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# Synthesis and Mercury (II) Trifluoroacetate Mediated Cyclization of N-Aryl - Allenylmethyl Carbamide

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# SYNTHESIS & MERCURY (II) TRIFLUOROACETATE MEDIATED CYCLIZATION OF N-ARYL N-ALLENYLMETHYL CARBAMIDE

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**ABSTRACT**: A three step sequence is described for conversion of substituted phenyl carbamide into 1-cyano-4-methylidene-1,2,3,4-tetrahydro quinoline involving N-propargylation, allene formation followed by mercury (II) trifluoro acetate catalysed cyclization.

As a part of a general study of exploring the scope and synthetic utility of [3,3]-sigmatropic rearrangement involving participation of allene double bonds,[1] we undertook a study of aza-Claisen rearrangement of a substrate containing an allene moiety. In general, aromatic aza-Claisen rearrangements are considered less facile than those of their oxygen counterparts.[2] However, if the lone pair on the nitrogen atom is trapped by protonation,[3] quaternization[4] or N-oxide formation,[5] the rearrangement is accelerated considerably.

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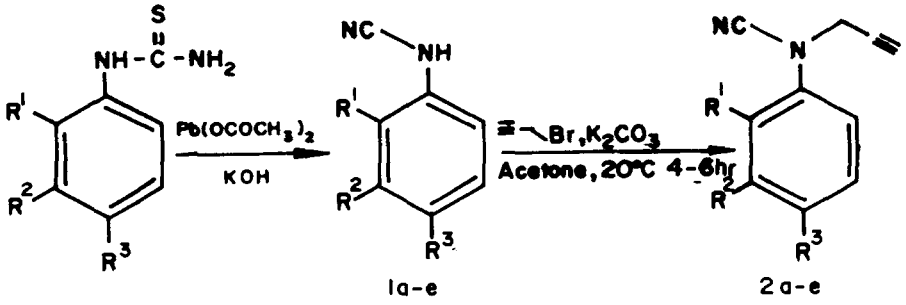
Scheme-I




Essentially, the success of aza-Claisen rearrangement depends on the weakening of the carbon-nitrogen bond a situation obtainable by using Lewis acids viz $ZnCl_2$.[6] It was anticipated that a strong $\pi$ electron withdrawing substituent of modest steric demands hooked on to the nitrogen atom can facilitate the rearrangement. A thorough survey of literature, surprisingly showed that the aza-Claisen rearrangement with $\pi$ electron acceptor like nitrile group (-CN) attached to the nitrogen atom has not been studied so far. In this communication we describe a facile preparation of N-aryl-N-allenylmethyl carbamide and its transformation to the corresponding 1-cyano-4-methylidene-1,2,3,4-tetrahydro quinoline.

Alkylation of the carbanilide **1a**, with propargyl bromide in the presence of anhydrous $K_2CO_3$ in acetone or acetonitrile at room temperature gave the N-propargylated product **2a** in high yield

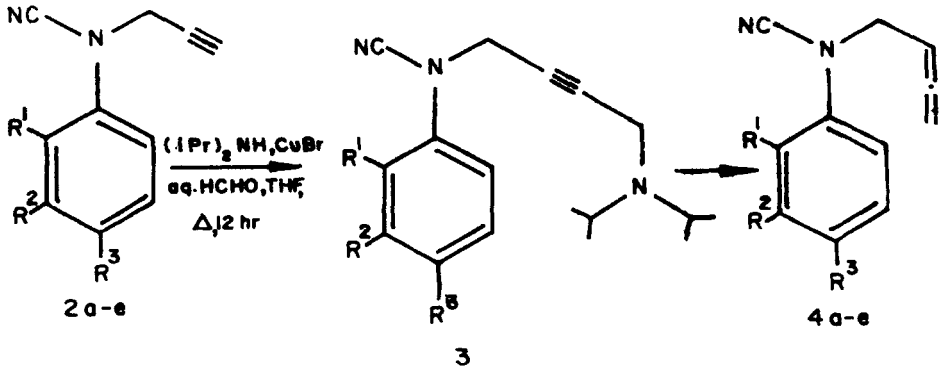
**Table I**

| Entry | Starting material | $R^1$ | $R^2$ | $R^3$ | Reaction time | Product | Yield | m.p. (°C) |
|---|---|---|---|---|---|---|---|---|
| 1 | 1a | H | H | H | 4h | 2a | 84 | 48 |
| 2 | 1b | H | H | $CH_3$ | 4h | 2b | 87 | 61 |
| 3 | 1c | H | H | $OCH_3$ | 4h | 2c | 89 | 92 |
| 4 | 1d | CH=CH-CH=CH | | H | 6h | 2d | 72 | Liquid |
| 5 | 1e | H | H | Cl | 5h | 2e | 85 | 58 |

(Scheme 1). The general applicability of the reaction was established by treating various substituted carbanilides Table I. In all these reactions the yield of the product was not increased by refluxing for 2 hours. The structures of the products were established by spectral methods.[9]

Earlier Hansen *et al.*, reported the transformation of the acetylenic function to an allene in nitrogen containing compounds although the reaction was fraught with difficulties.[3a] The N-phenyl N-allenyl methyl carbamide **4a** was prepared in one step by reacting compound **2a** with aqueous HCHO, diisopropyl amine and CuBr in THF at reflux temperature. Work up gave the desired allene as a pale yellow liquid in 65% yield. The generality of allene formation was established by reacting compound **2b-d** under conditions similar to that adopted for **2a**. However, compound **2e** gave only 20% yield of the allene (Scheme 2).

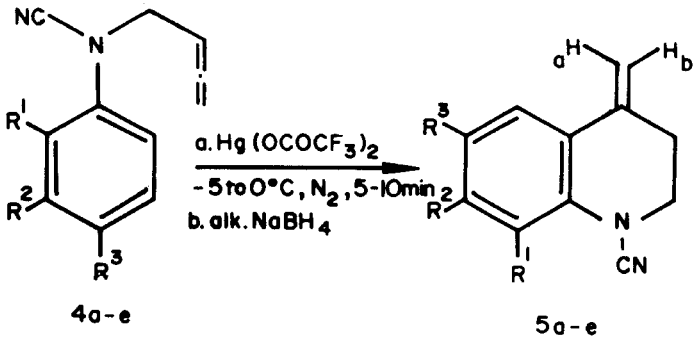
Scheme - 2




Decreasing the reaction time or lowering the temperature resulted in the isolation of Mannich product **3**. Compounds **4 a-e** were characterized by spectral data.[9]

The effect of solvent on the outcome of thermal [3,3] rearrangement has been studied quite extensively. Various high boiling solvents like o-dichlorobenzene, N,N-diethyl aniline, N-N-dimethyl aniline, PEG-200 and decalin were used for the rearrangement and no characterizable product was obtained at higher temperature at various time intervals. Attempts to effect an aza-Claisen rearrangement in the presence of $AgBF_4$ or $AlCl_3$ failed to give any rearranged product. $Hg(OCOCF_3)_2$ has been reported to catalyze the rearrangement in oxygen analogue[7] and oxy-Cope rearrangement.[8] This prompted the use of this reagent. Incidentally, it was found that when the allene was

Scheme - 3




4a-e 5a-e

treated with mercury (II) trifluoro acetate either at room temperature or at higher temperature furnished a mixture of products (by TLC).

However, treatment of allene **4a** with $Hg(OCOCF_3)_2$ at -5 to 0°C resulted in complete consumption of the starting material as revealed by TLC. Quenching the reaction mixture with alkaline $NaBH_4$ followed by work up afforded a light brown liquid which on purification by column chromatography over silica gel furnished the cyclized compound **5a** as a pale yellow liquid in 55% yield (Scheme 3). The structural assignment was based on spectral data (IR and NMR).[9]

The reaction with other allenes **4b-e**, proceeded smoothly to provide the cyclized product by the attack of the allenic $\pi_{1,2}$ rather than $\pi_{2,3}$. This revealed that the transformation probably proceeds through a mercuric ion promoted electrophillic cyclization.

Study on synthetic utility of mercury (II) trifluoroacetate in aza-Claisen rearrangement as well as the synthesis of Eupolauramine[10] by the above route is currently in progress.

## EXPERIMENTAL

### General procedure for N-alkylation. Synthesis of 2a-e

A mixture of aryl cyanamide **1a-e** (0.01 mol) and anhydrous potassium carbonate (0.01 mol) in dry acetone or acetonitrile (30 ml) was stirred at 20°C for 15 minutes. To this mixture was added a solution of propargyl bromide (0.011 mol) in dry acetone or acetonitrile (20 ml) dropwise over a period of 30 minutes. Stirring was continued for a period of 4-6 hours. The separated inorganic salts were filtered off and the solvent was distilled off. The residue was taken up in ether, washed with water and dried ($MgSO_4$). Evaporation of the solvent and crystallization from hexane-ethyl acetate yielded the desired compound.

### General procedure for allene formation. Synthesis of 4a-e

A mixture containing compound **2a** (1 mol equivalent), freshly prepared CuBr (0.5 mol), diisopropyl amine (1.6 mol) and formaldehyde (37 wt% solution in water) (1.5 mole) in THF or Dioxan was refluxed for 12 hr. After cooling the inorganic material was filtered, shaken with saturated brine, and the filtrate (organic layer) was dried ($MgSO_4$) and concentrated. The crude product was purified by chromatography over

silica gel using hexane-ethyl acetate as the eluent, which yielded compound **4a** in 65% yield. Similarly **4b-e** were obtained from **2b-e** respectively.

**General Procedure for Cyclisation using $Hg(OCOCF_3)_2$. Synthesis of 5a-e**

To a chilled (-5 to 0°C) solution of $Hg(OCOCF_3)_2$ (1.27 g, 3 mmol) in dry $CH_2Cl_2$ (30 ml) under $N_2$ atmosphere was added, with magnetic stirring compound **4a** (0.5 g, 2.94 mmol) in dry $CH_2Cl_2$ (5 ml). After 5 minutes when no trace of **4a** could be detected (TLC) the reaction mixture was quenched using alkaline 2M $NaBH_4$ solution and continued the stirring for 10 more minutes. The inorganic black material was filtered off. The organic layer was washed with water twice, dried ($MgSO_4$) and concentrated at reduced pressure. The crude material was purified by column chromatography over silica gel and elution with petrol; ethyl acetate gave compound **5a**. 0.275 g (55% yield) similarly **4b-e** were cyclised to **5b-e** respectively.

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## REFERENCES


1. a. Balakumar, A., Janardhanam, S. and Rajagopalan, K., *J. Org. Chem.* 1993, 58, 5482.

   b. Janardhanam, S., Devan, B. and Rajagopalan, K., *Tetrahedron Lett*, 1993, 6761.

   c. Huche, M. and Cresson, P., *Bull. Soc. Chim.*, France, 1974, 2040.

   d. Sleeman, M.J. and Meehan, G.V., *Tetrahedron Lett.*, 1989, 30, 3345.

   e. Dulcere, J.P. and Crandall, J.K., *J. Chem. Soc. Chem. Comm.*, 1990, 561.

   f. Ochiai, M., Ito, T., Takaoka Y. and Masaki, Y., *J. Am. Chem. Soc.*, 1991, 113, 1319.

2. a. Rhoads, S.J. and Raulins, N.R., *Org. React.*, 1974, 22,1.

   b. Bennett, G.B., *Synthesis*, 1977, 589.

   c. Lutz., R.P., *Chem. Rev.*, 1984, 84, 205.

   d. Przheval'skii, N.M. and Grandberg, I.I., *Russ. Chem. Rev.*, 1987, 56, 477.

3. a. Barmettler, P. and Hansen, H.J., *Helv. Chim. Acta*, 1990, 73, 1515.

   b. Chen, Y., Huesmann, P.L. and Mariano, P.S., *Tetrahedron. Lett.*, 1983, 24, 1021.

4. a. Koneko, K., Katayama, H., Saito, Y., Fujita, N. and Kato, A., *J. Chem. Soc. Chem. Comm.*, 1986, 1308.

   b. Katayama, H., *Chem. Pharm. Bull.*, 1978, 26, 2027.

5. Majumdar, K.C., Chattopadhyay, S.K. and Khan, A.T., *J. Chem. Soc., Perkin Trans.*, 1, 1989, 1285.

6. a. Beholz, L.G. and Stille, J.R., *J. Org. Chem.*, 1993, 58, 5095.

b. Elliot, M. and James, N.F., *J. Chem. Soc. (c)*, 1967, 1780.

c. Schmid, M., Hansen, H.J. and Schmid, H. *Helv. Chim. Acta*, 1973, 56, 104.

7. a. Balasubramanian, T. and Balasubramanian, K.K. *Tetrahedron Lett.* 1991, 32, 6641.

b. Bates, D.K. and Jones, M.C., *J. Org. Chem.*, 1978, 43, 3775.

8. Bluthe, N., Malacriae, M., and Gore, J., *Tetrahedron*, 1984, 40, 3277.

9. Spectral data for selected compounds.

2a : IR($CCl_4$, $\upsilon_{max}$, $cm^{-1}$); 3300 (-C≡CH), 2220 (-C≡N), 1590 (Aromatic C=C). $^1H$ NMR ($CDCl_3$, 400 MHz) δ: 7.22-7.18 (m, 2H, Ar-H), 6.98-6.94 (m,3H, Ar-H), 4.14 (d,2H, -N-$CH_2$), 2.41 (t,1H,-C≡CH). $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ; 138.23 (s), 129.09 (d), 123.5(d), 115.31 (d), 112.15(s), 75.46(d), 75.33(s), 39.23 (t).

2b: $^1H$ NMR ($CDCl_3$, 300 MHz), 7.13 (ABq, 4H, Ar-H), 4.34 (d, 2H, -$NCH_2$), 2.55 (t, 1H -C≡CH), 2.34 (s, 3H, Ar-$CH_3$).

4a: IR ($CCl_4$, $\upsilon_{max}$, $cm^{-1}$); 2220, 1950, 1590, 1490, 1210, 1180. $^1H$ NMR ($CDCl_3$, 400 MHz) δ; 7.2 (m, 2H, Ar-H), 6.96 (m, 3H, Ar-H), 5.15 (m, 1H, HC=), 4.76 (m, 2H, =$CH_2$), 4.03 (m, 2H, -$NCH_2$).
$^{13}C$ NMR ($CDCl_3$, 100.6 MHz) δ; 209.179(s), 139.113(s), 129.155 (d), 123.159(d), 115.479(d), 112.883(s), 84.423 (d), 77.577 (t), 48.084 (t).

4b: IR ($CHCl_3$, $\upsilon_{max}$, $cm^{-1}$): 2220, 1950,
$^1H$ NMR ($CDCl_3$, 300 MHz) δ; 7.11 (ABq, 4H, Ar-H), 5.21-5.30 (m, 1H, =CH-) 4.86-4.9 (m, 2H, =$CH_2$) 4.11-4.15 (m, 2H, -N-$CH_2$), 2.28 (S, 3H, Ar-$CH_3$).
$^{13}C$-NMR (75.4 MHz, $CDCl_3$); 209.2(s), 136.7(s), 132.8(s), 129.72(d), 115.7(d), 113.3(s), 84.55 (d), 77.51(t), 48.39 (t), 20.1(q).

5a: IR ($CHCl_3$, $\upsilon_{max}$, $cm^{-1}$), 3020, 2020, 1600, 1490, 1320, 1280, $^1$NMR ($CDCl_3$, 90 MHz) δ; 5.48 (s, 1H, $H_b$), 4.92 (s, 1H, $H_a$), 3.72 (t, 2H, - N-$CH_2$), 2.65 (t, 2H, allylic $CH_2$), 7.3 - 6.9 (m, 4H, Ar -H).

5b: IR ($CHCl_3$, $\upsilon_{max}$, $cm^{-1}$), 3020, 2020, 1595.
$^1$H NMR ($CCl_4$/TMS, 90 MHz) δ; 7.3 (s, 1H, Ar-H), 7.0 (s, 2H, Ar-H), 5.4 (s, 1H, $H_b$), 4.8 (s, 1H, $H_a$), 3.7 (t, 2H, -N-$CH_2$), 2.6 (t, 2H, Allylic - $CH_2$), 2.0 (s, 3H, Ar-$CH_3$).

10. a) Bowden, B.F., Picker, K., Ritchie, E. and Taylor, W.C. *Aust. J. Chem.*, 1975, 28, 2681.

b) Bowden, B.F., Freeman, H.C. and Jones, R.D.G., *J. Chem. Soc., Perkin Trans. 2.*, 1976, 658.

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