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THE PALLADIUM-CATALYSED CONJUGATE ADDITION TYPE REACTION OF 2-(N-ACYLAMINO)-ARYLMERCURY COMPOUNDS WITH α,β-ENONES: A NEW ENTRY TO THE QUINOLINE SKELETON

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Abstract—Pd-catalysed reaction of arylmercurials with α,β-enones in an acidic two-phase system gives conjugate addition products useful for the synthesis of quinolines, 3,4-dihydroquinolines, and 1,2,3,4-tetrahydroquinolines.

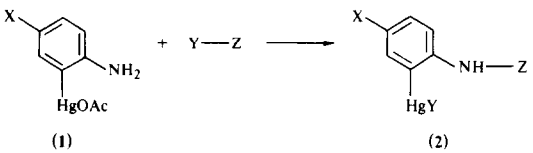
Recent publications from this laboratory[1,2] described a new synthesis of β-aryl ketones through a conjugate addition type reaction of arylmercury compounds to α,β-unsaturated ketones in the presence of catalytic amounts of palladium salts. As a wide variety of functional groups can be tolerated in the aryl moiety transferred to the enonic β-carbon atom, consecutive intramolecular reaction at the carbonyl group may be expected to occur when an aryl mercury compound containing a suitable nucleophile in the orto position is used as the aryl donor. This proved to be the case with o-hydroxyarylmercury chlorides whose utilization prompted us a new entry to 2-chromanols and 2-chromenes.[3]

Similar reactions with 2-aminoarylmercurials would be expected to produce quinoline derivatives. However, it was anticipated[2] that the acidic medium would prevent the addition reaction from occurring with arylmercury compounds containing a free amino group while good results were obtained with N-acetyl derivatives. Therefore, protection of the amino group is a necessary step to attain conjugate addition type products and cyclization would occur after removal of the protecting group.

Clearly the protecting group must be such that it can survive the addition step and that it can be easily and selectively removed to allow the nucleophilic attack of the nitrogen on the carbonyl carbon atom. Owing to the acidic conditions used for the conjugate addition, stability of the amino protecting group could be expected to give rise to difficulties.

We now report that benzyloxycarbonyl, ethoxycarbonyl, and trifluoroacetyl groups can be successfully used for the purpose under our acidic two-phase conditions and that deprotection of the amino group of the obtained addition products affords quinoline derivatives.

Benzyloxycarbonyl, ethoxycarbonyl, and trifluoroacetyl derivatives of 2-aminoarylmercury compounds **2** were prepared in good yield from mercurials **1a–d** chosen for this study and benzyloxycarbonyl chloride, ethoxycarbonyl chloride, and trifluoroacetic anhydride respectively (Scheme 1).



Scheme 1.

The results are summarized in Table 1.

The addition reactions of **2** with α,β-enones **3** were carried out under our usual acidic two-phase conditions (Scheme 2) and the results are summarized in Table 2.

A variety of reaction conditions were tested to allow deprotection-cyclization of compounds **4**. Interestingly, the oxidation level of the heterocyclic ring in the quinoline skeleton can be varied easily depending on the selected conditions (Scheme 3). Although no detailed investigation was performed, the results obtained clearly show that compounds **4** are very useful and versatile synthetic intermediates for the synthesis of quinoline derivatives. Thus, treatment of **4** with 37% HBr in AcOH at room temperature (Z = $COOCH_2Ph$) or at 50° (Z = COOEt) gave rise to 3,4-dihydroquinoline hydrobromides **5** (Table 3), while treatment of **4** with HBr in $MeNO_2$ gave rise to fully oxidized quinoline derivative **6** (Table 4).

In addition, N-ethoxycarbonyl tetrahydroquinoline **7** and tetrahydroquinoline **8** were obtained on treatment of **4** with zinc powder and 37% HBr in AcOH depending upon the nature of the protecting group: addition products containing N-ethoxycarbonyl group afforded **7** (Table 5) while addition products containing N-benzyloxycarbonyl group afforded **8** (Table 6). It is possible, however, to prepare N-benzyloxycarbonyl tetrahydroquinolines by using a weaker acidic medium (see preparation of **9**, Scheme 5. Compounds **7** can be converted into tetrahydroquinoline derivatives **8** simply by treatment with 37% HBr in AcOH at 50°.

Incidentally, it may be reported here that compounds **7f**, **g**, and **h** and **8c** were isolated as *cis* and *trans* isomers.

Table 1. N-Acylation of 2-aminoarylmercury compounds 1[a]

Entry	Compound (1)[b] X	M.p. of (1) (lit. m.p.) (°C)	Compound (2) Y	Z	M.p. of (2) (°C)
a	Me	187–189	Cl	$COOCH_2Ph$	237–239
b	Cl	207–208 (207)[5]	Cl	$COOCH_2Ph$	228–230
c	HgOAc[c]	210–211 (209)[6]	Cl	$COOCH_2Ph$	297–299
d	MeCO	171–173	Cl	$COOCH_2Ph$	284–286
e	Me		Cl	COOEt	268–269
f	Cl		Cl	COOEt	320–323
g	Cl		$OCOCF_3$	$COCF_3$	167–169

a) 2-(N-acylamino)arylmercury compounds (2a–f) were prepared in 85–92% yield according to the procedure described by Boarland and McOmie[4] for the synthesis of 2-(N-acetylamino)arylmercury compounds allowing a suspension of (1) in a 1% Na_2CO_3 solution to react with the suitable acylating agent for about 15 h. Compound (2g) was obtained in 87% yield (5h) according to the procedure described by Vecchiotti[5].

b) Compounds (1a–b) were prepared as described by Vecchiotti[5] while compounds (1c–d) were prepared as described by Bruice[6].

c) After treatment of (1c) with benzyloxycarbonyl chloride, the HgOAc group was substituted for HgCl group.

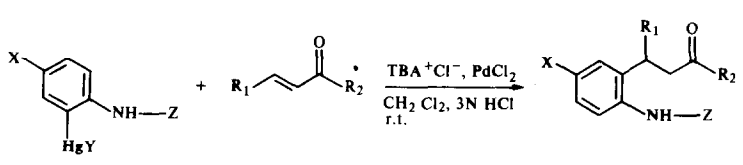
In all cases studied, the isomers containing diequatorial Ph and R_2 groups were found to be preferred by about 2:1. Conformations were established from the coupling constants of the heterocyclic ring protons and on the basis of the literature data.[9]

When acid sensitive compounds are concerned, the amino group may be protected through the formation of its trifluoroacetyl derivative and the deprotection-cyclization step can be carried out under basic conditions.

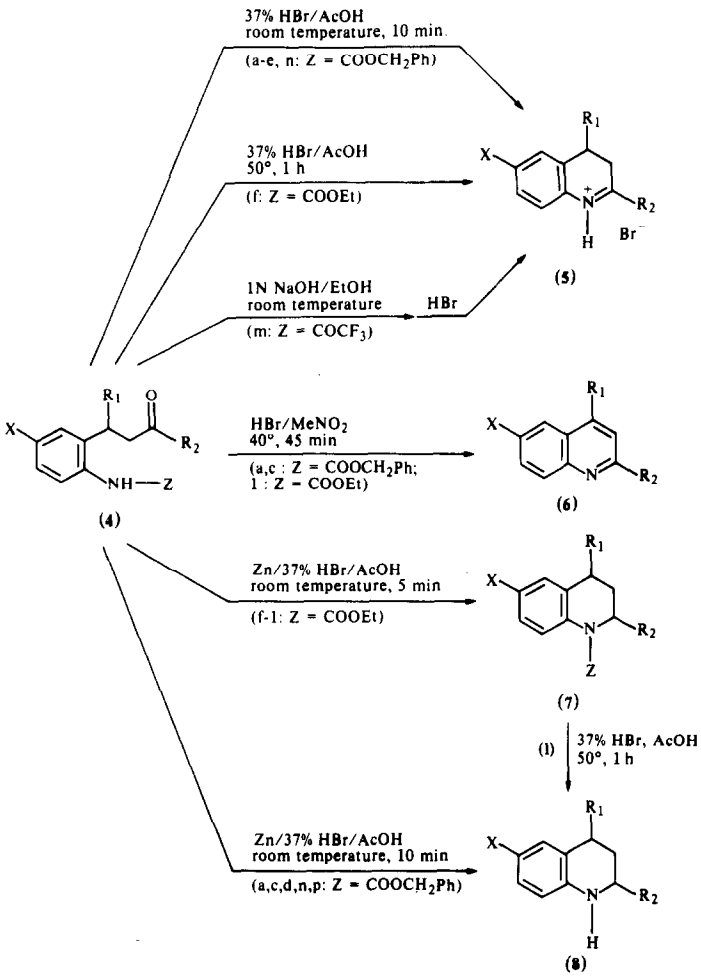
Finally, as it was found in the palladium-catalysed synthesis of 2-chromanols and 2-chromenes,[3] even in this case the presence of two chloromercury groups in the aromatic ring to be transferred provides a convenient synthesis of molecules difficult to be prepared using known methods. The reaction was tested by reacting methyl, vinyl ketone with 2-(N-benzyloxycarbonylamino) - 5 - chloromercuryphenylmercury chloride (entry o, Table 2). Compound **4o** was obtained in 85% yield and its deprotection-cyclization reaction was attempted under conditions shown in Scheme 5.

In the presence of zinc powder and 37% HBr in AcOH, the usual reductive cyclization was observed as well as the reduction of the carbonyl group on the side chain. Compound **8o'** was isolated in 84% yield. When compound **4o** was reacted under milder conditions (zinc powder, 10% HBr in AcOH) we were able to isolate the tetrahydroquinoline **9** containing the unchanged ketonic and benzyloxycarbonyl groups. Tetrahydroquinoline **8o** was obtained by treating **9** with 37% HBr in AcOH at room temperature.

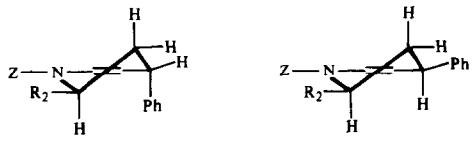
In conclusion, the described results suggest that this method is a simple and convenient new route to a variety of quinoline derivatives and a valuable alternative to the known procedures.



Scheme 2.



Scheme 3.



7(f,f',g,g'): Z = COOEt; R_2 = Me

7(h,h'): Z = COOEt; R_2 = CH_2Ph

8(c,c'): Z = $H_2^+Br^-$; R_2 = Me

Scheme 4.

Table 2. Palladium-catalysed addition of

Entry	Arylmercury compound (2) X	Z	α,β-Enone (3) R_1	R_2	Reaction time (h)	Yield of (4) (%)[b,c]	M.p. (°C)
a	Me	$COOCH_2Ph$	H	Me	8	86	54-55
b	Cl	$COOCH_2Ph$	Ph	Ph[7]	9	84	oil
c	Cl	$COOCH_2Ph$	Ph	Me	5	93	55-56
d	Cl	$COOCH_2Ph$	H	Me	8	88	92-93
e	Me	$COOCH_2Ph$	Ph	Ph[7]	9	85	oil
f	Me	COOEt	Ph	Me	7	87	119-120
g	Cl	COOEt	Ph	Me	6	87	123-124
h	Me	COOEt	Ph	CH_2Ph[8]	6	91	153-154
i	Cl	COOEt	H	Me	5	86	92-93
l	Me	COOEt	H	Me	5	84	51-52
m	Cl	$COCF_3$	Ph	Me	6	88	125-126
n	Me	$COOCH_2Ph$	H	Et	6	87	51-53
o	HgCl	$COOCH_2Ph$[f]	H	Me	6	85	61-63
p	MeCO	$COOCH_2Ph$	H	Me	7	89	93-94

a) Reactions were carried out at room temperature, with a 50 mol % excess of
b) Yields are calculated on the starting α,β-enone and are given on the isola
c) Satisfactory C, H, and N analyses and mass spectra in agreement with the p
d) Unless otherwise noted, IR spectra were recorded in nujol.
e) Liquid film.
f) Reaction was carried out by using a 2:1 (3):(2) molar ratio. Under these
isolated as the main product.

2-(N-acylamino)arylmercury compounds 2 to α,β-enones 3[a]

IR $\nu(cm^{-1})$[d]	^{1}H-NMR ($CDCl_3$) δ (ppm)
3295, 1705, 1690, 1520, 1235, 1050, 805, 745, 715, 690	7.93 (bs, 1H), 7.53 (d, 7.5 Hz, 1H), 7.50-7.20 (m, 5H), 7.05-6.85 (m, 2H), 5.17 (s, 2H), 2.70 (s, 4H), 2.23 (s, 3H), 2.00 (s, 3H)
3320, 1720, 1675, 1500, 1210, 1040, 820, 745, 690[e]	8.00-7.00 (m, 19H), 5.20 (s, 2H), 4.95 (q, 6 Hz, 8 Hz, 1H), 3.85 (q, 8 Hz, 18 Hz, 1H), 3.63 (q, 6 Hz, 18 Hz, 1H)
3300, 1710, 1510, 1220, 1050, 820, 750, 700	7.70 (bs, 1H), 7.60 (d, 9 Hz, 1H), 7.40-7.00 (m, 12H), 5.17 (s, 2H), 4.70 (t, 7.5 Hz, 1H), 3.12 (d, 7.5 Hz, 2H), 1.98 (s, 3H)
3320, 1715, 1700, 1520, 1220, 1035, 810, 765, 730, 690	8.17 (bs, 1H), 7.67 (d, 8 Hz, 1H), 7.45-7.00 (m, 7H), 5.20 (s, 2H), 2.70 (s, 4H), 2.03 (s, 3H)
3330, 1720, 1675, 1510, 1205, 1040, 810, 745, 690[e]	7.95-6.85 (m, 19H), 5.18 (s, 2H), 4.97 (q, 6.7 Hz, 7.5 Hz, 1H), 3.80 (q, 7.5 Hz, 17.6 Hz, 1H), 3.57 (q, 6.7 Hz, 17.6 Hz, 1H), 2.10 (s, 3H)
3260, 1715, 1700, 1520, 1300, 1230, 1055, 815, 765, 730, 700	7.48 (d, 7.5 Hz, 1H), 7.30-6.87 (m, 8H), 4.75 (t, 7.5 Hz, 1H), 4.20 (q, 7.0 Hz, 2H), 3.21 (d, 7.5 Hz, 2H), 2.22 (s, 3H), 2.05 (s, 3H), 1.27 (t, 7.0 Hz, 3H)
3250, 1705, 1505, 1290, 1230, 1165, 815, 760, 725, 700	7.70-7.05 (m, 9H), 4.75 (t, 7.2 Hz, 1H), 4.20 (q, 7.0 Hz, 2H), 3.20 (d, 7.2 Hz, 2H), 2.07 (s, 3H), 1.28 (t, 7.0 Hz, 3H)
3320, 1710, 1510, 1235, 1210, 1050, 815, 760, 740, 695	7.47 (d, 8.0 Hz, 1H), 7.30-6.70 (m, 13H), 4.77 (dd, 8.4 Hz, 6.6 Hz, 1H), 4.17 (q, 7.0 Hz, 2H), 3.57 (s, 2H), 3.30 (dd, 8.4 Hz, 17.3 Hz, 1H), 3.10 (dd, 6.6 Hz, 17.3 Hz, 1H) 2.15 (s, 3H), 1.25 (t, 7.0 Hz, 3H)
3300, 1705, 1690, 1530, 1250, 1100, 825, 775	8.10 (bs, 1H), 7.65 (d, 9.0 Hz, 1H), 7.20-7.05 (m, 2H), 4.20 (q, 7.0 Hz, 2H), 2.80 (s, 4H), 2.10 (s, 3H), 1.30 (t, 7.0 Hz, 3H)
3300, 1705, 1690, 1530, 1210, 1075, 825, 815, 775	7.84 (bs, 1H), 7.52 (d, 7.5 Hz, 1H), 7.07-6.85 (m, 2H), 4.20 (q, 7.0 Hz, 2H), 2.77 (s, 4H), 2.25 (s, 3H), 2.05 (s, 3H), 1.30 (t, 7.0 Hz, 3H)
3330, 1720, 1700, 1515, 1160, 910, 820, 720, 700	9.97 (bs, 1H), 7.62 (d, 8.5 Hz, 1H), 7.35-7.05 (m, 7H), 4.70 (t, 7.0 Hz, 1H), 3.33 (d, 7.0 Hz, 2H), 2.14 (s, 3H)
3260, 1720, 1700, 1590, 1520, 1290, 1210, 1030, 805, 750, 700	7.92 (bs, 1H), 7.63-6.85 (m, 8H), 5.20 (s, 2H), 2.70 (s, 4H), 2.28 (q, 7.5 Hz, 2H), 2.23 (s, 3H), 0.95 (t, 7.5 Hz, 3H)
3270, 1710, 1520, 1300, 1220, 1035, 825, 750, 700	8.00 (bs, 1H), 7.58 (d, 7.5 Hz, 1H), 7.47-6.87 (m, 7H), 5.20 (s, 2H), 2.75 (s, 8H), 2.08 (s, 3H), 2.04 (s, 3H)
3320, 1725, 1715, 1670, 1585, 1530, 1220, 1040, 770, 750, 700	8.53 (bs, 1H), 8.00 (d, 9.0 Hz, 1H), 7.75 (m, 2H), 7.50-7.25 (m, 5H), 5.23 (s, 2H), 2.83 (m, 4H), 2.50 (s, 3H), 2.08 (s, 3H)

the organomercury compound in the presence of 5 mol % of $PdCl_2$ and 10 mol % of TBA^+Cl^-.
ted products.
roposed structures were obtained.

conditions 4-[5-(3-oxo-butyl)-2-(N-benzyloxycarbonylamino)]-phenyl butan-2-one was

Table 3. 3,4-Dihydroquinoline hydrobromides 5[a]

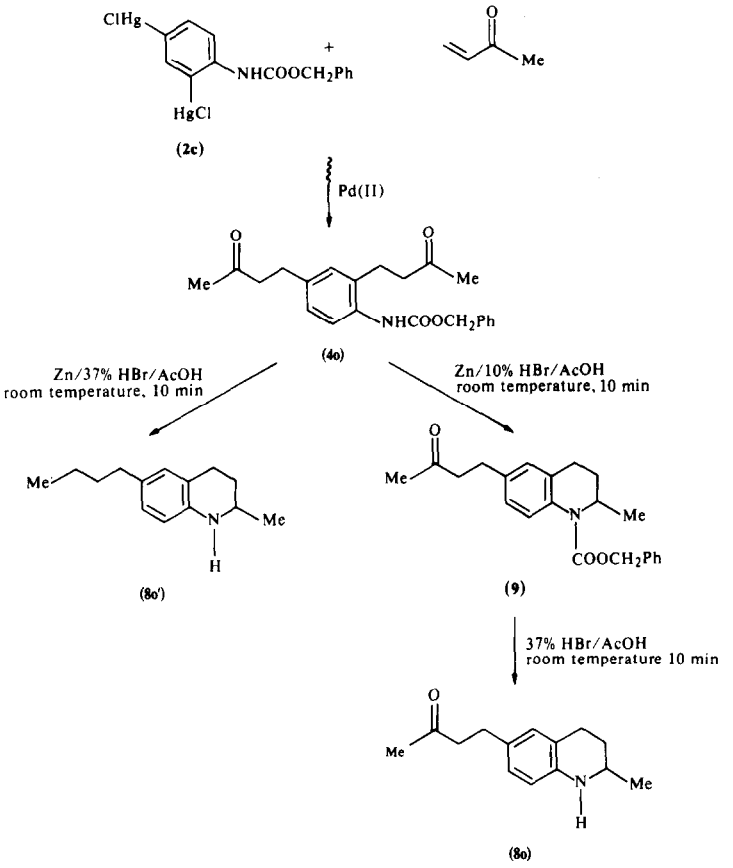
Product[b]	Yield (%)[c]	M.p. (°C)	IR ν (cm^{-1})[d]	^{1}H-NMR ($CDCl_3$) δ (ppm)
5a	96	176–178	2630, 1665, 1030, 900 835, 755, 705	15.60(bs, 1H), 7.87 (d, 9,0 Hz, 1H), 7.00 (m, 2H), 3.10 (m, 4H), 3.00 (s, 3H), 2.37 (s, 3H)
5b	92	168–170	2680, 1630, 1600, 885, 760, 740, 605	15.60 (bs, 1H), 8.78 (d, 8.4 Hz, 1H), 8.45 (d, 7.5 Hz, 2H), 7.70–6.90 (m, 10H), 4.65 (dd, 7.5 Hz, 10.5 Hz, 1H), 4.00 (dd, 7.5 Hz, 18.5 Hz, 1H), 3.70 (dd, 10.5 Hz, 18.5 Hz, 1H)
5c	95	175–178	2600, 1600, 1030, 855, 815, 755, 695	15.65 (bs, 1H), 8.05 (d, 8.1 Hz, 1H), 7.50–6.90 (m, 7H), 4.68 (dd, 8.2 Hz, 11.2 Hz, 1H), 3.58 (dd, 8.2 Hz, 19.1 Hz, 1H), 3.32 (dd, 11.2 Hz, 19.1 Hz, 1H), 2.97 (s, 3H)
5d	88	196–198	2650, 1020, 815, 750, 715	15.60 (bs, 1H), 7.80 (d, 9.0 Hz, 1H), 7.33 (m, 2H), 3.13 (m, 4H), 2.90 (s, 3H)
5e	91	182–185	2685, 1635, 1600, 825, 790, 750, 700	15.35 (bs, 1H), 8.78 (d, 8.1 Hz, 1H), 8.45 (d, 7.5 Hz, 2H), 7.70–7.10 (m, 9H), 6.90 (s, 1H), 4.55 (dd, 6.7 Hz, 9.0 Hz, 1H), 3.92 (dd, 6.7 Hz, 17.5 Hz, 1H), 3.67 (dd, 9.0 Hz, 17.5 Hz, 1H), 2.30 (s, 3H)
5f[e]	67	169–173	2650, 1670, 1030, 810, 760, 700	15.63 (bs, 1H), 8.00 (d, 8.2 Hz, 1H), 7.45–7.00 (m, 6H), 6.80 (s, 1H), 4.50 (dd, 7.9 Hz, 9.7 Hz, 1H), 3.53 (dd, 7.9 Hz, 18.7 Hz, 1H), 3.23 (dd, 9.7 Hz, 18.7 Hz, 1H), 2.90 (s, 3H), 2.25 (s, 3H)
5n	95	164–166	2680, 1670, 1620, 945, 900, 840	15.40 (bs, 1H), 7.93 (d, 9.0 Hz, 1H), 7.10 (m, 1H), 3.33 (q, 7.5 Hz, 2H), 3.13 (m, 4H), 2.35 (s, 3H), 1.41 (t, 7.5 Hz, 3H)

a) Reactions were carried out by treating compounds (4) with a 37% HBr solution in AcOH at room temperature for about 10 min.
b) Satisfactory C, H, and N analyses were obtained.
c) Yields are calculated on the starting compounds (4) and are given on the isolated products.
d) Nujol.
e) The reaction was carried out at 50°C.

Table 4. Quinolines 6[a]

Product[b]	Yield (%)[c]	M.p.[d] (°C)	IR ν(cm^{-1})[d,e]	^{1}H-NMR ($CDCl_3$) δ(ppm)
6a	74	225-229	2610, 1600, 840	7.93 (d, 9.0 Hz, 1H), 7.90 (d, 8.2 Hz, 1H), 7.50 (m, 2H), 7.20 (d, 8.2 Hz, 1H), 2.70 (s, 3H), 2.50 (s, 3H)
6c	77	270-272	2580, 1600, 1160, 860, 755, 700	7.97 (d, 9.0 Hz, 1H), 7.80 (d, 2.2 Hz, 1H), 7.50 (dd, 2.2 Hz, 9.0 Hz, 1H), 7.40 (m, 5H), 7.12 (s, 1H), 2.67 (s, 3H)
6l	82	237-239	2640, 1595, 880, 780, 755	8.20 (m, 3H), 7.80 (s, 1H), 7.70-7.40 (m, 10H), 2.50 (s, 3H)

a) Reactions were carried out by treating compounds (4) with HBr in nitromethane at 40° for about 45 min.
b) Satisfactory C, H, and N analyses and mass spectra in agreement with the proposed structures were obtained.
c) Yields are calculated on the starting compounds (4) and are given on isolated products.
d) As the hydrobromide.
e) Nujol.



Scheme 5.

Table 5. N-Ethoxycarbonyl-1,2,3,4-tetrahydroquinolines 7[a]

Product[b]	Yield (%)[c]	M.p. (°C)	IR ν (cm^{-1})	^{1}H-NMR ($CDCl_3$) δ (ppm)
7f[f] (trans)	28	123-124	1695, 1280, 1055, 830, 780, 710[d]	7.48 (d, 8.4 Hz, 1H), 7.30-6.95 (m, 6H), 6.78 (m, 1H), 4.50 (sext, 1H), 4.19 (m, 2H), 4.07 (dd, 6 Hz, 8.5 Hz, 1H), 2.33 (m, 1H), 2.23 (s, 3H), 1.95 (dt, J_t = 6 Hz, J_d = 13.5 Hz, 1H), 1.25 (t, 7.5 Hz, 3H), 1.21 (d, 6 Hz, 3H)
7f'[f] (cis)	69	157-158	1695, 1280, 1060, 830, 780, 710[d]	7.42-7.18 (m, 6H), 6.99 (m, 1H), 6.30 (m, 1H),4.55 (m, 1H), 4.24 (m, 2H), 3.74 (dd, 3 Hz, 13 Hz, 1H), 2.49 (qd, 3 Hz, 8.2 Hz, 12.8 Hz, 1H), 2.16 (s, 3H), 1.70 (td, J_d = 9.9 Hz, J_t = 12.8 Hz, 1H), 1.31 (t, 7 Hz, 3H), 1.27 (d, 6.2 Hz, 3H)
7g[f] (trans)	30	142-144	1700, 1330, 1310, 1250, 1105, 1050, 835, 765, 710[d]	7.60 (d, 8.5 Hz, 1H), 7.40-7.03 (m, 6H), 6.94 (d, 2.2 Hz), 4.56 (sext, 1H), 4.22 (m, 2H), 4.09 (dd, 6 Hz, 9 Hz, 1H), 2.31 (qd, 5.2 Hz, 9 Hz, 13.5 Hz, 1H), 1.99 (dt, J_t = 6 Hz, J_d = 13.5 Hz, 1H), 1.27 (t, 7 Hz, 3H), 1.22 (d, 6Hz, 3H).
7g'[f] (cis)	66	176-178	1700, 1325, 1245, 1095, 1055, 890, 835, 765, 710[d]	7.50-7.05 (m, 7H), 6.48 (m, 1H), 4.55 (m, 1H), 4.26 (m, 2H), 3.72 (dd, 3 Hz, 12.7 Hz, 1H), 2.51 (qd, 3Hz, 8.2 Hz, 12.7 Hz, 1H), 1.72 (td, J_d = 9.7 Hz, J_t = 12.7 Hz, 1H), 1.31 (t, 7 Hz, 3H), 1.28 (d, 5.9 Hz, 3H)
7h[f] (trans)	29	96-98	1700, 1500, 1325, 1140, 1050, 820, 755, 705[e]	7.52 (d, 8.5 Hz, 1H), 7.28-6.98 (m, 11H), 6.79 (m, 1H), 4.66 (m, 1H), 4.09 (m, 3H), 2.98 (dd, 7.2 Hz, 13.2 Hz, 1H), 2.67 (dd, 7.6 Hz, 13.2 Hz, 1H), 2.23 (s, 3H), 2.20 (qd, 5.7 Hz, 8.7 Hz, 13.5 Hz, 1H), 2.04 (dt, J_t = 6 Hz, J_d = 13.5 Hz, 1H), 1.16 (t, 7.1 Hz, 3H).
7h'[f] (cis)	65	108-109	1700, 1500, 1325, 1265, 1130, 1045, 825, 775, 750, 708[e]	7.44-7.13 (m, 11H), 7.00 (m, 1H), 6.33 (m, 1H), 4.71 (qd, 1H), 4.20 (m, 2H), 3.70 (dd, 3 Hz, 12.7 Hz, 1H), 3.24 (dd, 5 Hz, 12.7 Hz, 1H), 2.58 (dd, 8.8 Hz, 12.7 Hz, 1H), 2.30 (qd, 3.2 Hz, 8.1 Hz, 13 Hz, 1H), 2.15 (s, 3H), 1.75 (td, J_d = 9.6 Hz, J_t = 12.7 Hz, 1H), 1.28 (t, 7.1 Hz, 3H)
7i	95	oil	1700, 1320, 1215, 1090, 1045, 815, 765[e]	7.58 (d, 8.5 Hz, 1H), 7.10 (m, 2H), 4.62 (sext, 6.4 Hz, 1H), 4.21 (q, 7.2 Hz, 2H), 2.62 (m, 2H), 2.15 (m, 1H), 1.53 (m, 1H), 1.27 (t, 7.2 Hz, 3H), 1.12 (d, 6.4 Hz, 3H)
7l	98	oil	1700, 1500, 1320, 1225, 1310, 1045, 815, 765, 730[e]	7.47 (d, 8.1 Hz, 1H), 6.92 (m, 2H), 4.58 (sext, 6.4 Hz, 1H), 4.17 (m, 2H), 2.57 (m, 2H), 2.23 (s, 3H), 2.10 (m, 1H), 1.47 (m, 1H), 1.23 (t, 7.2 Hz, 3H), 1.10 (d, 6.7 Hz, 3H)

a) Reactions were carried out by treating compounds (4) with zinc powder, 37 % HBr in AcOH at room temperature for about 5 min.
b) Satisfactory C, H and N analyses and mass spectra in agreement with the proposed structures were obtained.
c) Yields are calculated on the starting compounds (4) and are given on the isolated products.
d) Nujol.
e) Liquid film.
f) Cis and trans isomers were isolated through semipreparative HPLC by using a 1x25 cm column packed with LiChrosorb Si-60 (10 μ) and eluting with n-hexane/EtOAc mixtures (5 ml/min).

Table 6. 1,2,3,4-Tetrahydroquinolines 8[a]

Product[b]	Yield (%)[c]	M.p.[d] (°C)	IR ν (cm^{-1})	^{1}H-NMR ($CDCl_3$) δ (ppm)
8a	92	174–176	2700, 2500, 1210, 1150, 955, 825[d,e]	6.77 (m, 2H), 6.38 (d, 9.0 Hz, 1H), 3.38 (bs, 1H), 3.30 (m, 1H), 2.70 (m, 2H), 2.18 (s, 3H), 2.0–1.35 (m, 2H), 1.13 (d, 6.0 Hz, 3H). 10.85 (bs, 1H), 7.61 (d, 8.0 Hz, 1H), 7.08 (m, 2H), 3.71 (m, 1H), 2.88 (t, 6.7 Hz, 2H), 2.30 (s, 3H), 2.21 (m, 2H), 1.72 (d, 7.0 Hz, 3H)[d].
8c[g] (trans)	28	208–210	3405, 1600, 1310, 1280, 815, 765, 705[f]	11.30 (bs, 2H), 7.88 (d, 8.5 Hz, 1H), 7.37–7.23 (m, 5H), 7.10–7.02 (m, 2H), 4.30 (t, 5.7 Hz, 1H), 3.94 (m, 1H), 2.55 (qd, 6.2 Hz, 9.0 Hz, 14.8 Hz, 1H), 2.32 (qd, 3.0 Hz, 5.5 Hz, 14.8 Hz, 1H), 1.72 (d, 6.7 Hz, 3H)[d].
8c'[g] (cis)	58	200–205	3405, 1600, 1300, 1270, 815, 745, 705[f]	11.30 (bs, 2H), 7.86 (d, 8.7 Hz, 1H), 7.39–7.21 (m, 6H), 6.92 (m, 1H), 4.15 (dd, 6.2 Hz, 11.6 Hz, 1H), 3.85 (m, 1H), 2.56 (dt, J_t = 12.0 Hz, J_d = 14.5 Hz, 1H), 2.36 (qd, 2.2 Hz, 6.2 Hz, 14.5 Hz, 1H), 1.88 (d, 6.5 Hz, 3H)[d].
8d	89	184–186	3405, 1610, 1305, 1140, 880, 810[f]	6.90 (m, 2H), 6.33 (d, 9.0 Hz, 1H), 3.60 (bs, 1H), 3.30 (m, 1H), 2.68 (m, 2H), 1.80 (m, 1H), 1.50 (m, 1H), 1.13 (d, 7.0 Hz, 3H).
8n	96	206–207	2650, 2480, 1205, 810[d,e]	6.80 (m, 2H), 6.40 (d, 9.0 Hz, 1H), 3.60 (bs, 1H), 3.10 (m, 1H), 2.72 (m, 2H), 2.18 (s, 3H), 1.90 (m, 1H), 1.50 (m, 3H), 0.96 (t, 7.5 Hz, 3H).
8o[h]	93	161–163[i]	3380, 1710, 1615, 1310, 1155, 810[f]	6.78 (m, 2H), 6.38 (d, 9.0 Hz, 1H), 3.35 (m, 2H), 2.75 (m, 6H), 2.10 (s, 3H), 2.07–1.30 (m, 2H), 1.18 (d, 6.0 Hz, 3H).
8p	88	208–210	3390, 1700, 1615, 1305, 1145, 820, 735[e]	6.83 (m, 2H), 6.38 (d, 9.0 Hz, 1H), 3.67 (bs, 1H), 3.37 (m, 1H), 2.70 (m, 2H), 2.05 (s, 3H), 2.00–1.35 (m, 2H), 1.17 (d, 6.5 Hz, 3H).

a) Reactions were carried out by treating compounds (4) with zinc powder, 37% HBr in AcOH at room temperature for about 10 min.
b) Satisfactory C, H, and N analyses were obtained.
c) Yields are calculated on the starting compound (4) and are given on the isolated products.
d) As the hydrobromide.
e) Nujol.
f) Liquid film.
g) Cis and trans isomers were isolated through semipreparative HPLC by using a 1x25 cm column packed with LiChrosorb Si-60 (10 μ) and eluting with n-hexane/EtOAc 97/3 (5 ml/min).
h) When (4o) was treated under the above conditions, even reduction of the carbonyl of the side chain was observed and after usual work-up (see preparation of (7)) 2-methyl-6-n-butyl-1,2,3,4-tetrahydroquinoline (8o') was obtained in 84% yield: m.p. : oil; IR (liquid film) ν (cm^{-1}): 3400, 1610, 1310, 805; ^{1}H-NMR ($CDCl_3$) δ (ppm): 6.78 (m, 2H), 6.37 (d, 9.0 Hz, 1H), 3.46 (bs, 1H), 3.30 (m, 1H), 2.70 (m, 2H), 2.48 (t, 7.0 Hz, 2H), 1.85 (m, 1H), 1.70–1.25 (m, 5H), 1.33 (d, 7.0 Hz, 3H), 0.90 (t, 7.5 Hz, 3H). Compound (8o) was prepared from (9) according to the scheme 4.
i) As the 2,4-dinitrophenylhydrazone derivative.

EXPERIMENTAL

M.ps are uncorrected and were determined with a Büchi apparatus. Methylvinyl ketone, ethylvinyl ketone, and benzalacetone were used without further purification. Chalcone and 1,4 - diphenyl - but - 3 - en - 2 - one were prepared according to cited references. Organomercury compounds **1** and **2** were prepared according to cited references. Tetrabutylammonium chloride and $PdCl_2$ were purchased from Fluka and used as such. The products were purified on silica gel open columns (SiO_2-60, 70–230 mesh, Merck) eluting with cyclohexane/EtOAc mixtures or on semipreparative HPLC (stainless steel 1 × 25 cm column, packed with LiChrosorb Si-60, 10 μ) eluting with n-hexane/EtOAc mixtures. Semipreparative HPLC separations were performed using a Waters ALC/GPC-202 chromatograph equipped with a U6-K injector, a Model M6000 solvent delivery system, and a Model 401 refractive index detector.

IR spectra were recorded with a Perkin–Elmer 297 spectrometer. ^{1}H NMR spectra (measured in $CDCl_3$ with TMS as an internal standard) were usually recorded with a Varian EM 390 spectrometer and with a Bruker CXP-300 spectrometer when *cis* and *trans* isomers of tetrahydroquinolines **7f, f', g, g', h, h'** and **8c, c'** were analyzed.

General procedure of reaction of 2 - (*N - acylamino*) - *phenylmercury compounds* **2** *with* α,β*-enones* **3**

This is exemplified by the reaction of 2 - (N - benzyloxycarbonylamino)-5-chlorophenylmercury chloride with benzalacetone (entry c, Table 2). To a stirred solution of benzalacetone (1.0 g, 6.85 mmol) in dichloromethane (13 ml) were added 3N HCl (8.0 ml), TBA^+Cl^- (0.190 g, 0.685 mmol), $PdCl_2$ (0.060 g, 0.342 mmol), and 2 - (N - benzyloxycarbonylamino) - 5 - chlorophenylmercury chloride (5.10 g, 10.27 mmol). The mixture was stirred for 5 hr at room temperature, and the organic layer was separated, washed with 10% sodium thiosulphate and water, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on silica gel. Elution with 75/25 cyclohexane/EtOAc gave 4-[5]-chloro-2-(N-benzyloxycarbonylamino)-phenyl-4-phenylbutan-2-one (2.59 g, 93% yield).

General procedure of synthesis of 3,4-*dihydroquinoline hydrobromides* **5** *from* 4 - [2 - (*N - benzyloxycarbonylamino*)] - *aryl ketones* **4a–e, n**

This is exemplified by the synthesis of 2 - methyl - 4 - phenyl - 6 - chloro - 3,4 - dihydroquinoline hydrobromide (**5c**, Table 3). 4 - [5 - Chloro - 2 - (N - benzyloxycarbonylamino)] - phenyl - 4 - phenylbutan - 2 - one (**4c**) (0.5 g, 1.22 mmol) was treated with a 37% HBr solution in AcOH (2 ml) at about 20°. After 10 min, during which time evolution of gas was observed, dilution of the reaction mixture with Et_2O (20 ml; filtered through neutral alumina) afforded 0.390 g (95% yield) of 2 - methyl - 4 - phenyl - 6 - chloro-3,4-dihydroquinoline hydrobromide as a crystalline white solid.

2,6 - *Dimethyl* - 4 - *phenyl* - 3,4 - *dihydroquinoline hydrobromide* **5f** *from* 4 - [5 - *methyl* - 2 - (*N - ethoxycarbonylamino*)] - *phenyl* - 4 - *phenyl-butan-2-one* **4f**.

Compound **4f** (0.5 g, 1.54 mmol) was reacted with 37% HBr in AcOH (3 ml) at 50°. After a 1 hr period the reaction mixture was worked up as described above to yield 2,6 - dimethyl - 4 - phenyl - 3,4 - dihydroquinoline hydrobromide (0.325 g, 67% yield).

2-*Methyl-4-phenyl-6-chloro*-3,4-*dihydroquinoline hydrobromide* **5c** *from* 4 - [5 - *chloro* - 2 - (*N - trifluoroacetyl - amino*)] - *phenyl* - 4 - *phenylbutan* - 2 - *one* **4m**.

A soln of **4m** (0.5 g, 1.35 mmol) in 95% EtOH (10 ml) was treated with 1N NaOH (3 ml) and allowed to react at room temperature for 1 hr.[10] The reaction mixture was then poured into water and extracted with CH_2Cl_2. After separation, the organic layer was dried (Na_2SO_4), and concentrated at reduced pressure. The obtained oily residue was diluted with Et_2O and HBr was bubbled to give 2 - methyl - 4 - phenyl - 6 - chloro - 3,4 - dihydroquinoline hydrobromide (0.419 g, 92% yield) as white crystals.

General procedure for synthesis of quinolines **6a, c, l**.

This is exemplified by the synthesis of 2 - methyl - 4 - phenyl - 6 - chloroquinoline hydrobromide (**6c**, Table 4). Gaseous HBr was bubbled for 15 min through a soln of 4-[5-chloro-2-(N-benzyloxycarbonylamino)] - phenyl - 4 - phenylbutan - 2 - one **4c** (0.5 g, 1.22 mmol) dissolved in 15 ml of nitromethane at room temperature with stirring. Then the solution was warmed at 40°. After 0.5 hr the reaction mixture was diluted with Et_2O, washed with water, saturated Na_2CO_3 solution, water, dried (Na_2SO_4), and concentrated at reduced pressure to afford an oil which upon purification via open column chromatography (85/15 cyclohexane/EtOAc) on silica gel yielded 2 - methyl - 4 - phenyl - 6 - chloroquinoline (0.239 g, 77% yield). Treatment of the Et_2O solution of the obtained quinoline with gaseous HBr gave the insoluble hydrobromide salt.

General procedure of synthesis of N - ethoxycarbonyl - 1,2,3,4 - *tetrahydroquinolines* **7f, f', g, g', h, h', i, l**

This is exemplified by the synthesis of N - ethoxycarbonyl - 2,6 - dimethyl - 1,2,3,4 - tetrahydroquinoline (**7l**, Table 5). 4-[5-methyl - 2-(N - ethoxycarbonylamino)] phenylbutan - 2 - one **4l** (0.5 g, 2.01 mmol) was treated with zinc powder (0.655 g, 10.08 mmol) and 37% HBr in AcOH (3 ml) at room temperature. After a 5 min period, the reaction mixture was diluted with dichloromethane, washed with a saturated Na_2CO_3 solution, and water. The organic layer was separated, dried (Na_2SO_4), and concentrated at reduced pressure. The residue was purified through silica gel open column (cyclohexane/EtOAc 90/10) to give compound **7l** (0.458 g, 98% yield).

General procedure for synthesis of 1,2,3,4 - *tetrahydroquinolines* **8a, c, c', d, n, o', p**

This is exemplified by the synthesis of 2 - methyl - 4 - phenyl - 6 - chloro - 1,2,3,4 - tetrahydroquinoline (**8c, c'**, Table 6). 4 - [5 - chloro - 2-(N - benzyloxycarbonylamino)] - phenyl - 4 - phenylbutan - 2 - one **4c** (0.5 g, 1.22 mol) was treated with zinc powder (0.4 g, 6.12 mmol) and 37% HBr in AcOH (3 ml) at room temperature. After a 10 min period the reaction mixture was worked-up as described for N-ethoxycarbonyl-1,2,3,4-tetrahydroquinolines **7**. HPLC analysis (LiChrosorb Si-60, 10 μ, 0.45 × 25 cm, n-hexane/EtOAc 93/7, 2 ml/min) of the reaction mixture revealed the presence of two isomeric quinolines with K' = 4.27 (23%) and K' = 6.41 (67%). Purification through silica gel open column (cyclohexane/EtOAc 90/10) afforded *cis–trans* 2 - methyl - 4 - phenyl - 6 - chloro - 1,2,3,4 - tetrahydroquinoline (0.316 g, 86%), quantitatively separated through semipreparative HPLC (LiChrosorb Si-60, 10 μ, 1 × 25 cm, n-hexane/EtOAc 97/3, 5 ml/min).

2,6 - *Dimethyl* - 1,2,3,4 - *tetrahydroquinoline hydrobromide* **8a** *from N - ethoxycarbonyl* - 2,6 - *dimethyl* - 1,2,3,4 - *tetrahydroquinoline* **7l**

Compound **7l** (0.5 g, 2.14 mmol) was treated with 37% HBr in AcOH (3 ml) at 50° for 1 hr. After the mixture was cooled at room temperature, Et_2O was added and hydrobromide **8a** was obtained as white crystals (0.34 g, 65% yield).

N - benzyloxycarbonyl - 2 - *methyl* - 6 - (3 - *oxo* - *butyl*) - 1,2,3,4 - *tetrahydroquinoline* **9** *from* 4 - [5 - (3 - *oxo* - *butyl*) - 2 - (*N - benzyloxycarbonylamino*)] - *phenyl* - *butan* - 2 - *one* **4o**

Compound **4o** (0.5 g, 1.36 mmol) was treated with zinc powder (0.45 g, 6.88 mmol) and 10% HBr in AcOH (6 ml) at room temperature for 15 min. The reaction mixture was worked up as described for the synthesis of tetrahydroquinolines **7**. Compound **9** was isolated in 89% yield (0.426 g): oil; IR (liquid film) ν (cm^{-1}): 2930, 1700, 1500, 1320, 1130, 1040, 810; ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.51 (d, 8.0 Hz, 1H), 7.47–7.20 (m, 5H), 6.95 (m, 2H), 5.21 (q, 12.4 Hz, 2H), 4.63 (sext, 6.5 Hz, 1H), 2.68 (m, 6H), 2.22 (m, 1H), 2.09 (s, 3H), 1.52 (m, 1H), 1.14 (d, 6.5 Hz, 3H).

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