사용하였고, glycine은 Wako 제1급 시약을 사용하였다. 그외 1-phenylalanine, ethylether, dichloromethane, triethylamine 등 대부분은 Junsei 제1급 시약을 사용하였고, tetrahydrofuran은 Hayashi 제 특급을 사용하였다.

사용한 기기는 녹는점 측정장치(Shimadzu 제)와 적외선 분광기(Beckman accuLab$_{T.M}$1) 등이며, 화합물의 원소 P는 Smith의 semimicro법[27], N은 semimicro Kjeldahl법[28]에 의하여 분석하였다.

2. O,O′-Diethyl 1-Aminobenzylphosphonate Hydrochloride (ABP · HCl) (4)의 합성

벤즈알데히드 31.8g(0.3mol)과 triethyl phosphite 49.8g(0.3mol)을 부틸 알코올 60m*l*에 녹여 암모니아를 계속 통과시켜 주면서 14시간 동안 환류시켰다. 이때 얻은 노랑색의 반응물을 실온으로 냉각하고 12시간 방치시킨후 감압증발 농축시켜 점성이 큰 황색의 액체를 얻었다. 이것을 무수에탄올-에테르(v/v 1 : 1) 용액 200m*l*에 녹여 0~5°C로 냉각시켰다. 여기에 흰색 결정이 더 이상 석출되지 않을 때까지 건조한 염화수소 가스를 통과시킨 후 생긴 침전물을 여과하여 흰색의 생성물 8.4g(15%)를 얻고 여액을 감압증발농축시켜 남은 잔유물을 무수에탄올-에테르

(v/v 1 : 1)용액에 녹이면 현탁액이 되었다. 이것을 4°C에서 하룻밤 방치시킨 후 여과하여 얻은 고체를 다시 동일한 용매로 재결정하여 불순한 생성물 16.8g(30%)를 얻었다. 이들을 합하여 위의 재결정 용매로 재결정하였다(mp 160~161°C, (문헌치[29] 159~160°C).

3. O,O′-Diethyl N-(*p*-Acetamidobenzenesulfonyl) aminobenzylphosphonate (7) 및 그의 acid (8)의 합성

3.1 O,O′-Diethyl N-(p-acetamidobenzenesulfonyl)aminobenzylphosphonate (7)의 합성

실험 2에서 합성된 O,O′-diethyl DL-1-aminobenzylphosphonate hydrochloride (4) 1.4g (0.005 mol)을 5m*l*의 dichloromethane에 녹이면서 triethylamine 1.4 m*l* (0.01 mol)을 가했다. 이 용액에 *p*-acetamidobenzenesulfonyl chloride (6) 1.2g(0.005mol)을 5m*l*의 dichloromethane에 녹인 용액을 서서히 가했다. 이것을 0~5 °C로 냉각하면서 1시간 반응시킨 후 실온에서 5시간 강하게 교반시킨 다음 약 3시간 환류시켰다. 환류가 끝난 후 분액 깔때기로 옮겨 1 *N* HCl, 5% K_2CO_3 용액, 증류수 각각 10m*l*로 1번씩 세척했다.

이 노란색의 액체를 건조시키기 위하여 무수 Na_2SO_4를 넣어 수시간 방치 후 여과하여 여액을 감압증발농축시켜 남은 갈색의 점성이 큰 액체에 석유에테르를 가하여 결정화시켰다(재결정 용매 : Tetrahydrofuran-석유 에테르(v/v 1 : 1), (1.3g, 59.5%, mp 186~87°C)

IR(KBr) ; 900(S-N) ,1160, 1315(O=S=O), 1023(P−O−C), 1230(P=O), 1685 cm^{-1}(C=O)

원소분석 : $C_{19}H_{25}N_2O_6PS$ N; 6.72% (이론치 6.36%), P; 6.95%(이론치 7.04%).

3.2 N-(*p*-Acetamidobenzenesulfonyl) aminobenzylphosphonic Acid (8)의 합성

3.2.1 1-Aminobenzylphosphonic Acid (5)의 합성

실험 2에서 합성된 O,O′-diethyl DL-1-aminobenzylphosphonate hydrochloride (4) 2.8g (0.01 mol)과 15 % 염산 5m*l*와 빙초산 5 m*l*를 넣고 80~90 °C의 온도에서 30~40 분간 환류시켰다. 반응액을 식힌뒤 감압증발농축시켜 증발하고 남은 끈끈한 액을 5~7m*l*의 에탄올에 희석시켜 propylene oxide를 가하여 냉장고에 하룻밤 방치시킨 후 여과하여 얻은 흰 결정을 에탄올-물 (v/v 1 : 1) 용액에 재결정시켰다. (1.4 g, 80%, mp 271~73°C, (문헌치[29] 272~273°C) 0.1*N* 수산화나트륨 용액으로 적정하여 얻은 적정곡선으로부터 계산된 중화당량은 94.7(이론치 93.5)이었다.

원소분석 : $C_7H_{10}NO_3P$ N ; 7.4% (이론치 7.49%), P ; 16.42% (이론치 16.58%)

3.2.2 N-(*p*-Acetamidobenzenesulfonyl)aminobenzylphosphonic Acid (8)의 합성

3.2.1.에서 얻은 1-aminobenzylphosonic acid (5) 1.4g(7mmol)을 0.56 g (14mmol)의 수산화나트륨을 용해시킨 10m*l*의 수용액에 가하였다. 이 혼합물을 서서히 교반시켜 주면서 *p*-acetamidobenzenesulfonyl chloride (6) 1.63 g(7 mmol)을 조금씩 가했다. 이 혼합물을 3시간 동안 격렬히 저어주었다. 반응이 끝난 후 미반응 물질을 여과한뒤 여액에 2*N* HCl을 서서히 가하여 흰색 결정을 얻었다. 결정이 더 이상 석출되지 않으면 여과하여 에탄올-물(v/v 1 : 1)로 재결정하였다. (2.06g, 76.6% mp 191~192°C) 0.1*N* 수산화나트륨 용액으로 적정하여 얻은 적정곡선으로부터 계산된 중화당량은 191.18(이론치192.03)으로 나타났다.

IR(KBr) ; 905(S-N), 1155, 1320 (O=S=O), 1210 (P=O), 1670cm^{-1}(C=O)

원소분석 : $C_{15}H_{17}N_2O_6PS$ N ; 6.98%(이론치 7.29%), P ; 8.01% (이론치 8.07%)

4. 화합물 (13)~(16)의 합성

4.1 N-(*p*-Acetamidobenzenesulfonyl)amino acid (9~12)의 합성

4.1.1 N-(*p*-Acetamidobenzenesulfonyl)glycine (9)의 합성

수산화나트륨 0.8 g (0.02mol)을 5m*l*의 물에 녹인 후 이 용액에 glycine 0.75 g (0.01 mol)을 가했다. 이 혼합물을 서서히 저어 주면서 *p*-ace-

tamidobenzenesulfonyl chloride (**6**) 2.34g(0.01 mol)을 조금씩 여러차례 가했다. 발열반응이므로 반응 초기에 40~50분간 0~5 °C로 냉각하에 교반시켜 주고 그 후 실온에서 2시간 격렬하게 교반시켜 주었다. 반응이 끝난 후 미반응 물질을 여과하고 여액에 2 *N* HCl을 서서히 가하여 흰색의 결정을 얻었다. 에탄올-물 (v/v 1 : 1)로 재결정하여 순수한 상태로 (**9**)을 얻었다(2g, 73.5 %, mp 234~235°C), (문헌치[20] 235°C).

IR(KBr) ; 880(S-N), 1160, 1310(O=S=O), 1720(acid의 C=O), 1640 cm^{-1}(acetyl의 C=O)

4.1.2 N-(*p*-Actamidobenzenesulfonyl)-DL-alanine (10)의 합성

DL-Alanine 0.89g (0.01mol)과 *p*-acetamidobenzenesulfonylchloride (**6**) 2.34g (0.01mol)로부터 실험 **4.1.1.**과 동일한 방법으로 처리하여 뜨거운 물로 재결정하였다(1.58, 52%, mp 206~207°C(문헌치[17] 208°C).

IR(KBr) ; 890(S-N), 1150, 1320(O=S=O), 1725 (acid의 C=O), 1645 cm^{-1}(acetyl의 C=O).

4.1.3 N-(*p*-Acetamidobenzensulfonyl)-L-leucine (11)의 합성

L-Leucine 2.62 g (0.02 mol)과 *p*-acetamido benzenesulfonyl chloride (**6**) 4.67g (0.02mol)을 역시 실험 4-1-1과 동일한 방법으로 처리하여 에탄올-물(v/v 1 : 1)로 재결정하였다 (4.1g, 62 %, mp 212~213°C), (문헌치[18] 211~212°C).

IR(KBr) ; 910(S-N), 1145, 1310(O=S=O), 1720(acid의 C=O), 1670 cm^{-1}(acetyl의 C=O).

4.1.4 N-(*p*-Acetamidobenzenesulfonyl)-L-phenylalanine (12)의 합성

L-Phenylalanine 1.65g (0.01 mol)과 *p*-acetamidobenzenesulfonyl chloride (**6**) 2.34 g (0.01 mol)로 부터 실험 4-1-1과 동일하게 처리하여 에탄올-물(v/v 2 : 8)로 재결정하였다(3g, 83%, mp 196~197°C) .

IR(KBr) ; 890(S-N), 1145, 1310(O=S=O), 1725 (acid의 C=O), 1655 cm^{-1} (acetyl의 C=O).

4.2 화합물 (13)~(16)의 합성

4.2.1 O,O'-Die thyl N-[N-(*p*-acetamidobenzenesulfonyl) glycyl] aminobenzylphosphonate (13)의 합성

실험 **4.1.1.**에서 합성된 N-(*p*-acetamidobenzesulfonyl) glycine (**9**) 0.87g(3.2mmol)과 실험 **2.**에서 합성된 O,O'-diethyl DL-1-aminobenzylphosphonate hydrochloride (**4**) 0.9 g (3.2mmol)과 dicyclohexylcarbodiimide (DCC) 0.68g (3.3 mmol)을 tetrahydrofuran (THF) 20m*l*에 녹인후 triethylamine 0.46m*l* (0.3mmol)을 tetrahydrofuran (THF) 20m*l*에 녹인 후 triethylamine 0.46 m*l* (0.0030 mol)을 첨가하였다. 자석교반기로 실온에서 16시간 반응시킨 후 이 반응 혼합물에 40 %초산 1.5m*l*를 넣고 2시간 더 반응시켰다. 이것을 여과하여 여액을 감압증발 농축시킨 뒤 클로로포름 25m*l*를 가해 희석시킨 용액을 분별 깔때기에 옮긴 후 포화 $NaHCO_3$ 용액 25m*l*와 증류수 25m*l*로 각각 3회 세척하였다. 클로로포름 용액에 무수 magnesium sulfate를 넣고 하룻밤 방치시킨 후 여과하였다.

여액을 감압증발농축시키고 tetrahydrofuran 석유 에테르(v/v 1 : 1)로 재결정하였다(0.71g, 44%, mp 195~196°C).

IR(KBr) ; 1150, 1305(O=S=O), 1620(amide C=O), 1530, 3320(N-H), 2840, 2910(aliphatic C-H), 1660 (acetyl C=O), 1020 (P-O-C), 1240 (P=O), 1390 (CH_3), 1430 cm^{-1} (CH_2)

원소분석 ; $C_{21}H_{28}N_3O_7PS$ N ; 8.96% (이론치 8.45%), P ; 6.13% (이론치 6.24%).

4.2.2 O,O'-Diethyl N-[N-(*p*-Acetamidobenzenesulfonyl)-DL-alanyl] aminobenzylphospho-nate (14)의 합성

실험 **4.1.2**에서 얻은 N-(*p*-acetamidobenzenesulfonyl)-DL-alanine (**10**) 0.92g (3.2mmol)과 O,O'-diethyl DL-1-aminobenzylphosphonate hydrochloride (**4**) 0.84 g (3.2 mmol)과 di-

cyclohexylcarbodiimide를 실험 **4.2.1**과 동일하게 처리하였다 (0.49g, 32%, mp 173~174°C)

IR(KBr) ; 1160, 1310(O=S=O), 1630(amide의 C=O), 1530, 3340(N−H), 2930, 2860(aliphatic C−H), 1670 (acetyl의 C=O), 1020(P−O−C), 1220~1240(P=O), 1370, 1450(CH_3), 690, 835, 1600 cm^{-1}(phenyl) 원소분석 : $C_{22}H_{30}N_3O_7PS$ N ; 8.68%(이론치 8.22%), P ; 5.82%(이론치 6.07%).

4.2.3 O, O′-DiethylN-[N-(*p*-Acetamidobenzenesulfonyl)—L-leucyl] aminobenzylphonate (15)의 합성

실험 **4.1.3**에서 얻은 N-(*p*-acetamidobenzenesulfonyl)-L-leucine (**11**) 1.05g (3.2mmol)과 O, O′-diethyl DL-1-aminobenzylphosphonate hydrochloride (**4**) 0.84g (3.0mmol)을 tetrahydrofuran 용매에서 반응시켜 실험 **4.2.1**과 같이 처리하였다 (0.52g, 30%, mp 94~95°C).

IR(KBr) ; 1145, 1310 (O=S=O), 1620 (C=O), 1015(P−O−C), 1520 (N−H), 1360, 1450 (CH_3), 2840, 2920 (aliphatic C−H), 1230(P=O), 690, 830, 1590(phenyl), 1670 cm^{-1} (acetyl의 C=O).

^1H NMR($CDCl_3$) δ 7.5—8 (*m*, 각기 다른 2개의 phenyl), 4.9 (*d*, CH−P=O), 3.3~4.5 (*m*, NH, O=P−OCH_2, NHCHC=O), 2.2(*s*, CCH C=O(CH_3 C=O), 1.4(*m*, O=P−OCH_2−CH_3), 0.5~1.2 (*m*, $-CH_2-CH(CH_3)-CH_3$)

원소분석 : $H_{36}N_3O_7PS$ N ; 7.95% (이론치 7.59%), P ; 5.48% (이론치 5.60%).

4.2.4 O, O′-Diethyl N-[N-(*p*-Acetamidobenzenesulfonyl)-L-phenylalanyl] aminobenzylphosphonate (16)의 합성

실험 **4.1.4**에서 합성된 N-(*p*-acetamidobenzenesulfonyl) -L-phenylalanine(**12**) 1.16g (3.2mmol)과 O, O′-diethyl DL-1-aminobenzylphosphonate hydrochloride (**4**) 0.84g (3.0mmol)과 dicyclohexylcarbodiimide 0.68g (3.3mmol)을 tetrahydrofuran 용매에서 triethylamine 0.46ml (3.0mmol)을 첨가한 후 실험 4-2-1과 동일하게 처리하였다(0.92g, 53%, mp 139~140°C).

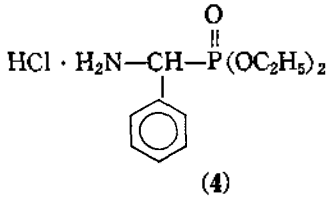
IR(KBr) : 1155, 1310 (O=S=O), 1625 (C=O), 3320, 1530 (N−H), 2680, 2930 (aliphatic N−H), 1370, 1450 (CH_3), 1020 (P−O−C), 1230 (P=O), 970 (C−O), 1670 (acetyl. C=O), 690, 840 1590 cm^{-1}(phenyl)

원소분석 : $C_{28}H_{34}N_3O_7PS$ N ; 6.86% (이론치 7.16%), P ; 5.14% (이론치 5.28%).

결과 및 고찰

Kabachnik과 Modved[30]는 dialkyl phosphite, 알데히드, 암모니아를 Mannich 반응을 이용하여 1-aminoalkylphosphonic acid를 합성하였다.

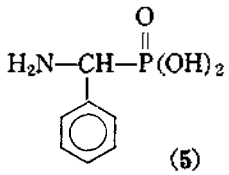
Kosolapoff[29]는 이 반응을 개량하여 가압반응으로 고압솥을 사용하여 벤즈알데히드, diethyl phosphite, 암모니아를 에틸알코올 용매하에서 반응시킨 후 염산 가스를 통과시켜서 O, O′-diethyl aminobenzyl phosphonate hydrochloride를 얻었으며, 김 등[31]은 이 방법에서 diethyl phosphite 대신 triethyl phosphite를 사용하여 27%의 수득율을 얻었다. 본 실험에서는 김의 방법[31]대로 벤즈알데히드, 암모니아, triethyl phosphite를 사용하여 부틸알코올 용매하에서 환류시켜 26%의 수득율로 O, O′-diethyl 1-aminobenzylphosphonate hydrochloride (ABP. HCl, **4**)를 합성하였다



(**4**)

Kosolapoff[29]는 여기서 합성된 O, O′-diethyl DL-1-aminobenzylphosphonate hydrochloride (**4**)을 진한 염산으로 12~15시간 가열하여 가수분해시켜 1-aminobenzylphosphonic acid를 64~65%의 수득율로 얻었다. 그러나 본 실험에서는 김등[32]이 실험한 대로 15% 염산-빙초산(v/v 1 :

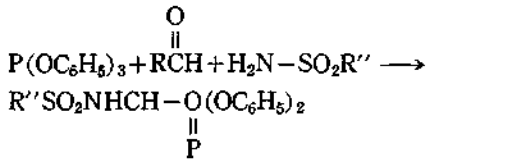
1) 용액을 사용하여 30~40분간 가열한뒤 propylene oxide로 처리하여 80 %의 1-aminobenzylphosphonic acid (5)를 얻을 수 있었다.



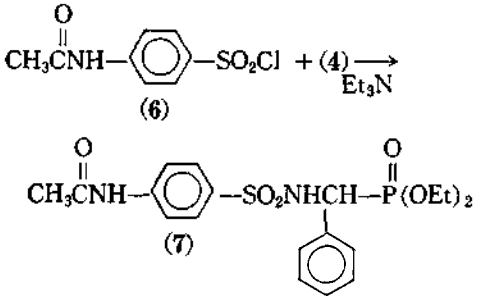
(5)

Kricheldorf[33]는 N-benzyloxycarbonylsulfonyl chloride와 amino acid ester hydrochloride를 triethylamine 존재하에 반응시켜 수종의 sulfonamide를 얻었다.

Spears[34]도 유사한 방법으로 sulfonamide를 합성한 바 있다. Birum[26]은 triphenyl phosphite와 알데히드, sulfonamide로 Mannich 반응을 이용하여 인(P)을 포함한 sulfonamide를 합성하였다.



본 실험에서는 *p*-acetamidobenzenesulfonyl chloride (6)를 dichloromethane 용매하에 소량의 triethylamine을 첨가하여 O,O′-diethyl DL-1-aminobenzylphosphonate hydrochloride (4)과 반응시켜 화합물 (7)를 얻었다.

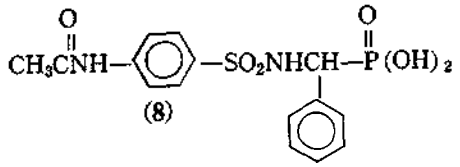


(6)

(7)

적외선 스펙트럼에서 출발 물질과는 달리 S−N 결합으로부터 연유되는 신축진동 흡수띠가 900 cm^{-1}에서 뚜렷히 나타났으며 O=S=O의 신축진동 흡수띠가 1160과 1315 cm^{-1}에서, P−O−C 및 P=O의 흡수띠는 1023 및 1230 cm^{-1}에서 각각 나타났다. 원소 분석치도 이론치와 잘 일치하였다. 앞에서 합성된 화합물 (4)과는 달리 수산화 나트륨 용액을 용매로 화합물 (6)과 (5)를 자석 교반기로 실온에서 반응시킨 다음 묽은 염산으로 결정화하여 화합물 (8)를 얻을 수 있었다.

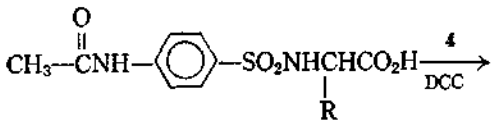
(6) + (5) ⟶

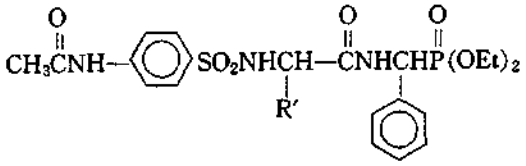


(8)

화합물 (9), (10), (11), (12)는 화합물 (6)과 아미노산 glycine, DL-alanine, L-leucine, L-phenylalanine과 Schotten-Bauman Condensation을 이용하여 쉽게 합성할 수 있었다. 본 실험에서, Kollof[16]와 Archer 등[18]이 실험한 대로 화합물 (6)과 아미노산을 수산화나트륨 수용액하에서 반응초기에 냉각시켜 주면서 강하게 저어주고 시간이 흐름에 따라 실온에서 반응시켜 묽은 염산으로 결정화시켜 주었다.

위의 반응들의 결과에서 모두 흰 결정을 얻을 수 있었으며 재결정 용매는 물 또는 물−알코올 혼합 용액을 사용하였다. 적외선 스펙트럼에서는 공통적으로 O=S=O의 신축진동 흡수띠가 약 1150, 1310 cm^{-1}에서, S−N의 신축진동 흡수띠는 약 900 cm^{-1}에서 볼 수 있었다. 여기서 합성된 (9), (10), (11), (12)와 O,O′-diethyl DL-1-aminobenzylphosphonate·hydrochoride (4)을 triethylamine 존재하에 tetahydrofuran 용매에서 dicyclohexylcarbodiimide (DCC)를 약간 과량으로 사용하여 화합물 (13), (14), (15), (16)을 얻을 수 있었다.





R=H (9)　　R′=H (13)

Me (**10**)	Me (**14**)
CH_2CHMe_2 (**11**)	CH_2CHMe_2 (**15**)
$CH_2C_6H_5$ (**12**)	$CH_2C_6H_5$ (**16**)

재결정 용매는 모두 석유 에테르-tetrahydrofuran 혼합물을 사용하였으며 또한 흰색 결정으로 얻을 수 있었다. Dicyclohexylcarbodiimide는 약간의 과량으로 사용하였으며 반응 후 미반응의 DCC는 초산을 소량 넣어 dicyclohexylurea로 바꾸어 실험을 진행하였다. 질소 및 인의 원소분석 결과는 이론치와 일치한 값을 얻었으며, 적외선 스펙트럼 분석에서는 예상대로 O=S=O의 신축진동 흡수띠가 1150, 1310 cm^{-1} 부근에서, P-O-C 및 P=O의 신축진동 흡수띠가 1020, 1230 cm^{-1} 부근에서, C=O의 신축진동 흡수띠는 1630 cm^{-1}에서 나타났고, N-H의 신축진동 흡수띠가 3340 cm^{-1} 부근에서, bending이 1530 cm^{-1}에서 각각 나타났으며[1] acetyl기의 C=O 신축진동 흡수띠가 1670 cm^{-}에서 나타났으며 acid의 C=O 신축진동 흡수띠는 볼 수 없었다. 또한 2800~3000 cm^{-1} 사이에는 aliphatic C-H 신축진동 흡수띠를 볼 수 있었고, 1370, 1450 cm^{-1}에서는 CH_3의 신축진동 흡수띠를 1600, 835, 690 cm^{-1}에서는 benzene기 를 볼 수 있었다.

본 실험에서 합성된 (**7**), (**8**) 및 (**13**), (**14**), (**15**), (**16**)들의 생물학적 실험이 추진될 예정이다.

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