

Synthesis and Studies of O-substituted Derivatives of Benzophenone Oxime

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In the present work, the synthesis of O-phthalimidoxyalkyl benzophenone oxime (IV) and O-(2,3-bis-phthalimidoxy) propylbenzophenone oxime (IX) are reported. These compounds contain two and three substituted amino-oxy groups respectively.

INTRODUCTION

In view of pharmacological, analytical, mechanistic and stereochemical utility of oximes¹⁻⁷ and also of imidoxy compounds⁸⁻¹¹, synthesis of phthalimidoxy derivatives of benzophenone oxime have been attempted.

RESULTS AND DISCUSSION

Benzophenone oxime, which was prepared by reported methods^{12,13}, was condensed with various halogen substituted compounds to yield oximino ($=N-O-R$) derivative. Benzophenone oxime is mild acidic and hence hydrogen can be replaced in presence of strong bases only. Many bases including sodium hydroxide, sodium carbonate. corresponding potassium compounds have been used. Yield of the product and recovery was poor. Here, we used sodium hydride which gave pure product, high yield and good recovery. Thus the referred oxime was treated with sodium hydride in an aprotic solvent. Evolution of hydrogen indicates the mild acidic character and replacement of hydrogen with that of sodium.

The reaction was carried out in many solvents and also in presence of different bases. When phthalimidoxyethyl bromide in dry acetone and crushed KOH was refluxed with oxime for 17–24 h; nucleophilic substitution at α -carbon occurred and O-alkyloxy phthalimido-benzophenone oxime was formed. In DMF media in both the bases, KOH and K_2CO_3 , gave competent result of this reaction with similar yield and same product. It was easy to perform this reaction in an ethereal solvent, tetrahydrofuran. In presence of base it gave better yields and separable products. Triethylamine and pyridine was also used as base but reaction was very slow; also the product was not perfectly solid. Whatever the solvent may be in the reaction was removed by downward distillation and the residual solid was recrystallized from suitable solvent. An attempt to hydrolyse the product by various routes did not yield any identifiable amino-oxy compound.

Reaction of allyl bromide with oxime to yield benzophenone oximino propene was faster than the rate observed in above case. This may be explained on the ease of nucleophilic substitution at allylic carbon atom. Here also the solvents used were same but acetone or tetrahydrofuran was preferred because of easy removal. The intermediate (VI) could not be isolated and was used for further reactions. Allyloxy compound (VI) was dissolved in carbon tetrachloride and a solution of bromine in carbon tetrachloride was slowly added while stirring. After the complete addition, the solution was stirred for next 2–3 h till the solution was completely colourless. Solvent was removed by distillation and the residual portion was dissolved in minimum amount of DMF. A dilute solution of N-hydroxyphthalimide in DMF and triethylamine was slowly added with shaking and it was kept for 24–30 h at room temperature with occasional shaking. The dark red colour disappeared but a red layer was present at the bottom of conical flask. It was stirred on a strong magnetic stirrer for 4–5 h or till the colour disappeared. The filtrate when poured on ice gave a dirty white solid of 2,3-bis-phthalimidoxy benzophenone oximino propane.

EXPERIMENTAL

All the m.p.s are uncorrected and determined in open capillaries. Purity of compounds was checked by TLC on silica gel. All the synthesized compounds have been characterised by microelemental and spectral studies.

Synthesis of benzophenone oxime (II): By reported method.

Synthesis of O-Phthalimidoxyalkyl benzophenone (IV): (0.1 mol, 19.7 g) benzophenone oxime and equivalent amount of sodium hydride were suspended in tetrahydrofuran and stirred with a strong magnetic stirrer. The stirring was continued till no effervescence was seen. Phthalimidoxyethyl bromide (0.1 mol, 27 g) in tetrahydrofuran was added stepwise and stirred for further 10 h. The solution was filtered while hot; the inorganic mass (NaBr) was tested and rejected. The filtrate was concentrated and cooled at room temperature. A crystalline compound separated out (m.p. 192°C); crystallised from benzene, (m.p. 194°C).

In a similar way, propyl and butyl derivatives of above said compounds were prepared.

Synthesis of O-allylbenzophenone oxime (VI): Sodium hydride (0.1 mole, 2.4 g) was suspended in tetrahydrofuran and stirred on a strong magnetic stirrer. Benzophenone oxime (0.1 mol, 19.7 g) was added slowly. Stirring was continued till the evolution of hydrogen was stopped. Allyl bromide (0.1 mol), was added dropwise while stirring. Here the reaction occurred very fast and a sticky solid was obtained after distillation of tetrahydrofuran.

Synthesis of O-(2,3-dibromopropyl) benzophenone oxime (VII): O-Allylbenzophenone (VI) was dissolved in chloroform and a calculated amount of bromine was added from a separating funnel to the stirring solution. Colour of the solution first decolourises fastly but gradually becomes slow. It was stirred up to complete decolourisation. Light yellow solid appeared (m.p. 109°C) which was used further without crystallisation.

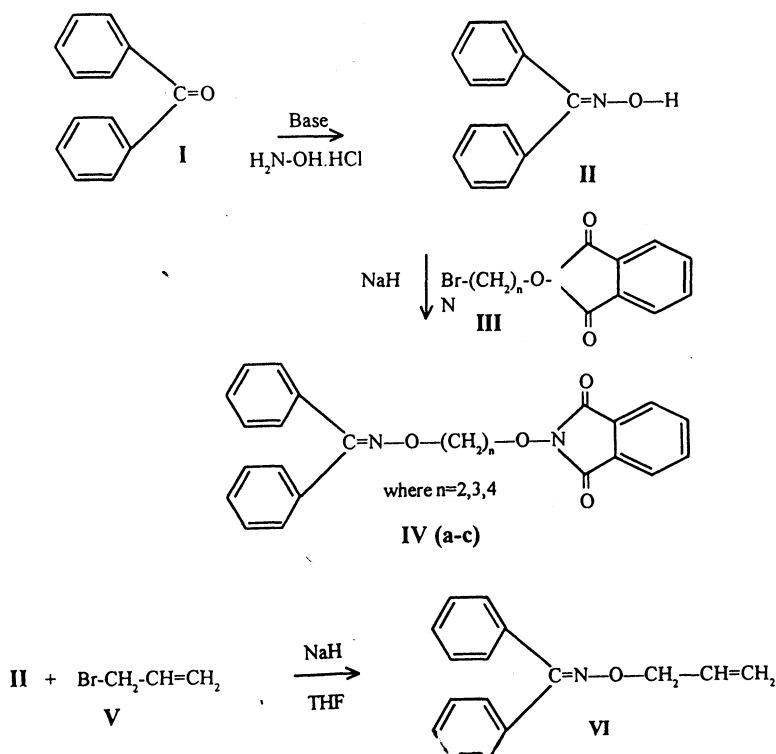
Synthesis of O-(2,3-(bis-phthalimidoxy)propyl) benzophenone oxime (IX): (0.1 mol, 39.7 gm) Dibromo compound (VII) was dissolved in 40 mL DMF. A

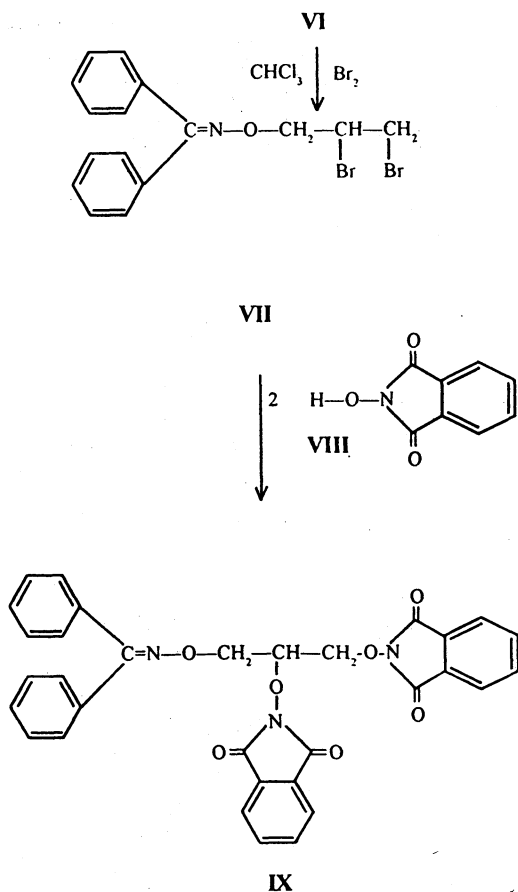
concentrated solution of N-hydroxyphthalimide in DMF (0.2 mole, 32.6 g) was added and the system was kept for 40–42 h with occasional shaking. Solid triethylammonium bromide was filtered off. The filtrate was poured on 800 g of crushed ice with constant stirring. Solid obtained was slippery which was converted to white dispersible solid by adding alcohol-water mixture (m.p. 172°C); crystallised from rectified spirit (m.p. 174°C).

TABLE-1
PHYSICAL DATA AND ELEMENTAL ANALYSIS OF SYNTHESIZED COMPOUNDS

| Compd. No. | m.f. | m.w. | Solvent of cryst. | m.p. (°C) | Yield (%) | N % | |
|------------|---|------|-------------------|-----------|-----------|------|-------|
| | | | | | | Obs. | Calc. |
| II | C ₁₃ H ₁₁ NO | 197 | Methanol | 142 | 92 | 7.04 | 7.10 |
| IVa | C ₂₃ H ₁₈ N ₂ O ₄ | 386 | Benzene | 194 | 77 | 7.45 | 7.50 |
| IVb | C ₂₄ H ₂₀ N ₂ O ₄ | 400 | Benzene | 202 | 65 | 6.95 | 7.00 |
| IVc | C ₂₅ H ₂₂ N ₂ O ₄ | 414 | Benzene | 209 | 73 | 6.72 | 6.76 |
| VI | C ₁₆ H ₁₅ NO | 237 | Sticky solid | – | – | 5.81 | 5.90 |
| VII | C ₁₆ H ₁₅ NOBr | 397 | Alcohol | 109 | 60 | 3.49 | 3.52 |
| IX | C ₃₂ H ₂₃ N ₃ O ₇ | 561 | Rectified spirit | 174 | 65 | 7.42 | 7.48 |

Following reaction sequences have been used:





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