

**Table 1. Conditions of the Mitsunobu Reaction for the Synthesis of (4b)**

| Entry | Condition     |           | Ratio <sup>a</sup> | Yield (%) <sup>b</sup> |
|-------|---------------|-----------|--------------------|------------------------|
|       | Reflux (12 h) | RT (12 h) |                    |                        |
| 1     | +             | -         | 1:1:1:1            | 18                     |
| 2     | -             | +         | 1:1:2:2            | 24                     |
| 3     | -             | +         | 1:1:1.5:1.5        | 46                     |
| 4     | -             | +         | 1:1.2:1.5:1.5      | 62                     |

<sup>a</sup> Molar ratio of compound **2**: p-chlorobenzyl alcohol: diisopropylazodicarboxylate: triphenylphosphin.

<sup>b</sup> Obtained after purification by chromatography on silica gel.

ortho positions on the benzene ring were low. In contrast, the electron-donating group had a good yield, particularly at the para position on the benzene ring.<sup>5</sup>

## EXPERIMENTAL SECTION

### Instruments

Infrared spectra were recorded on a Perkin-Elmer Model 882 (New York, U.S.A.) and a Nicolet 510 PFT (New York, U.S.A.) spectrophotometer. Proton NMR spectra were obtained on a Bruker AC-300 and a Bruker DRX-500 (Karlsruhe, Germany). Melting points were determined using a Yanaco MP-S3 (Tokyo, Japan) melting point apparatus. Mass spectra were obtained on a Joel JMS HX 110 FABMS (Tokyo, Japan) spectrometer.

### General Procedures

The reaction of compound **2** with alcohols (**3a**–**3c**): Alcohol was added to distilled tetrahydrofuran (20 mL), and then triphenylphosphin (0.4 mM) and compound **2** (0.3 mM) were added. After 10 min diisopropyl azodicarboxylate (0.4 mM) was added and the reaction was stirred for 12 h under N<sub>2</sub>. After the solvent was removed under reduced pressure and the resulting residue was triturated with 1:1 hexane/Et<sub>2</sub>O to remove the Ph<sub>3</sub>PO by-product, the crude product was purified by SiO<sub>2</sub> chromatography. The residue was crystallized from MeOH.

### N-4-methylbenzylcantharidinimide (4a)

Mp 120–122 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 1.10 (6H, s, CH<sub>3</sub> × 2), 1.66–1.77 (4H, m), 2.27 (3H, s,

**Table 2. Preparation of Cantharidinimides 4a–c**

| Entry | Substrate | Product   | Yield (%) <sup>a</sup> |
|-------|-----------|-----------|------------------------|
| 1     | <b>3a</b> | <b>4a</b> | 70                     |
| 2     | <b>3b</b> | <b>4b</b> | 62                     |
| 3     | <b>3c</b> | <b>4c</b> | 48                     |

<sup>a</sup> Obtained after purification by chromatography on silica gel.

C4-CH<sub>3</sub>), 4.55 (2H, s, OCH), 4.59 (2H, s, NCH<sub>2</sub>), 7.06 (2H, d, *J* = 7.5 Hz, phenyl H-3, H-5), 7.16 (2H, d, *J* = 7.5 Hz, phenyl H-2, H-6); IR (KBr): 1734 cm<sup>-1</sup> (amide); MS *m/z* (rel. int): 299 [M]<sup>+</sup> (30), 105 (100), 138 (60).

### N-4-chlorobenzylcantharidinimide (4b)

Mp 124–125 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 1.11 (6H, s, CH<sub>3</sub> × 2), 1.68–1.79 (4H, m, CH<sub>2</sub> × 2), 4.56 (2H, s, OCH), 4.60 (2H, s, NCH<sub>2</sub>), 7.45 (2H d, *J* = 6.8 Hz, phenyl H-2, H-6), 7.65 (2H, d, *J* = 6.8 Hz, phenyl H-3, H-5); IR (KBr), 1700 cm<sup>-1</sup> (amide); MS *m/z* (rel. int): 319 [M]<sup>+</sup> (20), 138 (40), 125 (50), 70 (100).

### N-4-nitrobenzyl-cantharidinimide (4c)

Mp 168–169 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 1.11 (6H, s, CH<sub>3</sub> × 2), 1.66–1.77 (4H, m, CH<sub>2</sub> × 2), 2.27 (3H, s, CCH<sub>3</sub>), 4.55 (2H, d, *J* = 2.2 Hz, OCH), 4.59 (2H, s, NCH<sub>2</sub>), 7.44 (2H, d, *J* = 8.5 Hz, phenyl H-2, H-6), 8.14 (2H, d, *J* = 8.6, phenyl H-3, H-5); IR (KBr): 1733 cm<sup>-1</sup> (amide); MS *m/z* (rel. int): 330 [M]<sup>+</sup> (5), 85 (30), 71 (70), 57 (100).

## ACKNOWLEDGEMENTS

We thank the National Science Council, R.O.C. for financial support (NSC 87-2314-B-038-011).

## REFERENCES AND NOTES

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