

## UV-VIS spectra and photoinitiation behaviors of acylphosphine oxide and bisacylphosphine oxide derivatives in unfilled, light-cured dental resins

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The aims of this study were to investigate the photoinitiation behaviors of acylphosphine oxide (APO) and bisacylphosphine oxide (BAPO) derivatives in comparison to D,L-camphorquinone (CQ)/tertiary amine (EDAB) system. Fifty six kinds of experimental unfilled, light-cured resins were prepared using APO, BAPO, CQ, EDAB, resin monomers, and adhesive monomers. The measurements of ultraviolet-visible (UV-VIS) spectroscopy, photopolymerization with differential scanning calorimeter (photo-DSC) and degree of conversion (DC) determination were performed. Results showed that the UV-VIS spectra of all APO and BAPO derivatives possessed  $\lambda_{\text{max}}$  ranging between 365 and 416 nm. Their photoinitiation behaviors were not influenced by acidic adhesive monomers formulated in unfilled Bis-GMA-based resins ( $p < 0.05$ ). Although BAPO exhibited higher reactivity than CQ/EDAB in unfilled 6-methacryloyloxyhexyl phosphonoacetate (6-MHPA)/2-hydroxyethyl methacrylate (HEMA) and 6-MHPA/glycerol monomethacrylate (GM)-based resins, it was found that there were no statistically significant differences in DC (%) between BAPO [44.2(6.5)–51.2(4.3)] and CQ/EDAB [42.4(4.4)–47.5(3.7)] ( $p < 0.05$ ). It was concluded that APO and BAPO photoinitiators exhibited reactivity comparable to that of CQ/tertiary amine system.

**Key words:** UV-VIS spectra, Photo-DSC, Degree of conversion

Received Feb 7, 2008; Accepted May 16, 2008

### INTRODUCTION

To develop advanced light-cured dental restorative and adhesive materials, numerous studies have tirelessly explored and sought for more active photoinitiator systems. In 1971, Dart and Nemcek<sup>1</sup>, researchers from Imperial Chemical Industries Co. Ltd. (ICI, UK), invented a visible-light curing initiator system:  $\alpha$ -diketon/tertiary amine, *i.e.*, DL-camphorquinone (CQ)/*N,N*-dimethylaminoethyl methacrylate (DMAMA). This invention opened a new vista in the field of dental materials, and CQ/tertiary amine system is now ubiquitous in the compositions of light-cured, dental resin-based materials. Although CQ/tertiary amine system has a lot of advantages, it is noted that the tertiary amines tend to react with an acidic group (*i.e.*, phosphoric acid, phosphonic acid, or carboxylic acid group) of adhesive monomers to form undesirable quaternary ammonium salt<sup>2</sup> or result in adverse interactions<sup>3,4</sup>.

Acylphosphine oxide (APO) and bisacylphosphine oxide (BAPO) derivatives have received considerable recent attention both because of their inherently interesting photochemistry and photophysics and because they are widely employed as photoinitiators in free radical polymerization processes of photoradiation industries<sup>5</sup>, and they have recently gained new

attention in dentistry. Commercially utilized APO [*i.e.*, 2,4,6-trimethylbenzoyl-diphenylphosphine oxide (TMDPO)] and BAPO [*i.e.*, bis(2,4,6-trimethylbenzoyl)-phenylphosphine oxide (BTMPO)] have also been shown to exhibit good photoinitiation activity when under dental halogen lamp irradiation. Unlike the CQ/tertiary amine system, which is so-called a hydrogen abstraction photoinitiator, APO and BAPO undergo  $\alpha$ -cleavage type of photoinitiation mechanism (Norrish type I system) which does not require accelerators such as tertiary amines—whereby the latter tend to result in adverse interactions with acidic monomers<sup>2-4</sup>.

Although there is increasing interest in the employment of APO and BAPO photoinitiators in dentistry, few investigations have been made on their photoinitiation behaviors in dental resins. Furthermore, to date, there was few scientific information with regard to comparing the  $\alpha$ -cleavage photoinitiation mechanism of APO and BAPO against the hydrogen abstraction reaction of CQ/tertiary amine system in unfilled dental resins containing acidic adhesive monomers.

The aims of this study, therefore, were to investigate systematically: (1) the photoinitiation behaviors of APO and BAPO derivatives in comparison to that of CQ/tertiary amine system; and (2) the effects of four kinds of acidic adhesive

monomers or two kinds of OH-containing monomers in unfilled resins on photopolymerization initiated by BAPO and CQ/tertiary amine. Evaluations in this study were carried out using the following means: the measurements of ultraviolet-visible (UV-VIS) spectroscopy, photopolymerization with differential scanning calorimeter (photo-DSC) and degree of conversion (DC) determination. The null hypothesis tested was that APO and BAPO photoinitiators exhibit reactivity comparable to that of CQ/tertiary amine system.

## MATERIALS AND METHODS

### Preparation of reagents (1): APO derivatives

Seven kinds of APO derivatives employed in this study were synthesized by Michaelis–Arbuzov reaction<sup>6</sup>, whereby a schematic illustration of the synthesis mechanism is shown in Fig. 1. All synthesized products were identified by the synthesis data previously reported by Henne *et al.*<sup>7</sup>. All reactions were carried out in dry toluene for 3–6 hours at 60°C. The reaction flask was covered with aluminum foil to shield ambient light in nitrogen atmosphere during all reactions, and purification procedures were carried out in a dark room that was shielded from ambient ultraviolet and visible light.

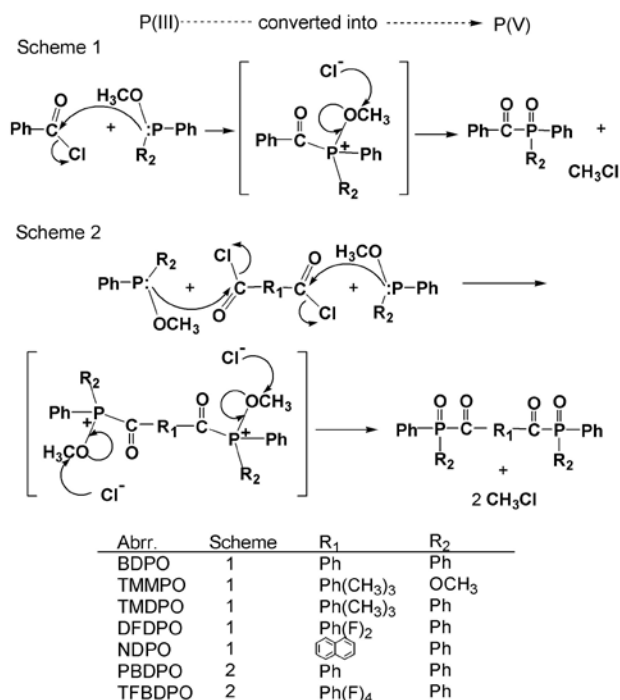


Fig. 1 Schematic illustration of the synthesis of acylphosphine oxide derivatives employed in this study by Michaelis–Arbuzov reaction according to two reaction schemes: scheme 1 used monoacid chlorides while scheme 2 used diacid chlorides.

A brief overview of the seven kinds of APO derivatives synthesized in this study were:

- (1) Benzoyl-diphenylphosphine oxide (BDPO): synthesized by the reaction of benzoyl chloride (BzC) with diphenylmethoxy phosphine (DPMP).
- (2) 2,4,6-trimethylbenzoyl-methoxy-phenylphosphine oxide (TMMPO): synthesized by the reaction of 2,4,6-trimethylbenzoyl chloride (TMC) with dimethoxyphenyl phosphine (DMPP).
- (3) 2,4,6-trimethylbenzoyl-diphenylphosphine oxide [TMDPO (Lab)]: synthesized by the reaction of TMC with DPMP.
- (4) Phthaloyl-bis(diphenylphosphine oxide) (PBDPO): synthesized by the reaction of terephthanoyl chloride (TPC) with DPMP in 1:2 molar ratio.
- (5) Tetrafluoroterephthanoyl-bis(diphenylphosphine oxide) (TFBDPO): synthesized by the reaction of tetrafluoroterephthanoyl chloride (TFPC) with DPMP in 1:2 molar ratio.
- (6) 2,6-difluoro benzoyl-diphenylphosphine oxide (DFDPO): synthesized by the reaction of 2,6-difluoro benzoyl chloride (DFBC) with DPMP.
- (7) (1-naphthoyl)diphenylphosphine oxide (NDPO): synthesized by the reaction of 1-naphthalene carboxyl chloride (NPCC) with DPMP.

The reaction reagents of aromatic monoacid chlorides (*i.e.*, BzC, TMC, DFBC, NPCC) and aromatic diacid chlorides (*i.e.*, TPC, TFPC), aromatic phosphines (*i.e.*, DMPP, DPMP) and commercial 2,4,6-trimethylbenzoyl-diphenylphosphine oxide [=TMDPO (Com)] were purchased from Wako Pure Chemicals Industries Ltd. (Osaka, Japan) and used without further purification. Synthesized APOs were identified by Fourier transform infra-red (FT-IR) spectroscopy (FTIR-8400S, Shimadzu Corp., Kyoto, Japan).

### Preparation of reagents (2): BAPO derivatives and CQ/tertiary amine systems

The BAPO derivatives of Irgacure 819 (IC 819) [*i.e.*, bis(2,4,6-trimethylbenzoyl)-phenylphosphine oxide; BTMPO] and Irgacure 1800 (IC 1800) [A: bis(2,6-dimethoxybenzoyl)-2,4,4-trimethyl-pentylphosphine oxide, B: 1-hydroxy-cyclohexyl-phenyl-ketone; A:B=1:3] (Ciba Specialty Chemicals Corp, NY, USA), D,L-camphorquinone (CQ) (Tokyo Chemical Industry Co. Ltd., Tokyo, Japan) and ethyl *p*-dimethylamino-benzoate (EDAB) (Wako Pure Chemicals Industries Ltd., Osaka, Japan) were purchased and used without further purification.

### Preparation of reagents (3): Adhesive monomers and other reagents

Adhesive monomers of 4-acryloyloxyethyl trimellitic

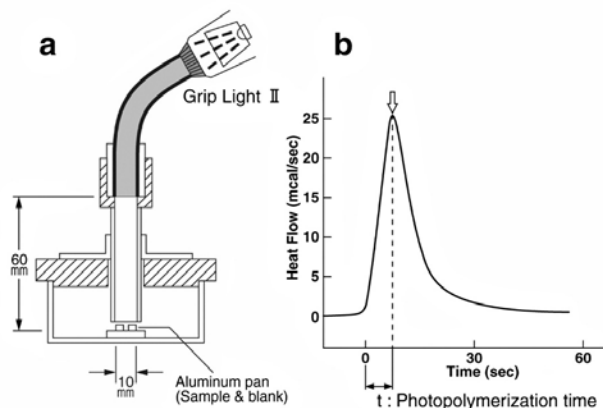


Fig. 2 Schematic illustration of the (a) photo-DSC measurement and (b) determination of polymerization time in this study.

acid (4-AET)<sup>8</sup>, 4-acryloyloxyethyl trimellitic anhydride (4-AETA)<sup>8</sup>, 4-methacryloyloxyethyl trimellitic anhydride (4-META)<sup>9</sup>, and 6-methacryloyloxyhexyl phosphonoacetate (6-MHPA)<sup>10</sup> were synthesized according to the respective methods previously reported. 2,2'-bis[4-(2-hydroxy-3-methacryloyloxypropoxy)phenyl]propane (*i.e.*, bisphenol-A-diglycidyl methacrylate; Bis-GMA)<sup>11</sup> was synthesized by adding bisphenol-A to glycidylmethacrylate in 1:2 molar ratio according to a method previously reported. Triethylene glycol dimethacrylate (*i.e.*, TEGDMA; 3G) (Shin-Nakamura Chemicals Co. Ltd., Wakayama, Japan) and two OH-containing monomers [*i.e.*, 2-hydroxyethyl methacrylate (HEMA) (Mitsubishi Rayon Co. Ltd., Tokyo, Japan) and glycerol monomethacrylate (GM) (Nihon Oil and Fat Co. Ltd., Tokyo, Japan)] were purchased and used without further purification.

#### Preparation of experimental light-cured unfilled resins

Eight kinds of experimental, unfilled, light-cured resins listed in Table 1 were prepared, in which the photoinitiators (1.0 wt%) without PBDPO and TFDPO, *i.e.*, BDPO, TMMPO, TMDPO (Lab), TMDPO (Com), DFDPO, NDPO, IC 819, and IC 1800 were dissolved in the mixture (Bis-GMA/TEGDMA=60/40, wt%) and mixed for 3 hours in a dark room. Then, 48 kinds of experimental, unfilled, light-cured resins listed in Tables 2–4 were prepared in a similar manner using the prepared reagents, *i.e.*, APOs, BAPOs, CQ, EDAB, Bis-GMA, TEGDMA (*i.e.*, 3G), 4-AET, 4-AETA, 4-META, 6-MHPA, HEMA, and GM.

For investigative comparison of BAPO against CQ/EDAB (Tables 3–4), experimental unfilled resins of Group A: Bis-GMA/3G (60/40, wt%)/6-

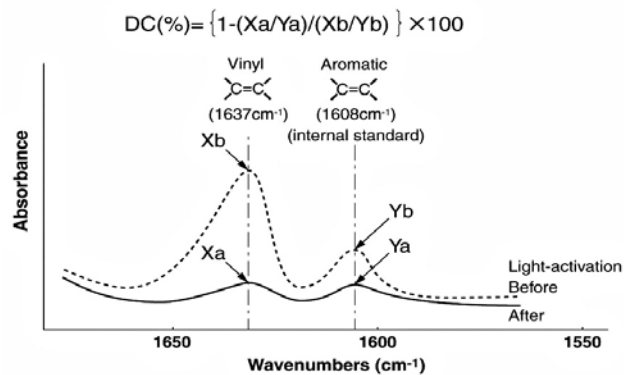


Fig. 3 Schematic illustration of determining the degree of conversion (DC, %) in this study. The DC was determined by the subtraction of FT-IR spectra measured before and after light activation for 30 sec.

MHPA/HEMA (50/50, wt%)=100/0–0/100, 2.0 wt% BAPO (IC 1800), Group B: Bis-GMA/3G (60/40, wt%)/6-MHPA/GM (50/50, wt%)=100/0–0/100, 2.0 wt% BAPO, Group A': Bis-GMA/3G (60/40, wt%)/6-MHPA/HEMA (50/50, wt%)=100/0–0/100, CQ/EDAB (0.5/1.0, wt%) and Group B': Bis-GMA/3G (60/40, wt%)/6-MHPA/GM (50/50, wt%)=100/0–0/100 CQ/EDAB, (0.5/1.0, wt%) were prepared.

#### UV-VIS spectra measurement

The ultraviolet and visible (UV-VIS) spectra of 10 kinds of APO and BAPO derivatives, *i.e.*, BDPO, TMMPO, TMDPO (Lab), TMDPO (Com), DFDPO, NDPO, PBDPO, TFBDO, IC 819, and IC 1800 were measured. The photoinitiator (1 mmol) was dissolved in dry toluene and placed in a crystal cell (cell thickness: 10 mm). UV-VIS spectra were then measured using an ultraviolet and visible light spectrophotometer (U-3310, Hitachi Co. Ltd., Tokyo, Japan).

#### Photopolymerization measurement with differential scanning calorimeter (photo-DSC)

Figure 2 depicts a schematic illustration of the (a) photo-DSC measurement and (b) determination of photopolymerization time in this study. The prepared sample ( $8.00 \pm 0.25$  mg or  $10.00 \pm 0.30$  mg) was weighed in an aluminum pan. Both blank and sample aluminum pans were placed in a differential scanning calorimeter (DSC; Thermoflex TAS 200 series DSC 8230D, Rigaku Co. Ltd., Tokyo, Japan) at room temperature, and irradiated with visible light (wavelength: 375–575 nm; light intensity: 80 mW/cm<sup>2</sup> or 100 mW/cm<sup>2</sup>) (Grip Light II, Shofu Inc., Kyoto, Japan) that was connected to DSC using a glass fiber (Fig. 1a). Distance between the sample in aluminum pan and pilot of the glass fiber was 60

mm. Polymerization time (sec) was determined based on the maximum value of heat flow measured using a photo-DSC curve (Fig. 1b). All experiments were carried out five times, and the mean and standard deviation values were calculated.

#### Degree of conversion (DC) measurement

Figure 3 depicts a schematic illustration for the determination of degree of conversion (DC, %). The DC was determined according to a method previously reported<sup>12,13</sup> using an FT-IR spectrophotometer (Shimadzu IR Prestage21). A small amount of sample resin (*ca.* 10 mg) was placed between two KBr disks (0 sec cure time) and transmission spectra were recorded with 20 scans at a resolution of 1 cm<sup>-1</sup>. After the IR spectral scan, the resin was irradiated (adjusted to 400 mW/cm<sup>2</sup>) through the transparent KBr disks for 30 seconds with the visible light curing unit (Grip Light II). After light curing, the specimens were again scanned for their FT-IR spectra. The quantity of the remaining double bonds was determined. Remaining unconverted double bonds were calculated by comparing the ratio of aliphatic C=C (vinyl) absorption (1637 cm<sup>-1</sup>) to aromatic C=C absorption (1608 cm<sup>-1</sup>) between cured and uncured specimens (*n*=5), in which the aromatic double bond stretching bands remain constant during polymerization reactions and serve as internal standard.

The DC was determined by subtracting the residual percentage of polymerizable aliphatic double bond from 100% and by the following equation:

$$DC (\%) = \{1 - (X_a/Y_a)/(X_b/Y_b)\} \times 100$$

where X<sub>a</sub> and X<sub>b</sub> are the bands of polymerizable aliphatic double bond after (X<sub>a</sub>) and before (X<sub>b</sub>) light activation, and Y<sub>a</sub> and Y<sub>b</sub> are the bands of aromatic double bond after (Y<sub>a</sub>) and before (Y<sub>b</sub>) light activation.

#### Statistical analysis

For the measured data of photo-DSC and degree of conversion, their means and standard deviations (*n*=5) were calculated. The results were subjected to one-way analysis of variance (ANOVA) followed by Newman-Keuls multiple comparison test.

## RESULTS

#### APO and BAPO derivatives and UV-VIS spectra results

Table 1 summarizes the appearance and melting points of the synthesized APOs. The seven APOs synthesized in this study were obtained in the yield range of 67.1–88.1% with: (1) BDPO at 78.5%; (2) TMMPO at 75.5%; (3) TMDPO at 88.1%; (4) PBDPO at 76.2%; (5) TFBDO at 67.1%; (6) DFDPO at

75.7%; and (7) NDPO at 75.0%. The melting point of TMDPO (Lab) agreed with that of the commercial reagent of TMDPO (Com). On the FT-IR spectra results, the absorbance of carbonyl band ( $\nu$ C=O: 1792 cm<sup>-1</sup>) of acid chloride group [-C(=O)-Cl] disappeared while that of acyl group [-C(=O)-R] ( $\nu$ C=O: 1670 cm<sup>-1</sup>) was recorded on the FT-IR spectra of APOs.

Figure 4 shows the results of UV-VIS spectra. To compare the UV-VIS spectra with the corresponding structural formulas of eight kinds of APOs and two kinds of BAPOs used in this study, the structural formulas are also given in Fig. 4. BDPO, TMMPO, TMDPO (Lab), PBDPO, TFBDO, DFDPO, and NDPO were synthesized in this study, whereas TMDPO (Com), IC 819, and IC 1800 were commercial reagents. Based on the absorption maximum wavelengths ( $\lambda_{max}$ ) given in Table 1, all APO and BAPO derivatives possessed  $\lambda_{max}$  ranging between 365 and 416 nm. Once again, synthesized TMDPO (Lab) was found to identify with the commercial reagent of TMDPO (Com) based on the agreement of  $\lambda_{max}$ . As for the  $\lambda_{max}$  values of BDPO, DFDPO, and IC 819 (=BAPO), they were greater than 400 nm.

#### Polymerization times of APO, BAPO, and CQ/Amine systems

Table 1 presents the photo-DSC results of eight APO and BAPO derivatives. The light intensity used was 100 mW/cm and sample weight was 10.00±0.30 mg. Using photo-DSC, the polymerization times under 10 seconds (5.9–9.9 sec) were shown as single sharp peaks. Short polymerization times were achieved by IC 819 (=BAPO) (5.9 sec), TMDPO (Lab) (6.7 sec), IC 1800 (6.8 sec), TMDPO (7.5 sec), and TMMPO (7.5 sec), hence demonstrating statistically higher reactivity than the other photoinitiators (*p*<0.05). In contrast, NDPO (70.0 sec) showed a prolonged polymerization time with broad photo-DSC peak. Since both PBDPO and TFBDO remained inactivated for a few days after synthesis, their photo-DSC data were not measured.

Table 2 presents the polymerization times (photo-DSC) by APO and BAPO initiators in unfilled Bis-GMA-based resins with or without 10 wt% of acidic adhesive monomer (*i.e.*, 4-AET, 4-AETA, 4-META, or 6-MHPA). Two APOs (TMMPO and TMDPO) and two BAPOs (IC 819 and IC 1800) were selected to be included in the formulations of Bis-GMA-based resins at a concentration of 1.0 wt%. During measurement, the light intensity used was 100 mW/cm and sample weight was 10.00±0.25 mg. Statistical analysis (ANOVA) showed that there were no significant difference among all experimental unfilled resins (*p*<0.05). It is indicated that two APOs and two BAPOs presented similar high photoinitia-

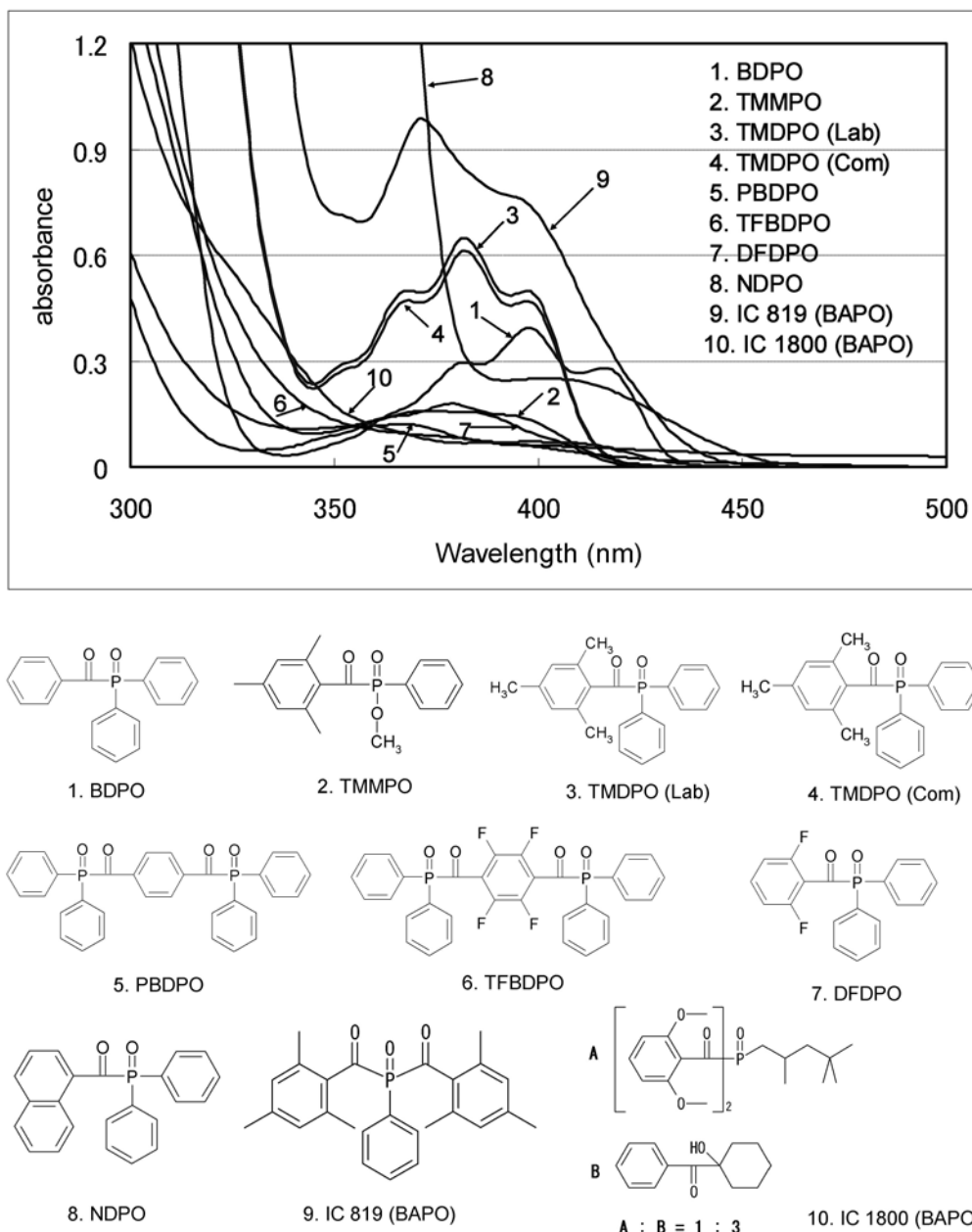


Fig. 4 The UV-VIS spectra of 10 kinds of APO and BAPO derivatives investigated in this study, together with their structural formulas. BDPO, TMMPO, TMDPO (Lab), PBDPO, TFBDO, DFDPO, and NDPO were synthesized in this study, whereas TMDPO (Com), IC 819, and IC 1800 were commercial reagents.

tion reactivity, and that they were not influenced by the presence of acidic adhesive monomers. It is also noteworthy that IC 819 in Bis-GMA/3G revealed the highest reactivity at 5.9 sec.

Table 3 shows the effects of the concentration of 6-MHPA/HEMA (50/50, wt%) or 6-MHPA/GM (50/50, wt%) in the mixed resin monomers of Bis-GMA/3G (60/40, wt%) initiated by BAPO (=IC 1800) at 2.0 wt% (Groups A and B) or CQ/EDAB (0.5/1.0, wt%) (Groups A' and B') by means of photo-DSC.

Results showed that increasing the concentration of OH-containing monomers (*i.e.*, HEMA and GM) tended to prolong the polymerization time in both BAPO and CQ/EDAB systems, and that statistical analysis (ANOVA) showed that there were significant differences among all the concentrations of 6-MHPA/OH-containing monomer in unfilled resins ( $p < 0.05$ ). In particular, all 100% HEMA and 100% GM initiated by both BAPO and CQ/EDAB indicated significantly prolonged polymerization times ( $p < 0.05$ ).

Table 1 Appearance and UV-VIS spectra, melting point, and photo-DSC results of APO and BAPO derivatives used

Photoinitiators	Classified as	Appearance	Melting point (°C)	UV-VIS spectra (λmax, nm)	Photo-DSC (sec)
BDPO	APO	light yellow oily product	—	382, 398, 416	9.9 (0.5) <sup>a</sup>
TMMPO	APO	light yellow oily product	—	373	7.5 (0.4) <sup>b</sup>
TMDPO (Lab)	APO	white needle crystals	86~88	368, 382, 397	6.7 (0.5) <sup>b,d</sup>
TMDPO (Com)	APO	white powders	88~92	368, 382, 397	7.5 (0.8) <sup>b</sup>
PBDPO	APO	light yellow powders	200~205	368	inactivated
TFBDPO	APO	light yellow powders	—	380	inactivated
DFDPO	APO	light brown oily product	—	365, 379, 391	9.3 (0.5) <sup>a</sup>
NDPO	APO	light yellow powders	163~166	401	70.0 (5.5) <sup>c</sup>
IC 819	BAPO	light yellow powders	—	371, 400	5.9 (0.3) <sup>d</sup>
IC 1800	BAPO	light yellow powders	—	398	6.8 (0.5) <sup>b,d</sup>

Note: Unfilled resins used: Bis-GMA/3G (60/40, wt% ), Concentration of photoinitiators: 1.0 wt%. BDPO, TMMPO, TMDPO (Lab), PBDPO, TFBDPO, DFDPO and NDPO are synthesized in this study, TMDPO (Com), IC 819 and IC 1800 are commercial reagents. Photo-DSC: n = 5, The light intensity used was 100 mWcm<sup>-1</sup>, and sample weight was 10.00 ± 0.30 mg. Group from the same column that are identified with the same superscript letters are not significantly different (p<0.05).

Table 2 Polymerization times (photo-DSC) [Mean (SD) in sec] of unfilled resins initiated by APO and BAPO photoinitiators

Composition (wt%)	APO		BAPO	
	TMDPO	TMMPO	IC 819	IC 1800
Bis-GMA/3G (=60/40)	6.4 (0.6) <sup>a</sup>	7.6 (0.3) <sup>a</sup>	5.9 (0.5) <sup>a</sup>	6.9 (0.4) <sup>a</sup>
4-AET/HEMA/BisGMA/3G (=10/10/48/32)	6.6 (0.3) <sup>a</sup>	7.7 (0.3) <sup>a</sup>	6.0 (0.2) <sup>a</sup>	7.5 (0.8) <sup>a</sup>
4-AETA/HEMA/BisGMA/3G (=10/10/48/32)	6.6 (0.5) <sup>a</sup>	7.6 (0.6) <sup>a</sup>	6.0 (0.3) <sup>a</sup>	7.3 (0.2) <sup>a</sup>
4-META/HEMA/BisGMA/3G (=10/10/48/32)	6.5 (0.4) <sup>a</sup>	7.8 (0.3) <sup>a</sup>	6.1 (0.5) <sup>a</sup>	7.4 (0.5) <sup>a</sup>
6-MHPA/HEMA/BisGMA/3G (=10/10/48/32)	6.5 (0.3) <sup>a</sup>	7.8 (0.3) <sup>a</sup>	6.1 (0.5) <sup>a</sup>	7.4 (0.4) <sup>a</sup>

Note: n = 5, Concentration of photoinitiator: 1.0 wt% in the mixed resins. The light intensity used was 100 mWcm<sup>-1</sup>, and sample weight was 10.00 ± 0.30 mg. TMDPO: 2,4,6-trimethylbenzoyl-diphenylphosphine oxide, TMMPO: 2,4,6-trimethylbenzoyl-methoxyphenylphosphine oxide, IC-819 (Irgacure 819): bis(2,4,6-trimethylbenzoyl)-phenylphosphine oxide, IC 1800 (Irgacure 1800): [A: bis(2,6-dimethoxybenzoyl)-2,4,4-trimethyl-phenylphosphine oxide, B: 1-hydroxy-cyclohexyl-phenylketone; A : B = 1:3]. Group from the same column that are identified with the same superscript letters are not significantly different (p<0.05).

Table 3 Polymerization times (photo-DSC) [Mean (SD) in sec] of unfilled resins initiated by BAPO (IC 1800) and CQ/EDAB initiator systems

Unfilled resins (a)/(b)	BAPO (IC 1800) initiator		CQ/EDAB system	
	Group A	Group B	Group A'	Group B'
100/0	7.3 (0.2) <sup>a</sup>	7.3 (0.3) <sup>a</sup>	9.8 (0.2) <sup>a</sup>	9.3 (0.4) <sup>a</sup>
80/20	8.0 (0.2) <sup>b</sup>	7.8 (0.2) <sup>b</sup>	11.0 (0.1) <sup>b</sup>	11.0 (0.2) <sup>b</sup>
60/40	9.4 (0.3) <sup>c</sup>	8.5 (0.3) <sup>c</sup>	14.7 (0.2) <sup>c</sup>	14.6 (0.4) <sup>c</sup>
40/60	11.8 (0.2) <sup>d</sup>	9.1 (0.2) <sup>d</sup>	20.6 (0.3) <sup>d</sup>	20.2 (0.2) <sup>d</sup>
20/80	14.9 (0.5) <sup>e</sup>	10.0 (0.2) <sup>e</sup>	29.2 (0.5) <sup>e</sup>	28.7 (0.4) <sup>e</sup>
0/100	21.3 (0.8) <sup>f</sup>	11.5 (0.1) <sup>f</sup>	44.4 (1.6) <sup>f</sup>	43.0 (0.0) <sup>f</sup>
100% OH-monomer	43.8 (1.2) <sup>g</sup>	20.8 (0.6) <sup>g</sup>	200.0 (5.6) <sup>g</sup>	195.2 (4.2) <sup>g</sup>

Note: n = 5, OH-monomer: Group A and A': 2-hydroxyethyl methacrylate (HEMA), Group B and B': glycerol monomethacrylate (GM). Group A and A': (a) Bis-GMA/3G (60/40, wt%)/(b) 6-MHPA/HEMA (50/50, wt% ), Group B and B': (a) Bis-GMA/3G (60/40, wt%)/(b) 6-MHPA/GM (50/50, wt%). Concentration of photoinitiators: BAPO (2.0 wt%), CQ/EDAB (0.5/1.0, wt%). IC 1800 is same definition described in Table 2. EDAB: ethyl N,N-dimethylaminobenzoate. The light intensity used was 80 mWcm<sup>-1</sup>, and sample weight was 8.00 ± 0.25 mg. Group from the same column that are identified with the same superscript letters are not significantly different (p<0.05).

Table 4 Degree of conversion (%) of unfilled resins initiated by BAPO (IC 1800) and CQ/EDAB initiator systems

Unfilled resins (a)/(b)	BAPO (IC 1800) initiator		CQ/EDAB system	
	Group A	Group B	Group A'	Group B'
100/0	47.8 (6.7) <sup>a</sup>	47.4 (5.2) <sup>a</sup>	45.6 (2.8) <sup>a</sup>	46.1 (3.1) <sup>a</sup>
80/20	46.9 (6.5) <sup>a</sup>	49.2 (1.0) <sup>a</sup>	45.4 (2.3) <sup>a</sup>	46.2 (4.4) <sup>a</sup>
60/40	46.2 (4.6) <sup>a</sup>	51.2 (4.3) <sup>a</sup>	44.9 (4.2) <sup>a</sup>	47.5 (3.7) <sup>a</sup>
40/60	46.6 (5.5) <sup>a</sup>	45.2 (4.1) <sup>a</sup>	42.4 (4.4) <sup>a</sup>	45.7 (3.6) <sup>a</sup>
20/80	44.2 (6.5) <sup>a</sup>	44.4 (2.4) <sup>a</sup>	43.3 (5.7) <sup>a</sup>	43.0 (4.8) <sup>a</sup>
0/100	did not test	did not test	did not test	did not test
100%OH-monomer	did not test	did not test	did not test	did not test

Note: n = 5, OH-monomer: Group A and A': HEMA, Group B and B' : GM. Group A and A' : (a) Bis-GMA/3G (60/40, wt%)/(b) 6-MHPA/HEMA (50/50, wt%), Group B and B' : (a) Bis-GMA/3G (60/40, wt%)/(b) 6-MHPA/GM (50/50, wt%), Concentration of photoinitiators: BAPO (2.0 wt%), CQ/EDAB (0.5/1.0, wt%). HEMA, GM, IC 1800 and EDAB are same definition described in Tables 2 and 3. The light intensity used was 80 mWcm<sup>-1</sup>, and sample weight was 8.00 ± 0.25 mg. Group from the same column that are identified with the same superscript letters are not significantly different (p<0.05).

It was also revealed that the BAPO initiator seemed to promote higher reactivity than the CQ/EDAB system in both HEMA-containing resins (Group A versus Group A') and GM-containing resins (Group B versus Group B').

#### Degree of conversion with BAPO and CQ/tertiary amine systems

Table 4 shows the effects on degree of conversion (DC) owing to the concentration of 6-MHPA/HEMA or 6-MHPA/GM in Bis-GMA/3G resins containing 2.0 wt% of BAPO (=IC 1800) (*i.e.*, Groups A and B) or CQ/EDAB at 0.5 or 1.0 wt% (*i.e.*, Groups A' and B'). The DC (%) values obtained ranged between 42.4(4.4) and 51.2(4.3): 44.2(7.5)–47.8 (6.7) for Group A, 44.4(2.4)–51.2(4.3) for Group B, 42.2(4.4)–45.6(2.8) for Group A', and 43.0(4.8)–47.5(2.7) for Group B'. Statistical analysis (ANOVA) showed that there were no significant differences among all the concentrations of 6-MHPA/OH-containing monomer in the unfilled resins initiated by both BAPO and CQ/EDAB initiator systems. Since the absorption of the aromatic double bond was used as an internal standard in FT-IR spectra, the DC of unfilled resins without Bis-GMA and 100% OH-containing monomers were not determined (indicated as “did not test” in Table 4).

## DISCUSSION

To design advanced dental adhesives and resin composites, it is now well recognized that advanced radical polymerization initiators are extremely valuable component<sup>10</sup>. The present study systematically investigated the absorption spectra and photo-initiation behaviors of APO and BAPO derivatives and then compared these results against those of

CQ/tertiary amine system.

This study investigated the UV-VIS spectra, photoinitiation activity and stability of APO and BAPO derivatives in unfilled, light-cured dental resins. Seven kinds of APO derivatives were synthesized by Michaelis–Arbuzov reaction<sup>6</sup> (Fig. 1), which is frequently used in organophosphorus chemistry<sup>14</sup>. Two reaction schemes were used in this study for synthesis. Scheme 1 employed monoacid chlorides and yielded BDPO, TMMPO, TMDPO, DFDPO and NDPO; scheme 2 employed diacid chlorides and yielded PBDPO and TFBDO (Fig. 1). Since they had the acylphosphine oxide moiety [ $>P(=O)-C(=O)-$ ] in the structure, ambient light-shielded flask and hydrophobic dry solvents were used during the reactions. 2,4,6-trimethylbenzoyl chloride (TMC) was a valuable intermediate that reacted with diphenyl methoxy phosphine (DPMP) to yield 2,4,6-trimethylbenzoyl-diphenylphosphine oxide (TMDPO). TMC further reacted with dilithiumphenyl phosphine (DLPP) or dichlorophenyl phosphine (DCPP), and the reaction product was oxidized with hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) to yield bis(2,4,6-trimethylbenzoyl)-phenylphosphine oxide (BTMPO) (=BAPO). In the course of transformation during the synthesis of both APO and BAPO derivatives, a trivalent phosphorus [P(III)] was converted into a pentavalent phosphorus [P(V)], which involved the conversion of  $>P-O-C$  linkage into  $>P(=O)-C$  linkage<sup>6</sup> (Fig. 1).

The UV-VIS spectra of 10 kinds of APO and BAPO derivatives possessed  $\lambda_{max}$  ranging between 365 and 416 nm (Fig. 4, Table 1). The  $\lambda_{max}$  of BDPO, NDPO, and IC 819 (=BAPO) were greater than 400 nm. While the structural formulas of synthesized APO derivatives showed differences, there were slight differences in  $\lambda_{max}$  from the ultraviolet region to the visible light region, which

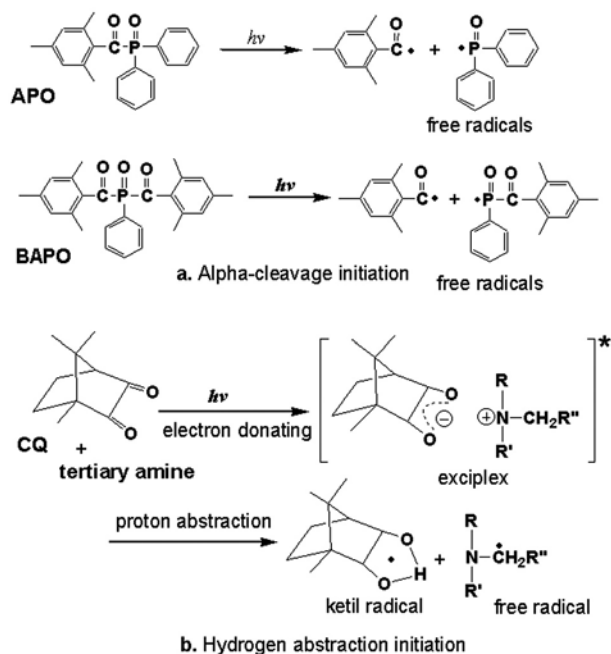


Fig. 5 Photoinitiation mechanisms of acylphosphine oxide (APO), bisacylphosphine oxide (BAPO), and D,L-camphorquinone (CQ)/tertiary amine systems. (a) APO and BAPO initiators undergo so-called  $\alpha$ -cleavage type of photoinitiation (Norrish type I photoreaction), which does not require reducing agents. (b) CQ/tertiary amine system undergoes so-called hydrogen abstraction mechanism which requires donating (reducing) agents, such as tertiary amines.

could be caused by the  $[>P(=O)-C(=O)-]$  moiety. On photo-DSC results, high photoinitiation reactivity was demonstrated by IC 819 (=BAPO), TMDPO (Lab), IC 1800, TMDPO (Com) and TMMPO (Table 1). In sharp contrast, NDPO exhibited a prolonged polymerization time (70.0 sec) with broad photo-DSC peak — which could be caused by the naphthoyl group in the structure, while  $\lambda_{\max}$  (401 nm) was slightly shifted to the visible light region.

On photoinitiator stability, an inherent disadvantage of acylphosphine oxides is that they are generally prone to undergoing solvolytic cleavage of the carbon-phosphorus bond  $[>P(=O)-C(=O)-]$  in the presence of nucleophilic compounds, such as water and alcohol<sup>15-17</sup>. However, it has been shown that the solvolytic stability of acylphosphine oxides is greatly enhanced by the introduction of methyl group, in the *ortho* position where the carbonyl group must be shielded from nucleophilic attack<sup>17</sup> — a phenomenon known as the substituent effect of stereochemistry. Although fluoride group was introduced as a substituted group in aromatic ring, one APO derivative (*i.e.*, TFBDDPO) was indicated as

“inactivated” after synthesis (Table 1). Therefore, APOs and BAPOs with 2,4,6-trimethylbenzoyl moiety (*i.e.*, TMMPO, TMDPO, IC 819, and IC 1800) had improved solvolytic stability sufficient for most practical applications<sup>17</sup>, rendering them more stable in hydrophobic resins such as Bis-GMA and TEGDMA. On the contrary, it was revealed that both bis(diphenylphosphine oxide) derivatives (*i.e.*, PBDPO and TFBDDPO) were inactivated for a few days after their synthesis. It was thus anticipated that BDPO, PBDPO, TFBDDPO, DFDPO, and NDPO might be unstable in the presence of nucleophilic compounds<sup>15-17</sup> because of the absence of methyl groups in the aromatic ring.

To investigate the photoinitiation reactivity (photo-DSC) of APO and BAPO derivatives in Bis-GMA-based resins with or without 10 wt% of acidic adhesive monomer, two APOs (*i.e.*, TMDPO and TMMPO) and two BAPOs (*i.e.*, IC 1800 and IC 819) were selected and incorporated at 1.0 wt% in the resins (Table 2). In conjunction, four kinds of acidic adhesive monomers bearing carboxyl group (4-AET), acid anhydride group (4-AETA, 4-META) and phosphonic acid group (6-MHPA) were used. It was shown that both APO and BAPO initiators presented similar high reactivity, and that the initiators were not influenced by the presence of acidic adhesive monomers. Therefore, there were no significant differences among the four adhesive monomers in unfilled Bis-GMA-based resins ( $p < 0.05$ ). It is also noteworthy that IC 819 in Bis-GMA/3G revealed the highest reactivity at 5.9 sec.

Since APO and BAPO undergo  $\alpha$ -cleavage type of photoinitiation mechanism (Norrish type I system) to form neutral free radicals (Fig. 5a), it was thought that they acted as photoinitiators without adverse interaction with the acidic adhesive monomers. Regarding the detailed mechanism, it is well established that TMDPO undergoes rapid  $\alpha$ -cleavage from a triplet excited state to afford the 2,4,6-trimethylbenzoyl radical  $[(CH_3)_3Ph-C\cdot(=O)]$  and diphenylphosphinoyl radical  $(Ph)_2P\cdot(=O)$ <sup>5,18</sup> (Fig. 5a). Sumiyoshi *et al.*<sup>19</sup> investigated to elucidate the kinetics and mechanism of the photolysis of TMDPO, which are capable of undergoing  $\alpha$ -cleavage type photoinitiation, in the presence of olefinic compounds (radical polymerizable monomers). Findings demonstrated rather high rate constants (in  $l\ mol^{-1}s^{-1}$ ) for the reaction of radicals with radical polymerizable monomers:  $6.0 \times 10^7$  (methyl methacrylate),  $2.3 \times 10^7$  (methacrylate), and  $6.0 \times 10^7$  (styrene). The quantum yield ( $\phi$ ) of radical formulation is  $\phi(TMDPO) = 0.5$  to  $0.7^5$ .

This study further compared the photoinitiation activity of BAPO (IC 1800) against that of CQ/EDAB system in terms of polymerization time (Table 3) and degree of conversion (Table 4). The effect of the



concentrations of 6-MHPA/HEMA and 6-MHPA/GM in Bis-GMA/3G resins activated by both photoinitiator systems on photopolymerization was further investigated. While there were no statistically significant differences among the four kinds of APO and BAPO photoinitiators or four kinds of adhesive monomers used on the polymerization time results of unfilled resins ( $p < 0.05$ ) (Table 2), IC 1800 for BAPO and 6-MHPA for adhesive monomer were employed for these two evaluations.

Regarding the concentration of BAPO and base resins, a recent study<sup>19</sup> noted that a BAPO (Irgacure 1850) initiator, at the 1.0% level, had significant shelf life problems when used with urethane dimethacrylate (UDMA) comonomer systems. Other composites formulated with the BAPO, but not containing UDMA did not exhibit this apparent stability problem. At the higher (2.0%) concentration level of BAPO, any diminution of available free radical is presumably not sufficient to adversely affect the photopolymerization process<sup>19</sup>. Therefore, 2% BAPO (IC 1800) and Bis-GMA-based resins were employed in this study (Tables 3 and 4).

On polymerization time, it was found that the concentration of 6-MHPA/OH-containing monomers (*i.e.*, HEMA, GM) significantly affected the polymerization behavior of unfilled resins initiated by both BAPO and CQ/EDAB, such that significant differences were observed for all the concentrations of 6-MHPA/OH-containing monomers ( $p < 0.05$ ). Prolonged polymerization time was mainly caused by the concentration of OH-containing monomers, because all 100% HEMA and 100% GM resins indicated significantly prolonged polymerization times ( $p < 0.05$ ) (Table 3). This was in sharp contrast to the non-existence of significant differences among the four acidic monomers (10 wt%) in Bis-GMA/3G resins initiated by BAPO ( $p < 0.05$ ) (Table 2). It was also shown that the BAPO initiator exhibited higher reactivity than CQ/EDAB system in unfilled HEMA- and GM-containing resins. This was suggested to be caused by the different photoinitiation mechanisms between the two photoinitiator systems (Fig. 5).

Unlike APO and BAPO photoinitiators, CQ as a photosensitizer requires an electron donating agent (reducing agent), such as tertiary amines, to initiate the hydrogen abstraction mechanism. In the photoinitiation mechanism of CQ/tertiary amine system, CQ ( $\lambda_{\text{max}} = 473 \text{ nm}$ ) absorbs the energy of visible rays to form excited states (CQ\*).  $\alpha$ -hydrogen of tertiary amine then donates CQ\* to form CQ-amine exciplex (excited state complex), which is subsequently decomposed to CQ ketyl radical and free radicals derived from tertiary amines. The free radicals can initiate the radical photopolymerization of monomers<sup>2)</sup> (Fig. 5b). It is recently noted that increasing the delay time before light curing of resin

composite degraded the bond strength to dentin. This was attributed to the quaternary ammonium salt that was formed by the interaction of acidic group ( $\pi$  donor) of adhesive monomers with tertiary amines ( $\pi$  acceptor)<sup>2)</sup>, which is an inherent disadvantage of CQ/amine system. Furthermore, in the present study, it was revealed that 100% HEMA (200 sec) and 100% GM (195.2 sec) resins initiated by CQ/EDAB system showed significantly prolonged polymerization times that were more influenced by OH-containing monomers than acidic adhesive monomers (Table 3).

On the degree of conversion (DC), it was determined by the subtraction of FT-IR spectra measured before and after light activation for 30 seconds (Fig. 3). Based on the results obtained, it was found that there were no significant differences between BAPO and CQ/EDAB systems among all the concentrations of 6-MHPA/HEMA and 6-MHPA/GM in Bis-GMA/3G resins ( $p < 0.05$ ) (Table 4), whereas polymerization time was significantly influenced by the concentration ( $p < 0.05$ ) (Table 3). It was revealed that the DC values [BAPO: 44.2(6.5)–51.2(4.3)%; CQ/EDAB: 42.4(4.4)–47.5(3.7)%] obtained in this study, after 30 seconds of photoirradiation, were almost comparable with the DC value [53 % after 20 sec of photoirradiation] previously reported by Park *et al.*<sup>12)</sup>. In the latter study, CQ/1-phenyl-1,2-propanedione (PPD) initiator was used, which was different from the photoinitiators and compositions employed in the present study<sup>12)</sup>. A recent study<sup>19</sup> also reported that as the higher level (2.0 %) of BAPO (IC 1850) performed as well as the CQ/amine system, this class of initiators may hold promise for use in dental composites.

Findings of this study could support the hypothesis that APO and BAPO photoinitiators exhibit reactivity comparable with that of CQ/tertiary amine system. Furthermore, it may be added that the BAPO initiator exhibited higher photoinitiator reactivity than CQ/EDAB system in unfilled HEMA- and GM-containing resins.

To develop more advanced, light-cured dental resins, further investigation efforts on photopolymerization should continue unabated with special focus on advanced photoinitiator technologies. This is because the development of more active photoinitiators is a chief prerequisite to the development of improved, light-cured dental resins.

## CONCLUSIONS

The present study systematically investigated the photoinitiation behaviors of APO and BAPO derivatives in comparison to CQ/EDAB system. Based on the findings in this study, the following conclusions were drawn:

- (1) The UV-VIS spectra of the 10 kinds of APO and BAPO derivatives investigated possessed  $\lambda_{\text{max}}$  ranging between 365 and 416 nm.
- (2) Short polymerization time (sec) was achieved with IC 819 (=BAPO) at 5.9 sec, TMDPO (Lab) at 6.7 sec, IC 1800 (=BAPO) at 6.8 sec, TMDPO (Com) at 7.5 sec, and TMMPO at 7.5 sec.
- (3) APO (*i.e.*, TMDP and TMMPO) and BAPO (*i.e.*, IC 819 and IC 1800) photoinitiators exhibited higher reactivity that was not influenced by the presence of 10 wt% acidic adhesive monomer (*i.e.*, 4-AET, 4-AETA, 4-META, or 6-MHPA) formulated in unfilled Bis-GMA-based resins ( $p < 0.05$ ).
- (4) BAPO (IC 1800) exhibited higher photoinitiator reactivity than the CQ/EDAB system in unfilled, 6-MHPA/HEMA or 6-MHPA/GM-containing Bis-GMA-based resins.
- (5) However, there were no significant differences between BAPO [44.2(6.5)–51.2(4.3)] and CQ/EDAB [42.4(4.4)–47.5(3.7)] in degree of conversion (%) ( $p < 0.05$ ).

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