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Note

Remote dianions and their application in the synthesis of macroheterocycles

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A useful sequence of reactions for the syntheses of nitrogen, oxygen and phosphorus macroheterocycles is described in one-pot. The key step involves the generation of dianion that reacts to dielectrophiles leading to compounds **3-9** in good yields.

Keywords: N, N'-*o*-phenylenebis(salicylideneimine), dianion, di-electrophiles, macrocyclic rings

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During the past decade, macroheterocyclic systems have attracted widespread attention due to versatile uses as models for biological systems, therapeutic reagents for the treatment of metal intoxication, synthetic ionophores and the selective extraction of heavy and precious metals[1-5]. Heterocyclization plays an important role in synthetic organic chemistry and provides irreplaceable approach to the preparation of heterocyclic systems[6,7]. Schiff bases are valuable synthons for the preparation of macroheterocyclic molecules[8,9]. The vigorous development of the chemistry of macroheterocyclic compounds has been observed in recent years[10,11]. Further it has been investigated that the macroheterocycles bind not only metal cations but also anions and even neutral organic molecules, forming complexes of the "host-guest" types[12,13]. Heteroatom-based remote dianion has become increasingly popular as strategic tools to the synthetic planner[14-19]. With the aim to broaden further the range of useful macroheterocycles and in continuation of our work[20-26] on the chemistry of heterocycles, we herein report the synthesis of new macroheterocycles *via* dianion-mediated cyclizations.

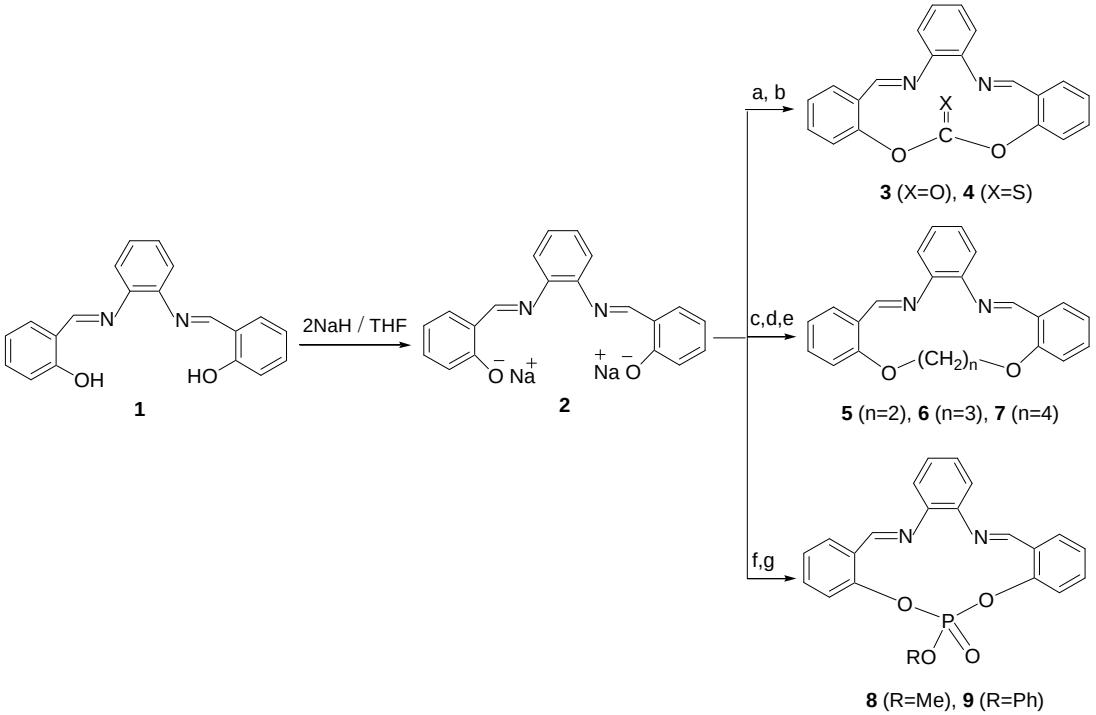
Results and Discussion

Considering the importance of macroheterocycles in organic synthesis, the possibility for the preparation of the previously unknown macrocyclic rings has been explored. The most common approach to the preparation of compounds **3-9** involves the reaction of nucleophilic dianion with dielectrophiles. N, N'-*o*-phenylenebis(salicylideneimine)[27,28] was prepared by the condensation of salicylaldehyde and *o*-phenylenediamine in 2:1 molar ratio. This synthesis involves the initial formation of dianion **2** from deprotonation of Schiff base **1** followed by nucleophilic attack on the suitable dielectrophiles leading to the formation of macroheterocycles (**3-9**, **Scheme I**). Products **3-9** were characterized by spectroscopic data and elemental analyses. When the dianion **2** was treated with 1,2-dibromoethene, it fails to react supporting the fact that vinylic halides do not undergo nucleophilic substitution reactions. The reaction is of great value because of its environmentally benign character as non-toxic chemicals are used and no waste is generated.

The spectral analysis showed IR bands for C=N, C=O and C=S groups in their respective regions that are listed in the experimental part. The stretching frequency for P=O in compounds **8** and **9** appears at 1283 and 1275 cm^{-1}, respectively. The NMR (^1H and ^{13}C) spectra of the compounds **3-9** were consistent with the suggested structures. The aromatic protons reveal signals in the region 6.75-8.08 ppm. Methylene protons attached to oxygen resonate as triplet (J=8.2 Hz) in the region 4.06-4.21 ppm. The aromatic ring has only four different kinds of carbon atom: the two *ortho* carbons are identical with each other and so are the two *meta* carbons; they are the two very closely spaced lines of high intensity near 132; the *para* carbon appears near 127, and the *ipso* carbon is the one of low intensity downfield than the others. Finally, the carbonyl carbons and azomethine carbon are furthest downfield, and are very weak. The two *ortho*- and two *para*-carbons are overlapping in all compounds. As anticipated, the ^{13}C NMR spectra support the structures by having the right number of signals for the carbon atoms present, and all in the appropriate regions.

Experimental Section

The chemicals ethyl chloroformate, carbon disulfide, 1,2-dibromoethane, 1,3-dibromopropane,



Scheme I (a) $ClCO_2Et$; (b) CS_2; (c) $BrCH_2CH_2Br$; (d) $Br(CH_2)_3Br$; (e) $Br(CH_2)_4Br$; (f) Cl_2PO_2Me; (g) Cl_2PO_2Ph

1,4-dibromobutane, methyldichlorophosphate and phenyldichlorophosphate were used as supplied (Aldrich). N, N'-*o*-phenylenebis(salicylideneimine) was prepared by the literature method[27,28]. All reactions were carried out under a dry, oxygen-free nitrogen atmosphere. All organic solvents were purified and dried according to established procedures[29]. TLC monitored the progress of the reactions on silica gel plates. Infrared spectra were recorded as KBr discs on a FT-IR Perkin-Elmer model RX-I spectrophotometer. Melting points were determined using a calibrated thermometer by Remi Digital Melting Point Apparatus and are uncorrected. Elemental analyses were performed by Central Drug Research Institute, Lucknow. NMR (^1H and ^{13}C) spectra were recorded on a JEOL AL 300 instrument. The chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane. Mass spectra were recorded at 70 eV ionizing voltage on a Jeol-D300 MS instrument.

4,5:8,9:12,13-Tribenzo-7,10-diaza-1,3-dioxacyclo-trideca-6,10-dien-2-one 3

Typical procedure: To a stirred solution of N, N'-*o*-phenylenebis(salicylideneimine) (316 mg, 1 mmole) in dry THF (25 mL) at room temperature, was added sodium hydride (48 mg, 2 mmoles) in THF (10 mL) dropwise by syringe. After completion of the addition, the solution was stirred at reflux for 7 hr, during which it became black in colour. The mixture was allowed to attain room temperature. Ethyl chloroformate (108.5 mg, 1 mmole) was added dropwise to the reaction vessel and the contents were further stirred at reflux for 2 hr. TLC confirmed the completion of the reaction. The solvent was evaporated *in vacuo* and the residue was column chromatographed (hexane/ethyl acetate 8:1) to give **3** (235 mg, 69%); m.p. 138-139°C; IR (KBr): 1762, 1621, 1596, 1243 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.65(s, 2H, CH=N), 7.56-6.75(m, 12H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.23, 160.65, 154.34, 142.46, 133.42, 132.48, 127.63, 119.42, 119.12, 118.86, 116.43; MS (EI, 70eV): *m/z* 342 (M^+, 26), 314, 298, 282, 208, 192, 77; Anal. Calcd for $C_{21}H_{14}N_2O_3$: C, 73.68; H, 4.12. Found: C, 73.42; H, 4.23.

4,5:8,9:12,13-Tribenzo-7,10-diaza-1,3-dioxacyclo-trideca-6,10-dien-2-thione 4: Same procedure as for **3** with 316 mg (1 mmole) of N, N'-*o*-phenylene-bis(salicylideneimine), 48 mg (2 mmoles) of sodium hydride, 76 mg (1 mmole) of carbondisulphide; yield: 225 mg (69%); m.p. 103-104°C; IR (KBr): 1630, 1602, 1261, 1237 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.43 (s, 2H, CH=N), 8.08-6.93 (m, 12H, Ar). ^{13}C

NMR (75 MHz, $CDCl_3$): δ 176.84, 161.06, 153.63, 142.26, 133.69, 132.46, 127.47, 119.67, 119.23, 119.12, 117.21; MS (EI, 70eV): *m/z* 358 (M^+, 24), 326, 310, 294, 278, 208, 192, 77; Anal. Calcd for $C_{21}H_{14}N_2O_2S$: C, 70.37; H, 3.93. Found: C, 70.12; H, 3.76.

3,4:9,10:13,14-Tribenzo-1,12-diaza-5,8-dioxacyclotetradeca-1,11-diene 5: Same procedure as for **3** with 316 mg (1 mmole) of N, N'-*o*-phenylenebis(salicylideneimine), 48 mg (2 mmoles) of sodium hydride, 188 mg (1 mmole) of 1,2-dibromoethane; yield: 230 mg (67%); m.p. 179-180°C; IR (KBr): 1626, 1592, 1248 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.52 (s, 2H, CH=N), 7.94-7.26 (m, 12H, Ar), 4.16 (t, *J*=8.2 Hz, 4H, $-OCH_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.43, 161.76, 153.78, 141.23, 134.21, 133.68, 127.94, 120.27, 120.04, 117.47, 57.84, 57.62; MS (EI, 70eV): *m/z* 342 (M^+, 22), 328, 314, 298, 283, 208, 192, 77; Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.29. Found: C, 77.43; H, 5.42.

3,4:10,11:14,15-Tribenzo-1,13-diaza-5,9-dioxacyclopentadeca-1,12-diene 6: Same procedure as for **3** with 316 mg (1 mmole) of N, N'-*o*-phenylenebis-(salicylideneimine), 48 mg (2 mmoles) of sodium hydride, 202 mg (1 mmole) of 1,3-dibromopropane; yield: 250 mg (70%); m.p. 192-193°C; IR (KBr): 1622, 1601, 1244 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.26 (s, 2H, CH=N), 7.86-7.21 (m, 12H, Ar), 4.06 (t, *J*=8.2 Hz, 4H, $-OCH_2$), 1.07 (m, 2H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.76, 162.07, 152.96, 142.21, 134.62, 133.43, 127.52, 120.18, 119.76, 117.42, 58.41, 58.16, 21.37; MS (EI, 70eV): *m/z* 356 (M^+, 18), 342, 328, 314, 282, 208, 192, 77; Anal. Calcd for $C_{23}H_{20}N_2O_2$: C, 77.51; H, 5.65. Found: C, 77.28; H, 5.37.

3,4:11,12:15,16-Tribenzo-1,14-diaza-5,10-dioxacyclohexadeca-1,13-diene 7: Same procedure as for **3** with 316 mg (1 mmole) of N, N'-*o*-phenylenebis(salicylideneimine), 48 mg (2 mmoles) of sodium hydride, 216 mg (1 mmole) of 1,4-dibromobutane; yield: 255 mg (69%); m.p. 184-185°C; IR (KBr): 1632, 1608, 1262 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.12 (s, 2H, CH=N), 7.78-7.32 (m, 12H, Ar), 4.21 (t, *J*=8.2 Hz, 4H, $-OCH_2$), 1.26 (m, 4H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.38, 162.84, 152.63, 142.43, 134.97, 133.81, 127.36, 120.64, 119.63, 117.82, 58.81, 58.68, 22.27, 22.15; MS (EI, 70eV): *m/z* 370 (M^+, 23), 356, 342, 328, 314, 282, 208, 192, 77; Anal. Calcd for $C_{24}H_{22}N_2O_2$: C, 77.81; H, 5.88. Found: C, 77.67; H, 5.78.

4,5:8,9:12,13-Tribenzo-2-methoxy-2-oxo-1,3,7,10-dioxadiaza-2-phosphacyclotrideca-6,10-diene 8: To a solution of dianion **2** prepared as above with 316 mg (1 mmole) of N, N'-*o*-phenylenebis(salicylideneimine) and 48 mg (2 mmoles) of sodium hydride in THF was added methyldichlorophosphate (149 mg, 1 mmole). The reaction mixture was allowed to reflux for 2 hr. Salts were filtered off and the solvent was removed under reduced pressure. The crude mixture was purified by column chromatography; yield: 280 mg (71%); m.p. 238°C (dec.); IR (KBr): 1638, 1609, 1283, 1230 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.26 (s, 1H, CH=N), 8.23 (s, 1H, CH=N), 7.86-7.07 (m, 12H, Ar), 3.58 (s, 3H, $-OCH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.84, 134.10, 131.24, 128.65, 124.90, 119.37, 116.76, 113.63, 108.92, 55.77; MS (EI, 70eV): *m/z* 393 (M^+ +1), 376, 361, 314, 208, 196, 168, 77, 53; Anal. Calcd for $C_{21}H_{17}N_2O_4P$: C, 64.28; H, 4.36. Found: C, 64.54; H, 4.68.

4,5:8,9:12,13-Tribenzo-2-phenoxy-2-oxo-1,3,7,10-dioxadiaza-2-phosphacyclotrideca-6,10-diene 9: To a solution of dianion **2** prepared as above with 316 mg (1 mmole) of N, N'-*o*-phenylenebis(salicylideneimine) and 48 mg (2 mmoles) of sodium hydride in THF was added phenyldichlorophosphate (211 mg, 1 mmole). The reaction mixture was allowed to reflux for 2 hr. Salts were filtered off and the solvent was removed under reduced pressure. The crude mixture was purified by column chromatography; yield: 330 mg (73%); m.p. 220°C (dec.); IR (KBr): 1633, 1606, 1275, 1227 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.32 (s, 1H, CH=N), 8.29 (s, 1H, CH=N), 7.92-7.13 (m, 17H, Ar), ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.54, 143.23, 135.42, 133.10, 131.74, 128.25, 124.40, 119.57, 116.36, 113.23, 108.52; MS (EI, 70eV): *m/z* 455 (M^+ +1), 439, 378, 362, 315, 220, 204, 180, 77, 53; Anal. Calcd for $C_{26}H_{19}N_2O_4P$: C, 68.72; H, 4.21. Found: C, 68.54; H, 4.36.

Conclusion

In conclusion, a simple work-up, low consumption of solvent, fast reaction rates, mild reaction condition, good yields, and selectivity of the reaction make this method an attractive and useful contribution to the preparation of a rare class of nitrogen, oxygen and phosphorus macroheterocycles.

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References

1 Lehn J M, *Supramolecular Chemistry*; (VCH, Weinheim) **1995**.

2 Das G, Tripathi P, Tripathi A & Bhardwaj P K, *Tetrahedron*, 56, **2000**, 1501.

3 (a) Inoue Y & Gokel G W, *Cation Binding by Macrocycles*; (Marcel Dekker, New York) **1990**.
(b) Gokel G W, *Crown Ethers and Cryptands*, (Royal Society of Chemistry, Cambridge) **1991**.

4 Guerriero P, Tamburini S & Vigalo P A, *Coord Chem Rev*, 139, **1995**, 17.

5 Yordanov A T & Roundhill D M, *Coord Chem Rev*, 170, **1998**, 93.

6 Tomilov Y V, Kostyuchenko I V & Nefedov O M, *Russ Chem Rev*, 69, **2000**, 461.

7 Suni M M, Nair V A & Joshua C P, *Tetrahedron*, 57, **2001**, 2003.

8 Pilkington NH & Robson R, *Aust J Chem*, 23, **1970**, 2255.

9 Konstantinova L S, Rakitin O A & Rees C W, *Chem Commun*, **2002**, 1204.

10 Voronkov M G & Knutov V I, *Russ Chem Rev*, 60, **1991**, 1293.

11 Vogtle F & Weber E, *Host-Guest Complex Chemistry: Synthesis, Structures and Application*, (Mir, Moscow) **1988**, 511.

12 Hiraoka M, *Crown Compounds. Their Characteristics and Applications*, (Mir, Moscow) **1986**, 363.

13 Zolotov Yu A, Ionov V P, Bodnya V A, Larikova G A, Nizeva N V, Viasova G E & Rybakova E V, *Zh Anal Khim*, 37, **1982**, 1543.

14 Thompson C M, Frick J A & Woytowicz C E, *Synth Commun*, 18, **1988**, 889.

15 Thompson C M, *Tetrahedron Lett*, 28, **1987**, 4243.

16 Thompson C M, Green D L C & Kubas R, *J Org Chem*, 53, **1988**, 5389.

17 Green D L C & Thompson C M, *Tetrahedron Lett*, 32, **1991**, 5051.

18 Thompson C M, *Dianion Chemistry in Organic Synthesis*, (CRC Press, Boca Raton, Florida) **1994**.

19 Green D L C, Kiddle J J & Thompson C M, *Tetrahedron*, 51, **1995**, 2865.

20 Singh M S & Singh A K, *Synth Commun*, 30, **2000**, 53.

21 Singh M S & Singh A K, *Heterocycles*, 53, **2000**, 851.

22 Singh M S & Singh A K, *Synth Commun*, 39B, **2000**, 551.

23 Singh M S & Pandey G, *Synth Commun*, 30, **2000**, 3589.

24 Singh M S, Singh B K & Singh A K, *Indian J Chem*, 41B, **2002**, 1507.

25 Singh M S & Singh A K, *Synthesis*, **2004**, 837.

26 Singh M S & Singh A K, *Tetrahedron Lett*, 46, **2005**, 315.

27 Mederos A, Dominguez S, Hernandez-Molina R, Sanchiz J & Brito F, *Coord Chem Rev*, 193, **1999**, 857.

28 (a) Tarafder M T H & Khan A R, *Polyhedron*, 10, **1991**, 819.
(b) Sailaja S, Reddy M R, Raju K M & Reddy KH, *Indian J Chem*, 38A, **1999**, 156.

29 (a) Armarego W L F & Perrin D D, *Purification of Laboratory Chemicals*, 4th Edn, (Butterworth, Heinemann: Oxford OX2 8DP) **1977**.
(b) Furniss B S, Hannaford A J, Smith P W G & Tatchell A R, *Vogel's Text Book of Practical Organic Chemistry*, 5th Edn, (Longman, UK) **1989**.