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Synthesis of 2(3H)-Imidazolethiones and 2(3H)-Imidazolones from ß,γ-Alkynyl Carbanilides

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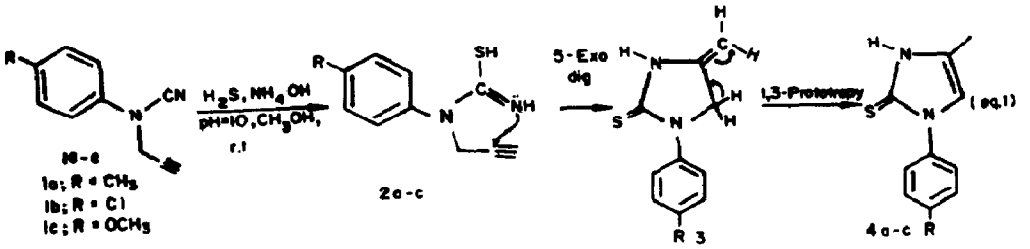
Abstract : ß, γ-Acetylenic carbanilides cyclize and subsequently isomerize to 2(3H)-Imidazolethiones and 2(3H)-Imidazolones upon treatment with ammoniacal H_2S and KOH in t-BuOH respectively.

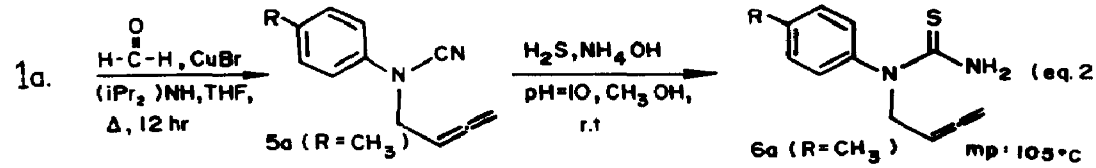
Base catalysed intramolecular addition-cyclization strategy has been receiving a great deal of attention as a potential methodology for construction of five membered heterocycles.[1,2] A number of 2(3H)-imidazolethiones have attracted considerable attention because of their pronounced antithyroid activity,[3] thus setting them apart as important synthetic targets. This prompted the communication of our findings viz., an expedient synthesis of 2(3H)-imidazolethiones and 2(3H)-imidazolones from compounds **1a-c**.

N-propargyl carbanilide **1a** was prepared in almost quantitative yield from carbanilide with propargyl bromide and K_2CO_3 in acetone or acetonitrile.[4] Compound **1a** was dissolved in methanol and the solution adjusted to pH=10 by adding NH_4OH. H_2S was passed at room temperature until a sample of the mixture no longer showed TLC spot corresponding to the starting material. The mixture was then poured onto ice and the solid which separated was filtered, dried and recrystallised from chloroform to afford 2(3H)-imidazolethione **4a** (m.p: 228°C, $CHCl_3$, 82% yield) (equation 1). The general applicability of this reaction was established with R=Cl and R=OCH_3. Addition of few drops of 1N NaOH during the reaction enhances the rate and the reaction goes to completion in one hour.

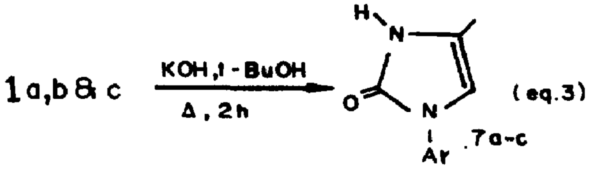


Critical analysis of ^{13}C NMR data, appearance of an NH proton in ^1H NMR at δ 12.0 and failure to get the reduced product with $NaBH_4$ clearly showed the product to have structure **4**. The reaction shows the initial attack of -SH on the nitrile carbon and cyclization occurs in a *5-exo-dig* pathway leading to intermediate **3** which on subsequent isomerization affords compound **4**. The presence of the NH proton was confirmed by D_2O exchange in ^1H NMR.

Extension of this reaction to the ß-allenyl system was investigated (eq2). The allenyl compound **5a** was prepared following conventional methods.[4,5] This system failed to cyclize under conditions described as in equation 1, but resulted in the thio urea **6a** in 70% yield.[6]



The drive for cyclization and the propensity to isomerization warrant further exploration of compound **1a-c**. The cyclization of compounds **1a-c** were also effected with powdered KOH in t-BuOH[7] at reflux temperature for 2 h. After work up, it afforded 2(3H)-imidazolones **7a-c** as the only products in almost quantitative yield (Eq.3). All the compounds gave satisfactory spectral[6] and analytical data.



In conclusion, this study demonstrates that the 5-*exo-dig* cyclization operates both in ammoniacal H_2S and KOH in t-BuOH thereby resulting in formation of 2(3H)-imidazolethiones and 2(3H)-imidazolone derivatives respectively under mild conditions and could therefore find useful applications in organic synthesis. Further work is in progress with compounds bearing good leaving group at the termini carbon of the alkyne in compound **1**.

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References

1. Short, K.M.; Ziegler, C.B.Jr. *Tetrahedron Lett.*, 1993, 34, 75-78.
2. Marshall, J.A.; DuBay, W.J. *J. Org. Chem.*, 1993, 58, 3435-3443.
3. a. Jackman, M.; Klenk, M.; Fishburn, B.; Tullar, B.F.; Archer, S. *J. Am. Chem. Soc.*, 1948, 70, 2884.
   b. Stanley, M.M.; Astwood, E.B. *Endocrinology* 1949, 44, 588-589.
   c. For a comprehensive review on 2(3H)-imidazolone and 2(3H)-imidazolethione, see Klaus Hofmann, "The Chemistry of Heterocyclic compounds" Imidazole and its derivative, part 1; Interscience Publishers, Inc., London. 1953, pp.63-91.
4. Devan, B.; Rajagopalan, K. *Synth. Commun.*, 1993, in Press.
5. a. Janardhanam, S.; Devan, B.; Rajagopalan, K. *Tetrahedron. Lett.*, 1993, 34, 6761-6764.
   b. Balakumar, A.; Janardhanam, S.; Rajagopalan, K. *J. Org. Chem.* 1993, 58, 5482-5487.
   c. Dikshit, D.K. *Ind. J. Chem.*, Sect. B., 1983, 22, 1144.
6. Spectral data of some selected compounds :
   4b : Solid (m.p. 208°C, $CHCl_3$) IR (KBr, υ_{max},cm^{-1}); 1630, 1390, 1330, 1250, 1120, 1090, 1070. ^{1}H NMR (90 MHz, $CDCl_3$), δ; 12.0 (br s, 1H,-NH) (disappears on exchange with D_2O), 7.42 (ABq, 4H, Ar-H), 6.55 (s, 1H, vinylic H), 2.19 (s,3H,-CH_3). ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ : 160. 32 (s,C_2), 136.09 (s), 133.95 (s), 129.17 (d), 127.07 (d), 125.95 (s), 115.32 (d), 9.81 (q).
   6a : IR ($CHCl_3$, υ_{max},cm^{-1}); 3500, 3380, 1950, 1585, 1460, 1360. ^{1}H NMR (300 MHz, $CDCl_3$) δ; 7.2 (ABq, 4H, Ar-H), 5.73-5.46 (br s, 2H, -NH_2), 5.44-5.13 (m, 1H, =), 4.77-4.73 (m, 2H, =), 4.70-4.66 (m, 2H, -N-CH_2), 2.39 (s-3H, Ar-CH_3). ^{13}C NMR ($CDCl_3$, 22.5 MHz) 209.44, 182.19, 139.02, 138.26, 130.78, 127.37, 85.76, 70.01, 54.34, 20.92.
   7c : Solid (m.p.218°C, $CHCl_3$-MeOH), IR ($CHCl_3$, υ_{max},cm^{-1}); 3450, 1680, 1510, 1400 ^{1} H NMR (90 MHz, $CDCl_3$) δ; 10.2 (br.s, 1H, NH) (exchange with D_2O), 7.1 (ABq, 4H, Ar-H), 6.08 (s, 1H, vinylic H), 3.8 (s, 3H,-OCH_3). 2.03 (s, 3H,-CH_3). ^{13}C NMR (DMSO-d_6, 22.5 MHz), 156.13, 152.07, 130.72, 121.89, 117.83, 113.88, 105.97, 55.04, 10.35.
7. Hall, J.H., Gisler, M., J. Org. Chem., 1976, 41, 3769-3770.

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