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Synthetic Applications of C,C-Bis(Iminophosphoranes):Preparation of [5+5] Rigid Bicyclic Guanidines and 1,3,6-Benzothiadiazepino[3,2-*a*] benzimidazole Derivatives

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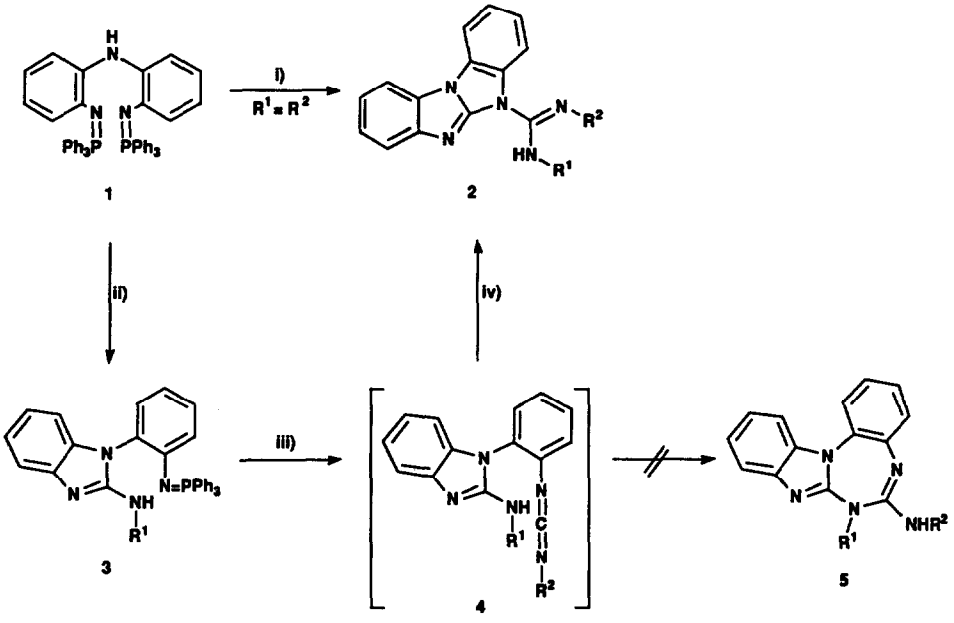
Abstract: Aza Wittig-type reaction of bis(iminophosphorane) **1**, derived from bis(2-aminophenyl)amine with two equivalents of isocyanate directly provided benzimidazo[1,2-*a*]benzimidazole derivatives **2**. However, the reaction with one equivalent of isocyanate or carbon disulfide afforded C-aryl iminophosphoranes **3** or **6**, respectively, derived from the 1-phenylbenzimidazole ring, which underwent cyclization by the action of one equivalent of isocyanate to give the [5+5] rigid bicyclic guanidines **2** or 1,3,6-benzothiadiazepino[3,2-*a*]benzimidazoles **8**.

Compounds containing a cyclic guanidine moiety are of considerable interest because of a range of chemical properties and biological activities. In this context, they have been used as versatile very strong bases[1] and they serve as binding sites for anionic functional groups e.g. rigid bicyclic guanidines have been utilized as enantioselective and/or substrates specific oxoanion hosts[2]. In addition, artificial enzymes that possess two guanidinium-like moieties have been synthesized in an attempt to activate phosphate linkages[3] electrophilically. On the other hand, the cyclic guanidine unit is found in a variety of naturally occurring compounds such as the potent ion-channel blockers saxitoxin, ptilocaulin, tetradotoxin and the polycyclic marine-derived guanidine ptilomycalin A, which has been reported to exhibit remarkable antitumor, antiviral and antifungal activities[4]. In addition, certain secondary metabolites of marine origin are non-traditional guanidine-based alkaloids that possess a broad spectrum of powerful biological activities[5], in which the guanidine group is most frequently found in the guise of a 2-aminoimidazole ring that is generally substituted with alkyl groups on carbon or nitrogen.

In order to further enhance the synthetic utility of our recently discovered iminophosphorane-mediated dihydropyrimido annulation based on the reaction of C,C-bis(iminophosphoranes) with isocyanates, which allowed the preparation of rigid [6+6] bicyclic guanidines[6], we have embarked upon a program to develop this chemistry. The next logical step would be the application of such methodology to the synthesis of rigid [5+5] bicyclic guanidines namely N-derivatives of the benzimidazo[1,2-*a*]benzimidazole ring system. The preparation of some derivatives of this ring system, by photolysis of 2-(1-benzotriazolyl)benzimidazoles[7] or by heating N^1,N^2,N^3-tris(pentafluorophenyl)guanidine[8], has only been briefly described.

In our approach, the bis(iminophosphorane) **1** was chosen as suitable starting material. This compound was easily prepared by the following three-step sequence: a) coupling of *o*-nitrofluorobenzene with *o*-nitroaniline in dimethyl sulfoxide in the presence of potassium *t*-butoxide[9], b) reduction with hydrazine in the presence of palladium on charcoal[10], and c) reaction of the resulting bis(2-aminophenyl)amine with triphenylphosphine dibromide in the presence of triethylamine (78%).

Bis(iminophosphorane) **1** reacted with two equivalents of aromatic or aliphatic isocyanates in dichloromethane at room temperature to give directly the tetracyclic compound **2**, bearing two guanidine-like moieties, in 58-65%. However, when the reaction was carried out with one equivalent of the same type of isocyanates, under the above mentioned conditions, iminophosphoranes **3**, derived from the benzimidazole ring, were isolated in 50-68% yield. Trace levels of compound **2** were detected in the crude products. The ^{1}H NMR spectra suggested the exocyclic amino group of **3**; e.g. for **3a** (R = isopropyl) the methine signal appeared as a complex multiplet and the amino group occurred as a doublet (J = 4.8 Hz). Treatment of iminophosphoranes **3** with a second equivalent of isocyanate in dichloromethane at room temperature afforded **2** in good yields (Scheme 1). The ^{1}H and ^{13}C NMR spectra of compounds **2a-c** indicated that the two aryl groups are non equivalent. However, comparison of these data

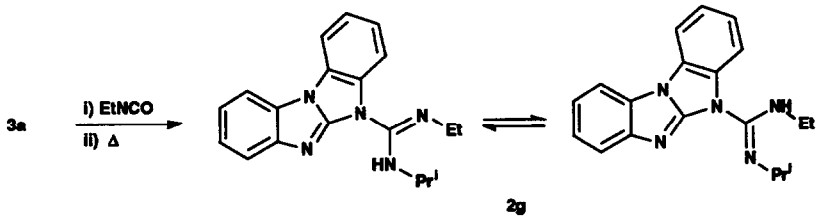


i) 2 R^1-NCO, CH_2Cl_2, r.t.; ii) R^1-NCO, CH_2Cl_2, r.t.; iii) R^2-NCO, CH_2Cl_2, r.t.; iv) Δ

Scheme 1

with those corresponding to previously reported structures bearing a N-substituted guanidine moiety[11] or a fused [1,3,5]benzotriazepine[12], which should be related to compounds **2** and **5**, respectively, do not permit the structural unambiguous assignment for these species. Nevertheless, compound **2g**, isolated when the iminophosphorane **3a**

reacted with ethyl isocyanate, gives rise to signals in the ^{1}H- and ^{13}C-NMR spectra corresponding to two different ethyl and isopropyl groups which clearly indicate the existence of two tautomers in solution, which is in agreement with a type **2** structure rather than a type **5** , which would give two signals corresponding to the R^2 substituent in the two possible tautomers but only one signal for the R^1 substituent (Scheme 2). These data together with the fact

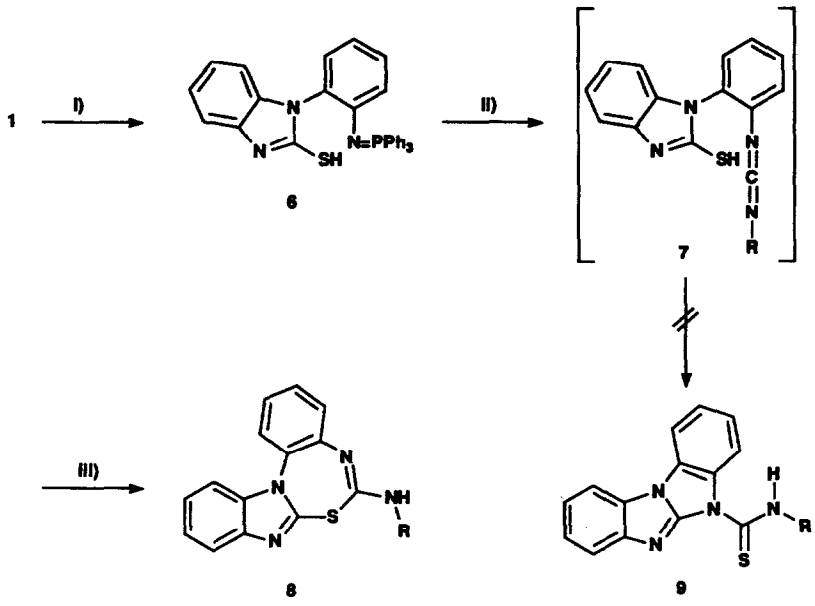


Scheme 2

that the mass spectra of **2** show the base peak at m/z 207 (M^+ - R-N=C=N-R') strongly support the proposed structure for compounds **2**. However, all attempts to remove the exocyclic guanidino fragment from **2**, either by thermal treatment or acid-promoted, failed as it occurred in most of the related bicyclic guanidines reported, in which the elimination of the corresponding exocyclic guanidino moiety took place only in one case and in very low yield, when were pyrolyzed at slightly higher temperatures than their melting point. In that case, the X-ray structure analysis of the resulting parent tetracyclic guanidine confirmed the proposed structure[13] with which structure **2** is related.

The conversion **1**→**2** could probably involve an initial aza Wittig-type reaction between one iminophosphorane group of **1** and the first equivalent of the isocyanate to give a carbodiimide which underwent cyclization by nucleophilic attack of the secondary amino group on the central carbon atom of the carbodiimide moiety to give **3**. Aza Wittig-type reaction between the iminophosphorane **3** and the second equivalent of the isocyanate led to the intermediate carbodiimide **4** which cyclised to **2** either by nucleophilic attack of the exocyclic amino group on the carbodiimide followed by ring-contraction of the resulting seven membered ring or by an intramolecular [2+2] cycloaddition between the carbodiimide and the exocyclic C=N double bond moieties and further ring-opening of the four-membered ring[13].

On the other hand, bis(iminophosphorane) **1** also reacted with carbon disulfide at 40°C to give the iminophosphorane **6** which was isolated as crystalline solid in 70% yield. Formation of compound **6** could be explained by an initial aza Wittig-type reaction between one iminophosphorane group of **1** and carbon disulfide to give an isothiocyanate as highly reactive intermediate which cyclised by nucleophilic attack of the amino group on the central carbon atom of the isothiocyanate moiety to give **6**. When compound **6** was treated with aromatic isocyanates in dichloromethane at room temperature the corresponding carbodiimide **7** was formed, as evidenced by IR spectroscopy. This compound remained unaltered at room tempeature for a long period of time. However, when dichloromethane solutions of **7** were heated at reflux temperature the corresponding tetracyclic compounds **8**, derived from the previously unreported 1,3,6-benzothiadiazepino[3,2-*a*]benzimidazole ring system, were isolated as crystalline solids in 65-71% (Scheme 2). The conversion **6**→**8** can be understood by initital formation of the carbodiimide **7** which undergoes ring-closure by nucleophilic attack of the thiol group on the carbodiimide fragment. Spectral data of compounds **8** support the proposed structure and rule out the alternative structure **9**. In conclusion, the work described here affords a simple but effective new and general route to [5+5] bicyclic



I) CS_2, 40°C; II) R-NCO, CH_2Cl_2, r.t.; III) Δ

Scheme 3

guanidines, derived from the benzimidazo[1,2-*a*]benzimidazole ring system, bearing an additional exocyclic guanidino fragment. These relatively complex structures are assembled in a simple one-pot procedure in good yields, mild reaction conditions and from a readily available starting material.

EXPERIMENTAL

All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained as Nujol emulsions or films on a Nicolet 5DX spectrophotometer. NMR spectra were recorded on a Bruker AC 200 (200 MHz) or a Varian Unity 300 (300 MHz). Mass spectra were recorded on a Hewlett-Packard 5993C spectrometer. Microanalyses were performed on a Perkin-Elmer 240C instrument.

2,2'-Bis(triphenylphosphoranylidenamino)diphenylamine **1**.

Bromine (1.60g, 10 mmol) in dry benzene (15 ml) was added dropwise to a stirred solution of triphenylphosphine (2.62 g, 10 mmol) in the same solvent (30 ml) at 0°C under nitrogen. The mixture was stirred for 1 h and then allowed to warm to room temperature. A solution of bis(2-aminophenyl)amine (1.0 g, 5 mmol) and triethylamine (2.0 g, 20 mmol) in dry benzene (35 ml) was then added. After heating under reflux for 5 h triethylammonium bromide was deposited and separated by filtration. The filtrate was concentrated to dryness and the residual material was treated with hot ethanol (20 ml) and the formed solid was separated by filtration, air-dried and recrystallized from chloroform/*n*-hexane to give **1** in 78% yield as green prisms, m.p. 260-262°C. (Found: C,

79.83; H, 5.59; N, 5.62. $C_{48}H_{39}N_3P_2$ requires: C, 80.10; H, 5.46; N, 5.84). i.r. (Nujol): 3245, 1568, 1523, 1483, 1437, 1115, 1019, 718; ^{1}H n.m.r. δ ($CDCl_3$):6.30 (br. s, 1H), 6.48 (d, 2H, J=7.5 Hz), 6.67 (t, 2H, J=7.5 Hz), 7.16-7.23 (m, 22H), 7.74-7.76 (m, 12H); ^{31}P n.m.r. δ ($CDCl_3$) -0.43; m/z (%): 719 (M^+, 6), 262 (30), 183 (100).

General Procedure for the Preparation of N-Substituted Benzimidazo[1,2-a]benzimidazoles **2a-e.**

To a solution of bis(iminophosphorane) **1** (1.0 g, 1.39 mmol) in dry dichloromethane (15 ml) the appropriate isocyanate (2.78 mmol) was added in one portion. The reaction mixture was stirred at room temperature under nitrogen for 48 h. The solvent was removed under reduced pressure and the residual product was chromatographed on a silica gel column with *n*-hexane/ethyl acetate (7:4) as eluent to give **2** which were recrystallized from *n*-hexane/chloroform (1:1)

2a: (R^1=R^2=4-$H_3C.C_6H_4$) (65%), m.p. 181-183°C (colourless needles) (Found: C, 78.43; H, 5.27; N, 16.13. $C_{28}H_{23}N_5$ requires: C, 78.30; H, 5.40; N, 16.30); i.r. (Nujol) 3290, 1636, 1511, 752 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 2.33 (s, 3H), 2.34 (s, 3H), 7.06 (d, 2H, J=8.6 Hz), 7.11 (d, 2H, J=8.6 Hz), 7.18-7.36 (m, 4H), 7.46 (d, 2H, J=8.6Hz), 7.51 (d, 2H, J=8.6 Hz), 7.64-7.69 (m, 2H), 7.75-7.80 (m, 2H), 7.82 (br s, 1H); ^{13}C n.m.r. δ ($CDCl_3$): 20.8, 20.9, 111.5, 119.4, 119.5, 119.8, 122.0, 123.2, 123.4, 124.0, 127.2, 127.6, 129.5, 130.0, 132.1, 133.3, 133.8, 133.9, 136.5, 137.8, 140.6, 142.8, 146.2, 150.0; m/z (%): 429 (M^+, 5), 223 (20), 207 (100), 91 (10).

2b: (R^1=R^2=4-$H_3CO.C_6H_4$) (63%), m.p. 189-191°C (colourless prisms) (Found: C, 72.69; H, 4.98; N, 14.94. $C_{28}H_{23}N_5O_2$ requires: C, 72.87; H, 5.02; N, 15.17); i.r. (Nujol) 3273, 1630, 1510, 754 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 3.74 (s, 3H), 3.76 (s, 3H), 6.83 (d, 2H, J=9.3 Hz), 7.26 (d, 2H, J=9.3 Hz), 7.33 (d, 2H, J=9.3Hz), 7.39-7.44 (m, 4H), 7.65 (d, 2H, J=9.3 Hz), 7.70-7.74 (m, 4H), 7.78 (br s, 1H); ^{13}C n.m.r. δ ($CDCl_3$): 55.4, 55.5, 111.3, 112.9, 114.1, 114.5, 119.6, 121.8, 122.0, 123.0, 123.7, 124.0, 127.0, 128.3, 129.0, 130.7, 131.9, 133.0, 140.4, 142.7, 147.9, 151.1, 156.2, 157.2; m/z (%): 461 (M^+, 4), 255 (83), 207 (100), 107 (8).

2c: (R^1=R^2=4-$F.C_6H_4$) (58%), m.p. 194-196°C (colourless prisms) (Found: C, 71.23; H, 3.77; N, 15.88. $C_{26}H_{17}F_2N_5$ requires: C, 71.39; H, 3.92; N, 16.01); i.r. (Nujol) 3288, 1630, 1591, 744 cm^{-1}; ^{1}H n.m.r. δ (DMSO-d_6): 7.06-7.15 (m, 4H), 7.30-7.57 (m, 12H), 9.18 (br s, 1H); ^{13}C n.m.r. δ (DMSO-d_6): 111.4, 115.4 ($^2J_{C\text{-}F}$=22.6 Hz), 115.5 ($^2J_{C\text{-}F}$=22.6 Hz), 118.2, 119.4 ($^3J_{C\text{-}F}$=8.2 Hz), 121.4 ($^3J_{C\text{-}F}$=8.2 Hz), 122.1, 123.1, 123.2, 124.0, 129.3, 129.7, 132.6, 135.0, 136.6 ($^4J_{C\text{-}F}$=2.6 Hz), 139.3 ($^4J_{C\text{-}F}$=2.6 Hz), 140.8, 142.4, 148.0, 151.3, 157.8 ($^1J_{C\text{-}F}$=239.3 Hz), 158.3 ($^1J_{C\text{-}F}$=239.3 Hz); m/z (%): 437 (M^+, 4), 231 (10), 207 (100), 95 (47).

2d: (R^1=R^2=$H_2C.C_6H_5$) (65%), m.p. 222-224°C (colourless prisms) (Found: C, 78.43; H, 5.27; N, 16.13. $C_{28}H_{23}N_5$ requires: C, 78.30; H, 5.40; N, 16.30); i.r. (Nujol) 3341, 1625, 1577, 736 cm^{-1}; ^{1}H n.m.r. δ (DMSO-d_6): 4.22 (d, 2H, J=4.5 Hz), 4.53 (s, 2H), 6.81-7.50 (m, 18H), 8.45 (d, 1H, J=4.5 Hz) ; ^{13}C n.m.r. δ (DMSO-d_6): 42.7, 45.6, 107.6, 115.3, 118.9, 120.5, 121.1, 122.3, 126.4, 126.9, 127.0, 127.2, 128.0, 128.3, 129.0, 129.6, 133.0, 134.1, 138.2, 139.8, 140.4, 143.4, 147.3, 150.6; m/z (%): 429 (M^+, 2), 223 (10), 207 (100), 91(98).

2e: (R^1=R^2=C_6H_{11}) (64%), m.p. 202-204°C (colourless prisms) (Found: C, 75.40; H, 7.34; N, 16.70. $C_{26}H_{31}N_5$ requires: C, 75.51; H, 7.56; N, 16.93); i.r. (Nujol) 3280, 1622, 1520, 738 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$):1.17-1.30 (m, 12H), 1.60-1.91 (m, 10H), 7.26-7.29 (m, 4H), 7.59-7.69 (m, 4H), 8.65 (br s, 1H); ^{13}C n.m.r. δ ($CDCl_3$): 24.1, 24.8, 29.0, 29.7, 32.7, 33.6, 49.1, 52.0, 111.0, 119.1, 121.3, 122.4, 122.6, 126.9, 128.1, 128.4, 132.8, 133.9, 140.9, 142.1, 147.5, 150.0; m/z (%): 413 (M^+, 2), 207 (100), 83 (29).

General Procedure for the Preparation of Iminophosphoranes **3.**

To a solution of bis(iminophosphorane) **1** (0.81 g, 1.13 mmol) in dry dichloromethane (15 ml) an equimolecular amount of the appropriate isocyanate (1.13 mmol) was added in one portion. The resultant mixture

was stirred at room temperature under nitrogen for 48 h. The work-up was similar to that described for the preparation of compounds **2**.

3a: (R^1=*i*-Pr) (50%), m.p. 241-243°C (colourless prisms) (Found: C, 77.68; H, 5.79; N, 10.44. $C_{34}H_{31}N_4P$ requires: C, 77.55; H, 5.93; N, 10.64); i.r. (Nujol) 3281, 1615, 1488, 1115, 749 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 0.90 (d, 3H, J=6.2 Hz), 1.81 (d, 3H, J=6.2 Hz), 4.12 (m, 1H), 5.26 (d, 1H, J=4.8 Hz), 6.63 (d, 1H, J=7.6 Hz), 6.75 (t, 1H, J= 7.6 Hz), 7.39-7.57 (m, 21H); ^{13}C n.m.r. δ ($CDCl_3$): 23.0, 23.4, 44.6, 108.7, 115.8, 117.7, 118.8, 120.5, 122.8, 123.0, 128.5 ($^3J_{C\text{-}P}$=12 Hz), 128.6 ($^4J_{C\text{-}P}$=3 Hz), 130.2 ($^1J_{C\text{-}P}$=100 Hz), 130.9 ($^3J_{C\text{-}P}$=18 Hz), 131.8, 132.4 ($^2J_{C\text{-}P}$=9.5 Hz), 134.6, 136.1, 147.2, 154.9; m/z (%): 526 (M^+, 5), 262 (42), 183 (100).

3b: (R^1=4-$H_3C.C_6H_4$) (68%), m.p. 190-192°C (colourless needles) (Found: C, 79.68; H, 5.79; N, 10.44. $C_{38}H_{31}N_4P$ requires: C, 79.42; H, 5.44; N, 9.75); i.r. (Nujol) 3347, 1602, 1437, 1109, 746 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 2.22 (s, 3H), 6.68 (d, 1H, J=7.5 Hz), 6.78 (t, 1H, J=7.5Hz), 6.9-7.7 (m, 25H), 8.45 (br s, 1H); ^{13}C n.m.r. δ ($CDCl_3$): 20.7, 109.6, 116.8, 118.6, 120.2, 120.3, 121.3, 121.4, 121.5, 128.4, 128.9 ($^3J_{C\text{-}P}$=12 Hz), 129.1 ($^3J_{C\text{-}P}$=18 Hz), 129.4, 131.3 ($^1J_{C\text{-}P}$=100 Hz), 132.1, 132.2 ($^4J_{C\text{-}P}$=3 Hz), 132.5 ($^2J_{C\text{-}P}$=9.5 Hz), 134.2, 136.3, 137.7, 147.0, 151.8; m/z (%): 574 (M^+, 20), 262 (16), 183 (100).

Preparation of N-Substituted Benzimidazo[1,2-a]benzimidazoles **2f** *and* **2g**.

To a solution of the appropriate iminophosphorane **3** (1.4 mmol) in dry dichloromethane (20 ml) the corresponding isocyanate was added dropwise (1.4 mmol). The reaction mixture was stirred at room temperature under nitrogen for 6 h and then refluxed for 6 h. After cooling, the solvent was removed under reduced pressure and the remaining solid was chromatographed on a silica gel column with *n*-hexane/ethyl acetate (7:4) as eluent, and finally recrystallized from *n*-hexane/chloroform (1:1).

2f: (R^1 = 4-$H_3C.C_6H_4$, R^2 = 4-$H_3CO.C_6H_4$) (64%), m.p. 154-156°C (colourless prisms) (Found: C, 75.30; H, 5.15; N, 15.49. $C_{28}H_{23}N_5O$ requires: C, 75.49; H, 5.20; N, 15.72); i.r. (Nujol) 3242, 1642, 1511, 735 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 2.1 (s, 3H), 3.7 (s, 3H), 6.73 (d, 2H, J=9 Hz), 6.87 (d, 2H, J=8.4 Hz), 7.04 (d, 2H, J=9 Hz), 7.28 (d, 2H, J=8.4 Hz), 7.39-7.43 (m, 2H), 7.46-7.51 (m, 2H), 7.64-7.86 (m, 4H), 8.0 (br s, 1H); ^{13}C n.m.r. δ ($CDCl_3$): 20.9, 55.6, 111.2, 114.5, 120.9, 122.5, 124.2, 124.4, 125.0, 125.1, 125.9, 128.2, 128.4, 129.6, 131.9, 132.0, 135.0, 135.6, 137.6, 141.0, 142.0, 147.7, 150.9, 156.9; m/z (%): 445 (M^+, 10), 239 (8), 207 (100), 107 (7), 91 (53).

2g: (R^1 = $(H_3C)_2CH$, R^2 = C_2H_5) (48%), m.p. 168-170°C (colourless prisms) (Found: C, 71.20; H, 6.48; N, 21.95. $C_{19}H_{21}N_5$ requires: C, 71.45; H, 6.63; N, 21.93); i.r. (Nujol) 3245, 1638, 1530, 746 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.20 (t, 3H, J=7.0Hz), 1.25(d, 6H, J=6.6 Hz), 1.26 (d, 6H, J=6.6 Hz), 1.32 (t, 3H, J = 7.0 Hz), 3.31-3.48 (m, 2H), 3.92-4.11 (m, 4H), 4.60 (d, 1H, J=4.8Hz), 5.32 (br s, 1H), 7.18-7.20 (m, 8H), 7.51-7.54 (m, 4H), 7.57-7.62 (m, 4H); ^{13}C n.m.r. δ ($CDCl_3$): 22.2, 22.3, 22.4, 22.5, 22.6, 37.4, 37.5, 44.1, 49.8, 111.2, 118.9, 119.0, 121.2, 121.3, 122.4, 122.6, 122.7, 126.8, 126.9, 127.0, 128.5, 128.7, 132, 132.1, 132.2, 132.9, 133.1, 133.9, 134.0, 140.4, 140.7, 142.2, 142.5, 147.4, 147.8, 150.8, 151.7; m/z (%): 319 (M^+, 6), 207 (100), 113 (8), 43 (25).

Preparation of Iminophosphorane **6**.

Method A.- To a solution of bis(iminophosphorane) **1** (1.0 g, 1.39 mmol) in dry dichloromethane (20 ml) carbon disulfide (0.11 g, 1.39 mmol) was added. The reaction mixture was stirred at 40°C under nitrogen for 24 h, and then the solvent was removed under reduced pressure and the residue chromatographed on a silica gel column, using *n*-hexane/ethyl acetate (4:7) as eluent, and finally recrystallized from *n*-hexane/chloroform (1:1) to give **6** in 68% yield.

Method B- A well stirred solution of bis(iminophosphorane) **1** (1.0 g, 1.39 mmol) in carbon disulfide (25 ml)

was heated at 40°C under nitrogen for 20 h. After cooling, the precipitated solid was collected by filtration and recrystallized from *n*-hexane/chloroform (1:1) to give **6** in 70% yield; m.p. 282-284°C (colourless needles). (Found: C,74.13 ; H, 4.67 ; N, 8.16. $C_{31}H_{24}N_3PS$ requires: C, 74.24; H, 4.82 ; N, 8.38); i.r. (Nujol): 3222, 1591, 1437, 1113, 741 cm^{-1} ; ^1H n.m.r. δ ($CDCl_3$): 6.60 (d, 1H, J=7.5 Hz), 6.82 (t, 1H, J=7.5 Hz), 7.0-7.48 (m, 21H), 11.88 (s, 1H) ; ^{13}C n.m.r. δ ($CDCl_3$): 109.4, 111.7, 117.1, 122.2, 122.3, 122.5, 122.7, 128.4 ($^3J_{C-P}$=12 Hz), 129.1 ($^3J_{C-P}$=18 Hz), 129.8, 131.1 ($^1J_{C-P}$=100 Hz), 131.6 ($^4J_{C-P}$=3 Hz), 132.5 ($^2J_{C-P}$=9.5 Hz), 134.8, 136.5, 148.0, 169.5; m/z (%): 501 (M^+, 23), 262 (9), 183 (100).

General Procedure for the Preparation of 1,3,6-Benzothiadiazepino[3,2-a]benzimidazole Derivatives **8.**

To a solution of iminophosphorane **6** (0.5 g, 1 mmol) in dry dichloromethane (15 ml) the corresponding isocyanate (1 mmol) was added. The resultant reaction mixture was stirred at room temperature under nitrogen for 12 h and then heated at reflux temperature for 6 h. After cooling, the solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column with *n*-hexane/chloroform (1:1) as eluent to give **8**.

8a: (R = 4-$H_3C.C_6H_4$) (71%), m.p. 225-227°C (colourless needles). (Found: C, 70.55 ; H, 4.39 ; N,15.60. $C_{21}H_{16}N_4S$ requires: C, 70.77; H, 4.52; N, 15,72); i.r. (Nujol):3154, 1630, 1616, 744 cm^{-1} ; ^1H n.m.r. δ ($CDCl_3$/TFA): 2.35 (s, 3H), 6.89 (d, 2H, J= 8.5 Hz), 6.92 (d, 2H, J=8.5 Hz), 7.30-7.66 (m, 8H); ^{13}C n.m.r. δ ($CDCl_3$/TFA): 20.7, 111.6, 115.0, 119.6, 121.4, 123.5, 123.6, 124.5, 124.8, 127.1, 127.7, 129.0, 133.0, 134.6, 136.9, 140.7, 142.1, 144.2; m/z (%): 356 (M^+, 98), 324 (10),225 (100), 209 (20), 150 (15), 106 (30), 91 (18).

8b: (R = 4-$H_3CO.C_6H_4$) (65%), m.p. 220-222°C (colourless needles). (Found: C, 67.55 ; H, 4.29 ; N,15.15. $C_{21}H_{16}N_4OS$ requires: C, 67.73; H, 4.33; N, 15.05); i.r. (Nujol):3250, 1636, 1591, 748 cm^{-1} ; ^1H n.m.r. δ (DMSO-d_6): 3.71 (s, 3H), 6.88 (d, 2H, J= 9.0 Hz), 7.34-7.78 (m, 10H), 10.21 (br s, 1H); ^{13}C n.m.r. δ (DMSO-d_6): 55.2, 111.4, 113.8, 114.6, 119.8, 121.3, 123.3, 124.2, 124.4, 125.0, 126.8, 127.5, 128.1, 135.1, 140.9, 142.9, 144.0, 155.4; m/z (%): 372(M^+, 45), 340 (10), 225 (100), 150 (17), 122 (26), 107 (16).

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