

HIGHLY REACTIVE ELECTROGENERATED ZINC: PREPARATION AND ITS USE IN CROSS-COUPLING REACTIONS

Aishah Abdul Jalil¹, Sugeng Triwahyono², Kurono Nobuhito³, Takasugi Shingo³, and Tokuda Masao³

¹Department of Chemical Engineering, Faculty of Chemical and Natural Resources Engineering,

²Ibnu Sina Institute for Fundamental Science Studies, Universiti Teknologi Malaysia, 81310 UTM Skudai, Johor

³Division of Molecular Chemistry, Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan

ABSTRACT

Highly reactive zinc metal was prepared by electrolysis of a *N,N*-dimethylformamide (DMF) solution containing naphthalene and a supporting electrolyte in a one-compartment cell fitted with a platinum cathode and a zinc anode. This highly reactive electrogenerated zinc (EGZn/Naph) was used for transformation of bromoalkanes into the corresponding organozinc bromides, which can not be achieved by the use of usual zinc metals. Reaction of the organozinc compounds were thus prepared with various aryl iodides in the presence of 5 mol% of palladium catalyst to give the corresponding cross coupling products in high yields. Arylzinc iodides were also prepared by the use of this highly reactive zinc, and they were reacted with other iodides to give the corresponding cross-coupled biaryls in good yields.

Keywords : Highly Reactive Zinc, Preparation, Cross-Coupling, Palladium Catalyst

1.0 INTRODUCTION

Organozinc compounds are very useful organometallic compounds for the forming reaction of carbon-carbon bonds [1]. Organozinc halides can usually be prepared by direct insertion of zinc metal into organic halides, but commercially available zinc metal is generally poorly reactive [2]. Therefore, activation of the metal is necessary for preparation of organozinc halides. Various method of zinc activation, such as the reduction of zinc halide with alkaline metal or alkali metal naphthalenide, have been reported [3]-[5]. These methods, however, require high temperatures and long reaction times, or vigorous stirring during the reaction.

A new method for preparation of reactive zinc by electrolysis and its use in facile isoprenylation [6] and allylation of aldehydes and ketones was reported elsewhere [7],[8]. It was shown that this electrogenerated reactive zinc (EGZn) was an aggregation of very fine crystalline zinc particles with a large surface area [8]. A facile preparation of organic compounds from functionalized alkyl iodides by using EGZn and their cross-couplings with aryl halides (Scheme 1), was also reported [9].

However, no organozinc compounds have been obtained from alkyl bromides or were only obtained in very low yields from the corresponding organic bromides, even by the use of reactive EGZn. Recently, the authors have developed a new electrochemical method for preparation of more highly reactive zinc by using naphthalene as a mediator. Such methods for preparing reactive zinc are very convenient and useful in organic synthesis. In this paper, the authors report a new method for preparing highly reactive zinc by electrolysis and its use in cross-coupling reaction of bromoalkanes with aryl iodides as well as in aryl-aryl cross-coupling reaction.

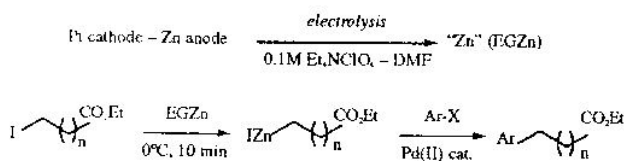
2.0 EXPERIMENTAL

A. General methods

IR spectra were recorded on a JASCO IR-810 infrared spectrometer (neat between NaCl plates). ¹H NMR spectra were recorded on a JEOL JNM-EX270 (270 MHz) and JNM-LA400FT NMR (400 MHz). ¹H chemical shift is reported in ppm (δ) using tetramethylsilane as an internal standard. High and low resolution mass spectra were determined with a JEOL JMS-AX500 or JEOL JMS-SX102A spectrometer. Products were isolated by kugelrohr distillation or thin layer chromatograph and column chromatograph (Merck Kieselgel 60 PF₂₅₄).

B. Solvent and reagents

Commercially available anhydrous *N,N*-dimethylformamide (DMF) and tetrahydrofuran (THF) packed under a nitrogen atmosphere (Kanto Chemical) were used without further purification. Tetraethylammonium perchlorate was prepared according to the previous reported method [9]. The zinc plate (Nilaco) is commercially available in more than 99.9%



Scheme 1

purities, and was washed with 2N HCl, methanol, acetone and dried before electrolysis. Ethyl 4-bromobutanoate, ethyl 3-bromo-propanoate, 4-bromobutanenitrile, bromocyclohexane, bromohexane, iodobenzene are commercially available, and were purified by distillation prior to use. 4-Iodoacetophenone and 4-iodoanisole are also commercially available and were used without further purification. Naphthalene (Junsei Chemical, 99%) was used after recrystallisation from methanol.

C. Preparation of electrogenerated highly reactive zinc (EGZn/Naph)

A normal one-compartment cell equipped with a magnetic stirrer and a serum cap was used. Electrogenerated highly reactive zinc (6 mmol) was prepared by the electrolysis of a DMF solution (10 ml) containing 0.1M Et₄NClO₄ (230 mg) and naphthalene (12 mmol) in a one-compartment cell fitted with a platinum plate cathode (2x2 cm²) and a zinc plate anode (2x2 cm²). Electrolysis was carried out at -10°C at a constant current of 60 mA/cm² under nitrogen atmosphere. The quantity of electricity passed was 0.012 F, which corresponded to 2 F per mol of zinc metal. The amount of EGZn/Naph was calculated from the weight of dissolved zinc anode metal. A solution containing EGZn/Naph was directly used for the preparation of organozinc compound after the zinc anode was removed from the electrolysis cell.

D. General procedure for cross-coupling reaction using EGZn/Naph

To a DMF solution containing EGZn/Naph was added ethyl 4-bromobutanoate (**1a**) (5 mmol) and the mixture was stirred at 50°C under nitrogen atmosphere for 1 h. DMF solution (5 ml) of aryl iodide (4 mmol) and Pd(P(*o*-Tol)₃)₂Cl₂ (0.11 mmol) was added, and the reaction mixture was stirred at 70°C for 3 h. The resulting mixture was quenched with HCl solution and filtered. The filtrate was extracted with diethyl ether (50 ml x 3) and the combined organic layers were washed with water (100 ml x 3), saturated Na₂S₂O₃ solution (100 ml x 1) and saturated NaCl (100 ml x 1) and dried over MgSO₄. After evaporation of diethyl ether, the crude product was purified by column chromatograph on silica gel with ethyl acetate-hexane (1:4) to give ethyl 4-phenylbutanoate **4**.


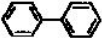
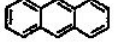

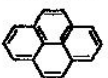
3.0 RESULTS AND DISCUSSIONS

A. ELECTROCHEMICAL PREPARATION OF HIGHLY REACTIVE ELECTROGENERATED ZINC (EGZn/Naph)

Electrochemically generated highly reactive zinc (EGZn/Naph) was readily prepared by electrolysis of a *N,N*-dimethylformamide (DMF) solution containing naphthalene and 0.1M tetraethyl ammonium perchlorate (TEAP) in a one-compartment cell fitted with a platinum cathode and a zinc anode. Electrolysis at -10°C at a constant current of 60 mA/cm² in a nitrogen atmosphere was found to give highly reactive zinc. However, other polyaromatic compounds such as biphenyl, phenanthrene, and pyrene could also be used as

mediators to obtain activated EGZn/PA (PA: polyaromatic compound). The reactivities of these EGZn/PA are summarised in Table 1. They were effective for the formation of organozinc compounds except anthracene, but naphthalene was chosen for the present transformation from the point of view of availability.

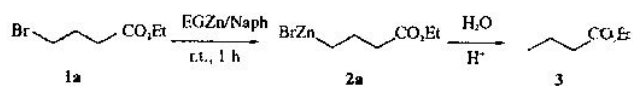
Table 1. Effect of various polyaromatic compounds on the reactivity of EGZn/Naph*

| Entry | Polyaromatic | Conversion (%) ^a |
|-------|---|-----------------------------|
| 1 |  | 52 |
| 2 |  | 57 |
| 3 |  | 8 |
| 4 |  | 68 |
| 5 |  | 84 |

EGZn (6 mmol), Polyaromatic (12 mmol), Ethyl 4-bromobutanoate (**1a**) (5 mmol), 0.1M TEAP-DMF. * Conversion was determined by Gas chromatograph

At the cathode, a one-electron reduction of naphthalene molecule occurred to give naphthalene radical anion preferentially. The formation of the naphthalene radical anion was shown by the dark green color appeared on the surface of the cathode. On the other hand, at the anode, dissolution of the zinc metal occurred to give zinc ions, which were reduced by the naphthalene radical anions to give zero-valence highly reactive zinc, EGZn/Naph. The EGZn/Naph was an aggregation of very fine zinc particles with much smaller sizes than those of EGZn and was dispersed in the DMF solution [8]. Although the nature and the structure of EGZn/Naph are not clear at the present stage, it was found to be very reactive towards an oxidative addition to organic bromides.

The high reactivity of EGZn/Naph in the forming reaction of organozinc bromide (**2a**) from ethyl 4-bromobutanoate (**1a**) was compared with the reactivity of other zinc metals (Scheme 2). The results are summarised in Table 2.



Scheme 2

These results show that the use of commercially available zinc or EGZn with the addition of naphthalene was not effective in terms of reactivity and that the presence of naphthalene molecules in the electrochemical reduction step is required for the preparation of much higher reactive zinc.

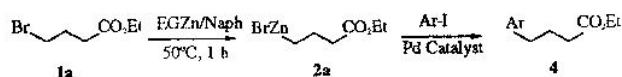
Table 2. Transformation of bromoester 1a to organozinc 2a under various conditions^a

| Entry | Zn | Temperature (°C) | Time (h) | Conversion of 1a (%) ^b |
|-------|--------------------------|------------------|----------|-----------------------------------|
| 1 | Zn + Naph ^c | r.t. | 18 | 0 |
| 2 | Zn + Naph ^c | 70 | 3 | 0 |
| 3 | EGZn + Naph ^d | r.t. | 3 | 37 |
| 4 | EGZn/Naph | r.t. | 1 | 95 |

^aEthyl 4-bromobutanoate (1a) (5 mmol) was reacted in DMF (10 ml) with zinc metal (6 mmol). ^bDetermined by gas chromatograph analysis. ^cCommercially available Rare Metallic zinc (6 mmol) in the presence of naphthalene (12 mmol) was used. ^dEGZn (6 mmol) in the presence of naphthalene (12 mmol) was used

B. Cross-coupling of Functionalised Bromoalkanes with Aryl Iodides using EGZn/Naph

Ethyl 4-bromobutanoate (1a) can efficiently be transformed into the corresponding organozinc 2a by a reaction with EGZn/Naph at 50°C. Cross-coupling of 2a with iodobenzene, 4-acetyliodobenzene or 4-methoxyiodobenzene at 70°C for 2 h in the presence of 5 mol% Pd(P(*o*-Tol))₂Cl₂ catalyst gave the corresponding cross-coupled products 4 in 75–97% isolated yields (Scheme 3) (Table 3, entries 1–3).

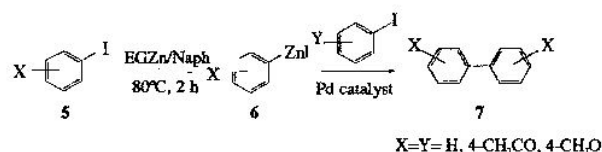


Scheme 3

Table 3. Cross-coupling of functionalised bromoalkanes (1a–1e) with Aryl Iodides using EGZn/Naph^a

| Entry | Bromide | ArI | Product | Isolated Yield (%) |
|-------|---|--|---|--------------------|
| 1 | Br(CH ₂) ₃ CO ₂ Et (1a) | C ₆ H ₅ I (5a) | C ₆ H ₅ (CH ₂) ₃ CO ₂ Et (4a) | 97 |
| 2 | Br(CH ₂) ₃ CO ₂ Et (1a) | <i>p</i> -CH ₃ COC ₆ H ₄ I (5b) | <i>p</i> -CH ₃ COC ₆ H ₄ (CH ₂) ₃ CO ₂ Et (4b) | 84 |
| 3 | Br(CH ₂) ₃ CO ₂ Et (1a) | <i>p</i> -CH ₃ OC ₆ H ₄ I (5c) | <i>p</i> -CH ₃ OC ₆ H ₄ (CH ₂) ₃ CO ₂ Et (4c) | 75 |
| 4b | Br(CH ₂) ₂ CO ₂ Et (1b) | C ₆ H ₅ I | C ₆ H ₅ (CH ₂) ₂ CO ₂ Et (4d) | 84 |
| 5 | Br(CH ₂) ₂ CO ₂ Et (1b) | <i>p</i> -CH ₃ COC ₆ H ₄ I | <i>p</i> -CH ₃ COC ₆ H ₄ (CH ₂) ₂ CO ₂ Et (4e) | 81 |
| 6 | Br(CH ₂) ₂ CO ₂ Et (1b) | <i>p</i> -CH ₃ OC ₆ H ₄ I | <i>p</i> -CH ₃ OC ₆ H ₄ (CH ₂) ₂ CO ₂ Et (4f) | 63 |
| 7 | Br(CH ₂) ₃ CN (1c) | C ₆ H ₅ I | C ₆ H ₅ (CH ₂) ₃ CN (4g) | 89 |
| 8 | Br(CH ₂) ₃ CN (1c) | <i>p</i> -CH ₃ COC ₆ H ₄ I | <i>p</i> -CH ₃ COC ₆ H ₄ (CH ₂) ₃ CN (4h) | 91 |
| 9 | Br(CH ₂) ₃ CN (1c) | <i>p</i> -CH ₃ OC ₆ H ₄ I | <i>p</i> -CH ₃ OC ₆ H ₄ (CH ₂) ₃ CN (4i) | 97 |
| 10 | Br(CH ₂) ₃ CH ₃ (1d) | C ₆ H ₅ I | C ₆ H ₅ (CH ₂) ₃ CH ₃ (4j) | 89 |
| 11 | Br(CH ₂) ₃ CH ₃ (1d) | <i>p</i> -CH ₃ COC ₆ H ₄ I | <i>p</i> -CH ₃ COC ₆ H ₄ (CH ₂) ₃ CH ₃ (4k) | 85 |
| 12 | Br(CH ₂) ₃ CH ₃ (1d) | <i>p</i> -CH ₃ OC ₆ H ₄ I | <i>p</i> -CH ₃ OC ₆ H ₄ (CH ₂) ₃ CH ₃ (4l) | 71 |
| 13 | C ₆ H ₁₁ Br (1e) | C ₆ H ₅ I | C ₆ H ₅ C ₆ H ₁₁ (4m) | 77 |
| 14 | C ₆ H ₁₁ Br (1e) | <i>p</i> -CH ₃ COC ₆ H ₄ I | <i>p</i> -CH ₃ COC ₆ H ₄ C ₆ H ₁₁ (4n) | 71 |
| 15 | C ₆ H ₁₁ Br (1e) | <i>p</i> -CH ₃ OC ₆ H ₄ I | <i>p</i> -CH ₃ OC ₆ H ₄ C ₆ H ₁₁ (4o) | 76 |

^a Bromides 1a–1e (5 mmol), except 1b were reacted at 50°C for 1 h with EGZn/Naph (6 mmol), and the resulting DMF solutions containing 2a–2e were reacted with ArI (4 mmol) in the presence of 5 mol% Pd(P(*o*-Tol))₂Cl₂ at 70°C for 2 h. ^b Bromides 1b (5 mmol) was reacted at 0°C for 1 h with EGZn/Naph (6 mmol), and subsequent cross-coupling reaction is similar as above

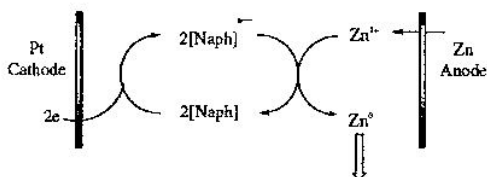


Scheme 4

The results are summarised in Table 4. Lower yield was observed from the reaction of organozinc compound of 4-methoxy-iodobenzene with iodobenzene (entry 3).

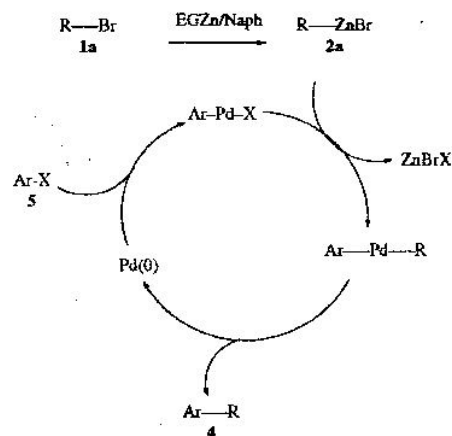
D. Reaction Pathways

Probable reaction pathways of the preparation of EGZn/Naph are shown in Scheme 4. Electrolysis of a DMF solution with a platinum cathode and a zinc anode results in anodic dissolution of zinc metal to give zinc ions. On the other hand, at the cathode, a one-electron reduction of naphthalene molecule occurs to give radical anion of naphthalene, which was shown by the appearance of the dark green color on the surface of the cathode [10]. Reduction of zinc ion with naphthalene radical anion would give zero-valent reactive zinc (EGZn/Naph).



Scheme 4

Probable reaction pathways of the present cross-couplings are shown in Scheme 5. Oxidative addition of Pd(0) to aryl halides would give Ar-Pd-X, which undergoes metal exchange reaction with organozinc bromide 2 to give an intermediate Ar-Pd-R. Reductive elimination of Ar-Pd-R would give the cross-coupling product, ethyl 2-arylpropenoates 4.



Scheme 5

4.0 CONCLUSION

A new electrochemical method for preparation of highly reactive zinc (EGZn/Naph) by using naphthalene as a mediator in the electrolysis was developed. The corresponding organozinc bromide could readily be prepared under mild conditions by the reaction of ethyl 4-bromobutanoate with EGZn/Naph. Subsequent cross-coupling reaction of the organozinc bromide with various aryl halides readily took place in the presence of a palladium catalyst to give the corresponding cross-coupled products in high yields.

ACKNOWLEDGEMENT

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(Note: The spectral data of the products are shown in Table 5 on page 69)

Table 4. Palladium catalysed Aryl-aryl Cross-coupling reaction using EGZn/Naph^a


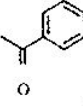
| Entry | ArI | Product | Isolated Yield (%) | |
|-------|---|---|---|-----------------|
| 1 | C ₆ H ₅ I | <i>p</i> -CH ₃ COC ₆ H ₄ I | <i>p</i> -CH ₃ COC ₆ H ₄ C ₆ H ₅ | 82 |
| 2 | <i>p</i> -CH ₃ COC ₆ H ₄ I | <i>p</i> -CH ₃ OC ₆ H ₄ I | <i>p</i> -CH ₃ COC ₆ H ₄ C ₆ H ₄ OCH ₃ - <i>p</i> | 70 |
| 3 | <i>p</i> -CH ₃ OC ₆ H ₄ I | C ₆ H ₅ I | <i>p</i> -CH ₃ OC ₆ H ₄ C ₆ H ₅ | 51 ^b |

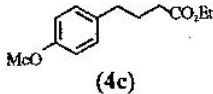
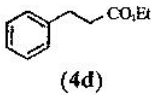
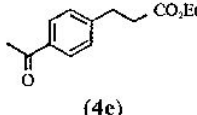
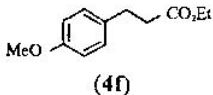
^a Iodobenzene, 4-acetyl iodobenzene or 4-methoxyiodobenzene (5 mmol), were reacted at 80°C for 2 h with EGZn/Naph (6 mmol), and the resulting DMF solutions were reacted with ArI (4 mmol) in the presence of 5 mol% Pd(P(*o*-Tol)₃)₂Cl₂ at 70°C for 2 h. ^b Cross-coupling was carried out in THF solution

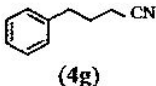
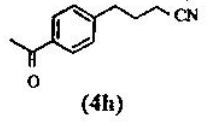
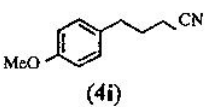
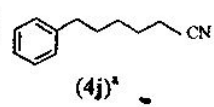
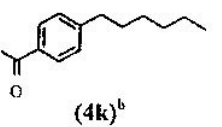
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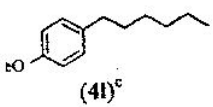
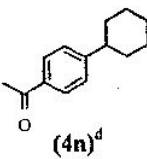
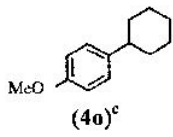
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Table 5. Spectral data of the products

| Product | bp°C/ mmHg | ¹ H NMR (ppm) | IR (neat, cm ⁻¹) | MS (70 eV), m/e | Analysis |
|---|---------------|--|--|---|--|
|  (4a) | 97/4 | 7.23 (5H, m), 4.12 (2H, q, <i>J</i> =7.26 Hz), 2.65 (2H, t, <i>J</i> =7.59 Hz), 2.32 (2H, t, <i>J</i> =7.59 Hz), 1.96 (2H, quin, <i>J</i> =7.59 Hz), 1.25 (3H, t, <i>J</i> =7.26 Hz). | 1734, 1498, 700 | EIMS 192 (M ⁺ , 60), 147 (76), 117 (18), 104 (100), 91 (85), 88 (79), 70 (25). HRMS Calcd for C ₁₂ H ₁₆ O ₃ <i>m/z</i> 192.1124. Found <i>m/z</i> 192.1137. | C ₁₂ H ₁₆ O ₃ : C, 74.97; H, 8.39 Found: C, 74.75; H, 8.45 |
|  (4b) | 126/0.2 | 7.89 (2H, d, <i>J</i> =8.42 Hz), 7.28 (2H, d, <i>J</i> =8.42 Hz), 4.13 (2H, q, <i>J</i> =7.26 Hz), 2.72 (2H, t, <i>J</i> =7.76 Hz), 2.59 (3H, s), 2.32 (2H, t, <i>J</i> =7.42 Hz), 1.99 (2H, m), 1.26 (3H, t, <i>J</i> =7.26 Hz). | 1734, 1683, 1607, 1571, 1413 | EIMS 234 (M ⁺ , 58), 219 (19), 189 (12), 147 (100), 131 (26), 118 (7), 105 (6), 90 (9). HRMS Calcd for C ₁₄ H ₁₈ O ₃ <i>m/z</i> 234.1274. Found <i>m/z</i> 234.1265. | C ₁₄ H ₁₈ O ₃ : C, 71.77; H, 7.74. Found: C, 71.83; H, 7.83. |

| Product | bp°C/ mmHg | ¹ H NMR (ppm) | IR (neat, cm ⁻¹) | MS (70 eV), m/e | Analysis |
|---|---------------|--|--|--|---|
|  (4c) | 99/0.2 | 7.09 (2H, dd, $J=1.98, 4.61$ Hz), 6.83 (2H, dd, $J=1.98, 4.61$ Hz), 4.12 (2H, q, $J=7.10$ Hz), 3.78 (3H, s), 2.59 (2H, t, $J=7.43$ Hz), 2.30 (2H, t, $J=7.59$ Hz), 1.92 (2H, m), 1.25 (3H, t, $J=7.10$ Hz). | 1734, 1613, 1514, 1247, 1037 | EIMS 222 (M^+ , 30), 177 (20), 134 (100), 121 (63), 91 (10). HRMS Calcd for C ₁₃ H ₁₈ O ₃ m/z 222.1198. Found m/z 222.1227. | C ₁₃ H ₁₈ O ₃ : C, 70.25; H, 8.16 Found: C, 70.22; H, 8.16 |
|  (4d) | 85/2.6 | 7.24 (5H, m), 4.12 (2H, q, $J=7.26$ Hz), 2.95 (2H, t, $J=7.59$ Hz), 2.62 (2H, t, $J=7.59$ Hz), 1.23 (3H, t, $J=7.26$ Hz). | 1737, 1605, 1498 | EIMS 178 (M^+ , 48), 133 (16), 104 (100), 91 (53). HRMS Calcd for C ₁₁ H ₁₄ O ₂ m/z 178.1046. Found m/z 178.1020. | C ₁₁ H ₁₄ O ₂ : C, 74.13; H, 7.92 Found: C, 73.91; H, 7.92. |
|  (4e) | 108/0.25 | 7.89 (2H, d, $J=8.29$ Hz), 7.30 (2H, dd, $J=8.29$ Hz), 4.13 (2H, q, $J=7.10$ Hz), 3.01 (2H, t, $J=7.76$ Hz), 2.64 (2H, t, $J=7.76$ Hz), 2.58 (3H, s), 1.23 (3H, t, $J=7.10$ Hz). | 1735, 1684, 1608, 1571, 1415 | EIMS 220 (M^+ , 49), 205 (100), 177 (11), 149 (9), 131 (18). HRMS Calcd for C ₁₃ H ₁₆ O ₃ m/z 220.1151. | C ₁₃ H ₁₆ O ₃ : C, 70.89; H, 7.32 Found: C, 70.68; H, 7.36. |
|  (4f) | 79/0.16 | 7.12 (2H, d, $J=8.29$ Hz), 6.82 (2H, d, $J=8.29$ Hz), 4.12 (2H, q, $J=7.26$ Hz), 3.78 (3H, s), 2.89 (2H, t, $J=7.76$ Hz), 2.58 (2H, t, $J=7.76$ Hz), 1.23 (3H, t, $J=7.26$ Hz). | 1736, 1613, 1515, 1248, 1037 | EIMS 208 (M^+ , 31), 134 (39), (100) 121 HRMS Calcd for C ₁₂ H ₁₆ O ₃ m/z 208.1141. Found m/z 208.1120. | C ₁₂ H ₁₆ O ₃ : C, 69.21; H, 7.74 Found: C, 69.17; H, 7.80. |

| Product | bp°C/ mmHg | ¹ H NMR (ppm) | IR (neat, cm ⁻¹) | MS (70 eV), m/e | Analysis |
|--|---------------|--|---|---|---|
|  (4g) | 75 /0.2 | 7.25 (5H, m), 2.78 (2H, t, J=7.26 Hz), 2.32 (2H, t, J=7.26 Hz), 1.98 (2H, qui, J=7.26 Hz) | 2244, 1603, 1497 | EIMS 145 (M ⁺ , 36), 104 (25), 91 (100). HRMS Calcd for C ₁₀ H ₁₁ N m/z 145.0879. | C ₁₀ H ₁₁ N: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.72; H, 7.64; N, 9.61. |
|  (4h) | 120 /0.2 | 7.92 (2H, d, J=7.92 Hz), 7.30 (2H, d, J=7.92 Hz), 2.86 (2H, t, J=7.26 Hz), 2.60 (3H, s), 2.34 (2H, t, J=7.26 Hz), 2.01 (2H, qui, J=7.26 Hz). | 2246, 1683, 1608, 1499, 1458 | EIMS 187 (M ⁺ , 18), 172 (100), 144 (7), 131 (4), 116 (9). HRMS Calcd for C ₁₃ H ₁₃ ON m/z 187.0967. | C ₁₃ H ₁₃ ON: C, 76.98; H, 7.00; N, 7.48. Found: C, 76.43; H, 7.09; N, 7.48. |
|  (4i) | 95 /0.2 | 7.10 (2H, dd, J=2.97, 11.55 Hz), 6.84 (2H, dd, J=2.97, 11.55 Hz), 3.79 (3H, s), 2.72 (2H, t, J=7.26 Hz), 2.30 (2H, t, J=7.26 Hz), 1.95 (2H, qui, J=7.26 Hz). | — | EIMS 175 (M ⁺ , 17), 121 (100), 91 (15), 77 (15). HRMS Calcd for C ₁₁ H ₁₃ ON m/z 175.1023. Found m/z 175.1010. | C ₁₁ H ₁₃ ON: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.20; H, 7.48; N, 7.95. |
|  (4j) ^a | — | 7.22 (5H, m), 2.60 (2H, t, J=7.59 Hz), 1.59 (2H, m), 1.32 (6H, m), 0.88 (3H, t, J=6.93 Hz). | 1588, 1572, 1487, 1469, 1244, 1175 | EIMS 162 (M ⁺ , 36), 91 (100). HRMS Calcd for C ₁₂ H ₁₈ m/z 162.2749. Found m/z 162.1394. | — |
|  (4k) ^b | — | 7.88 (2H, d, J=8.58 Hz), 7.27 (2H, d, J=8.58 Hz), 2.65 (2H, t, J=7.59 Hz), 2.58 (3H, s), 1.62 (2H, m), 1.30 (6H, m), 0.88 (3H, t, J=7.26 Hz). | 1685, 1608, 1572, 1413, 1377, | EIMS 204 (M ⁺ , 70), 189 (100), 148 (8), 133 (32), 91 (25), 43 (10). HRMS Calcd for C ₁₄ H ₂₀ O m/z 204.3114. Found m/z 204.1517. | C ₁₄ H ₂₀ O: C, 82.30; H, 9.87. Found: C, 82.15; H, 9.97. |

| Product | bp°C/ mmHg | ¹ H NMR (ppm) | IR (neat, cm ⁻¹) | MS (70 eV), m/e | Analysis |
|--|---------------|---|---|--|--|
|  (4l) ^c | — | 6.99 (2H, d, J=8.58 Hz), 6.72 (2H, d, J=8.91 Hz), 3.68 (3H, s), 2.44 (2H, t, J=7.59 Hz), 1.46 (2H, m), 1.20 (6H, m), 0.78 (3H, t, J=6.60 Hz). | | EIMS 192 (19) 121 (100). HRMS Calcd for C ₁₃ H ₂₀ O <i>m/z</i> 192.1514. Found <i>m/z</i> 192.1487 | C ₁₃ H ₂₀ O: C, 81.20; H, 10.48. Found: C, 80.69; H, 10.54. |
|  (4n) ^d | — | 7.89 (2H, d, J=8.25 Hz), 7.29 (2H, d, J=8.25 Hz), 2.58 (3H, s), 2.56 (1H, m), 1.83 (4H, m), 1.39 (6H, m). | 1690, 1610, 1461, 1267, 824 | EIMS 202 (M ⁺ , 83), 187 (100), 159 (13), 131 (49), 115 (26), 105 (17), 91 (29), 77 (13), 43 (13). HRMS Calcd for C ₁₄ H ₁₈ O <i>m/z</i> 202.29. Found <i>m/z</i> 202.1353. | C ₁₄ H ₁₈ O: C, 83.12; H, 8.97. Found: C, 82.89; H, 8.99. |
|  (4o) ^c | — | 7.13 (2H, d, J=8.58 Hz), 6.84 (2H, d, J=8.58 Hz), 3.78 (3H, s), 2.44 (1H, m), 1.78 (5H, m), 1.32 (5H, m). | 1515, 1461, 1249, 1045 | EIMS 190 (90), 147 (100), 134 (17), 121 (72), 108 (7), 91 (13). HRMS Calcd for C ₁₃ H ₁₈ O <i>m/z</i> 190.1358. Found <i>m/z</i> 190.1354. | C ₁₃ H ₁₈ O: C, 82.06; H, 9.53. Found: C, 82.04; H, 9.64. |

^{cc} Separated by column chromatography on silica gel with hexane/ethyl acetate as eluant (5:1)