Tetrahedron Letters No. 5, pp 443 - 446. 0040-4039/79/0129-0443$02.00/0

SYNTHESES BY MEANS OF N-BENZYLIDENEBENZYLAMINE IN A TWO-PHASE SYSTEM

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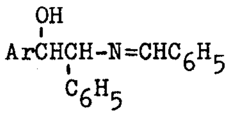
Some years ago Kauffmann et al.[1] have reported that, in THF under the action of lithium diisopropylamide, N-benzylidenebenzylamine (1) was easily metalated to afford 2. The addition of 2 to alkenes, alkynes, azomethines and nitriles resulted in some pyrrole and imidazole derivatives [2]. However, 2 failed to react with aromatic aldehydes and the reaction with benzophenone was successful only in the case when sodium amide, as catalyst, and ether as solvent was used [1]. In this paper we report the first results of our study on the possibility of using 1 as a nucleophile in aldol-type reactions under the conditions of phase-transfer catalysis, which is now well recognized and widely applied in organic synthesis [3,4,5].

$$C_6H_5CH{=}NCH_2C_6H_5 \qquad\qquad [C_6H_5CH^{\cdot}\!=\!N^{\cdot}\!=\!CHC_6H_5]^-Li^+$$

1 2

With aromatic aldehydes 1 gave the corresponding 2-amino-1-aryl-N-benzylidene-2-phenylethanols (3a-f), isolated as mixtures of diastereoisomers in 26-84% yield. In a typical procedure aq.NaOH (3 ml, 50%) was added to a mixture

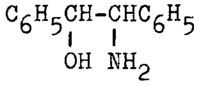


$$ArCH(OH)CH(C_6H_5){-}N{=}CHC_6H_5$$

3

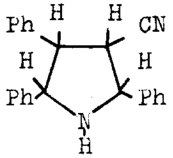
a: Ar = C_6H_5
b: Ar = $2\text{-}C_{10}H_7$
c: Ar = $2\text{-}ClC_6H_4$
d: Ar = $4\text{-}ClC_6H_4$
e: Ar = $4\text{-}CH_3C_6H_4$
f: Ar = $4\text{-}CH_3OC_6H_4$

of 1 (10 mmol), the corresponding aldehyde (10 mmol) and triethylbenzylammonium chloride - TEBA (0,5 mmol). The reaction mixture was stirred or left to stand at room temperature until it completely solidified (20-60 min), then it was worked up as previously described [6] to yield 3. In the cases when no crystallyzation took place, the reaction was prolonged for 24 hr. On the other hand, when CH_2Cl_2 or CH_3CN were used as solvents, the yields of 3 were much lower, especially in the case of CH_2Cl_2. Since compounds of this type are known to be readily hydrolyzed [1,7,8], the alcohols 3 are interesting as precursors of substituted aminoethanols. Thus, when 3a was refluxed with HCl (2N, 80°, 1 hr), 2-amino-1,2-diphenylethanol (4) was obtained in 80% yield.

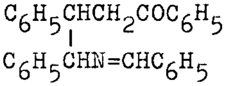


$C_6H_5\underset{|\,OH}{CH}-\underset{|\,NH_2}{CH}C_6H_5$

4



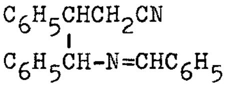
6a,b



$\begin{array}{l}C_6H_5CHCH_2COC_6H_5\\ \quad\;\; |\\ C_6H_5CHN=CHC_6H_5\end{array}$

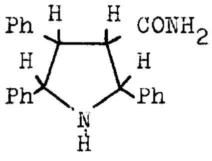
5

Under the same conditions 1 reacted with benzylideneacetophenone to give a mixture of the isomers of 1-benzylideneamino-1,2-diphenyl-3-benzoylpropane (5). The yields of 5, obtained in CH_2Cl_2, CH_3CN or in the absence of solvent were approximately the same and varied in the ranges 40-44%. The interaction of 1 with cinnamonitrile, however, led to differant products depending on the reaction conditions. When the reaction was carried out in the absence of solvent, two isomers of the tetrahydro-3-cyano-2,4,5-triphenylpyrrole (6a, m.p. 163-165°, 8% and 6b, m.p. 123-125°, 14%) were formed. In CH_2Cl_2 in addition to 6a (7%),



$\begin{array}{l}C_6H_5CHCH_2CN\\ \quad\;\; |\\ C_6H_5CH-N=CHC_6H_5\end{array}$

7



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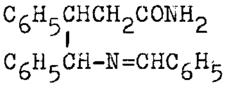
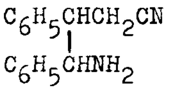


$\begin{array}{l}C_6H_5CHCH_2CONH_2\\ \quad\;\; |\\ C_6H_5CH-N=CHC_6H_5\end{array}$

9

the corresponding Michael adduct (7) was obtained in 25% yield, as a mixture of diastereoisomers. The open chain product (7) was the only isolable product in CH_3CN, the yield being 32% when the reaction was carried out at room temperature and 19% under reflux. No trace of both 6a or 6b was detected by tlc or nmr analysis of the crude reaction product. On the other hand, attempts to convert 7 into 6 (CH_2Cl_2, aq.NaOH, TEBA, 24 hr) failed.

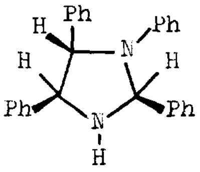
Treatment both of 6a and 7 with conc. sulfuric acid at room temperature afforded the amides 8 and 9, respectively. In contrast, when 7 was refluxed with HCl (2N, 80°, 4 hr), a mixture of the isomeric nitriles of 4-amino-3,4-diphenylbutyric acid (10, 60%) was formed.



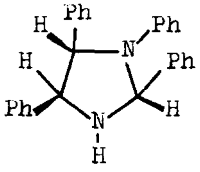
$$\begin{array}{l} C_6H_5CHCH_2CN \\ \quad\;\; | \\ C_6H_5CHNH_2 \end{array}$$

10

Recently it has been found that under two-phase catalysis conditions 2-alkylbenzazoles, benzylcyanide and other CH-acidic compounds undergo facile addition to the C=N bond of Schiff bases to give in good yields the corresponding open chain products [9]. On the other hand, in THF in the presence of lithium diisopropylamide 1 reacted with N-benzylideneaniline to yield both isomers of 2,3,4,5-tetraphenylimidazolidine - 11a (m.p. 115-117°, 44%) and 11b (m.p. 170°,



11a



11b

19%). In a two-phase system with TEBA as catalyst the interaction of 1 and N-benzylideneaniline led also to a cycloaddition product, identical with the higher melting isomer of 2,3,4,5-tetraphenylimidazolidine (11b, 45%). In this case the same decreasing of the yield of 11b was observed when CH_3CN or CH_2Cl_2 were used as solvents (34% and 11%, respectively).

All new compounds reported here (3a-f, 5, 6a,b, 7, 8 and 9) gave satisfactory elemental analysis. Their ir and nmr spectra are in agreement with the proposed structures. Further studies toward the determination of the scope of this and other related reactions are currently in progress.

References

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(Received in UK 27 November 1978)