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TRIFLIC ACID CATALYZED DOUBLE-CYCLIZATION OF N,N-DIBENZYL-2-PROPYNYLAMINE AND RELATED COMPOUNDS

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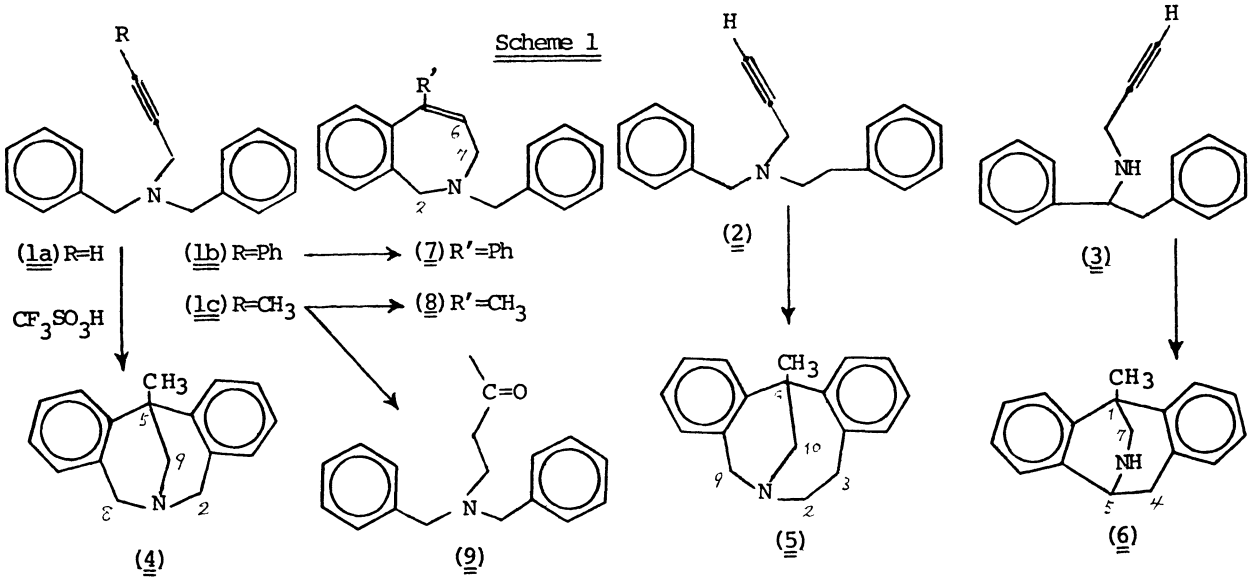
Triflic acid catalyzed double-cyclization reactions of N,N-dibenzyl-2-propynylamine, N-benzyl-N-phenethyl-2-propynylamine, and N-(α-benzylphenethyl)-2-propynylamine afforded 1-aza-5-methyldibenzo[c,f]bicyclo[3.3.1]nona-3,6-diene, 1-aza-6-methyldibenzo[d,g]bicyclo[4.3.1]deca-4,7-diene and 6-aza-1-methyldibenzo-[b,i]bicyclo[3.3.2]nona-2,8-diene in high isolated yields, respectively.

The utilization of alkynes for carbon-carbon bond formation in organic syntheses has been developed, but the reactivities of vinyl cation generated from alkynes have not been well established.[1] In our previous report[2] were described the perchloric acid catalyzed double-cyclization reactions of N,N-dibenzylaminoacetaldehyde diethylacetals to pharmacologically active 1-azadibenzo[c,f]bicyclo-[3.3.1]nona-3,6-diene in high isolated yields, independent of the nature of the substituents on the aromatic ring. We wish to describe here that N,N-dibenzyl-2-propynylamine (1a),[3] N-benzyl-N-phenethyl-2-propynylamine (2),[3] and N-(α-benzylphenethyl)-2-propynylamine (3), by employing triflic acid as cyclization catalyst,[4] are each effectively double-cyclized to afford 1-aza-5-methyldibenzo[c,f]-bicyclo[3.3.1]nona-3,6-diene (4), 1-aza-6-methyldibenzo[d,g]bicyclo[4.3.1]deca-4,7-diene (5), and 6-aza-1-methyldibenzo[b,i]bicyclo[3.2.2]nona-2,8-diene (6),[5] in high isolated yields (Scheme 1).

Scheme 1



In a typical procedure, compound 1a(1 mmol) was dissolved in 1.5g(10 mmol) of triflic acid at below 0°C and the reaction mixture was allowed to stand overnight at room temterature. The mixture was poured into cracked ice and basified with aq. NaOH, followed by extraction with dichloromethane. The resulting dichloromethane solution was concentrated and the residue was chromatographed on an alumina column to give 4, yield 95%, colorless needles, mp 123°C, m/e 235, NMR(δ, in $CDCl_3$) 1.70 (3H,s,CH_3) 3.24(2H,s,C_9-H_2) 3.95(2H,d,J=17Hz,$C_{2,8}$-H_{endo}) 4.58(2H,d,J=17Hz,$C_{2,8}$-H_{exo}) 7.0-7.6(8H,m)[6]. 5: yield 89%, colorless viscous oil, m/e 249, NMR(δ, in $CDCl_3$) 1.60(3H,s,CH_3) 2.20(1H,m,C_3-H) 2.85 (1H,m,C_3-H) 3.00-3.30(2H,m,C_2-H_2) 3.35(2H,m,C_{10}-H_2) 3.92(1H,d,J=16Hz,C_9-H_{endo}) 4.52(1H,d,J=16Hz,C_9-H_{exo}) 6.9-7.4(8H,m), HCl salt mp 189°C. 6: yield 95%, colorless viscous oil, m/e 235, NMR(δ, in $CDCl_3$) 1.73(3H,s,CH_3) 2.15(1H,s,exchanged with D_2O,NH) 2.90(1H,d,J=12Hz,C_7-H) 3.40(2H,dd,J=3Hz,17Hz, C_4-H_2) 3.50(1H,d,J=12Hz,C_7-H) 4.25(1H,t,J=3Hz,C_5-H) 7.0-7.5(8H,m), HCl salt mp >300°C.

However, in spite of the smooth double-cyclization reaction of 1a to 4, N,N-dibenzyl-3-phenyl-2-propynylamine(1b)[7], in triflic acid at room temterature for 1.5 hrs did not give any double-cyclized products, but afforded benz[c]azepine derivative(7) almost quantitatively.[8] 7: yield 95%, yellow viscous oil, m/e 311, NMR(δ, in $CDCl_3$) 2.75(2H,d,J=8Hz,C_7-H_2) 3.50(2H,s,N-CH_2-Ph) 3.60(2H,s,C_2-H_2) 6.30(1H,t,J=8Hz,C_6-H) 7.0-7.5(14H,m). Furthermore, the reaction of N,N-dibenzyl-2-butynylamine[7] (1c) in triflic acid at room temperature for 3 hrs gave a trace of benz[c]azepine derivative(8) (3%) and 4-benzylamino-2-butanone(9)[9] (52%), which were no longer subject to the double-cyclization to 1-aza-5-methyl-dibenzo[c,f]bicyclo[3.3.2]deca-3,6-diene. 8: unstable oil, m/e 249, NMR(δ,in $CDCl_3$) 2.20(3H,s,CH_3) 2.75(2H,d,J=6Hz,C_7-H_2) 3.50(2H,s,N-CH_2-Ph) 3.60(2H,s,C_2-H_2) 6.90(1H,t,J=6Hz,C_6-H) 7.1-7.5(10H,m) (Scheme 1).

Further studies along the scope and the limitation of the strong acid catalyzed double-cyclization reactions are in progress.

References and Notes

1) P.J.Stang and A.G.Anderson, J. Am. Chem. Soc., 100, 1520(1978) and the references cited therein.
2) H.Takayama, M.Takamoto, and T.Okamoto, Tetrahedron Lett., 1978, 1307.
3) 1a and 2 were prepared by the reactions of 3-bromopropyne with dibenzylamine and N-benzylphenethylamine in boiling aq. alcohol in the presence of K_2CO_3, respectively(yield: 1a 90%, 2 71%).
4) Yields of 4 from 1a by GLC analyses: 0%(CH_3SO_3H, FSO_3H), 14%($SnCl_4$) 89%(PPA), 97%<(CF_3SO_3H).
5) 3 was cyclized with PPA to afford 6 in 68% yield, contaminated with some undetermined products. J.R.Brooks, D.N.Harcourt, and R.D.Weigh, J. Chem. Soc., Perkin Trans. 1, 1973, 2588.
6) 4 was unequivocally synthesized by the $HClO_4$ catalyzed double-cyclization reaction of 1-benzylamino-2-propanone(unpublished result).
7) 1b was synthesized by Mannich reaction of dibenzylamine, paraformaldehyde, and phenylacetylene in the presence of $CuCl_2$(90%). 1c was synthesized by the reaction of 1a with n-BuLi and CH_3I(65%).
8) When 7 in triflic acid was heated at 70°-80°C, the reaction was complicated.
9) 9: mp 52°C, m/e 267, NMR(δ, in $CDCl_3$) 1.90(3H,s) 2.60(4H,m) 4.50(4H,m) 7.0-7.5(10H,m), was unequivocally synthesized by the Michael reaction of dibenzylamine with methyl vinyl ketone. Even when triflic acid anhydride was added to the reaction mixture, 9 was produced in 60% yield. Therefore, the reaction may proceed via the attack of $CF_3SO_3^-$ to the vinyl cation intermediate (P.J.Stang and R.Summerville, J. Am. Chem. Soc., 91, 4600 (1969)).

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