Tetrahedron Letters No. 38, pp 3571 - 3574.
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0040-4039/78/0915-3571$02.00/0

A NEW ROUTE TO 2,4-DIBENZYLTETRAHYDROQUINOLINE. REVERSIBILITY OF THE HOMOLYTIC AROMATIC BENZYLATION.

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The benzyl radical addition to ethylene is a reversible process at 90°C[1]. Considering that the addition of a free radical to benzene has been estimated[2] to be less exothermic of ca. 11 Kcal/mole than the corrqsponding addition of a benzyl radical to ethylene, the addition of a benzyl radical to an aromatic ring should be reversible. In fact the homolytic benzylation is pratically unknown in benzene series but, because of the nucleophilic character of the benzyl radical, it is a well known type of reaction with protonated heteroaromatic bases[3].

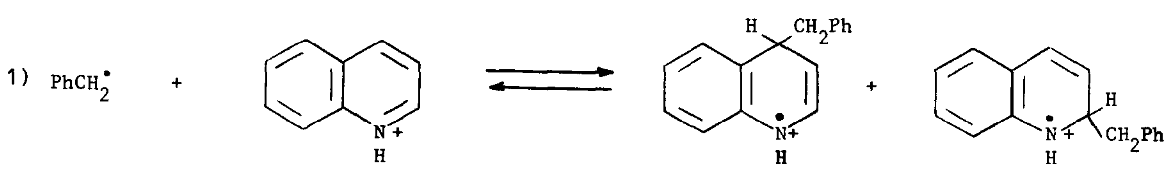
In this communication we report an unusual synthesis of 2,4-dibenzyltetrahydroquinoline from the benzyl radical addition to quinoline and preliminary evidences that this addition also is a reversible process.

The benzyl radical was generated from the oxidation of phenylacetic acid with $Ti^{3+}/Na_2S_2O_8$ system[4] (methods A, B), $Ag^{+}/Na_2S_2O_8$ system[3] (methods C, D) and uncatalized $Na_2S_2O_8$ system (method E).

4-benzylquinoline (III), 2-benzylquinoline (IV), 2,4-dibenzyltetrahydroquinoline (VI), bibenzyl (VII), benzaldehyde (VIII), benzylalcohol (IX) and benzylphenylacetate (X) account for all the generated benzyl radicals.

(VII) arises from benzyl radical dimerization, (VIII), (IX) and (X) from its oxidation, (III) and (IV) from homolytic substitution[3]. (VI) is the main product in reducing medium (Table,Method A) and we suppose it is formed according to the Scheme. Its unusual formation shows a very new method for the synthesis of this class of compounds. In fact 2,4-dibenzylquinoline cannot be the precursor because the high ratio quinoline/$Na_2S_2O_8$ prevents its formation and moreover we have verified that 2,4-dibenzylquinoline is not reduced to (VI) in the experimental conditions.

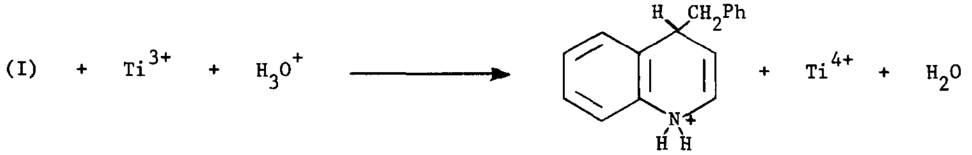
SCHEME



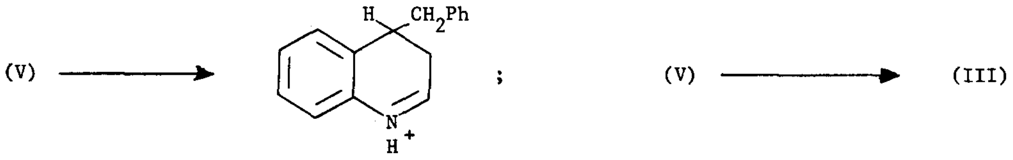
(I) (II)

(I) ⟶ (III)   (II) ⟶ (IV)

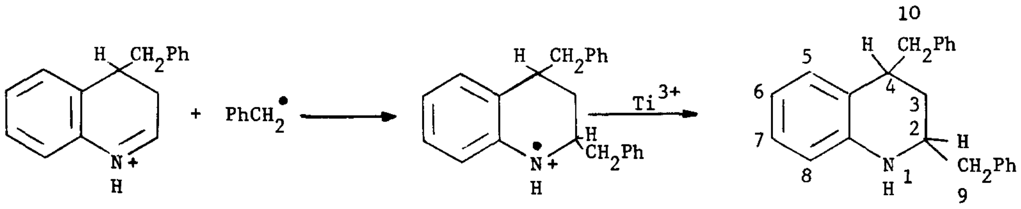
2)



(V)



3)



(VI)

The above mechanism is based on the following grounds:

a) the reduction of a radical like (I) to dihydroderivative by Ti^{3+} has already been shown[5] with acridine as substrate.

b) in absence of Ti^{3+}, (VI) is not formed at all (methods C, D, E).

c) the ratio of 4-benzylquinoline and 2,4-dibenzyltetrahydroquinoline to 2-benzylquinoline (Table, last column) remains constant independentely from the experimental conditions, even when the product (VI) is not formed.

This fact strongly suggests that (VI) is derived from (I) and the ratio in the lat column of the Table is always determined by reaction 1). The ratio between the addition products to quinoline and all the other products derived from benzyl radical dimerization (Table, last but one column) strongly increases with the reducing character of the reaction medium (from 0.43, method E, to 31, method A) This behaviour is well explained by considering the effect of Ti^{3+} salt on the reversible addition of the benzyl radical to quinoline. In fact in presence of Ti^{3+}, the fast reaction 2) shifts equilibrium 1) to the right increasing the addition products.

A decrease of the addition products as the temperature increases (methods C, D) further supports the reversibility of the reaction 1).

TABLE

PRODUCTS (moles %) FROM BENZYL RADICAL AND QUINOLINE *

Method	(VI)		(IV)		(III)		(VII)	(VIII)	(IX)	(X)	$\frac{(IV)+(III)+2(VI)}{2(VII)+(VIII)+(IX)+2(X)}$	$\frac{(III)+(VI)}{(IV)}$
	b)	a)	b)	a)	b)	a)						
A	49.5	(51.3)	14.3	(14.9)	32.6	(33.8)	1.2	2.4	-	-	31.0	5.7
B	10.1	(11.3)	12.9	(14.4)	66.4	(74.3)	5.6	5.0	-	-	6.3	5.9
C	-	-	13.4	(15.6)	72.4	(84.4)	1.3	5.7	3.6	3.6	4.5	5.4
D	-	-	9.0	(16.0)	47.0	(84.0)	0.8	0.9	40.5	1.8	1.2	5.2
E	-	-	4.6	(15.0)	26.0	(85.0)	0.4	16.0	51.6	1.4	0.43	5.6

* A (4mol.) solution of quinoline in water. Molar ratio quinoline/H_2SO_4/$Na_2S_2O_8$/$PhCH_2COOH$ = 1/5/0.33/2 .

a) The yields of the products (VI), (IV) and (III) are based on converted quinoline (33%) and given in parentheses in moles % .

b) The molar % yields not in parentheses of the products (VI), (IV), (III), (VII), (VIII), (IX) and (X) are based on the converted $PhCH_2COOH$ (16.5%) .

A: $Na_2S_2O_8$ is added to the reaction mixture containing $TiCl_3$ (0.003 mol.) . Temp. 55 °C.
B: $TiCl_3$ (0.003 mol.) is added to the reaction mixture containing $Na_2S_2O_8$. Temp. 55 °C.
C: Catalysis by Ag^+ . Temp. 55 °C.
D: " " " . Temp. 80 °C.
E: Uncatalyzed reaction. Temp. 80 °C.

A tipycal experiment is as follows:

Reaction with $Ti^{3+}/Na_2S_2O_8$ system. (method A): into a 50 ml. three-necked flask containing a bar magnet and fitted with a refrigerator, a thermometer and a pressure-equalising dropping funnel, was introduced quinoline (0.01 mol), phenylacetic acid (0.02 mol), concentrated H_2SO_4 (0.05 mol) in water (8 cc) and 4 ml. of a 15% w/v $TiCl_3$ solution. The solution was deaerated by passage of nitrogen for 1/2 hour. A $Na_2S_2O_8$ (0.003 mol) solution in water (10 ml.) deaerated in the same way was added dropwise over a period of 10 min. under vigorous stirring. The mixture was stirred for a further 10 min., cooled, made alkaline (NaOH) and extracted with chloroform. The residue from evaporation of the solvent was submitted to analytical procedures (g.l.c. and t.l.c. preparative).

All the data summarized in the Table are the medium value of three independent experiments and the result of g.l.c. analysis reproducible to within ± 3 %.

Spectroscopic properties of (VI): ^{13}C nmr ($CDCl_3$, 25.18 MHz), δ (ppm), 48.4 (d, C-2), 44.5-43.3 (t,t, C-9 + C-10), 37.9 (d, C-4), 31.1 (t, C-3); ^1H nmr ($CDCl_3$, 100 MHz, TMS as internal standard), δ (ppm), 3.6 (2H, H-2 + N-H), 3.2-2.4 (5H, H-4 + $2CH_2Ph$), 1.8-1.5 (2H, dd, 2H-3), 7.5-6.8 (12H, H-7 + H-5 + 10 H arom.), 6.6 (1H, dd, H-6), 6.4 (1H, d, H-8); IR (nujol) $\bar{v}$ 3400 cm^{-1} (m, N-H); MS m/e 313 (molecular ion), 223, 222, 131 and 130.

Acnowledgment: the authors wish to thank Prof. Minisci for helpful discussions.

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(Received in UK 13 July 1978; accepted for publication 20 July 1978)