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Unexpected Condensation Reaction of Two Units of 1,2-Dihydrophosphinine 1-Oxides in the Presence of Tetracyanoethylene

György Keglevich,[1] János Kovács,[1] Áron Szöllősy,[2] Attila Kovács,[3] Andrea Szabó,[2] Krisztina Ludányi,[4] István Kádas,[5] and László Tőke[5]

[1]*Department of Organic Chemical Technology, Budapest University of Technology and Economics, 1521 Budapest, Hungary*

[2]*Department of General and Analytical Chemistry, Budapest University of Technology and Economics, 1521 Budapest, Hungary*

[3]*Research Group for Technical Analytical Chemistry of the Hungarian Academy of Sciences at the Department of General and Analytical Chemistry, Budapest University of Technology and Economics, 1521 Budapest, Hungary*

[4]*Chemical Research Center, Hungarian Academy of Sciences, 1525 Budapest, Hungary*

[5]*Research Group of the Hungarian Academy of Sciences at the Department of Organic Chemical Technology, Budapest University of Technology and Economics, 1521 Budapest, Hungary*

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ABSTRACT: *In the presence of tetracyanoethylene, the reaction of two molecules of dihydrophosphinine oxide* **2B** *followed an unexpected route to afford diphosphatricyclododecatrienes* **4** *instead of the corresponding Diels–Alder cycloadducts (***3***). Structures of the products (***4***) have been elucidated by a joint application of spectroscopy and quantum chemical calculations.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:29–35, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10062

Correspondence to: György Keglevich; e-mail: keglevich@oct.bme.hu.

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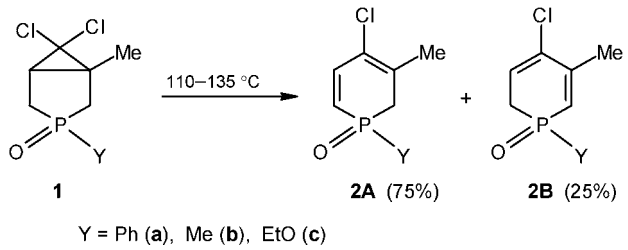
INTRODUCTION

Bridged P-heterocycles, such as 2-phosphabicyclo-[2.2.2]octene 2-oxides, are of synthetic use as precursors of low-coordinate fragments, methylenephosphine oxides, that can be used in phosphorylations [1–3]. The "traditional" phosphabicyclooctenes are obtained by the Diels–Alder reaction of 1,2-dihydrophosphinine oxides with maleic acid derivatives [1,2]. Recently, we have aimed at the synthesis of new types of precursors, such as diaza derivatives [4,5] or the dimers of dihydrophosphinine oxides [5,6]. In this paper, we describe the reactions of dihydrophosphinine oxides with tetracyanoethylene, which is a versatile dienophile that sometimes gives quite unexpected results [7–9].

RESULTS AND DISCUSSION

In our experiments, a 3:1 mixture of dihydrophosphinine oxides **2A** and **2B**, obtained by the cyclopropane



SCHEME 1 [7–9].

ring opening of 3-phosphabicyclo[3.1.0]hexane 3-oxide (**1**), was used as the starting material (Scheme 1) [10–12].

This mixture of the double-bond isomers (**A** and **B**) of dihydrophosphinine oxides **1a–c** was reacted with tetracyanoethylene in boiling benzene for 6 days to prepare the corresponding [4 + 2] cycloadducts (**3**). The work-up procedure afforded, however, a quite different product (**4a–c**) that was formed by the condensation of two molecules of dihydrophosphinine oxide **2Ba–c**, incorporating also a tetracyanoethylene unit (Scheme 2). Based on isomer **2B**, the yields of products **4a–c** were ca. 25% after purification by chromatography. Structures of the unexpected products (**4a–c**) were evaluated by joint spectroscopic and quantum chemical studies.

^{31}P, ^{13}C, and ^{1}H NMR spectral parameters, together with the high-resolution molecular ion peak match, suggested the formation of the diphosphatricyclododecatriene skeleton; the four possibilities for **4a** are shown in Fig. 1. The two phosphorus atoms are coupled by 38.6 Hz. It is clear that four carbon

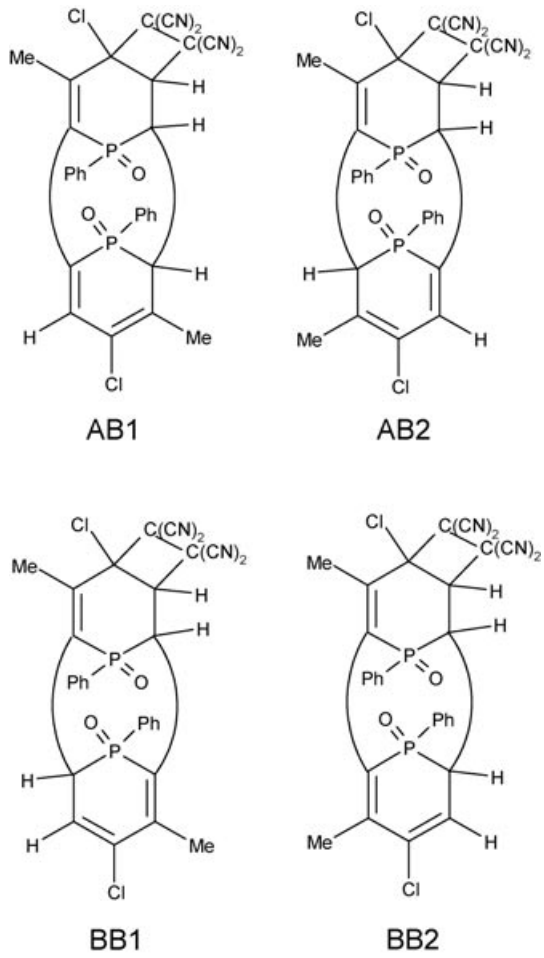
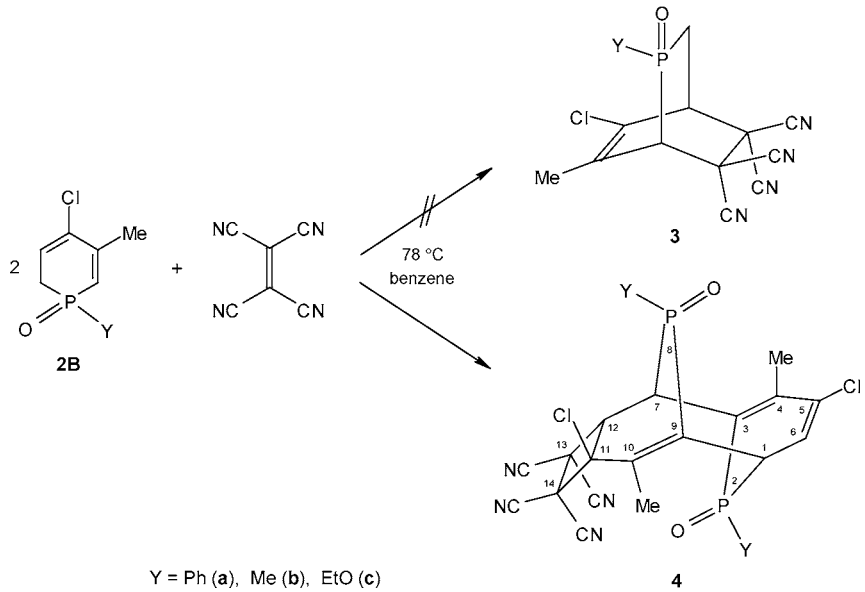


FIGURE 1 Possible connections of the 1,2-dihydrophosphinine 1-oxide moieties in the product.



SCHEME 2

atoms are connected to phosphorus, two sp^3 CH signals at 40.5 and 43.7 ppm, as well as two quaternary sp^2 signals at 154.3 and 164.1 ppm. Assignments of one quaternary and three CH signals in the sp^3 region as well as those of the only CH= and the five quaternary signals in the sp^2 region were achieved by HMQC spectra and characteristic J_{CP} couplings. The protonated carbon signals at 40.5, 43.7, and 128.7 ppm are correlated with the proton signals at 4.25, 3.60, and 7.35 ppm, respectively. The carbon atoms at δ_C 40.5 and 43.7 are coupled with both phosphorus atoms, indicating that the two phosphorus atoms are part of the same ring. The above experiments were, however, inconclusive as to the type of skeleton (**AB1, AB2, BB1**, and **BB2**, where **AB** or **BB** marks the connecting units of the dihydrophosphinine oxides, while "**1**" or "**2**" indicates the manner of the connection of the two dihydrophosphinine moieties, see Fig. 1) and on the relative orientation of the P=O/phenyl and the tetracyanoethylene moieties. Based on the number of centers of chirality, altogether 64 different structural isomers could be anticipated. Although some experimental information on the steric arrangements can be obtained from NOE measurements, the presence of a large number of possible structures required the application of theoretical calculations.

Our quantum chemical calculations served two important goals: to select the most stable structures and to obtain reliable geometrical data (interatomic distances) for the interpretation of the NOESY data. First, the symbols used for the various structural characteristics are defined: **c** or **b** means the conformation of the "diphosphacyclohexane" ring (chair or boat, respectively). **ee, ea, ae**, and **aa** show the orientation (equatorial/axial) of the P_2-phenyl and the P_8-phenyl groups, respectively. **Ex** or **En** refers to the exo- or endofusion of the tetracyanoethylene moiety. Because of the large size of the molecule and the large number of possible structural isomers, initial quantum chemical computations have been performed by using the quick PM3 semiempirical method [13]. Altogether, 43 initial structures were generated, and, on the basis of the first results, the potentially high-energy ones were omitted from further consideration. The minimum characters of the optimized structures were confirmed by frequency analyses. The lowest energy and some additional characteristic structures (altogether 20) have been reoptimized at the more reliable HF/3-21G* level of theory. No symmetry constrain was used during the geometry optimizations. The reliability of the HF/3-21G* results was checked by HF/6-31G* calculations on selected structures. The computations have been performed using the Gaussian98 program package [14]. Relative energies of the most significant isomers are compiled in Table 1.

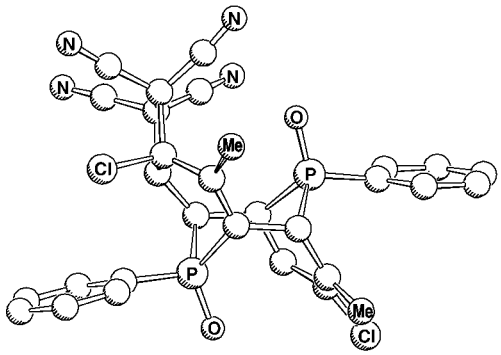
We can say that, in general, the HF/6-31G* calculations supported the reliability of the HF/3-21G* relative energies. The differences between the two levels do not exceed 10 kJ/mol. The results of the PM3 semiempirical calculations are, however, of restricted reliability, as the relative energies obtained in this way deviate considerably from those obtained by the ab initio methods. Literature data suggest the greater reliability of ab initio computed relative energies over the ones obtained by the PM3 method [15].

Comparing the results of the HF/6-31G* and the HF/3-21G* calculations, we found the most stable structures to be **AB2c-eeEx** and **BB1c-eeEx**. It is noted that the PM3 calculations also suggested **AB2c-eeEx** to be the most stable isomer. From Table 1, one can establish that even more structures, including **AB1c-eeEx, AB2c-eaEx**, and **BB2c-eeEx**, should be considered as possible reaction products.

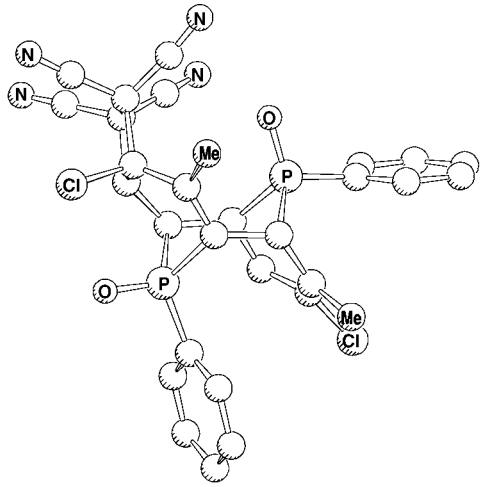
Upon comparison of the various dimer skeletons (**AB1c, AB2c, BB1c, BB2c**) with **eeEx** substituent orientation, it can be seen that they are within 12.5 kJ/mol (HF/6-31G* results). This indicates that the relative stabilities of the various structures may be less dependent on the dimer constitution, but are primarily determined by the steric interactions between the phenyl/P=O substituents and the tetracyanoethylene moiety. Selected structures with the most characteristic steric interactions are shown in Fig. 2

TABLE 1 Results of the Quantumchemical Calculations on Some of the Representative Structures of **4a**

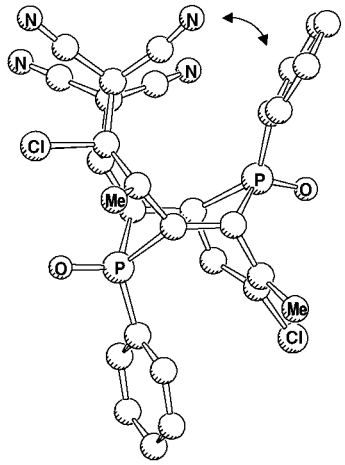
	ΔE (kJ/mol)		
Structure	*PM3*	*HF/3-21G**	*HF/6-31G**
AB1c-eaEn	55.9	37.8	
AB1c-eaEx	44.5	16.4	23.0
AB1c-eeEx	42.7	8.0	12.5
AB1c-eeEn	87.4	112.4	
AB2b-aaEn	42.7	107.3	
AB2b-eeEx	6.5	132.8	125.5
AB2c-aaEx	301.2	531.3	
AB2c-aaEn	33.0	107.9	
AB2c-eaEx	0.3	10.0	11.0
AB2c-eaEn	11.7	21.4	25.4
AB2c-aeEn	64.3	194.5	
AB2c-eeEn	40.5	93.7	
AB2c-eeEx	0.0	0.2	0.0
BB1b-aaEn	67.0	149.6	
BB1c-aaEn	48.6	131.6	
BB1c-eeEx	12.0	0.0	4.6
BB1c-eeEn	53.0	95.5	
BB2c-eaEx	59.5	35.6	
BB2c-eeEn	94.3	107.2	
BB2c-eeEx	51.7	4.5	10.7



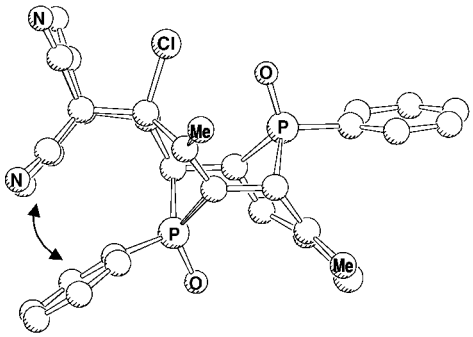
AB2c-eeEx (0.2 kJ/mol)



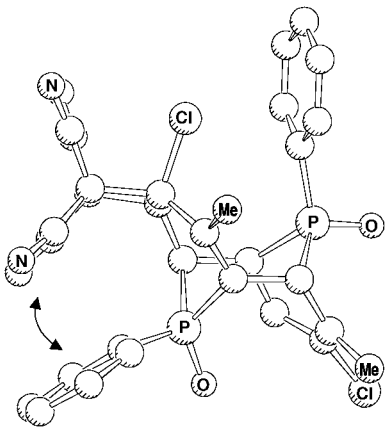
AB2c-eaEx (10.0 kJ/mol)



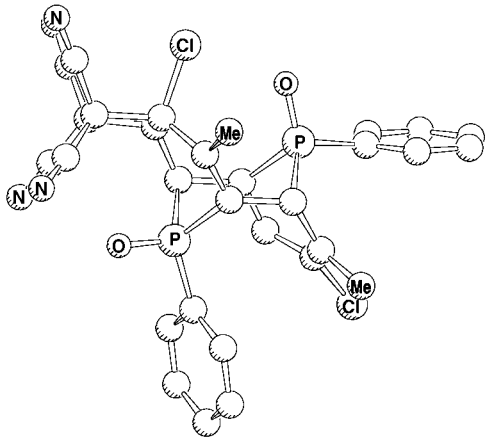
AB2c-aaEx (531.3 kJ/mol)



AB2c-eeEn (93.7 kJ/mol)

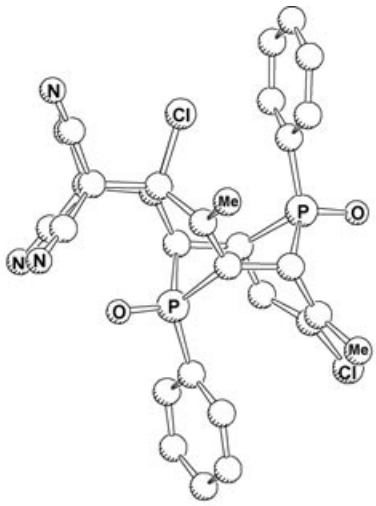


AB2c-aeEn (194.5 kJ/mol)

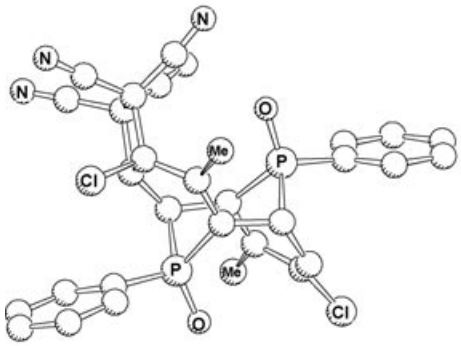


AB2c-eaEn (21.4 kJ/mol)

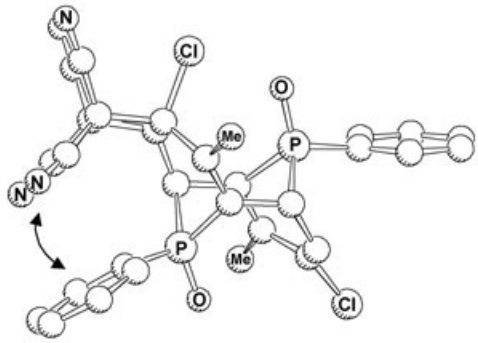
FIGURE 2 Selected structures for the product of the 1-phenyl-1,2-dihydrophosphinine 1-oxide–tetracyanoethylene reaction. *(Continued)*



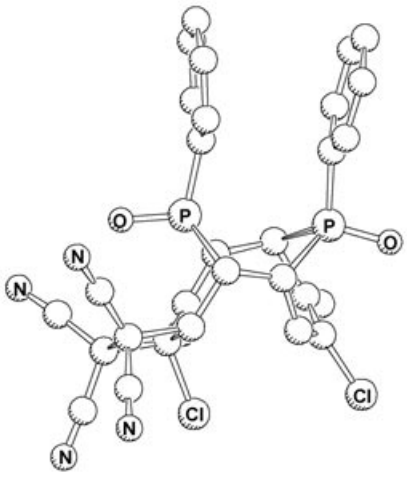
AB2c-aaEn (107.9 kJ/mol)



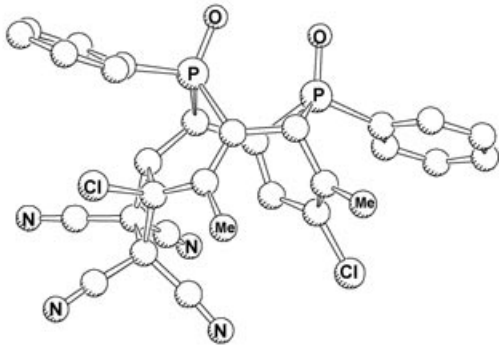
BB1c-eeEx (0.0 kJ/mol)



BB1c-eeEn (95.5 kJ/mol)



AB2b-aaEn (107.3 kJ/mol)



AB2b-eeEx (132.8 kJ/mol)

FIGURE 2 Continued

(accompanied by the HF/3-21G* relative energies). Two important features should be emphasized:

i. The equatorial orientation of the phenyl group is generally more favored than the axial one (Table 1).
ii. The steric proximity of a phenyl and the tetracyanoethylene moiety is not much favored. The most stable structures contain the tetracyanoethylene moiety oriented towards the P=O group of the farther hetero ring.

In a relatively stable structure (**AB2c-eeEx**), the "diphosphacyclohexane" ring forms a chair, the phenyl rings are in the equatorial position, and the fusion of the cyclobutane ring is exo. Upon putting first the P_8-phenyl group and then the P_2 one into the axial position (**AB2-eaEx** and **AB2-aaEx**, respectively) the energy content of the species increases dramatically. In the diaxial conformer, the steric hindrance between the phenyl substituent and the cyclobutane ring is rather unfavorable. Similarly, the change of the anellation of the cyclobutane ring in **AB2c-eeEx** results in unfavorable **AB2c-eeEn**. The energy content is further increased on placing the P_2-phenyl ring into the axial position (**AB2c-aeEn**). The change at the P_8-center however results in a considerable relief of the energy, as in **AB2c-eaEn** where there is no steric hindrance between the phenyl substituent and the cyclobutane ring. However, a further change at the P_2-center again leads to an unfavorable structure (**AB2c-aaEn**) where both phenyl groups are axial. Going to the **BB1-ee** structures, it can be seen that the exofusion is more advantageous than the endoconnection of the corresponding rings.The boat structure for the "diphosphacyclohexane" ring is not much favored; its relative energies are above 100 kJ/mol with respect to the analogous chair structures. This high instability may stem from the unfavored steric interactions of the axial substituents on the phosphorus atom (both phenyl and oxygen atom).

In summary, the calculations indicate that the product formed in the reaction has most probably a chair "diphosphacyclohexene" ring with the phenyl groups in equatorial positions and with the exofusion of the tetracyanoethylene moiety. It was the joint analysis of the computed interatomic distances in the lowest energy structures and the integrated NOE intensities from the 2D ^{1}H–^{1}H NOESY spectrum that finally unambiguously suggested **BB1c-eeEx** as the structure of the product isolated from the reaction mixture. Of course, besides the thermodynamic factors, kinetic effects may also affect the outcome of the reaction. The possibility of the presence of isomer **AB2c-eeEx** in a small quantity in the reaction mixture cannot be excluded. It is worthy of mention that only the **B** isomer was involved in the novel condensation reaction.

Our results demonstrate that the 1,2-dihydrophosphinine oxides **2A** and **2B** are useful starting materials for the syntheses of bridged P-heterocycles, such as diphosphatricyclododecatrienes. The reaction involves a condensation reaction between the two molecules of the substrate and also incorporating a tetracyanoethylene moiety. It may be recalled that the Diels–Alder reaction of two isomeric units of the dihydrophosphinine oxide led to phosphabicyclooctenes [5]. The mechanism of the novel reaction discussed is yet to be studied further. One possibility is that the reaction of one of the dihydrophosphinine oxide moieties with tetracyanoethylene precedes the condensation involving the loss of two molecules of hydrogen.

EXPERIMENTAL

The ^{31}P, ^{13}C, and ^{1}H NMR spectra were taken on a Bruker DRX-500 spectrometer operating at 202.4, 125.7, and 500 MHz, respectively. Chemical shifts are downfield relative to 85% H_3PO_4 or TMS. The couplings are given in Hz. Mass spectrometry was performed on a ZAB-2SEQ instrument. The starting dihydrophosphinine oxides were prepared as described earlier [10–12].

General Procedure for the Preparation of Diphosphatricyclododecatrienes **4a–c**

The 10 ml benzene solution of 1.70 mmol of the dihydrophosphinine oxides **2a–c** and 0.24 g (1.87 mmol) of tetracyanoethylene was stirred at the boiling point for 6 days. The residue obtained after the evaporation of the solvent was purified by column chromatography to afford the products **4a–c**.

4a: Yield 21% (based on **2Ba**); δ_P ($CDCl_3$) 27.1 (P_2), 16.3 (P_8), $^3J_{PP}$ = 38.6 Hz; δ_C ($CDCl_3$) 19.0 (J = 3.6, C_4–Me), 25.9 (J' = 2.4, C_{10}–Me), 40.5 (J = 3.6, J' = 64.2, C_7), 43.7 (J = 64.2, J' = 2.4, C_1), 55.3 (J = 2.4, J' = 8.5, C_{11}), 61.5 (J' = 3.6, C_{12}), 92.7 (J' = 4.8, C_{14}), 98.1 (J = 8.5, C_{13}), 108.9 (J = 6.1, CN), 109.7 (J = 14.5, CN), 110.1 (J = 7.3, CN), 110.5 (J = 15.7, CN), 124.7 (J = 107.8, $C_{1'}$), 127.5 (J = 12.1, C_5), 128.1 (J' = 109.0, $C_{1''}$), 128.7 (J = 3.6, C_6), 130.0 (J = 12.1, $C_{2'}$[a]), 130.2 (J' = 13.3, $C_{2''}$[a]), 130.6 (J = 10.9, $C_{3'}$[b]), 131.7 (J' = 9.7, $C_{3''}$[b]), 134.7 (J = 3.6, $C_{4'}$[c]), 134.9 (J' = 2.4, $C_{4''}$[c]), 135.3 (J = 6.1, C_4), 154.2 (J' = 15.7, C_{10}), 154.3 (J' = 70.2, C_9), 164.1 (J = 83.6, C_3), J: coupled by P_2, J': coupled by P_8, [a–c]may be

reversed; $(M+H)^+_{found} = 601.0483$, $C_{30}H_{21}Cl_2N_4O_2P_2$ requires 601.0517 for the ^{35}Cl isotopes.

4b: Yield 16% (based on **2Bb**); δ_P ($CDCl_3$) 37.9 (P_2), 25.5 (P_8), $^3J_{PP} = 39.5$; $(M+H)^+_{found} = 477.0091$, $C_{20}H_{17}Cl_2N_4O_2P_2$ requires 477.0204 for the ^{35}Cl isotopes.

4c: Yield 25% (based on **2Bc**); δ_P ($CDCl_3$) 31.3 (P_2), 22.8 (P_8), $^3J_{PP} = 61.2$ Hz; δ_C ($CDCl_3$) 16.3 (CH_3CH_2), 18.6 (C_4–CH_3), 25.5 (C_{10}–CH_3), 39.6 ($J' =$ 101.6, C_7), 41.6 ($J = 96.6$, C_1), 55.5 ($J = J' = 5.9$, C_{11}), 61.4 (C_{12}), 65.0 ($J = 7.1$, CH_2O), 66.5 ($J = 5.3$ CH_2O), 90.6 ($J' = 6.3$, C_{14}), 95.9 ($J = 7.4$, C_{13}), 109.5 ($J = 16.4$, CN), 109.8 ($J = 5.8$, CN), 110.2 ($J = 17.1$, CN), 110.5 ($J = 6.8$, CN), 125.4 ($J = 13.8$, C_5), 127.9 (C_6), 133.5 ($J = 9.8$, C_4), 152.2 ($J' = 96.7$, C_9), 153.8 ($J' = 17.1$, C_{10}), 163.1 ($J = 114.4$, C_3); $(M+H)^+_{found} =$ 537.0315, $C_{22}H_{21}Cl_2N_4O_4P_2$ requires 537.0415 for the ^{35}Cl isotopes.

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