PHASE-TRANSFER-CATALYSED REACTIONS OF DIHALOCARBENES WITH 3,4-DIHYDROPYRIDIN-2-ONES

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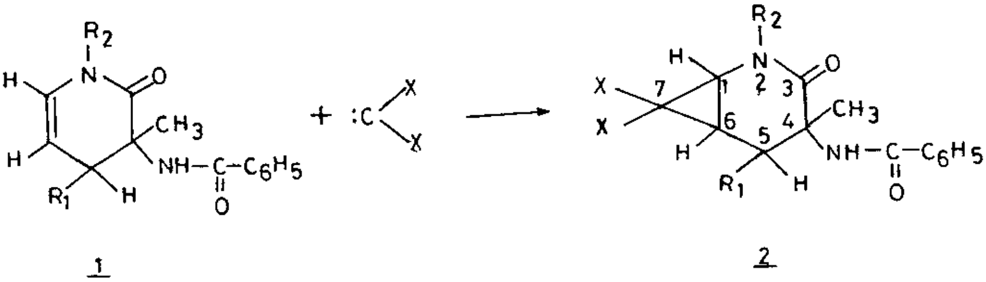
Abstract - Dihalocarbenes produced by two phase system (TPS) technique readily reacted with double bond of 3,4-dihydropyridin-2-ones 1 to give 2-azabicyclo-[4.1.0] heptanes 2 in good yields.

Pyridone ring is an important feature of many naturally occurring alkaloids and biologically active substances[1-3]. Therefore several groups have tried to provide fairly general procedures for their syntheses and pharmacological evaluations[4-7]. During our investigations on 1-aza-1, 3-butadienes we encountered a new and fairly general reaction which provides facile synthesis of a variety of 3,4-dihydropyridin-2-ones[8-11].

Since these molecules were easily available to us in high yields, we wanted to further exploit their chemistry for synthesizing novel fused heterocycles. In this connection we tried the reactions of carbenes generated from haloform and alkoxides[12] but could not succeed. The carbenes produced by two phase system (TPS) provide a convenient method for the preparation of dihalocyclopropanes[13,14]. We report here reaction of dihalocarbenes produced by this technique with 3,4-dihydropyridin-2-ones where 2-azabicyclo[4.1.0] heptanes 2 are obtained in good yields. We have chosen typical pyridones 1 having alkyl and aryl substituents to show the general applicability of this reaction (Scheme I).

When pyridone 1a ($R_1 = C_6H_5$, $R_2 = CH_3$) (3.20 g, 0.01 mole) reacted with dichlorocarbene generated from chloroform (25 ml) and 50% sodium hydroxide (6.4 g, 0.08 mole) in two phase system in the presence of catalytic amount of aliquat-336 (tricaprylylmethylammonium chloride) (0.1 g, 0.25 m mole) for 80 h, on usual work up gave a white crystalline solid, mp 197-198°C, in 85% yield. The structural assignment 2a to this product rests on elemental as well as spectral data. Anal. Calcd for $C_{21}H_{20}N_2O_2Cl_2$: C, 62.68; H, 4.97; N, 6.96; Cl, 17.41. Found : C, 62,89; H, 4.88; N, 6.85; Cl, 17.48. The ir (KBr) 3270, 1690, 1648 cm^{-1}; ^1H nmr (360 MHz, d_6-acetone) δ 1.50 (3H,s), 2.87 (1H,dd,J=10Hz, 8Hz), 3.08 (3H,s), 3.55 (1H, d, J=10Hz), 4.72 (1H, d, J=8Hz), 7.12 (1H,s), 7.29-7.50 (8H, m), 7.68 (2H,m). CIMS : m/e 367 (M^+-35, 20%), 331 (15), 237(60), 185 (100) and 77 (70).



2	R_1	R_2	X	Yield (%)	Mp (°C)	Reaction time (h)
a =	C_6H_5	CH_3	Cl	85	197-198	80
b =	C_6H_5	CH_3	Br	78	203-204	80
c =	CH_3	C_6H_{11}	Cl	80	192-193	72
d =	CH_3	C_6H_{11}	Br.	75	205-206	72
e =	C_6H_5	C_6H_5	Cl	25	190-191	96
f =	C_6H_5	C_6H_5	Br	25	201-202	96

Scheme I

Similarly products 2b-f were prepared, their microanalytical and spectral data are recorded in table I. However in case of 2e and 2f the yields obtained were poor (25%), the products were obtained by preparative tlc on silica gel and unreacted pyridone was recovered. This can be attributed to the presence of N-aryl group where possible delocalization of nitrogen lone pair into the aromatic ring will further reduce enamine character of the double bond.

ACKNOWLEDGEMENTS

Authors are thankful to Dr. T.W. Doyle, Director, Bristol Laboratories, Syracuse, New York for recording 360 MHz ^{1}H nmr spectra, CIMS and helpful discussions. We are also thankful to Analytical Chemistry Division of this Laboratory for spectral analyses.

Table I. Microanalytical and spectral data of 2-azabicyclo[4.1.0] heptanes (<u>2b-f</u>)

Compound	Molecular formula	Analysis % Calcd. (Found)				IR ν_{max} (cm^{-1})	^{1}H nmr(d_6-acetone/TMS) δ (ppm)	MS m/e M^{+} Halogen
		C	H	N	Halogen			
<u>2b</u>	$C_{21}H_{20}N_2O_2Br_2$	51.22 (51.02)	4.06 (4.08)	5.69 (5.88)	32.52 (32.75)	3270,1690, 1648	1.50(3H,s), 2.87(1H,dd,J=10Hz,8Hz), 3.08(3H,s),3.55(1H,d,J=10Hz),4.73 (1H,d,J=8Hz),7.12(1H,s),7.28-7.48 (8H,m), 7.70(2H,m)	411
<u>2c</u>	$C_{21}H_{26}N_2O_2Cl_2$	61.76 (61.80)	6.37 (6.28)	6.86 (6.68)	17.16 (17.13)	3275,1685, 1645	1.22-2.24(16H,m), 2.81(1H,m),3.30 (1H,d,J=10Hz),3.48(1H,dd,J=10Hz,8Hz), 4.12(1H,d,J=8Hz),7.33-7.53(4H,m), 7.84(2H,m)	373
<u>2d</u>	$C_{21}H_{26}N_2O_2Br_2$	50.60 (50.82)	5.22 (5.37)	5.62 (5.71)	32.13 (32.00)	3275,1683, 1645	1.23-2.24(16H,m),2.80(1H,m),3.30 (1H,d,J=10Hz), 3.40(1H,dd,J=10Hz, 8Hz), 4.11(1H,d,J=8Hz),7.32-7.52 (4H,m), 7.83(2H,m)	417
<u>2e</u>	$C_{26}H_{22}N_2O_2Cl_2$	67.24 (67.39)	4.74 (4.67)	6.03 (6.18)	15.08 (15.19)	3270,1690 1645	1.65(3H,s), 3.05(1H,dd,J=10Hz,7Hz), 4.13(1H,d,J=10Hz),4.82(1H,d,J=7Hz), 7.25-7.51(14H,m), 7.71(2H,m)	429
<u>2f</u>	$C_{26}H_{22}N_2O_2Br_2$	56.32 (56.54)	3.97 (3.98)	5.05 (5.25)	28.88 (28.69)	3270,1690 1645	1.65(3H,s), 3.05(1H,dd,J=10Hz,7Hz), 4.13(1H,d,J=10Hz),4.82(1H,d,J=7Hz), 7.25-7.51(14H,m), 7.72(2H,m)	473

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Received, 27th May, 1983