ADDITION OF PHTHALIMIDO NITRENE TO SUBSTITUTED CYCLOPENTADIENES

Krishna Narasimhan* and Perumal Raja kumar
Department of Organic Chemistry
University of Madras, Madras-600 025, India

Abstract - The aziridines 3, 3a and 3b obtained by the cycloaddition of phthalimidonitrene to cyclopentadiene derivatives 2, 2a and 2b undergoes facile ring expansion, when treated with sodium hydride to give substituted pyridine derivatives 4, 4a and 4b respectively. Hydrazinolysis of the aziridines gives the cyclopentadiene derivatives through the intermediacy of N-aminoaziridines 5, 5a and 5b. Oxidation of the aziridines 3, 3a with lead tetraacetate gives the aziridine 6 and 6a.

Phthalimidonitrene 1, generated by the oxidation of N-aminophthalimide with lead tetraacetate undergoes facile cycloaddition with a variety of olefins[1]. The aziridines derived by the cycloaddition of 1 to substituted cyclopentadienes could be used as a potential synthon for the construction of substituted heterocyclic systems. We wish to report the synthetic utility of phthalimidonitrene for the construction of pyridine ring system.

Phthalimidonitrene 1 adds smoothly to tetraphenylcyclopentadiene 2 to give a yellow crystalline product which showed the presence of phthalimido carbonyls in ir and ^{1}Hnmr spectrum of this material displayed a sharp singlet at δ4.1 for the allylic protons in addition to the aromatic protons. The appearance of singlet for the allylic protons in nmr indicated 1,2-addition. The proposed structure 3 received further support by the appearance of molecular ion peak at m/z 530 in the mass spectrum. When the aziridine 3 was treated with sodium hydride a product (60%) mp 180°C was obtained, which showed the absence of carbonyl group in ir and displayed multiplet for the aromatic protons in ^{1}Hnmr. The product has been identified as 2,3,4,6-tetraphenylpyridine and confirmed by comparing with an authentic sample[2]. The present approach to pyridine derivatives would offer more advantages than the conventional method[3].

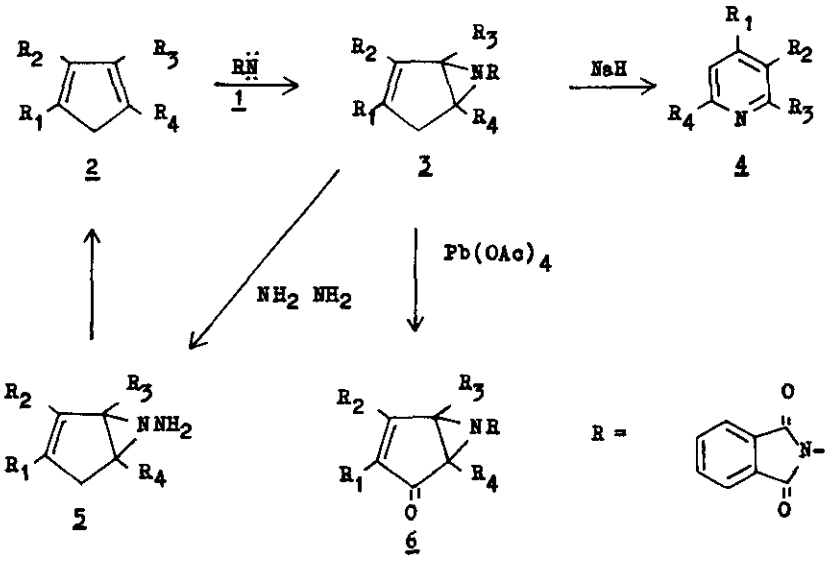
The potentiality of the above synthetic route was further explored with the aziridine 3a derived from phthalimidonitrene and 7,9-diphenyl-8H-cyclopenta [a] acenaphthylene, 2a. The aziridine 3a when treated with sodium hydride

in dry THF gave the pyridine derivative 4a. The structure was further confirmed by comparing the spectral data with that of authentic sample[2]. An extension of the above procedure for the construction of pyridine ring from the aziridine 3b derived from indene could result in isoquinoline. The aziridine derived from phthalimidonitrene and indene was mentioned by Jones et al.[4] and by Ebert et al.[5]. In the current investigation aziridine 3b was prepared by the reaction of phthalimidonitrene with indene. The aziridine 3b when refluxed with sodium hydride in THF gave isoquinoline 4b (58%). The neutral fraction purified by distillation was found to be a mixture of indene and dihydroindene 4:1 as revealed by nmr spectra and GLC analysis. The use of other bases like sodamide, sodium ethoxide decreased the percent yield of isoquinoline (32%).

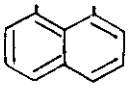
The aziridine 3 when treated with hydrazine hydrate in ethanol at 50°C gave a viscous oil which on purification yielded tetraphenylcyclopentadiene (60%). The formation of tetraphenylcyclopentadiene could result either by a thermal cycloreversion route or through an intermediacy of unstable N-aminoaziridine 5. Since the aziridine 3 has been found to be thermally stable, the intermediacy of 5 was investigated. The formation of N-aminoaziridine 5 has been evidenced by carrying out the reaction at -25°C. The crude product in ir displayed the $-NH_2$ stretching at 3350 and 3290 cm^{-1} and the absence of phthalimidocarbonyls. Cyclo reversion of such unstable N-aminoaziridines has been reported by Eschenmoser[6]. In a similar way aziridine 3a derived from 7,9-diphenyl-8H-cyclopenta [a] acenaphthylene, when treated with hydrazine hydrate in ethanol gave the diene 2a, through the intermediacy of the N-amino compound 5a. However the aziridine 3b derived from indene, when treated with hydrazine hydrate, gave indene and dihydroindene 3:1. Dihydroindene could result by the sequential attack of hydrazine hydrate or sodium hydride at the phthalimido carbonyls followed by the aziridine ring cleavage and abstraction of proton from the solvent whereas indene could be obtained from the unstable N-aminoaziridine 5b.

The aziridine 3 when treated with lead tetraacetate gave an yellow crystalline solid (70%) which showed the presence of phthalimido carbonyls and an enone carbonyl. The nmr spectrum showed the absence of allylic protons and the presence of aromatic protons. The product was found to be the aziridine 6. The structure was further supported by the molecular ion peak at m/z 544 and

confirmed by the independent synthesis of 6 from tetraphenylcyclopentadienone and phthalimidonitrene. The formation of 6 could be explained by the allylic oxidation of 3 by lead tetraacetate. Similar oxidation of the aziridine 3a with lead tetraacetate gave the aziridine 6a as indicated by the appearance of enone carbonyl in ir spectrum. The structure 6a was further confirmed by the independent synthesis of 6a from acecyclone and phthalimidonitrene. The reaction sequence is summarised in the following scheme.



2, 3, 4, 5, 6 $R_1 = R_2 = R_3 = R_4 =$ Ph

2a, 3a, 4a, 5a, 6a $R_1 = R_4 =$ Ph, R_2 & $R_3 =$ 

2b, 3b, 4b, 5b, 6b R_1 & $R_2 = C_4H_4$, $R_3 = R_4 =$ H

EXPERIMENTAL SECTION

All melting points are uncorrected. Ir spectra were recorded on Beckman Ir-20 spectrometer and ^{1}Hnmr spectra were obtained using Perkin-Elmer R-32 (90 MHz) spectrometer. Chemical shifts are reported in δ units downfield from internal Me_4Si and the J values are given in hertz.

Recommended general procedure for the nitrene reaction

N-aminophthalimide (0.01 mol) was stirred with anhydrous dichloromethane (15 ml/g) and the olefin (0.011 mol) was added. Lead tetraacetate

(0.012 mol) was then added to the stirred suspension at 5-10°C during 10 min. After stirring for further 15 min the reaction mixture was filtered and the residue was washed with dichloromethane. The combined filtrate was then washed sequentially with water and with saturated solution of sodium bicarbonate to remove any traces of acetic acid. The dichloromethane layer was then dried (Na_2SO_4) and evaporated to dryness. The residue was examined by tlc and the subsequent purification was effected as described for each aziridine.

Reaction of phthalmidonitrene with 1, 1', 1'', 1'''-(1,3-cyclopentadiene-1,2,3,4-tetrayl)-tetrakisbenzene or 1,2,3,4-tetraphenylcyclopentadiene (2)

Addition of phthalimidonitrene from N-aminophthalimide (1.62 g) and lead tetraacetate (5.33 g) to the diene 2 (4.07 g) gave the aziridine 3 (4.77 g, 90%) mp 97°C (Petrol). Ir (KBr) ν max 3000, 1765, 1725, 1610 cm^{-1}; ^{1}Hnmr ($CDCL_3$): 4.1 (2H,S), 7.1-7.5 (24H,m); mass spectrum: m/z 530 (M^+). Anal. calcd. for $C_{37}H_{26}N_2O_2$: C, 83.8; H, 4.9; N, 5.3. Found: C, 83.2; H, 4.5; N, 5.0%.

Reaction of phthalimidonitrene with 7,9-diphenyl-8H-cyclopenta (a) acenaphthylene (2a)

Addition of phthalimidonitrene from N-aminophthalimide (1.62 g) and lead tetraacetate (5.33 g) to the diene 2a (3.76 g) gave the aziridine 3a (4.01 g; 82%), mp 140°C (Petrol, ethyl acetate; 9.1). Mass spectrum: m/z 502 (M^+). Anal. calcd. for $C_{35}H_{22}N_2O_2$: C, 83.6; H, 4.4. Found C, 83.1; H, 4.2%.

Reaction of phthalimidonitrene with indene (2b)

Addition of phthalimidonitrene from N-aminophthalimide (1.62 g) and lead tetraacetate (5.33 g) to indene (1.27 g) gave the aziridine 3b (1.38 g, 50%), mp 186°C (Petrol, ethyl acetate; 8.2). Lit.[5] mp 187-88°C.

General procedure for the reaction of the aziridines with sodium hydride

To a magnetically stirred suspension of sodium hydride (0.025 mol) in anhydrous tetrahydrofuran (50 ml) a solution of the aziridine (0.02 mol) in tetrahydrofuran (20 ml) was added in a dropwise manner during a period of 30 min under nitrogen atmosphere. The reaction mixture was stirred for 2 h at room temperature, then refluxed for 30 min, poured onto ice (200 g) and extracted with ether (2 x 25 ml). The combined ether layer washed with

water, dried (K_2CO_3) and evaporated.

Reaction of the aziridine 3 with sodium hydride

Reaction of the aziridine 3 (10.6 g) with sodium hydride (0.60 g) in THF (70 ml) gave 2,3,4,6-tetraphenylpyridine (4.58 g, 60%), mp 182°C, Lit.[2] mp 183-84°C.

Reaction of the aziridine 3a with sodium hydride

Reaction of the aziridine 3a (10.0 g) with sodium hydride (0.60 g) in THF (70 ml) gave the substituted pyridine 4 (4.25 g, 60%), mp 162°C.

Reaction of the aziridine 3b with sodium hydride

Reaction of the aziridine 3b (5.52 g) with sodium hydride (0.60 g) in THF (70 ml) gave isoquinoline (1.50 g, 58%), indene (0.70 g, 32%) and dihydroindene (0.24 g, 10%).

Reaction of the aziridine 3b with sodium ethoxide

A mixture of the aziridine 3b (13.8 g), sodium ethoxide(3.4 g) in dry ethanol (100 ml) was refluxed for 1.5 h. The reaction mixture was poured onto ice (500 g) and extracted with ether (2 x 100 ml). The isoquinoline (1.85 g, 32%) formed was separated with 2N HCl from indene (2.9 g) and dihydroindene (0.8 g). The reaction was repeated similarly with sodamide.

General procedure for the hydrazinolysis of the aziridines

A solution of hydrazine hydrate (0.04 mol) in ethanol (10 ml) was added to a magnetically stirred suspension of the aziridine (0.03 mol) in ethanol (20 ml) at 45°C for 1 h. The reaction mixture was worked up as usual and purified.

Hydrazinolysis of the aziridine 3

Hydrazinolysis of the aziridine 3 (15.9 g) with hydrazine hydrate (2.0 ml) in ethanol (30 ml) gave the diene 2 (0.66 g, 60%), mp 181°C (Petrol-benzene; 8:2).

Hydrazinolysis of the aziridine 3a

Hydrazinolysis of the aziridine 3a (5.02 g) with hydrazine hydrate (0.75 ml) in ethanol (15 ml) gave the diene 2a (1.71 g, 47%), mp 210°C (Petrol-benzene; 9:1).

Hydrazinolysis of the aziridine 3b

Hydrazinolysis of the aziridine 3b (5.52 g) with hydrazine hydrate (1.5 ml) in ethanol (25 ml) gave a viscous oil (2.33 g) after distillation gave indene (0.47 g, 20%) and dihydroindene (1.86 g, 80%).

Low temperature hydrazinolysis of the aziridine 3

To a solution of the aziridine 3 (2.65 g) in ethanol (15 ml) at -25°C, a solution of hydrazine hydrate (0.5 ml) in ethanol (2 ml) was added and stirred magnetically for 5 min. The reaction mixture was extracted immediately with dichloromethane and washed with ice water to remove hydrazine hydrate and dried (K_2CO_3) for a short period. A viscous oil was obtained after removing the solvent at low temperature (-10°C). Ir ($CHCl_3$) ν max 3350, 3290, 1610 cm^{-1}.

General procedure for the oxidation of the aziridines

To a solution of the aziridine (0.01 mol) in dry dichloromethane (30 ml), lead tetraacetate (0.01 mol) was added and stirred for 30 min. The reaction mixture was filtered and washed with water, bicarbonate solution and dried (Na_2SO_4). The residue obtained by the evaporation of the ether was purified by crystallisation.

Oxidation of the aziridine 3

Oxidation of the aziridine 3 (5.30 g) with lead tetraacetate (4.44 g) in dichloromethane (30 ml) gave the aziridine 6 (3.80 g, 70%), mp 121°C. Lit.[7] mp 122°C.

Oxidation of the aziridine 3a

Oxidation of the aziridine 3a (5.02 g) with lead tetraacetate (4.44 g) in dichloromethane (30 ml) gave the aziridine 6a (3.60 g, 72%), mp 196°C. Uv λ_{max}^{EtOH} 266 (22,900), 315 (26,720) and 420 nm (18,000). Ir (KBr) ν max 3020, 1780, 1730, 1650, 1620, 1580 cm^{-1}. Mass spectrum m/e 516 (M^+).

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REFERENCES

1. A.S.Drieding, L.Hoesch and N.Eggner, Helv. Chim. Acta, 1978, 61, 795.

2. N.Zecher and F.Krokuke, Chem. Ber., 1961, 94, 698.

3. D.C.Horwell and C.W.Rees, Chem. Commun., 1969, 1428.

4. D.W.Jones, Chem. Commun., 1972, 884.

5. G.R.Meyer, C.A.Kellert and R.W.Ebert, J. Heterocycl. Chem., 1979, 16, 461.

6. A.Eschenmoser, D.Felix, R.K.Muller, J.Horn, R.Joss and J.Schreiber, Helv. Chim. Acta, 1972, 55, 1276.

7. A.S.Drieding and L.Hoesch, Chimia, 1975, 29, 531.

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