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# Cesium carbonate mediated exclusive dialkylation of active methylene compounds

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**ABSTRACT**

Active methylene compounds are regioselectively dialkylated by variety of alkyl halides using cesium carbonate in quantitative yield. The reaction yielded exclusively dialkylated products with no intermediate monoalkyaltion or mixture of products.



## 1. Introduction

In recent years, cesium carbonate has found extensive applications as an excellent base for a variety of synthetic transformations [1-13] and has received even industrial acceptance. In most of the cases, it is superior to other bases in terms of yield, reaction time, reaction temperature and sensitivity towards moisture, thus compensating the rather high cost of this reagent compared to that of potassium carbonate or other cheaper bases. It is easy to handle using readily available commercial starting materials without requiring strict exclusion of moisture in the system. Its basic strength is shown by the fact that it is the base of choice for reactions that are too sensitive towards strong bases or reactions that require a "Balanced base," stronger than other carbonates and weaker than hydroxides or alkoxides. It is compatible with a variety of functional groups. It has widely been employed for selective mono alkylation of amines [1], O-alkylation of phenols [2], O-alkylation of carboxylic acids [3] and S-alkylation[4].

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Surprisingly, its use in C-C bond formation reactions has not been explored much, except for a few reports on the Michael addition[5] and a solitary report on the alkylation of acetamidomalonicester[6].

Alkylation of active methylene compounds are generally accomplished using bases like sodium hydride, sodium ethoxide, potassium tert-butoxide, potassium phosphate and potassium carbonate. In many of the cases, yields are only moderate and mixtures of mono, di and *O*-alkylated product as well as a small amount of condensation product are formed. Sometimes, separation and isolation of the pure product from this mixture poses problems. Therefore alternative approaches to these products need to be developed. In this letter we describe a highly efficient and practical Method for the dialkylation of active methylene compounds by using cesium carbonate in dimethylformamide.

## 2. Results and Discussion

Stirring a solution of acetyl acetone (10 mmol) in DMF (15 mL) with allyl bromide (25 mmol) and cesium carbonate (20 mmol) at r.t., for 45 mins resulted in complete consumption of acetyl acetone and afforded the diallylated product in nearly quantitative yield (Table 1, entry 1). As shown in Table 1, several active methylene compounds (β-diketones, β-ketoesters and nitriles) can undergo alkylation smoothly with several reactive halides in the presence of cesium carbonate at room temperature itself, affording the corresponding di *C*-alkylated products in good to excellent yield and in good purity in a reasonably short period of time. In the case of diethyl malonate and benzonitrile, no reaction occurred at ambient temperature, but complete conversion was observed at 70 ˚C (Table 1, entries **11-12**). In all cases, crude product itself was sufficiently pure (>95%), except in the case of alkylation with benzyl bromide (Table 1, entries **13-17**).

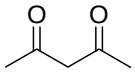
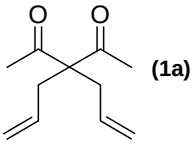
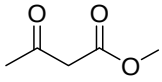
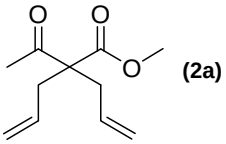
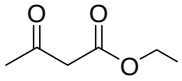
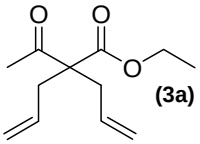
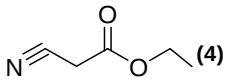
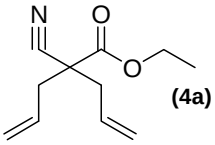
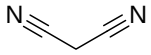
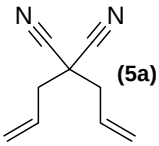
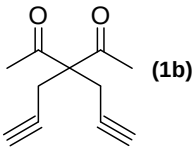
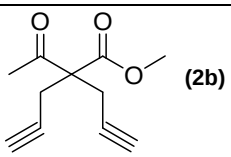
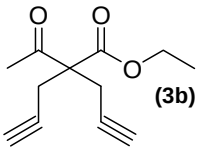
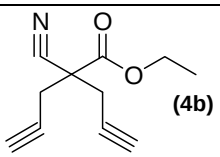
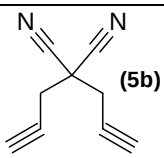
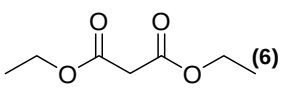
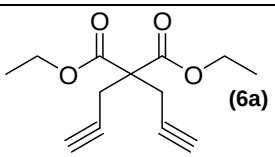

R = COMe, R' = COMe, R" = allyl = **1a**
R =COMe, R'= COOMe, R" = allyl = **2a**
R = COMe, R' = COOEt, R" = allyl = **3a**
R = CN, R' = COOEt, R" = allyl = **4a**
R = CN, R' = CN, R" = allyl = **5a**
R = COOEt, R' = COOEt, R" = propargyl = **6a**
R = Ph, R' = CN, R" = propargyl = **7a**
R = COMe, R' = COMe, R" = propargyl = **1b**
R = COMe, R'= COOMe, R" = propargyl = **2b**
R = COMe, R'= COOEt, R" = propargyl = **3b**
R = CN, R' = COOEt, R" = propargyl = **4b**
R = CN, R' = CN, R" = propargyl = **5b**

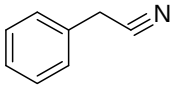
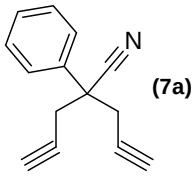
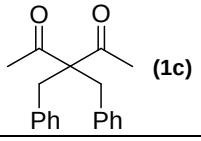
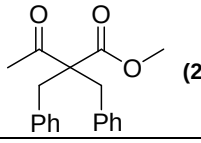
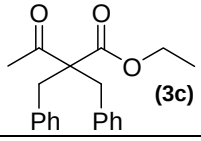
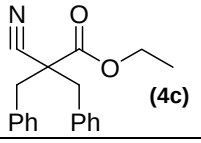
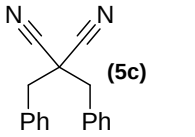
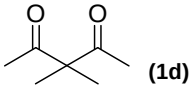
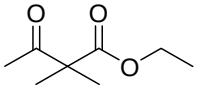
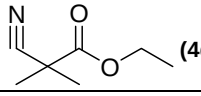
R = COMe, R'= COMe, R" = Bz = **2c**
R = COMe, R'= COOEt, R" = Bz = **3c**
R = CN, R' = COOEt, R" = Bz = **4c**
R = CN, R'= CN, R" = Bz = **5c**
R = COMe, R' = COMe, R"= Me = **1d**
R = COMe R'= COOEt, R" = Me = **3d**
R = CN, R' = COOEt, R" = Me = **4d**

**Scheme 1.** Dialkylation of active methylene compounds.

In these cases benzyl bromide was used in slight excess, and hence the product was accompanied with unreacted excess benzyl bromide which was easily removed by crystallization of the crude product from n-hexane/ethyl acetate (9:1).

**Table 1.** Alkylation of active methylene compounds

| Entry | Active methylene compounds | Alkyl halide (RX) | Condition | Product[a, b] | Yield (%) |
|---|---|---|---|---|---|
| 1 |  **(1)** | allyl bromide | r.t., 45 min |  **(1a)** | 99[c] |
| 2 |  **(2)** | allyl bromide | r.t., 2 h |  **(2a)** | 99[c] |
| 3 |  **(3)** | allyl bromide | r.t., 1 h |  **(3a)** | 99[c] |
| 4 |  **(4)** | allyl bromide | r.t., 1 h |  **(4a)** | 99[c] |
| 5 |  **(5)** | allyl bromide | r.t., 1 h |  **(5a)** | 99[c] |
| 6 | **(1)** | propargyl bromide | r.t., 45 min |  **(1b)** | 94[c] |
| 7 | **(2)** | propargyl bromide | r.t., 2 h |  **(2b)** | 99[c] |
| 8 | **(3)** | propargyl bromide | r.t., 1 h |  **(3b)** | 98[c] |
| 9 | **(4)** | propargyl bromide | r.t., 1 h |  **(4b)** | 99[c] |
| 10 | **(5)** | propargyl bromide | r.t., 1 h |  **(5b)** | 99[c] |
| 11 |  **(6)** | propargyl bromide | 70 °C, 16 h |  **(6a)** | 99[c] |

| | | | | | |
|---|---|---|---|---|---|
| 12 |  **(7)** | propargyl bromide | 70 °C, 24 h |  **(7a)** | 87[c] |
| 13 | **(1)** | benzyl bromide | r.t., 45 min |  **(1c)** | 84[c] |
| 14 | **(2)** | benzyl bromide | r.t., 2 h |  **(2c)** | 78[c] |
| 15 | **(3)** | benzyl bromide | r.t., 1 h |  **(3c)** | 60[c] |
| 16 | **(4)** | benzyl bromide | r.t., 1 h |  **(4c)** | 76[c] |
| 17 | **(5)** | benzyl bromide | r.t., 1 h |  **(5c)** | 89[c] |
| 18 | **(1)** | methyl iodide | r.t., 45 min |  **(1d)** | 95[c] |
| 19 | **(3)** | methyl iodide | r.t., 1 h |  **(3d)** | 98[c] |
| 20 | **(4)** | methyl iodide | r.t., 1 h |  **(4d)** | 96[c] |

[a]All reactions were performed on 10 mmol scale of active methylene compound.
[b]GC and proton NMR analysis of the crude product in the case of 1a-4d indicates absence of mono substituted product.
[c]Isolated yield.
[d]Recrystallized yield.

A comparison of the results of diallylation of acetyl acetone using present protocol and with various bases has been reported in Table 2. As shown in Table 1, a few other active methylene compounds (*β*-diketones, *β*-ketoesters and nitriles) also underwent a smooth alkylation with several reactive halides in the presence of cesium carbonate at room temperature, affording the corresponding di *C*-alkylated products in good to excellent yield and in good purity in a reasonably short period of time.

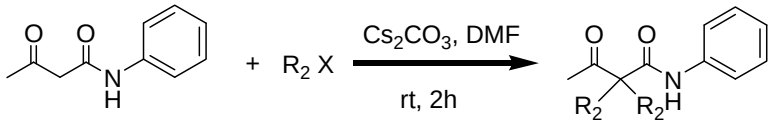
**Table 2.** Catalyst optimization for the synthesis of **3a** under solvent- media

| Entry | Base | Yield [a, b] (%) | |
|---|---|---|---|
| | | monoalkylated | dialkylated |
| 1 | $NaOCH_3$ | 39 | 36 |
| 2 | $NaOC_2H_5$ | 34 | 61 |
| 3 | $KOC_4H_9$ | 30 | 46 |
| 4 | NaH | _ | 24 |
| 5 | $K_2CO_3$ | 25 | 75 |
| 6 | $K_3PO_4$ | 23 | 34 |
| 7 | $Cs_2CO_3$ | _ | 99 |

[a]All the reaction were performed on 10 mmol scale of active methylene compound for a duration of 45 min.
[b]Crude GC purity.

As shown in Table 2, the dialkylation was fast in the case of cesium carbonate and proceeded to completion in 45 minutes itself compared to the reactions involving other bases. Further the reactions using other bases, led to a mixture of products, which could not be easily separated by normal purification methods. In the case of cesium carbonate, the reactions were clean and efficient. Importantly, in the present protocol the dialkylation reaction is free from any side product formation, such as monoalkylated product[14-33], O-alkylation[30] and condensation product. Bases like sodium ethoxide, potassium tert-butoxide, potassium phosphate and sodium hydride are known to give rise to considerable O-alkylation in DMF. We have observed only *C*-alkylation and very little, if at all, any O-alkylation.

Almost in all cases, the proton NMR spectrum and gas chromatogram of the crude product revealed its purity. The reactivity of the active methylene compounds towards the dialkylation under the present condition followed the anticipated trend, viz., *β*-diketone > ethyl acetoacetate = malononitrile = ethyl cyanoacetate > methyl acetoacetate > diethyl malonate > phenyl acetonitrile (see Table 1).Since cesium carbonate is known to be the base of choice for *N*-alkylation of amides[7], it was of interest to study the alkylation of acetoacetanilide. Treatment of acetoacetanilide with alkyl halides in DMF in the presence of cesium carbonate at r.t., for 2 h resulted in complete consumption of acetoacetanilide and afforded the corresponding di C-alkylated product without any *N*-alkylation and other side products (Scheme **2**).




$R_2$ = allyl, propargyl, benzyl, methyl

**Scheme 2.** Alkylation of active methylene compounds with amide functionality.

## 3. Conclusion

In summary we have found that dialkylation of active methylene compounds can be brought about efficiently, under mild conditions and under short duration, using cesium carbonate in DMF. No mono alkylated product was observed, hence the resulted products were attained with easy work up procedures.

## Acknowledgment

Ulaganathan Sankar is thankful to Dr. K.K. Balasubramanian and the Prinicipal, Pachaiyappa's college (Affiliated to University of Madras) for providing the facilities for the work.

## 4. Experimental Section

### *4.1 Materials and Methods*

All the reactions were carried out under nitrogen atmosphere, in all reaction N, N′-dimethylformamide was the choice of solvent. HPLC grade N, N′- dimethylformamide was used throughout all the reaction. Anhydrous cesium carbonates was purchased from commercial suppliers and was activated by heating at 180 °C for 2 hr prior to use. All the other reagents were AR grade commercial materials and were directly used without further purification. Melting points were determined with Buchi melting B-545. TLC was carried out on a Merck silica gel 60 $PF_{254}$ . $^1H$, $^{13}C$, Dept – NMR's was obtained from Bruker (400 MHz/300 MHz) spectrometer in $CDCl_3$. Low resolution mass spectra were recorded at ionizing voltage of eV by electron impact. Purity was recorded in Agilent-1200 series and Elemental analyses were recorded in vario micro super user.

*4.2 General procedure*

To a solution of active methylene compound (10 mmol) and cesium carbonate (20 mmol) in DMF (15 mL) at 0 $^{o}$C, alkyl halide (25 mmol) was added. The resulting mixture was stirred at r.t. (except Table 1 entry 11 and 12), under nitrogen atmosphere until reaction completion. The reaction was quenched by addition of water (30 mL) and then the mixture was extracted with MTBE (3x20 mL), washed with water (2x20 mL), saturated brine (2x20 mL), and dried over $Na_2SO_4$. Evaporation of the solvent under vacuum furnished analytically pure dialkylated product (**1a–4d**). All the products exhibited satisfactory spectral data.

*4.3 Physical and Spectral Data*

**3, 3-diallyl pentane-2, 4-dione (1a):** Pale yellow liquid, yield: 99% $^{1}$H NMR (400 MHz, $CDCl_3$): δ 2.03 (6H, s), δ 2.57 (4H, d), 5.01 (4H, 2d), 5.40 (2H, m). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 26.6, 34.5, 69.7, 118.6, 131.5, 204.9. DEPT NMR (100 MHz, $CDCl_3$): δ 26.58, 34.45, 118.60, 131.53. GC purity: (99.62%), Method: TRIAZWAX.M, RT- 9.5 min. GCMS m/z 181 $(M+H)^+$ , 165 $(M-CH_3)^+$ , 138 $(M+H-COCH_3)^+$ , 123 $(M-57)^+$ ,109 $(M-71)^+$, 97 $(M-83)^+$, 79 $(M-101)^+$.

**Methyl 2-acetyl-2-allyl pent-4-enoate (2a):** Pale brown liquid, yield: 99.53%. $^{1}$H NMR (300 MHz, $CDCl_3$): δ 2.1 (3H, s), 2.53 (4H, 2d), 3.6 (3H, s), 5.06 (4H, 2d), 5.51 (2H, m). $^{13}$C nmr (75 MHz, $CDCl_3$): δ 26.9, 35.9, 52.3, 63.3, 119.1, 132.1. DEPT NMR (100MHz, $CDCl_3$): δ 26.59, 35.80, 51.99, 118.79, 132.10. GC purity: (>96%), Method: TRIAZDBW.M, RT-7.49 min. GCMS *m/z* 196 $(M)^+$ , 181 $(M-CH_3)^+$, 164 $(M-OCH_3)^+$, 153 $(M-COCH_3)^+$, 137 $(M-59)^+$, 123 $(M-73)^+$, 113 $(M-83)^+$.

**Ethyl 2-actyl-2-allylpent-4-enoate (3a):** Pale yellow liquid, yield: 99.15%. $^{1}$H NMR (300 MHz, $CDCl_3$): δ 1.24 (3H, t), 2.13 (3H, s), 2.57 (4H, 2d), 4.16 (2H, q), 5.08 (4H, 2d), 5.5 (2H, m). $^{13}$C NMR (100 MHz, $CDCl_3$): δ13.9, 26.7, 35.8, 61.2, 63.1, 118.9, 132.2, 171.3, 203.6. DEPT NMR (100MHz, $CDCl_3$): δ13.89, 26.61, 35.78, 61.10, 118.81, 132.13. GC purity: (>96%), Method: TRIAZDBW.M, RT- 7.65 min. GCMS *m/z* 210 $(M)^+$, 168 $(M-COCH_3)^+$, 123 $(M-87)^+$, 95 $(M-115)^+$, 79 $(M-131)^+$.

**Ethyl 2-allyl-2-cyano pent-4-enoate (4a):** Colorless liquid yield: 99%, 1H NMR (300 MHz, $CDCl_3$): δ 1.27 (3H, t), 2.5 (2H, d), 2.6 (2H, d), 4.2 (2H, q), 5.2 (4H, d), 5.74 (2H, m). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 13.9, 40.5, 49.2, 62.5, 118.2, 120.7, 130.5, 167.7. DEPT NMR (100 MHz, $CDCl_3$): δ 13.99, 40.49, 62.46, 120.7, 130.52. GC purity: (>99%), Method: TRIAZDBW.M, RT- 7.96 min. GCMS *m/z* 192$(M-2)^+$, 165 $(M-CH_2CH_3)^+$, 152 $(M-45)^+$, 124 $(M-70)^+$, 120 $(M-COCH_3)^+$,106 $(M-88)^+$, 93 $(M-101)^+$, 80 $(M-114)^+$.

**Diallylmalonate (5a):** Pale brown liquid, yield 99%, $^{1}$H NMR (400 MHz, $CDCl_3$): δ 2.68 (4H, d), 5.39 (4H, 2d), 5.85 (2H, m).$^{13}$C NMR (100 MHz, $CDCl_3$): δ 37.3, 40.6, 114.8, 123.1, 128.6. DEPT NMR (100 MHz, CDCl3): δ 40.66, 123.16, 128.57.GC purity: (>96%), Method TRIAZDBW.M, RT-11.2 min. GCMS *m/z* 146.18 $(M-1)^+$, 131 $(M-15)^+$, 119 $(M-27)^+$, 105 $(M-41)^+$, 68 $(M-78)^+$.

**3,3-diprop-2-ynyl pentane-2,4-dione (1b)** : White solid, yield: 94% [Compound was purified by tituration by using petroleum ether]. Melting range: 74.5 - 75.8 °C. $^{1}$H NMR (400 MHz, $CDCl_3$): δ 2.03 (6H, s), 2.19 (6H, s), 3.1 (4H, s). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.1, 26.3, 70, 72.2, 78.8, 202.6. DEPT NMR (100 MHz, $CDCl_3$): δ 21.02, 26.35, 72.18, 78.82. GC purity: (>95%), Method: TRIAZWAX.M, RT- 8.2min. GCMS *m/z* 176 $(M)^+$ , 161 $(M-CH_3)^+$ , 134 $(M+H-COCH_3)^+$ , 119 $(M-57)^+$ ,95 $(M-81)^+$, 91 $(M-85)^+$.

**Methyl 2-acetyl-2-prop-2-ynylpent-4-ynoate (2b):** Pale yellow solid, yield: 99%, Melting range: 78.9- 81.2°C. $^{1}$H NMR (300 MHz, $CDCl_3$): δ 2.02 (2H, s), 2.2 (3H, s), 2.88 (4H, 2d), 3.77 (3H, s). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 21.7, 26, 53.1, 62.3, 71.9, 78.4, 169.5, 200.5. DEPT-NMR (100 MHz, $CDCl_3$): δ 21.76, 26.08, 53.13, 72.02, 78.41. GC purity: (>97%), Method: TRIAZDBW.M, RT- 9.27 min. GCMS *m/z* 191 $(M-1)^+$, 177 $(M-CH_3)^+$, 161 $(M-OCH_3)^+$, 150 $(M-COCH^3)^+$, 135 $(M-59)^+$, 118

$(M-74)^+$, 111 $(M-81)^+$, 91 $(M-101)^+$,79 $(M-113)^+$, 63 $(M-129)^+$. Elemental analysis: Calculated for $C_{11}H_{12}O_3$: C, 68.74%: H, 6.29%: Found: C, 68.66%: H, 6.26%.

**Ethyl 2-acetyl-2-prop-2-ynylpent-4-ynoate (3b):** Pale brown liquid, yield: 98.5%. $^1$H NMR (400 MHz, $CDCl_3$): δ 1.26 (3H, t), 2.03 (2H, s), 2.2 (3H, s), 2.9 (4H, 2d), 4.22 (2H, q).$^{13}$C NMR (100 MHz, $CDCl_3$): δ 13.9, 21.6, 25.3, 62.2, 71.5, 78.6, 169.2, 200.6. DEPT NMR (100 MHz, $CDCl_3$): δ 13.79, 21.53, 25.79, 62.04, 72.02, 78.38. GC purity: (>97%), Method-TRIAZDBW.M, RT- 9.39 mins. GCMS m/z 206 $(M)^+$, 191 $(M-CH_3)^+$, 177 $(M-CH_2CH_3)^+$, 164 $(M-COCH_3)^+$, 135 $(M-71)^+$, 97 $(M-99)^+$.

**Ethyl 2-cyano-2-prop-2-ynylpent-4-ynoate (4b):** Pale yellow liquid, yield: 99% $^1$H NMR (400 MHz, $CDCl_3$): δ 1.32 (3H, t), 2.22 (2H, s), 2.92 (4H, s), 4.3 (2H, q).$^{13}$C NMR (100MHz, $CDCl_3$): δ13.9, 25.7, 47.3, 63.6, 73.7, 76.2, 117.1, 165.9. DEPT NMR (100MHz, $CDCl_3$): δ 13.92, 25.71, 63.60, 73.71, 76.21. GC purity: (>99%), Method: TRIAZDBW.M, RT- 10.36 min. GCMS *m/z* 190$(M)^+$, 160 $(M-H-CH_2CH_3)^+$, 150 $(M-40)^+$, 144 $(M-46)^+$, 133 $(M-57)^+$,122 $(M-68)^+$, 116 $(M-74)^+$, 105 $(M-85)^+$, 89 $(M-101)^+$,78 $(M-112)^+$.

**Diprop-2-yn-1-ylmalononitrile (5b):** Pale brown solid, yield: 99%, $^1$H NMR (400 MHz, $CDCl_3$): δ 2.44 (2H, s), 3.09 (4H, s). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 27.4, 35.9, 73.8, 75.7, 113.4. DEPT NMR (100 MHz, CDCl3): δ 27.33, 73.89, 75.79. GC purity: (>99%), Method: TRIAZDBW.M, RT- 13.95 min. GCMS m*/z* 142.15 $(M-1)^+$, 115 $(M-27)^+$, 103 $(M-39)^+$, 88 $(M-54)^+$, 76 $(M-66)^+$.

**Diethyl diprop-2-ynyl malonate (6a):** Pale yellow solid, yield 99%, $^1$H NMR (400 MHz, $CDCl_3$): δ 1.20 (6H, t), 2 (2H, s), 2.94 (4H, s), 4.16 (4H, q).$^{13}$C NMR 100MHz, $CDCl_3$): δ 13.8, 22.4, 56.2, 61.9, 71.6, 78.3, 168.4. DEPT NMR (100 MHz, $CDCl_3$): δ 13.87, 22.37, 61.85, 71.68, 78.30. GC purity: (>99%), Method: TRIAZDBW.M, RT- 9.6 min. GCMS *m/z* 237 $(M+1)^+$, 207 $(M-CH_2CH_3)^+$, 197 $(M-39)^+$, 191 $(M-OCH_2CH_3)^+$, 162 $(M-COOCH_2CH_3)^+$, 151 $(M-85)^+$, 133 $(M-103)^+$, 123 $(M-113)^+$, 105 $(M-131)^+$, 91 $(M-145)^+$, 77 $(M-157)^+$, 65 $(M-171)^+$.

**2-phenyl-2-prop-2-ynyl pent-4-ynenitrile (7a):** Pale yellow solid, yield: 87%, $^1$H NMR (400 MHz, $CDCl_3$): δ 2.17 (2H, s), 2.97 (4H, 2d), 7.27-7.55 (5H, m) .$^{13}$C NMR (100 MHz, $CDCl_3$): δ 29.1, 45.6, 73.1, 77.1, 120.4, 125.7, 128.4, 128.6, 135.9.DEPT NMR (100 MHz, $CDCl_3$): δ 29.11(down), 73.02, 77.23, 125.75, 128.38, 128.58. GC purity: (>98%), Method: TRIAZDBW.M, RT- 13.50 min. GCMS m/z 192 $(M-H)^+$ 178 $(M-15)^+$, 165 $(M-28)^+$, 154 $(M-39)^+$, 127 $(M-66)^+$.

**3, 3-dibenzyl pentane-2, 4-dione (1c):** White solid, yield 84% [compound was purified by tituration by using petroleum ether]. $^1$H NMR (400MHz, $CDCl_3$): δ 2.14 (6H, s), 3.30 (4H, s), 7.03-7.28 (10H, m). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 28.4, 37.5, 72.1, 126.9, 128.5, 129.8, 136.1, 206.74. DEPT NMR (100 MHz, $CDCl_3$): δ 28.42, 37.46, 126.91, 128.49, 129.77. HPLC purity: (>99%), GCMS *m/z* 280$(M)^+$, 237 $(M-COCH_3)^+$, 189 $(M-CH_2Ph)^+$, 159 $(M-121)^+$, 147 $(M-133)^+$, 129 $(M-151)^+$, 91 $(M-189)^+$.

**Methyl 2,2-dibenzyl-3-oxobutanoate (2c) :** White solid, yield: 78% [compound was purified by tituration by using petroleum ether]. $^1$H NMR (400 MHz, $CDCl_3$): δ 1.96 (3H, s), 3.24 (4H, s), 3.69 (3H, s), 7.13-7.31 (10H, m). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 28.7, 39.4, 51.6, 65.7, 126.5, 127.9, 129.6, 135.8, 171.7, 205.2. DEPT NMR (100 MHz, $CDCl_3$): δ 28.73, 39.42, 51.63, 126.57, 127.95, 129.62. HPLC purity: (>99%), GCMS *m/z* 296 $(M)^+$, 264 $(M-OCH_3)^+$, 253 $(M-COCH_3)^+$, 221 $(M-59)^+$, 205 $(M-CH_2Ph)^+$, 192 $(M-104)^+$, 173 $(M-123)^+$, 144 $(M-152)^+$,131 $(M-165)^+$, 115 $(M-181)^+$,103 $(M-193)^+$, 91 $(M-205)^+$, 65 $(M-231)^+$. Elemental analysis: calculated for $C_{19}H_{20}O_3$: C, 77.00%: H, 6.80%. Found: C, 77.06%: H, 6.68%:

**Ethyl 2, 2-dibenzyl-3-oxobutanoate (3c):** White solid, yield 60% [compound was purified by tituration by using petroleum ether]. $^1$H NMR (400 MHz, $CDCl_3$) : δ 1.15 (3H, t), 1.64 (3H, s), 3.22 (4H, s), 4.09 (2H, q), 7.12-7.28 (10H, m). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 13.8, 29.1, 39.8, 61.3, 66.2,

126.9, 128.3, 130.1, 136.4, 171.7, 205.6. DEPT-NMR (100MHz, $CDCl_3$): δ 13.87, 29.10, 39.86, 61.31, 126.95, 128.34, 130.14. HPLC purity: (>99%), GCMS *m/z* 310 $(M)^+$, 267 $(M\text{-}COCH_3)^+$, 219 $(M\text{-}CH_2Ph)^+$, 173 $(M\text{-}137)^+$, 131 $(M\text{-}179)^+$, 91 $(M\text{-}219)^+$.

**Ethyl 2-benzyl-2-cyano-3-phenyl proponate (4c):** Colorless oil, yield: 76%, $^1H$ NMR (400 MHz, $CDCl_3$):δ 0.99 (3H, t), 3.13 (2H, d), 3.34 (2H, d), 4 (2H, q), 7.32-7.36 (10H ,m). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 13.7, 43.4, 53.3, 62.6, 118.6, 127.9, 128.6, 130.1, 134.1, 168.2. DEPT NMR (100 MHz, $CDCl_3$): δ 13.73, 43.35, 62.60, 127.91, 128.60, 130.06. HPLC purity: purity (>99%), GCMS m/z: 293 $(M)^+$, 202 $(M\text{-}CH_2Ph)^+$, 174 $(M\text{-}119)^+$, 91 $(M\text{-}202)^+$.

**Dibenzylmalononitrile (5c)**: White solid, yield: 89% [compound was purified by tituration by using petroleum ether]. $^1H$ NMR (400 MHz, $CDCl_3$): δ 3.27 (4H, s), 7.42 (10H, m).$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 41.2, 43.4, 115, 128.8, 129.1, 130, 132.1. DEPT NMR (100 MHz, $CDCl_3$): δ 43.41, 128.86, 129.02, 130.32. HPLC purity: purity (>99%), GCMS *m/z* 246.3 $(M)^+$, 91 $(M\text{-}155)^+$.

**3,3-dimethylpentane-2,4-dione (1d) :** Yellow liquid, yield: 95%, $^1H$ NMR (400 MHz, $CDCl_3$): δ 1.22 (6H, s), 2.01 (6H, s). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 20.9, 25.8, 62.2, 207.5. DEPT NMR (100MHz, $CDCl_3$): δ 20.98, 25.87. GC purity: (94.85%), Method: TRIAZHP5.M, RT -3.35 min. GCMS *m/z* 129 $(M=1)^+$ , 186 $(M\text{-}COCH_3)^+$, 71 $(M\text{-}59)^+$ .

**Ethyl 2,2-dimethyl-3-oxobutanoate (2d) :** colorless liquid, yield: 98%, $^1H$ NMR (400 MHz , $CDCl_3$): δ 1.24 (3H,t), 1.36 (6H, s), 2.16 (3H, s), 4 (2H, q). $^{13}C$ NMR 100 MHz, $CDCl_3$): δ 13.7, 21.5, 25.4, 26.7, 55.4, 61.1, 173.3, 205.4. DEPT NMR (100 MHz, $CDCl_3$): δ 13.76, 21.56 (up), 25.39, 26.70, 61.01. GC purity: (>95%), Method: TRIAZHP5.M, RT- 4.80 min. GCMS m/z :159 $(M+1)^+$, 116 $(M\text{-}COCH_3)^+$, 88 $(M\text{-}70)^+$, 73 $(M\text{-}85)^+$.

**Ethyl 2-cyano-2-methyl propanoate (3d):** Pale yellow liquid, yield: 96%, $^1H$ NMR (400 MHz, $CDCl_3$): δ 1.33 (3H, t), 1.63 (6H, s), 4.25 (2H, q). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 13.7, 24.5, 38.4, 62.5, 120.5, 169.4. DEPT-NMR (100 MHz, $CDCl_3$): δ 13.72, 24.51, 62.52 .GC purity:(>97%), Method:TRIAZHP5.M, RT- 4.27 min. GCMS *m/z* :142 $(M+1)^+$, 114 $(M\text{-}27)^+$, 96 $(M\text{-}OCH_2CH_3)^+$, 69 $(M\text{-}COOCH_2CH_3)^+$, 54 $(M\text{-}87)^+$.

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