A FREE RADICAL INITIATED DIMERISATION IN THE SYNTHESIS OF 4, 5-BIS(2, 4-DIACETYLCARBAZOL-1-YL)-1,4,5-OXDIAZEPANES.

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Abstract: 1-(2'-Hydroxyethylimino)-1,2,3,4-tetrahydrocarbazoles 1, readily prepared by the reaction of 1-oxo-1,2,3,4-tetrahydrocarbazoles with mono ethanolamine in absolute ethanol at reflux, react smoothly with acetyl chloride in acetic anhydride and pyridine by a free radical induced dimerisation mechanism to afford the corresponding novel 4,5-bis(2,4-diacetylcarbazol-1-yl)-1,4,5-oxdiazepanes, 3.

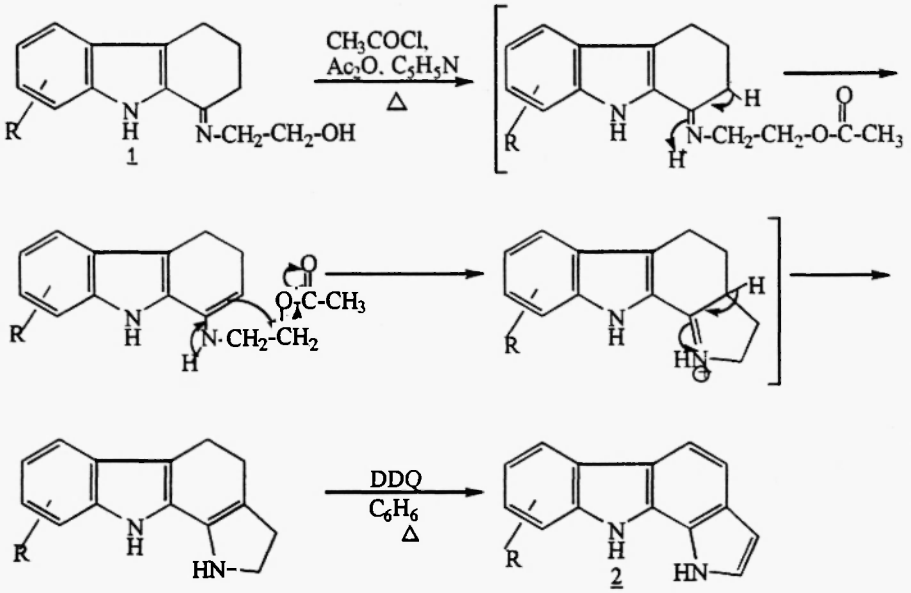
Introduction

The study of the behaviour of various ketoximes of 1-oxo-1,2,3,4-tetrahydrocarbazoles towards acetyl chloride and acetic anhydride has been in progress for some time in our laboratory.[1-4] 1-Hydroxyimino-1,2,3,4-tetrahydrocarbazoles have been found to react with acetyl chloride in acetic anhydride and pyridine to give 1-N, N-diacetylamino-2-hydroxy-3-acetylcarbazoles[1] and with acetic anhydride in pyridine to give 1-N,N-diacetylamino carbazoles.[2] 1-Hydroxyimino-1,2,3,4-tetrahydrocarbazoles have also been successfully utilized in synthesising oxazolo[4,5-*a*]carbazoles by reaction with acetyl chloride at room temperature.[3] Further, 2-acetoxy-3,4,5-trihydroazepino[2,3-*b*]indoles and 2-acetoxy-1-acetylamino-3,4-dihydrocarbazoles were realized from the reactions of 1-hydroxyimino-1,2,3,4-tetrahydrocarbazoles with acetic anhydride and anhydrous phosphoric acid.[4] Based on the above reactions involving the utility of 1-hydroxyimino-1,2,3,4-tetrahydrocarbazoles towards the synthesis of a class of interesting heterocyclic systems, we were intended to study the reactions of 1-(2'-hydroxyethylimino)-1,2,3,4-tetrahydrocarbazoles, the potential precursors which have received scant attention in deriving pyrazino[3,2,1-*j,k*]carbazoles,[5,6] with acetyl chloride and acetic anhydride in pyridine. Our interest in such reactions was further stimulated by the possibility of obtaining pyrrolo[2,3-*a*]carbazoles (Scheme 1).

Results and Discussion

Keeping the above objective in mind, 6-methyl-1-(2'-hydroxyethylimino)-1,2,3,4-tetrahydrocarbazole 1a[5] was reacted with acetyl chloride in acetic anhydride and pyridine at 80 °C. After 10 h, the reaction mixture has been worked out and the viscous liquid obtained was chromatographed over silica gel and the fraction eluted with petroleum ether - ethyl acetate (85:15) afforded a dense oil. The IR spectrum of the product exhibited a band at 1647 cm^{-1} indicating the presence of $COCH_3$ group. The ^1H - NMR spectrum of the product registered six singlets each corresponding to three protons at δ 1.81, δ 1.86, δ 1.91, δ 1.98, δ 2.39 and δ 2.73, an eight proton unresolved broad

SCHEME 1

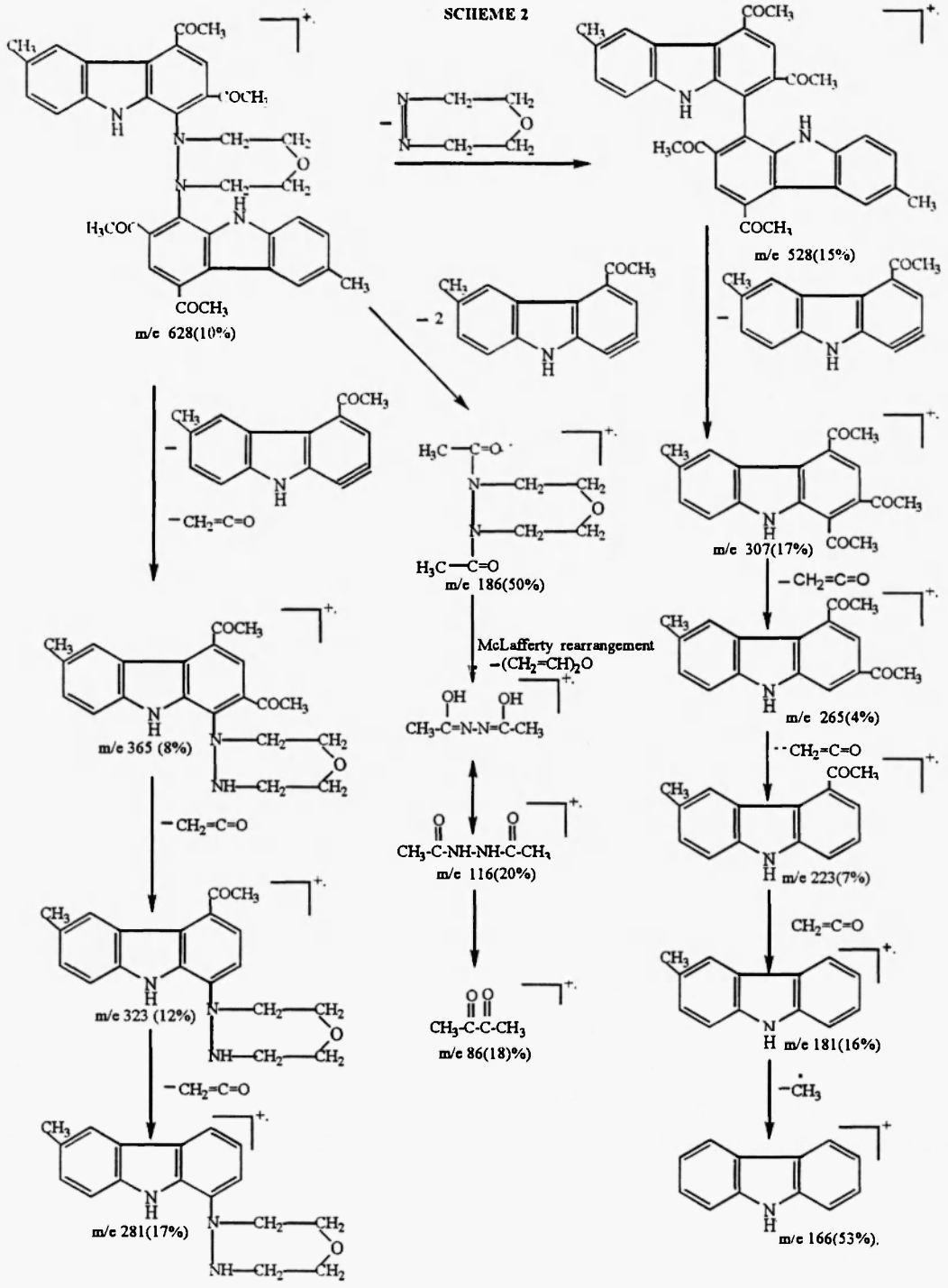


1a: R = 6-CH_3 2a: R = 7-CH_3
1b: R = 7-CH_3 2b: R = 8-CH_3
1c: R = 8-CH_3 2c: R = 9-CH_3
1d: R = 6-Cl 2d: R = 7-Cl
1e: R = H 2e: R = H

multiplet at δ 3.41 - 4.53, an eight proton aromatic envelop at δ 7.14 - 8.17 and two distinct one proton broad singlets at δ 10.16 and δ 10.70. The mass spectrum of the compound showed the molecular ion peak at m/e 628(10%). The elemental analysis: C 72.49, H 05.68, N 08.84 is compatible with the molecular formula $C_{38}H_{36}N_4O_5$. Based on the spectral and analytical data, we inferred that a dimeric product 3a would have formed during the reaction.

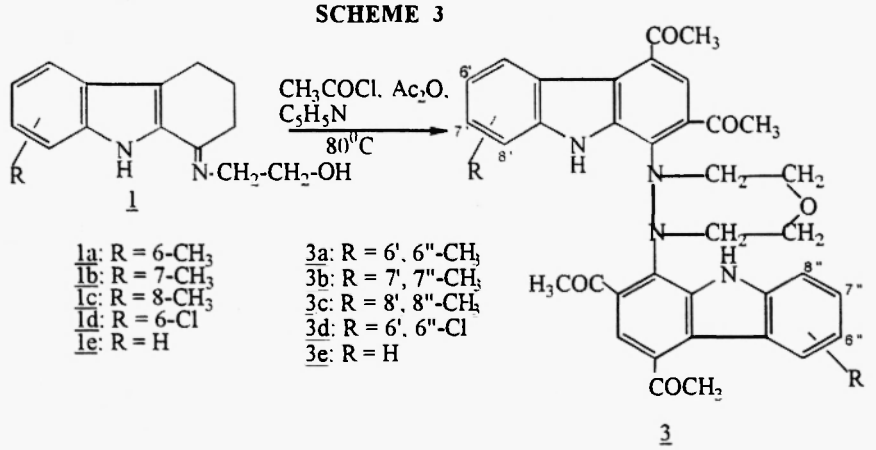
The dimeric structure 3a is further attested by the fragment modes exhibited by its mass spectrum (Scheme 2). An elegant proof for the formation of oxdiazepane ring was derived by assigning the ion of mass at m/e 186(50%) which could be formed from the molecular ion through the 1, 3 - migration of acetyl group. This radical ion eliminates divinyl ether by successive McLafferty rearrangements to give an ion radical at m/e 116(20%). An ion of mass at m/e 528(15%) could have their genesis from the molecular ion by the expulsion of oxdiazepane ring. The ion radical thus formed expels three CH_2=C=O molecules one by one, followed by methyl radical. The surprising observation was also made that conspicuous peak at m/e 365(8%) which corresponds to the elimination of two neutral fragments. The ion radical thus formed was suggested to fragment further via the ejection of two CH_2=C=O molecules in a consecutive manner.

SCHEME 2


m/e 628(10%)
m/e 528(15%)
m/e 307(17%)
m/e 265(4%)
m/e 223(7%)
m/e 181(16%)
m/e 166(53%).
m/e 186(50%)
McLafferty rearrangement
m/e 116(20%)
m/e 86(18)%)
m/e 365 (8%)
m/e 323 (12%)
m/e 281(17%)

The generality of the reaction was verified successfully with a series of compounds 1b, 1c, 1d and 1e (Scheme 3 and Table 1).

SCHEME 3



1

1a: R = 6-CH_3
1b: R = 7-CH_3
1c: R = 8-CH_3
1d: R = 6-Cl
1e: R = H

3a: R = 6', 6"-CH_3
3b: R = 7', 7"-CH_3
3c: R = 8', 8"-CH_3
3d: R = 6', 6"-Cl
3e: R = H

3

It is considered worthwhile to understand the mechanistic aspects of the above transformation. In the light of some expertise gained in the case of 1-hydroxyimino-1,2,3,4-tetrahydrocarbazoles,[1-4] we propose the following mechanistic pathway for the transformation 1 → 3 (Scheme 4). It is reasonable to assume that the reaction may proceed through the O-acetylation of 1-(2'-hydroxyethylimino)-1,2,3,4-tetrahydrocarbazole followed by prototropic shift to 4. The next step apparently involves the hydrogen radical abstraction from 4 to give the radical 5 and its subsequent coupling with the radical 6 formed *insitu* to give the 7. The conversion of the 7 to the dimerised product 3 can be interpreted in terms of cyclisation, aerial oxidation and Friedel-Crafts acylation.

Experimental

General procedure for the synthesis of 4, 5 - bis(2,4-diacetylcarbazol-1-yl)-1,4,5-oxdiazepanes:

1-(2'-Hydroxyethylimino)-1,2,3,4-tetrahydrocarbazole (1, 0.002 mol) was taken in a mixture of acetic anhydride (2 mL) and pyridine (3 mL). Acetyl chloride (0.14 mL, 0.002 mol) was added to the above mixture keeping the temperature at 0 °C. Then the reaction mixture was heated at 80 °C for 10 h and was poured into crushed ice and extracted with chloroform. The chloroform extract was washed with cold dil HCl. The residue obtained after evaporation of the solvent was chromatographed over a column of silica gel using petroleum ether - ethyl acetate mixture as eluant. Petroleum ether - ethyl acetate (85:15) mixture yielded the 4, 5-bis(2,4-diacetylcarbazol-1-yl)-1,4,5-oxdiazepanes 3 as dense oil.

SCHEME4

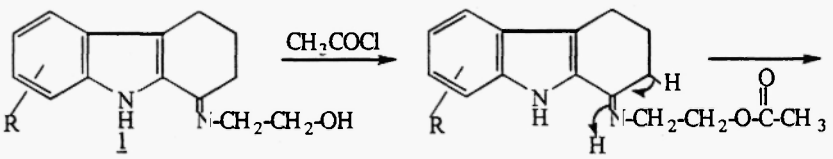


Table 1. Physical and spectral data of new 4, 5-bis(2,4-diacetylcarbazol-1-yl)-1,4,5-oxdiazepanes 3.

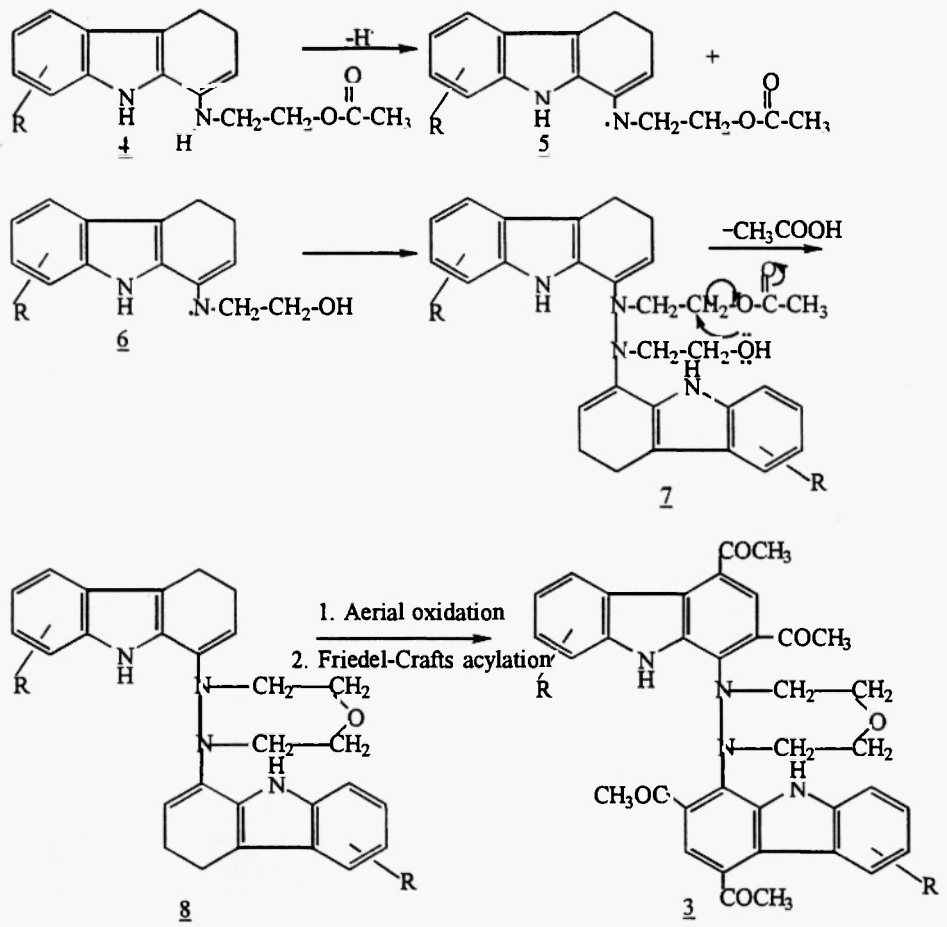
Compound	Yield %	IR[a]	MS(70eV)[b] m/e(M$^+$)	Molecular Formula	Analysis(%)[c] Calcd.	Found.	^{1}H-NMR[d] δ
3a	30	3250 1645	628	$C_{38}H_{36}N_4O_5$	C 72.59 H 05.77 N 08.91	72.49 05.68 08.84	1.81, 1.86, 1.91, 1.98, 2.39, 2.73(6 s, 18H, two CH_3, four $COCH_3$), 3.41-4.53(m, 8H, C_2-2H, C_3-2H, C_6-2H, C_7-2H), 7.14-8.17(m, 8H, Aromatic -H), and 10.16, 10.70(2 b s, two N-H)
3b	22	3290 1650	628	$C_{38}H_{36}N_4O_5$	C 72.59 H 05.77 N 08.91	72.45 05.70 08.82	1.77, 1.81, 1.94, 2.02, 2.58, 2.70(6 s, 18H, two CH_3, four $COCH_3$), 3.35-4.65(m, 8H, C_2-2H, C_3-2H, C_5-2H, C_7-2H), 7.12-8.10(m, 8H, Aromatic -H), and 10.19, 10.31(2 b s, two N-H)
3c	25	3270 1655	628	$C_{38}H_{36}N_4O_5$	C 72.59 H 05.77 N 08.91	72.48 05.68 08.79	1.82, 1.91, 1.96, 1.99, 2.70, 2.72(6 s, 18H, two CH_3, four $COCH_3$), 3.40-4.78(m, 8H, C_2-2H, C_3-2H, C_5-2H, C_7-2H), 7.08-8.15(m, 8H, Aromatic -H), and 10.15, 10.73(2 b s, two N-H)
3d	20	3275 1660	668	$C_{36}H_{30}N_4O_4Cl_2$	C 64.58 H 04.52 N 08.37	64.42 04.48 08.29	1.77, 1.82, 1.84, 1.98(4 s, 12H, four $COCH_3$), 3.55-4.37(m, 8H, C_2-2H, C_3-2H, C_6-2H, C_7-2H), 7.17-8.12(m, 8H, Aromatic -H), and 10.66, 11.21(2 b s, two N-H)
3e	22	3270 1665	600	$C_{36}H_{32}N_4O_5$	C 71.99 H 05.37 N 09.33	71.80 05.25 09.24	1.81, 1.84, 1.89, 1.98(4 s, 12H, four $COCH_3$), 3.42-4.53(m, 8H, C_2-2H, C_3-2H, C_6-2H, C_7-2H), 7.14-8.17(m, 10H, Aromatic -H) and 10.16, 10.76(2 b s, two N-H)

[a] : Recorded on a Perkin-Elmer 597 Infrared spectrophotometer;

[b] : Recorded on a Jeol-JMS-D 300 Mass spectrometer;

[c] : Satisfactory microanlyses were obtained on Carlo Erba 1106 and Perkin Elmer Model 240 CHN analyzers;

[d] : NMR spectra were recorded on Varian AMX400 FT-NMR spectrometer using tetramethylsilane as internal reference in $CDCl_3$ .The chemical shifts are quoted in parts per million(PPM).



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