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CONVENIENT SYNTHESIS OF β-ALKYL SUBSTITUTED DIHYDROCHALCONES

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General Methods. All reactions involving organolithium reagents were carried out by using standard techniques for the manipulation of air- and water-sensitive compounds.[1] All compounds reported here are fully characterized by mass spectrometry (using a gas chromatograph coupled to the BG Trio-2 mass spectrometer), and nuclear magnetic resonance spectroscopy (determined on a Brucker 200 spectrometer operating at 200 MHz for ^{1}H and 60 MHz for ^{13}C). The ^{13}C chemical shifts are referenced relative to $CDCl_3$ at δ=77.0). High-resolution mass spectra were measured on a ZAB-SEQ4F mass spectrometer. The GC analyses were carried out on a 5890 Hewlett Packard gas chromatograph, using a HP-5 column; conditions: T_i = 70 °C, T_f = 250 °C, rate = 10 °/min. Isolation of the reaction products was carried out by preparative TLC, using Silica Gel GF.

Materials. Tetrahydrofuran (THF) and hexane were purified as previously described [2] and were distilled from dark blue solutions of benzophenone ketyl under nitrogen immediately prior to use. Commercial E-cinnamaldehyde (ACS reagent grade) was distilled prior to use. Solid phenyllithium was prepared as described previously[3]. The concentration of PhLi was

[1] Shriver, D. F. *The Manipulation of Air Sensitive Compounds*, Wiley, New York, 1989.
[2] Pérez, D.G.; Nudelman, N.S. *J. Org. Chem.* **1988**, *53*, 408-413.
[3] Nudelman, N.S.; Vitale, A.A.; Doctorovich, F. *J. Organomet. Chem.* **1987**, *9*, 332.

determined by reaction with diphenylacetic acid[4]. All glassware, syringes and needles were dried in a vacuum oven and cooled in a dessicator. Compounds **2**,[5] **3**,[6] and **4**[7] were synthesized according to literature methods.

General procedure for the synthesis of alkylsubstituted dihydrochalcones. In a typical procedure, 3 mL of 1M PhLi in anhyd THF were placed in a septum-capped round-bottomed reaction flask provided of a stirring bar, under nitrogen atmosphere. 12 mL of THF and 132 mg (1 mmol) of (*E*)-cinnamaldehyde freshly distilled, were added all at once to the stirred solution. The temperature was kept at 20 °C. After 7 h, 1 mmol of the electrophile was added. The resulting solution was allowed to stir until decoloration at 20 °C before 0.2 mL of methanol was added. The product was purified by preparative TLC, using hexane-ethyl acetate, 95:5 as eluent. The alkylsubstituted dihydrochalcone obtained was crystallized from a mixture methanol-water. The compounds were fully characterized by melting point, ^{1}H and ^{13}C NMR spectroscopy and HRMS.

1,3-diphenyl-5-hepten-1-one (5). White crystals mp 54.5-55 °C. ^{1}H NMR ($CDCl_3$) (ppm): 2.18 (M, 3H), 2.39 (m, 2H), 3.29 (m, 2H), 3.43 (m, 1H), 5.37 (m, 2H), 7.23 (m, 5H), 7.49 (m, 3H), 7.90 (d, 2H, J=6.9 Hz). ^{13}C NMR ($CDCl_3$) (ppm): 17.84, 39.62, 41.32, 44.56, 126.21, 127.34, 127.53, 127.99, 128.34, 128.48, 128.72, 132.82, 137.34, 144.75, 199.11. MS *m/z* (I rel) : 264 (1), 145 (6), 144 (45), 143 (2), 130 (3), 129 (21), 128 (3), 115 (2), 106 (8), 105 (100), 104 (6), 103 (4), 91 (4), 79 (1), 78 (8), 77 (57), 65 (3), 63 (2), 55 (5), 53 (2), 52 (2), 51 (19), 50 (4). HRMS *m/z* for $C_{19}H_{20}O$ calcd 264.1514, found 264.1518.

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[4] Kofron, W.G.; Bacawlski, L.M. *J. Org. Chem.* **1976**, *41*, 1879-1880.
[5] Wasserman, H. H.; Aubrey, N. E. *J. Am. Chem. Soc.* **1955**, *77*, 590-594.
[6] Kohler, E. P.; Chadwell, H. M. *Org. Synth.* **1932**, Vol 1, 78-80.
[7] Weber, F. G.; Möschwitzer, G. *Tetrahedron* **1973**, *29*, 2479-2483.

1,3-diphenyl-1-hexanone (6). White crystals mp 65 °C. ^{1}H NMR ($CDCl_3$) (ppm): 0.87 (t, 3H, J=7.2 Hz), 1.23 (m, 2H), 1.67 (m, 2H), 3.30 (m, 3H), 7.26 (m, 5H), 7.45 (m, 3H), 7.91 (d, 2H, J=7.2 Hz). ^{13}C NMR ($CDCl_3$) (ppm): 14.01, 20.64, 38.59, 41.15, 45.98, 126.23, 127.58, 128.04, 128.42, 128.53, 132.89, 144.99, 211.59. MS *m/z* (I rel) : 252 (3), 210 (9), 209 (54), 133 (13), 132 (99), 131 (17), 121 (8), 120 (12), 118 (5), 117 (29), 115 (5), 106 (10), 105 (100), 104 (8), 103 (8), 92 (4), 91 (55), 78 (13), 77 (81), 65 (7), 51 (25), 50 (5). HRMS *m/z* for $C_{18}H_{20}O$ calcd 252.1514, found 252.1517.

1,3-diphenyl-4-methyl-1-pentanone (7). White crystals mp 25-26 °C. ^{1}H NMR ($CDCl_3$) (ppm): 0.81 (d, 3H, J=6.7 Hz), 1.00 (d, 3H, J=6.7 Hz), 1.96 (m, 1H), 3.17 (t, 1H, J=7 Hz), 3.37 (d, 2H, J= 7 Hz), 7.20 (m, 5H), 7.46 (m, 3H), 7.88 (dd, 2H, J= 1.3 and 8.2 Hz). ^{13}C NMR ($CDCl_3$) (ppm): 20.37, 20.94, 33.28, 42.58, 47.94, 126.13, 128.01, 128.07, 128.36, 128.47, 132.78, 137.50, 143.64, 208.81. MS *m/z* (I rel) : 252 (1), 210 (2), 209 (8), 133 (7), 132 (64), 131 (5), 117 (7), 106 (8), 105 (100), 104 (9), 103 (5), 91 (15), 78 (9), 77 (62), 65 (4), 55 (4), 51 (22), 50 (5). HRMS *m/z* for $C_{18}H_{20}O$ calcd 252.1514, found 252.1517.

1,3-diphenyl-1-heptanone (8). White crystals mp 57 °C. ^{1}H NMR ($CDCl_3$) (ppm): 0.84 (t, 3H, J=6.8 Hz), 1.23 (m, 4H), 1.70 (m, 2H), 3.28 (m, 3H), 7.26 (m, 5H), 7.51 (m, 3H), 7.90 (d, 2H, J=7.6 Hz). ^{13}C NMR ($CDCl_3$) (ppm): 13.90, 22.61, 29.67, 36.06, 41.34, 46.03, 126.21, 127.58, 128.39, 128.50, 132.81, 145.05, 199.14. MS *m/z* (I rel) : 266 (2), 210 (9), 209 (52), 147 (12), 146 (94), 131 (13), 121 (5), 120 (9), 118 (5), 117 (30), 115 (5), 106 (9), 105 (100), 104 (21), 103 (7), 92 (4), 91 (43), 79 (3), 78 (11), 77 (69), 65 (5), 55 (6), 52 (2), 51 (18), 50 (4). HRMS *m/z* for $C_{19}H_{22}O$ calcd 266.1671, found 266.1675.

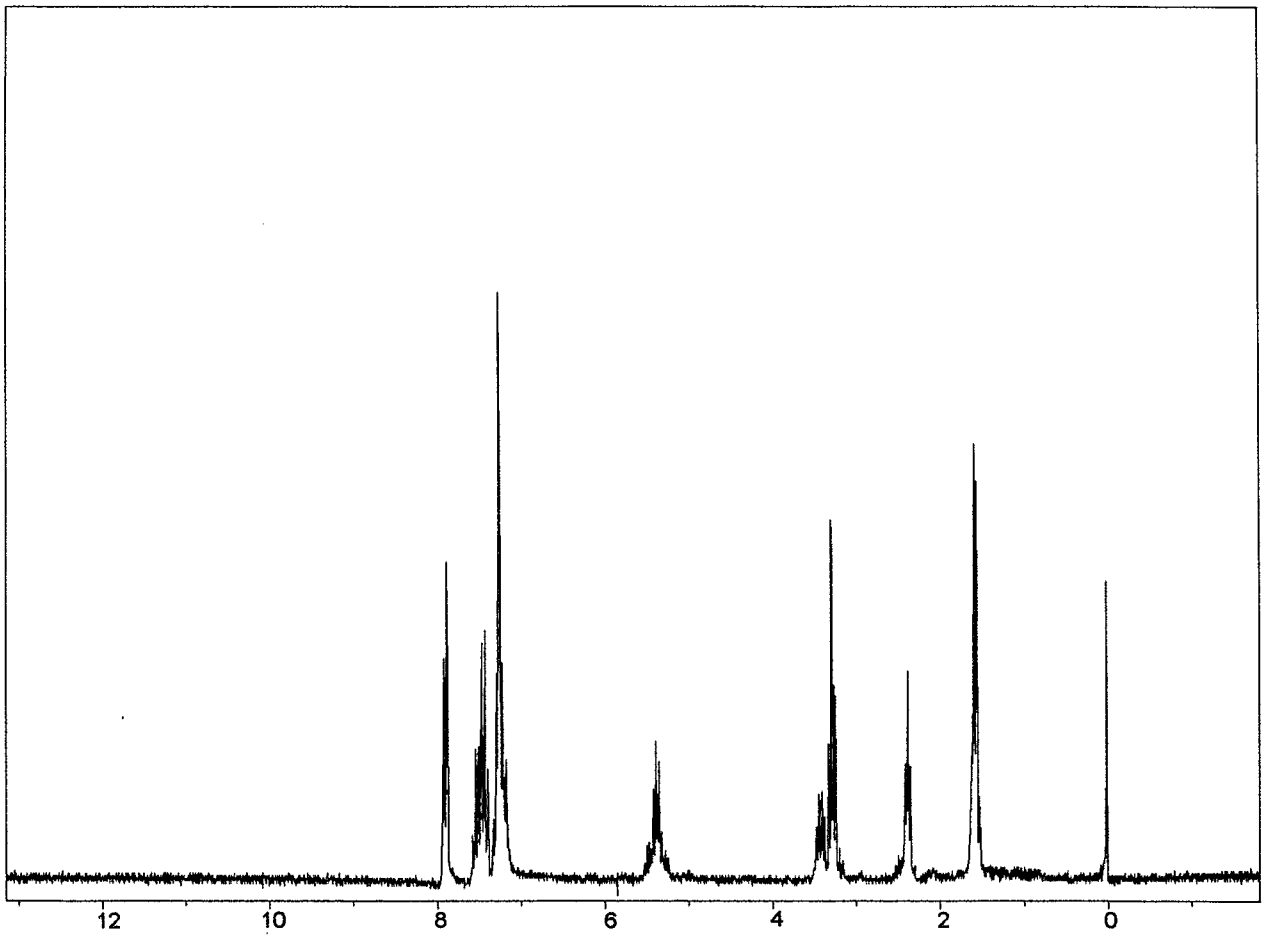
3-cyclohexyl-1,3-diphenyl-1-propanone (9). White crystals mp 126 °C. ^{1}H NMR ($CDCl_3$) (ppm): 1.12 (m, 5H), 1.60 (m, 6H), 3.21 (m, 1H), 3.35 (m, 2H), 7.19 (m, 5H), 7.44

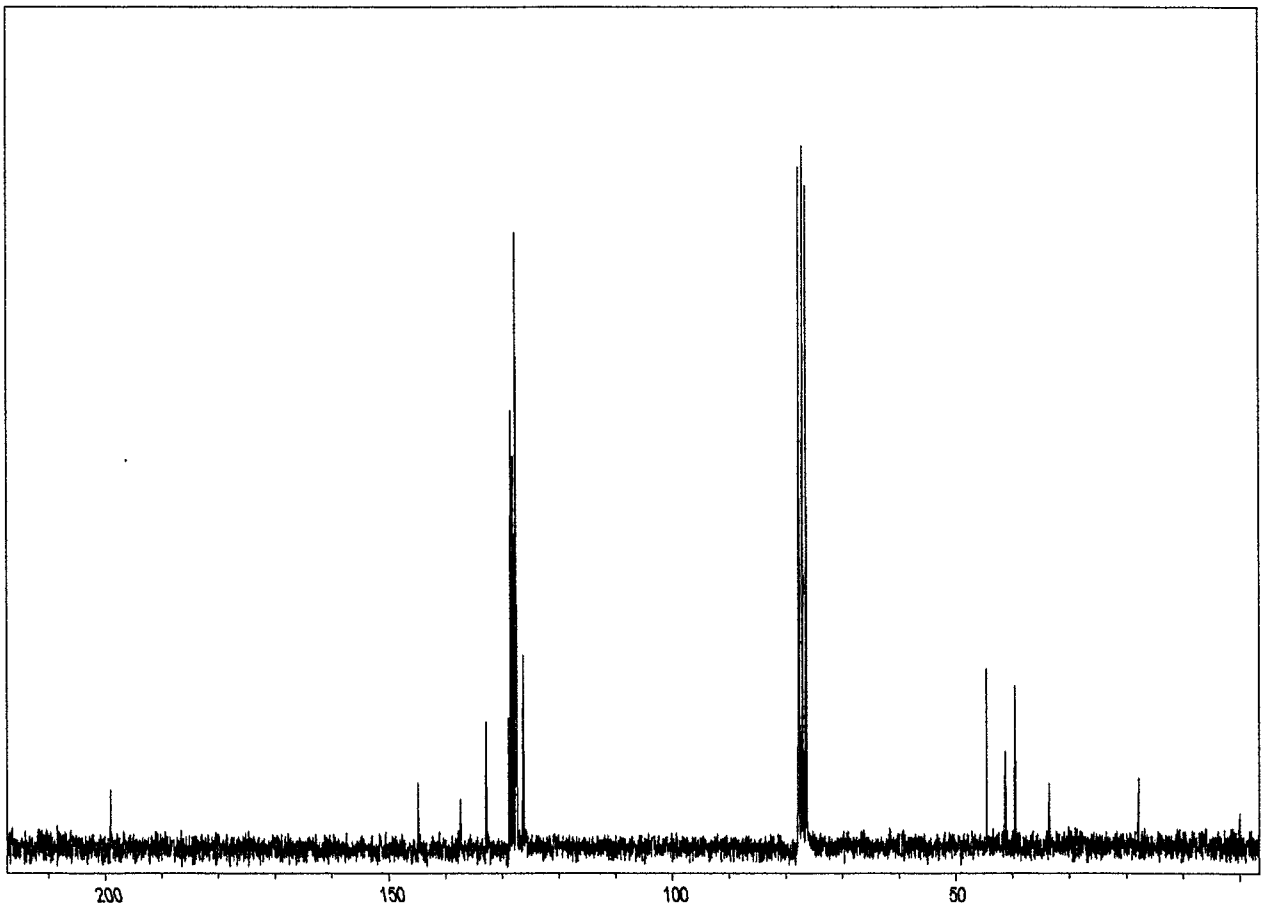
(m, 3H), 7.88 (d, 2H, J=6.7 Hz). ^{13}C NMR ($CDCl_3$) (ppm): 26.44, 26.60, 30.86, 31.42, 42.53, 43.17, 47.11, 59.32, 126.07, 128.01, 128.07, 128.47, 132.76, 143.86, 199.52. MS *m/z* (I rel) : 292 (1), 210 (12), 209 (23), 173 (16), 172 (87), 131 (5), 130 (4), 129 (6), 115 (5), 106 (13), 105 (100), 104 (28), 103 (6), 91 (28), 83 (4), 81 (17), 80 (12), 79 (4), 78 (10), 77 (64), 67 (5), 65 (5), 55 (37), 53 (4), 51 (16), 50 (3). HRMS *m/z* for $C_{21}H_{24}O$ calcd 292.1827, found 292.1830.

1,3,4-triphenyl-1-butanone (10). White crystals mp 113 °C. ^1H NMR ($CDCl_3$) (ppm): 3.01 (d, 2H, J= 5.8 Hz), 3.32 (d, 2H, J= 6.9 Hz), 3.69 (m, 1H), 7.21 (m, 10H), 7.42 (m, 2H), 7.50 (m, 1H), 7.86 (d, 2H, J= 8 Hz). ^{13}C NMR ($CDCl_3$) (ppm): 43.01, 43.06, 44.20, 126.10, 126.40, 127.66, 127.99, 128.17, 128.36, 128.50, 129.28, 132.92, 144.13, 208.19. MS *m/z* (I rel) : 250 (3), 131 (12), 130 (67), 129 (12), 128 (4), 115 (6), 106 (13), 105 (100), 103 (5), 91 (10), 78 (9), 77 (65), 65 (4), 51 (23), 50 (5). HRMS *m/z* for $C_{22}H_{20}O$ calcd 300.1514 , found 300.1510.

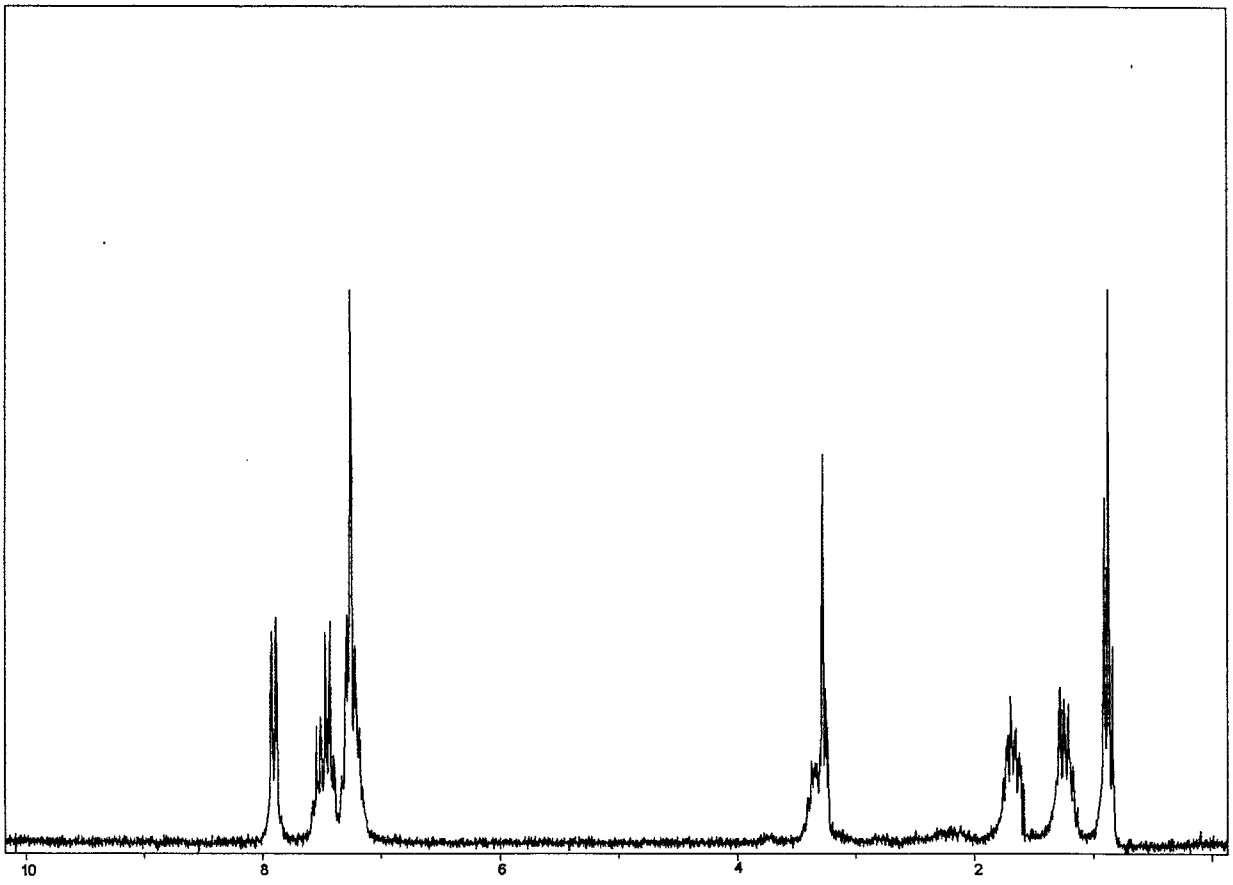
1,3-diphenyl-5-hexen-1-one (11). White crystals mp 68 °C. ^1H NMR ($CDCl_3$) (ppm): 2.48 (m, 2H), 3.30 (dd, 2H, J=2.9 and 6.5 Hz), 3.49 (m, 1H), 5.00 (m, 2H), 5.70 (m, 1H), 7.26 (m, 5H), 7.46 (m, 3H), 7.91 (d, 2H, J=6.9 Hz). ^{13}C NMR ($CDCl_3$) (ppm): 26.76, 40.73, 44.60, 116.77, 126.37, 127.55, 128.01, 128.42, 128.50, 132.84, 136.26, 144.37, 206.71. HRMS *m/z* for $C_{18}H_{18}O$ calcd 250.1358, found 250.1360.

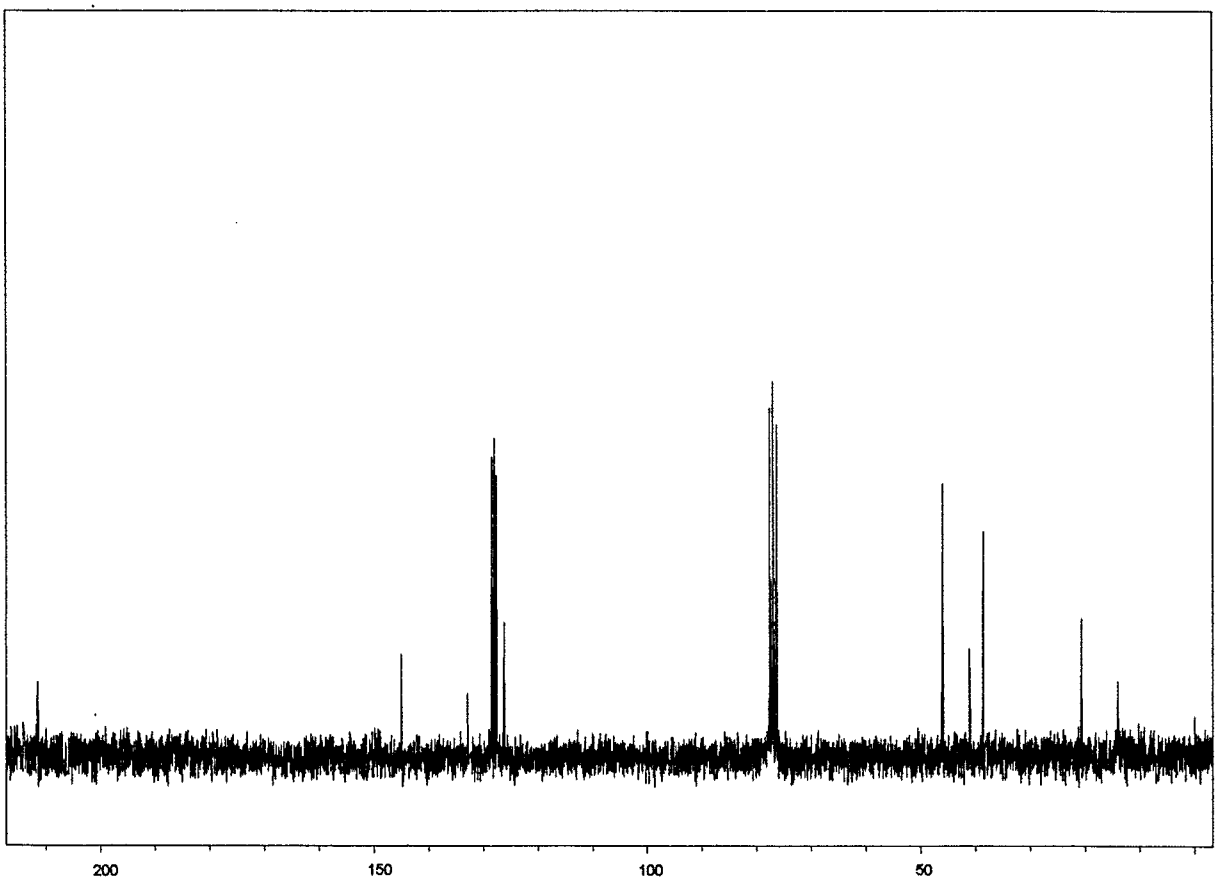
1,3-diphenyl-5-hepten-1-one (**5**)



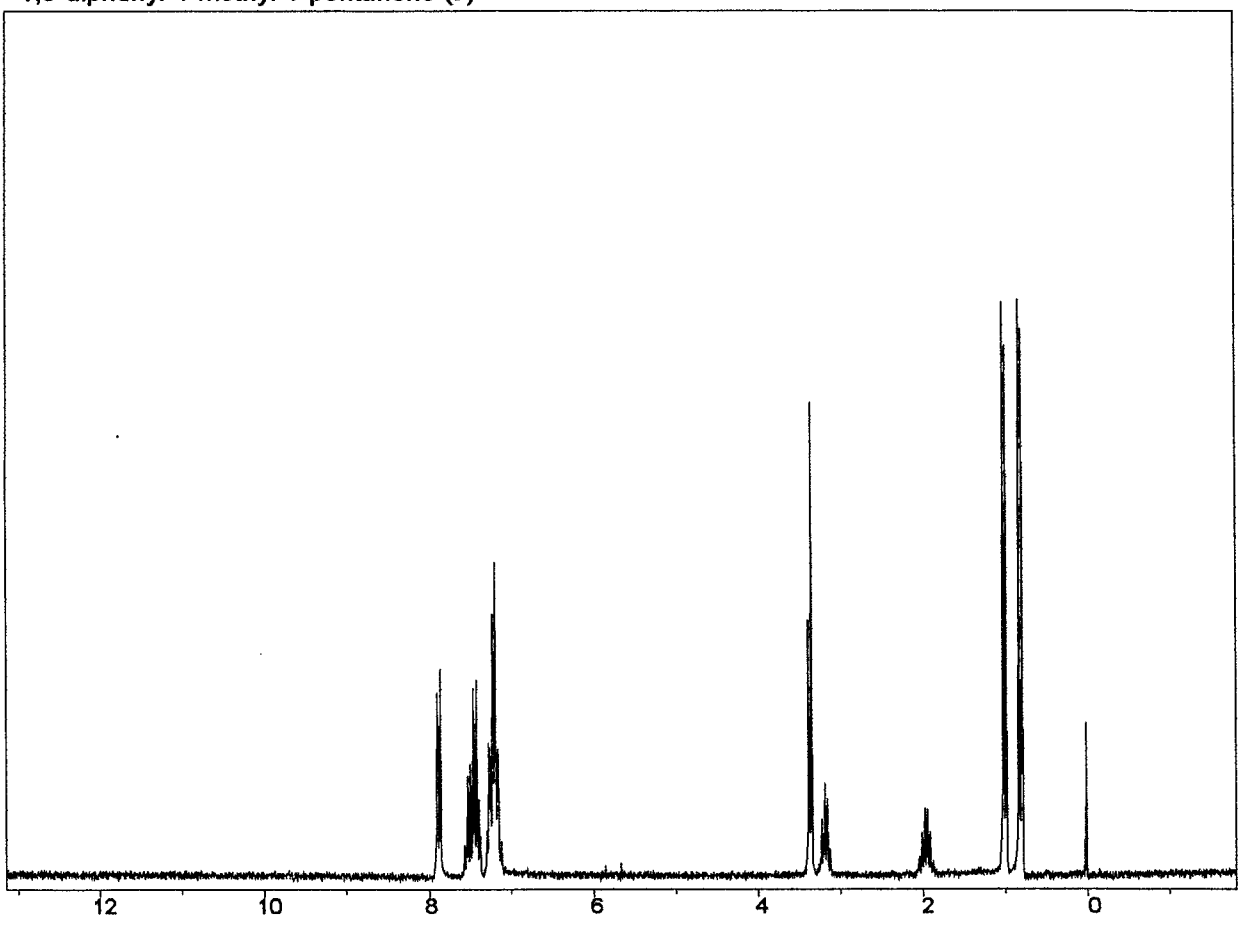


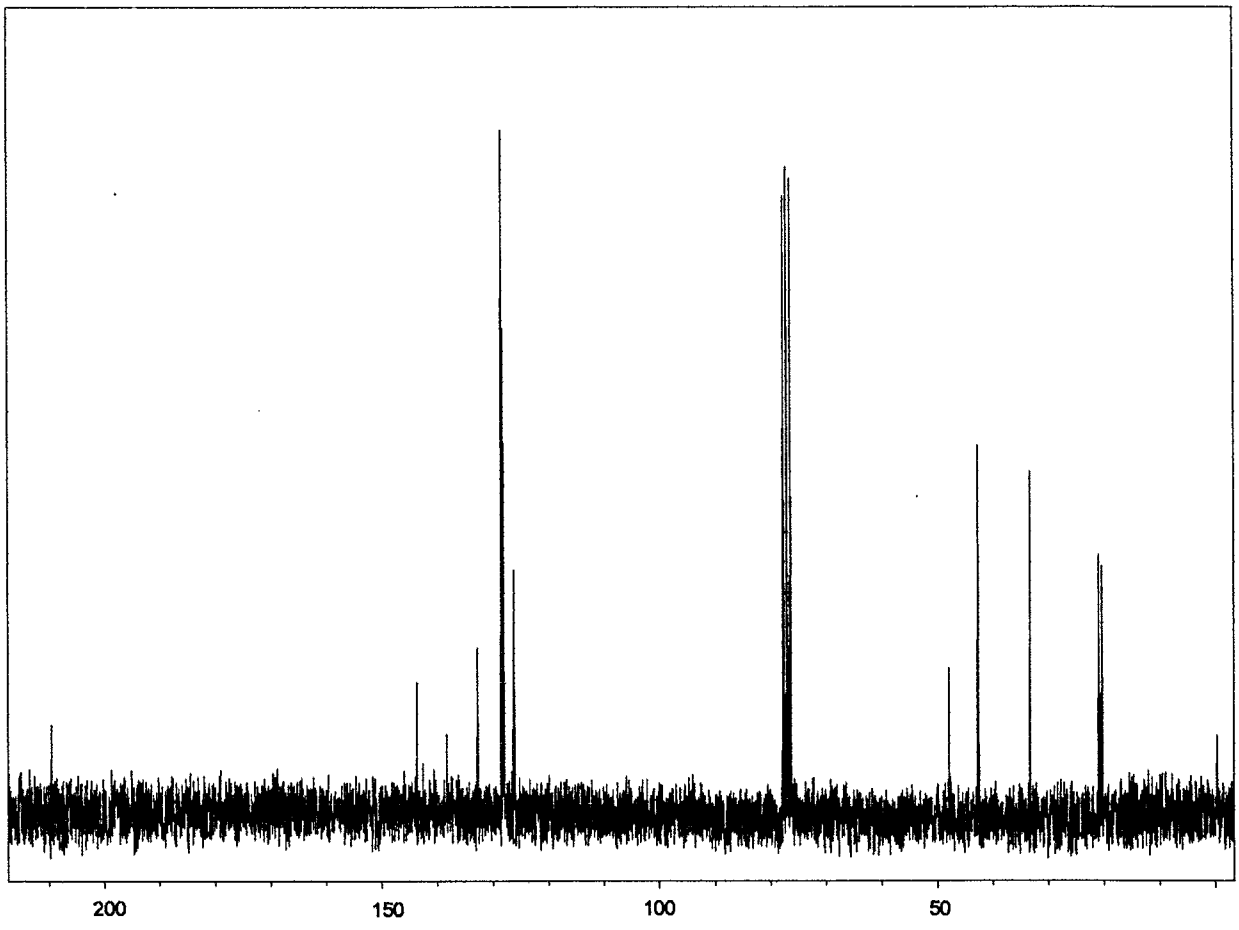
1,3-diphenyl-1-hexanone (**6**)



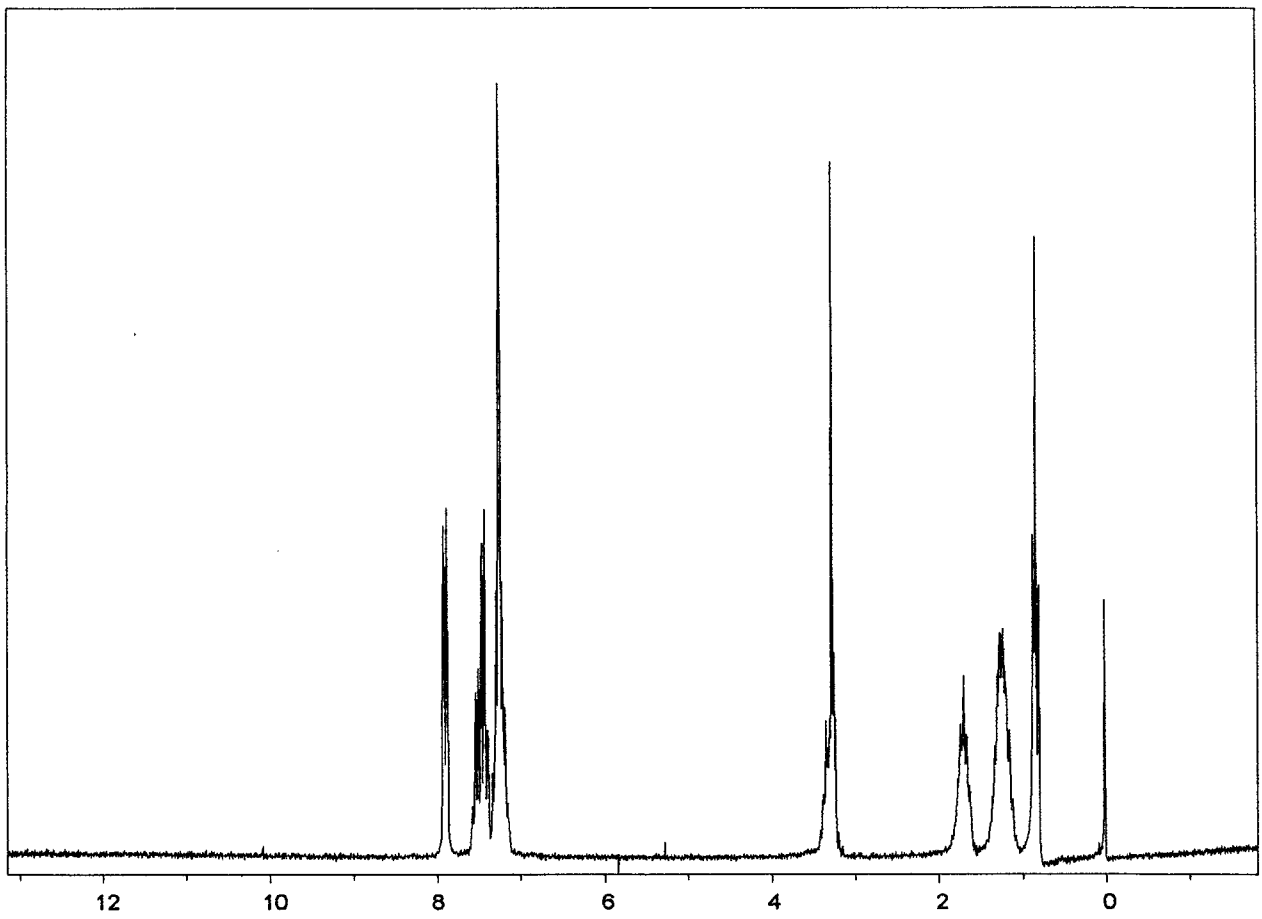


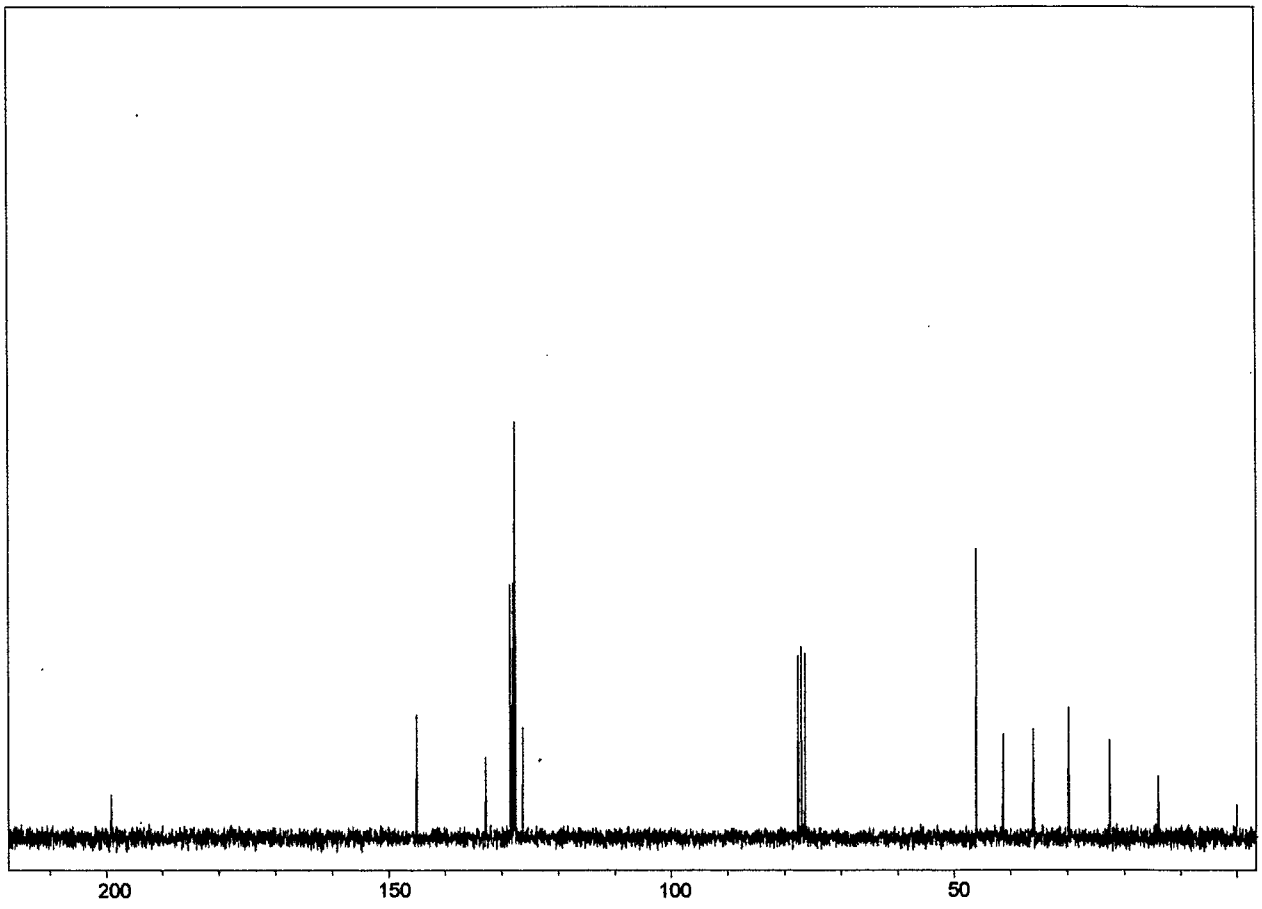
1,3-diphenyl-4-methyl-1-pentanone (7)



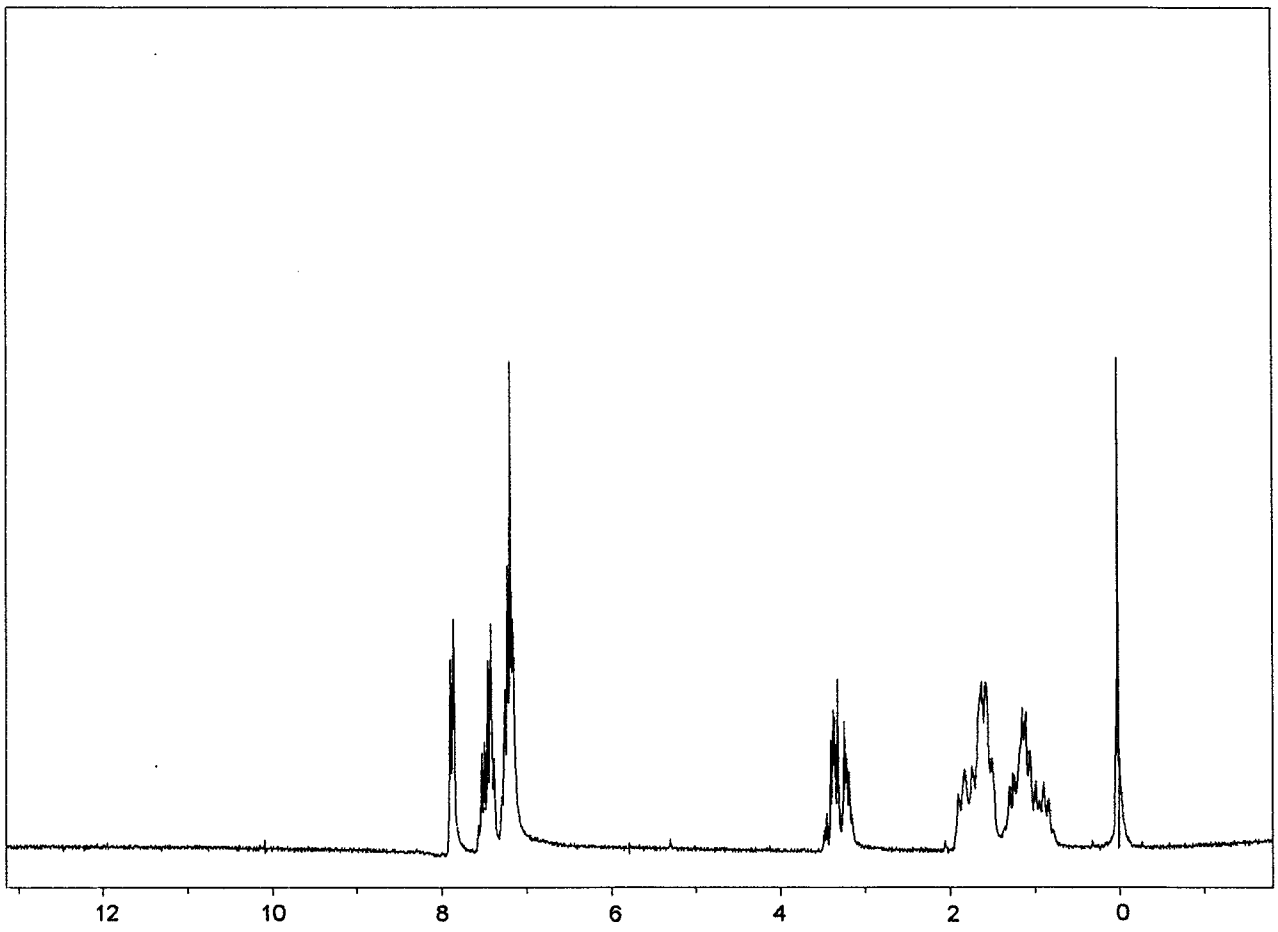


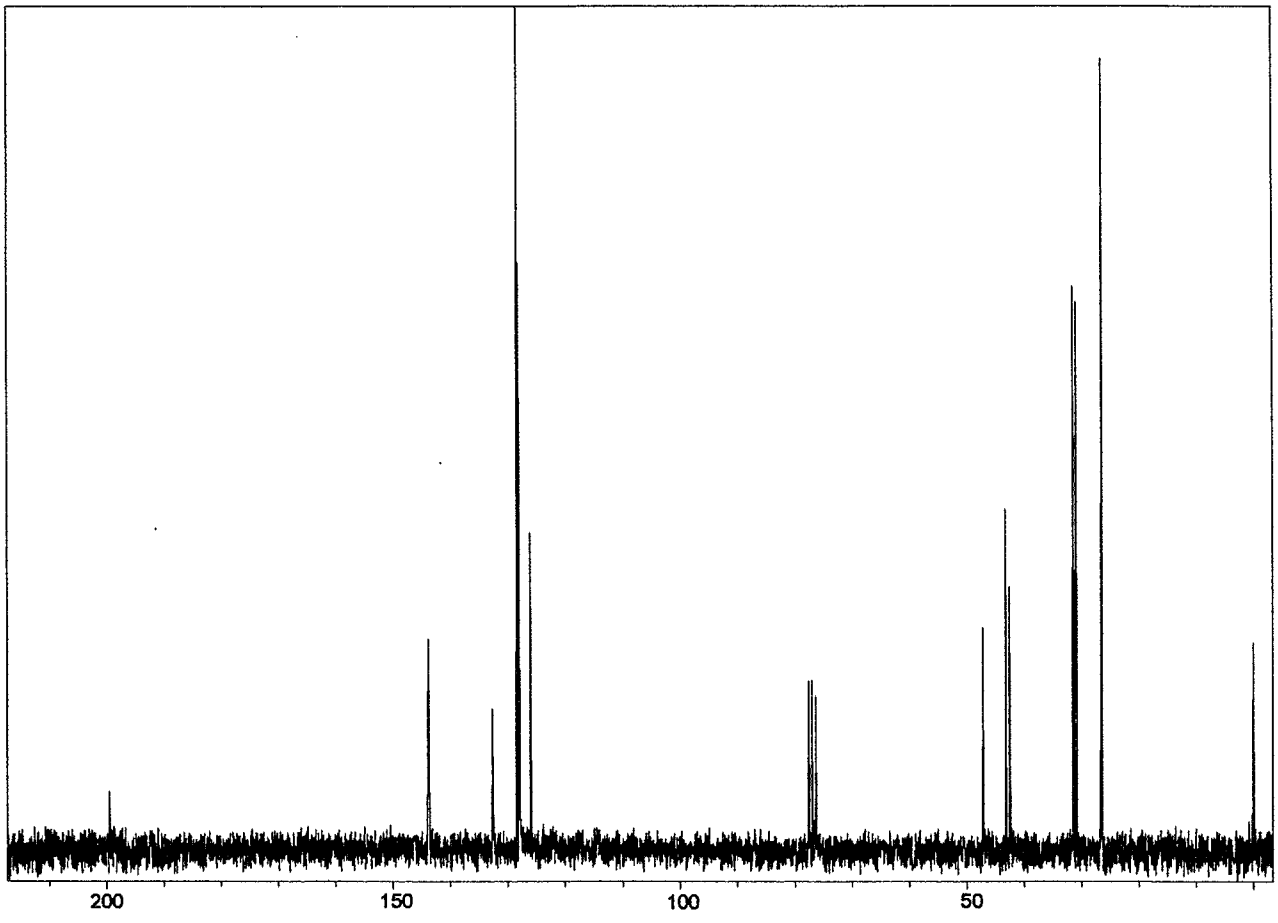
1,3-diphenyl-1-heptanone (**8**)



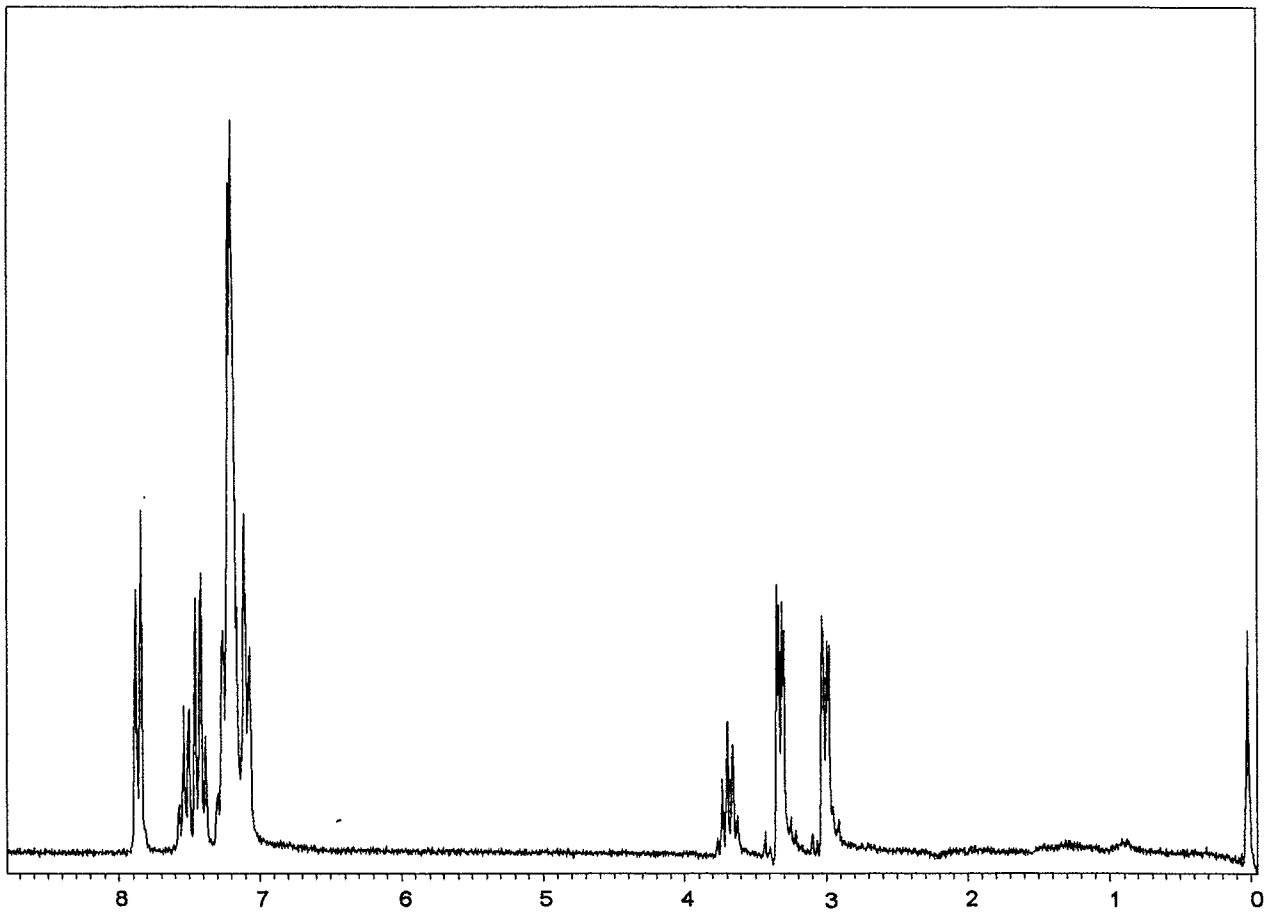


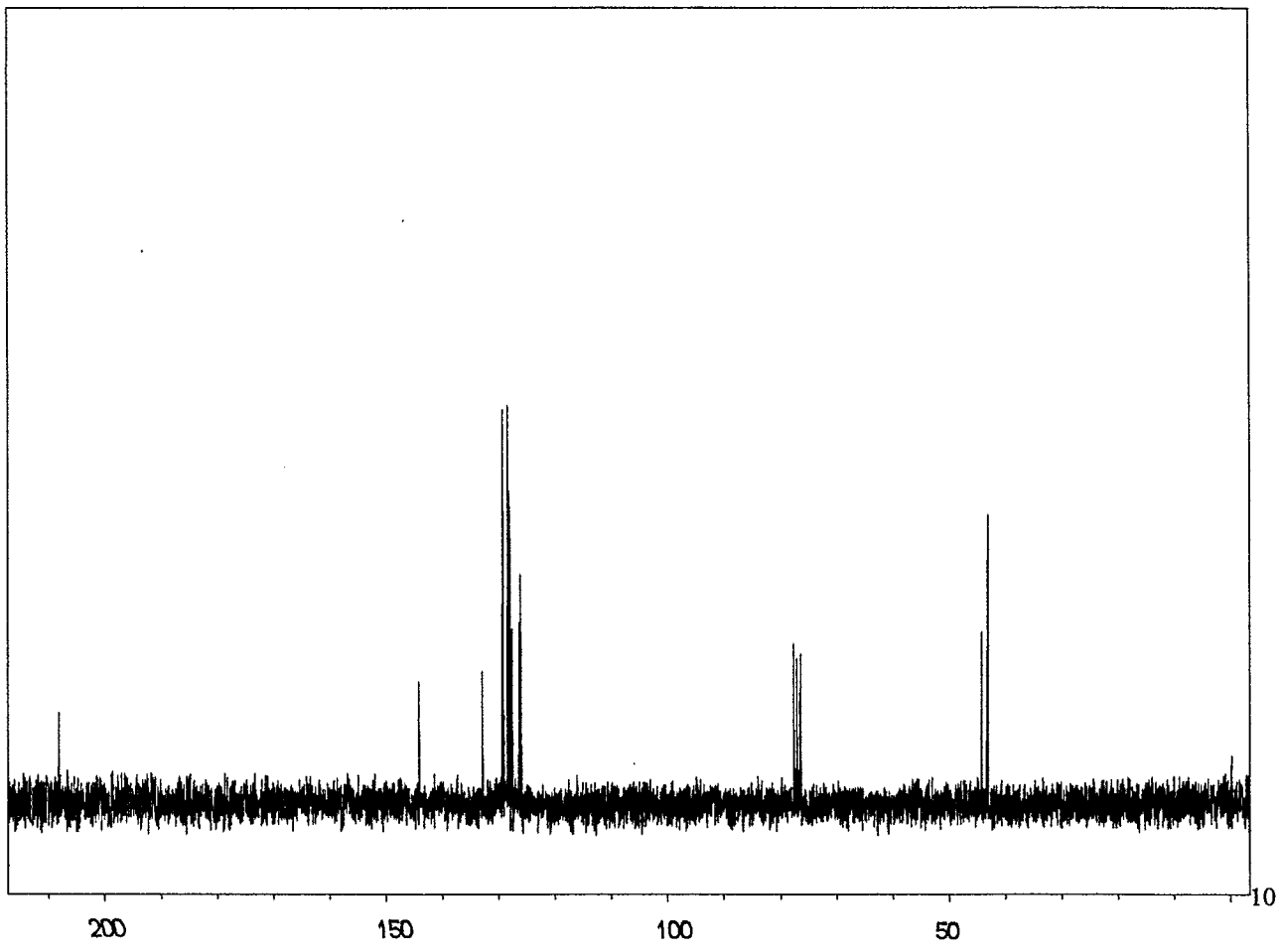
3-cyclohexyl-1,3-diphenyl-1-propanone (**9**)





1,3,4-triphenyl-1-butanone (**10**)





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1,3-diphenyl-5-hexen-1-one (**11**)