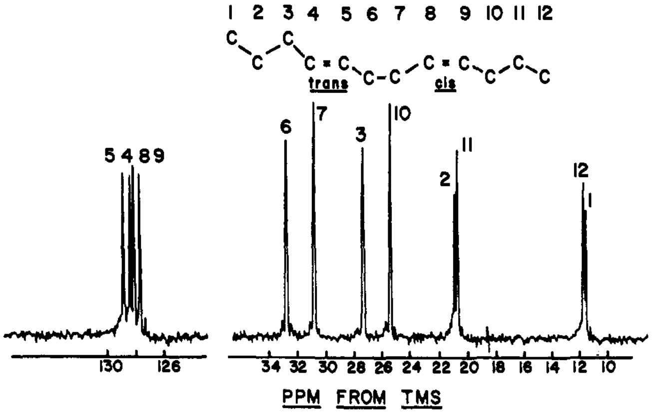

Figure 1. ^{13}C FT nmr spectrum at 25.15 MHz of *cis,trans*-4,8-dodecadiene in dioxane (50% w/v). Reprinted by permission of John Wiley and Sons, Inc.; from ref 7.

The ^{13}C FT nmr of **1**, given in Figure 1, shows all 12 carbon nuclei clearly.[7] The peaks near 128 ppm show that each of the four olefinic carbons has a slightly different electronic environment. The power of ^{13}C nmr is impressively demonstrated by the fact that the slight difference in methyl carbons (at 12 ppm) is easily discerned. The peaks are separated by 0.14 ppm (or 3.5 Hz). Positive assignment of these peaks to methyl carbons was shown by their quartet structure in an off-resonance decoupling experiment. The peaks of the adjacent methylene carbons (at 21 ppm) show a similar separation (0.15 ppm).

The four remaining peaks are due to methylene carbons 3, 6, 7, and 10. The fact there are four well-separated peaks conclusively shows that: (1) the adjacent carbons and the next-nearest neighbors have a considerable effect on the electronic environment, *e.g.*, carbons 3 and 6 are different from each other as are carbons 7 and 10, and (2) the carbons in a cis–trans linkage (6 and 7) are considerably different from each other. Calculated chemical shifts based upon empirical parameters determined from a series of unsubstituted hydrocarbons[8] do not take into account differences between cis and trans units. Additional terms should be added to the parameters to correct for these sizable effects.

This spectrum clearly confirms that this compound has the geometry of **1**. If it were cis–cis or trans–trans, the olefin region would have only two peaks and the aliphatic region only four. Furthermore, the peak intensities indicate about equal concentrations of cis and trans units, thus supporting cis–trans geometry.

The eight peaks in the aliphatic region are in a pattern of a set of four lower intensity peaks and a set of four higher intensity peaks, as judged by peak heights. Each set probably arises from one structure, cis or trans, reflecting a difference in relaxation times between the two structures. The set with the lower peak heights (1, 2, 3, 6) is assigned to the trans structure and the remaining set to the cis structure. This assignment is supported by ^{13}C nmr spectra of cis and trans 1,4 addition polybutadienes which show the *trans*-methylene carbons are downfield 5.4 ppm from *cis*-methylene carbons.[9]

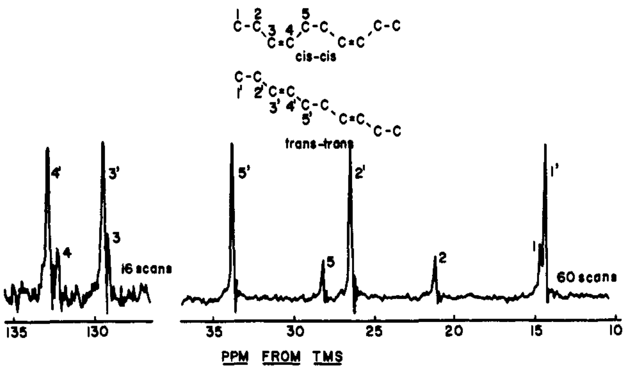

Figure 2. ^{13}C nmr spectrum of an isomeric mixture of 3,7-decadiene in dioxane (50% w/v). Reprinted by permission of John Wiley and Sons, Inc.; from ref 7.

A further assignment of peaks can be made by referring to Figure 2, which is the ^{13}C nmr spectrum of a mixture of isomers of 3,7-decadiene.[5b] The mixture contains about 90% of the trans–trans isomer (the tall peaks) and about 10% of either the cis–cis or the cis–trans isomer. Since only three small peaks are observed in the aliphatic region, it appears that the cis–cis isomer is the minor component. Again, the trans–trans peaks are downfield from the cis–cis peaks except for the methyl carbons, which are also reversed in the spectrum of **1**. Carbons 2 and 2′ which are "outside" carbons are shifted about 7.5 ppm upfield from the "inside" carbons, 5 and 5′. Therefore, in Figure 1 carbons 3, 10, 12, and 1 are assigned as shown by analogy with Figure 2. The carbons of the cis–trans linkage, 6 and 7, have a separation of 2.4 ppm and are assigned intuitively as shown.

In conclusion, ^{13}C FT nmr supports the previous assignment of the geometry in **2** and confirms the geometry of **1**.

Acknowledgment. We wish to acknowledge the assistance of R. K. Griffith in the synthesis work and the permission of The Firestone Tire & Rubber Co. to publish this communication.

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(7) The spectrum was taken with a JEOL JNM-PS/PFT 100 spectrometer at 25.15 MHz. It was obtained with 512 scans, a pulse repetition time of 2.1 sec, and 16,384 data points. TMS is used as the reference. The most likely assignment of peaks is shown in Figure 1. Reprinted from V. D. Mochel, *J. Polym. Sci., Part A-1*, 10, 1009 (1972).

(8) G. B. Savitsky and K. Namikawa, *J. Phys. Chem.*, 68, 1956 (1964).

(9) M. W. Duch and D. M. Grant, *Macromolecules*, 3, 165 (1970).

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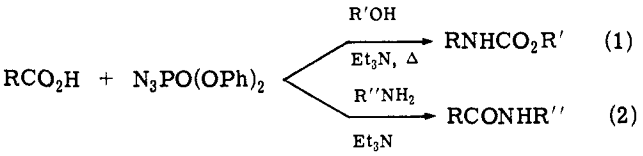
Diphenylphosphoryl Azide. A New Convenient Reagent for a Modified Curtius Reaction and for the Peptide Synthesis

Sir:

This communication describes some synthetic utilities of a hitherto unknown reagent, diphenylphosphoryl azide (DPPA). The new reagent is conveniently prepared in more than 90% yield by allowing diphenyl phosphorochloridate to react with a slight excess of sodium azide in acetone at room temperature, and is a stable, nonexplosive liquid, bp 157° (0.17 mm).

Several modes of reaction are available to DPPA depending upon the coreactant and reaction conditions. These include reactions in which the direct conversion of carboxylic acids to urethanes (1) occurs and also those in which the amide bond formation (2) takes place.



$$RCO_2H + N_3PO(OPh)_2 \xrightarrow[Et_3N,\ \Delta]{R'OH} RNHCO_2R' \quad (1)$$

$$RCO_2H + N_3PO(OPh)_2 \xrightarrow[Et_3N]{R''NH_2} RCONHR'' \quad (2)$$

The reaction procedure for the conversion of carboxylic acids to urethanes is quite simple, occurring by refluxing an equimolecular mixture of the carboxylic acid, triethylamine, and DPPA in the presence of the hydroxyl component for 5–25 hr.[1] After evaporation of the solvent, the neutral fraction obtained after aqueous acid and alkali work-ups is purified by recrystallization, distillation, or silica gel column chromatography to give the urethane.

Both aromatic and aliphatic carboxylic acids afforded urethanes in satisfactory yields. When the reaction was carried out in *tert*-butyl alcohol, the alcohol played the role of both the reactant and solvent. The product isolated was the *tert*-butylurethane giving the amine in high yield under mild acidic conditions.[2,3] The phenyl- or benzylurethane was generated by the similar treatment of the carboxylic acid with a slight excess of phenol or benzyl alcohol in dioxane. Typical yields were: *tert*-butyl carbanilate, 74% from benzoic acid; phenyl carbanilate, 57% from benzoic acid; benzyl carbanilate, 61% from benzoic acid; *tert*-butyl *N*-*n*-heptylcarbamate, 67% from *n*-caprylic acid; *tert*-butyl *N*-phenethylcarbamate, 61% from hydrocinnamic acid; *tert*-butyl *N*-styrylcarbamate, 70% from cinnamic acid; di-*tert*-butyl *N*,*N*′-tetramethylenedicarbamate, 53% from adipic acid; 4-carbobenzoxyaminooxazolidone-2,[4] 71% from *N*-carbobenzoxy-L-serine.

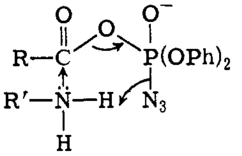
Apparent are several noteworthy features of the new method as compared with the classical conversions[5] of carboxylic acids to amine derivatives. This modified Curtius reaction is much simpler and less laborious than the classical one. The reaction proceeds under more or less neutral and nonoxidizing conditions, and neither strong alkali in the Hofmann reaction nor strong acid in the Schmidt reaction is required. Although pyridine-2-carboxylic acid failed to undergo the Schmidt reaction,[5] it smoothly gave *tert*-butyl *N*-pyridyl-2-carbamate in 73% yield by DPPA.

The intermediate of the above reaction is apparently the carboxylic acid azide[5] which is produced by the transfer of the azido group from DPPA to the carboxylic acid. The well-known azide method[6] is still the only reliable method extensively employed for the racemization-free fragment condensation in the peptide synthesis,[7] though the yield of the coupling is not always high. These facts led us to investigate the usefulness of DPPA in the peptide synthesis free of racemization. DPPA indeed allows the coupling in high yield of acylamino acids or peptides with amino acid or peptide esters in the presence of a base in a single operation and without racemization.

A preferred procedure is as follows. To a stirred mixture of the acylamino acid or peptide (1 equiv) and the amino acid or peptide ester hydrochloride (1.1–1.2 equiv) in dimethylformamide is added DPPA (1.1–1.2 equiv) in dimethylformamide at or below 0°, followed by the addition of triethylamine (2.1–2.2 equiv). The mixture was stirred at or below 0° for several hours, and at room temperature overnight.

Practically no racemization was observed during the fragment coupling (87% yield) of *N*-carbobenzoxy-L-leucyl-L-leucine with L-valyl-L-phenylalanine methyl ester hydrochloride,[8] and the supersensitive Young test[9] afforded *N*-benzoyl-L-leucylglycine ethyl ester in 83% yield with 94.5% L isomer. Moreover, the oxazolone formation mainly responsible for the racemization during the coupling could not be detected on the infrared absorption at 1830 cm^{-1}.[10] As the chloride ion effect[10] was not noticed in this reaction, this new method made it possible to use the amino component as its hydrochloride with 1 equiv of tertiary amine as well as the free ester. Usability of a highly polar solvent dimethylformamide in which even large peptides are often soluble widens the scope of this new method.

The method is quite general in the sense that it can be applied to the formation of peptides containing various functional groups. No difficulties were encountered when the side chains of asparagine, glutamine, valine, threonine, methionine, tryptophan, or histidine were present in the carboxyl component. Arginine showed no trouble when its guanido group was protected with the ordinary nitro group. Serine and tyrosine could be used as the amino component without any protection of their hydroxyl functions. Typical yields were:[11] (Z)-Asn-Phe-OMe, 80%; (Z)-Gln-Ser-OMe, 80%; (Z)-Val-Tyr-OMe, 69%; (Z)-Thr-Phe-OMe, 72.5%; (Z)-Met-Gly-OEt, 90%; Boc-Trp-Gly-OEt,[12] 89.5%; (Z)-Arg(NO$_2$)-Leu-OMe, 83%; (Z)-His-Leu-OMe, 95%.[13]



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(1) Reaction conditions were not optimized.

(2) E. Schröder and K. Lübke, "The Peptides," Vol. I, Academic Press, New York, N. Y., 1965, p 36.

(3) H. E. Baumgarten and A. Staklis, *J. Amer. Chem. Soc.*, **87**, 1141 (1965).

(4) $[\alpha]^{25}D$ −46.7° (*c* 0.6, ethyl acetate) [lit. $[\alpha]^{25}D$ −50° (*c* 0.6, ethyl acetate); see E. Baer, J. Maurukas, and D. D. Clarke, *Can. J. Chem.*, **34**, 1182 (1956)].

(5) C. A. Buchler and D. E. Pearson, "Survey of Organic Syntheses," Wiley-Interscience, New York, N. Y., 1970, pp 494–503, and references therein.

(6) T. Curtius, *Chem. Ber.*, **35**, 3226 (1902).

(7) For a recent review, see A. Marglin and R. B. Merrifield, *Annu. Rev. Biochem.*, **39**, 841 (1970).

(8) The product, (*Z*)-Leu-Leu-Val-Phe-OMe, had $[\alpha]^{20}D$ −25.2°; material prepared by the azide method had $[\alpha]^{20}D$ −25.4°; see A. Ide, K. Shigezane, S. Shigezane, T. Mizoguchi, and S. Saito, *Yakugaku Zasshi*, **90**, 850 (1970).

(9) M. W. Williams and G. T. Young, *J. Chem. Soc.*, 881 (1963).

(10) M. W. Williams and G. T. Young, *ibid.*, 3701 (1964).

(11) All optically active amino acids were of the L configuration.

(12) New compound, mp 118–119°, $[\alpha]^{20}D$ −12.8° (*c* 1, ethanol).

(13) All compounds have been characterized satisfactorily by elemental and spectral analysis.

DPPA may open up a host of interesting synthetic possibilities and create added flexibility in synthesis. The investigation is continued along a broad front to determine the full range of ability in synthetic chemistry and to clarify the underlying reaction mechanisms.[14]

[14] The exact mechanistic details of the peptide formation must remain speculative at this time. The intermediacy of the carboxylic acid azide is tentative, and it seems attractive to consider a concerted process.

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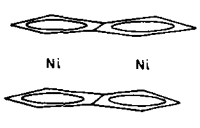
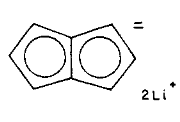
Sandwiches of Iron and Cobalt with Pentalene

Sir:

Of the few compounds in which a transition metal is sandwiched between the rings of a pair of nonbenzenoid aromatic hydrocarbons, the simplest is bis(pentalenylnickel) (I) which forms when dilithium pentalenide[1] (II) reacts with nickel chloride.[2] With ferrous chloride a structurally different product results, consisting of two molecules of pentalene and only one of iron. Cobalt analogs of both structures can also be made, and we are reporting here the preparation of these iron and cobalt compounds.

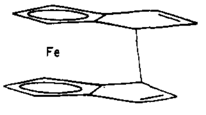


I



II

Bis(pentalenyl)iron was prepared by stirring dilithium pentalenide (5.4 mmol) in tetrahydrofuran (THF, 60 ml) with a slurry of ferrous chloride[3] (6.4 mmol) at −78° for 1 hr and at room temperature for 4 hr. After quenching with water, removal of solvent at reduced pressure, extraction with pentane, sublimation (50°, 0.02 mm) of the pentane-soluble extract, and recrystallization from hexane, we obtained an 18% yield of an orange-red crystalline solid, mp 127–128°, whose formula is two molecules of pentalene plus one of iron.[4] Its proton nmr spectrum shows a four-proton AB quartet, $|J| = 5.6$ Hz, at τ 3.14 and 3.85,[5] where olefinic protons resonate, and multiplets for the remaining protons at 6.01 and 6.3. The spectrum implies that the structure of the molecule is either III or IV and appears to exclude alternative structures, such as V, that lack a new carbon–carbon bond. The closest precedent is the structure of bis(azulene)iron, which has a four-carbon bridge between two ferrocene rings.[6,7] Although the two pentalene rings are presumably united by a carbon–carbon bond, in the molecule's mass spectrum, while the parent ion is the most abundant, the next most abundant (88% as intense at 75 eV) is pentalene cation, $C_8H_6^+$, in which that carbon–carbon bond is absent.[8,9]



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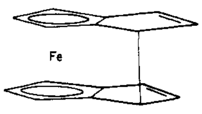
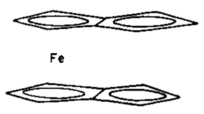


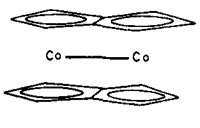
IV



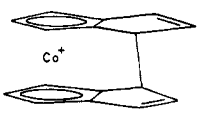
V

The same reaction with cobaltous chloride does not give an analogous product, but gives bis(pentalenylcobalt) (VI), instead. When dilithium pentalenide (9.6 mmol) in THF (10 ml) was stirred with a slurry of cobaltous chloride (10.8 mmol) and THF (30 ml) for 1 hr at room temperature, the solvent distilled, and the residue sublimed at 150° (10^{-3}–10^{-4} mm), we obtained in 4.3–10% yield bis(pentalenylcobalt) (VI), a green-black solid that does not melt below 270°.[10] The structure was assigned on the basis of the mass spectrum,[11] which shows the parent peak as the most abundant ion, the proton nmr spectrum, which consists of a triplet at τ 5.84 and doublet at 6.33, $|J| = 2.2$ Hz, in the intensity ratio 4.16:7.84, and the ir spectrum, which is remarkably similar to that of the nickel analog I.[2,12]

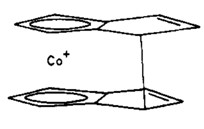
However, oxidizing VI with hydrogen peroxide removes a cobalt atom giving a bis(pentalenyl)cobalticinium ion, which can be isolated as the hexafluorophosphate in 21% yield,[13] and which is isoelectronic and presumably isostructural with bis(pentalenyl)iron. The similarity of the two structures is indicated by the similarity of their proton nmr spectra, the cobalticinium ion like the iron analog showing a four-proton AB quartet, $|J| = 5.5$ Hz, in the olefin region and appropriate resonances around τ 5 for the remaining eight protons.[15] The structure of this ion is thus either VII or VIII. The cobalticinium hexafluorophosphate is an orange solid that does not melt, but darkens when



VI



VII



VIII

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[1] (a) T. J. Katz and M. Rosenberger, *J. Amer. Chem. Soc.*, **84**, 865 (1962); (b) T. J. Katz, M. Rosenberger, and R. K. O'Hara, *ibid.*, **86**, 249 (1964).

[2] T. J. Katz and N. Acton, *ibid.*, **94** 3281 (1972).

[3] If ferric chloride is used in place of ferrous chloride, the yield is 12%.

[4] *Anal.* Calcd for $C_{16}H_{12}Fe$: C, 73.88; H, 4.65; Fe, 21.47. Found: C, 73.83; H, 4.77; Fe, 21.59.

[5] Intensities: 2.12, 2.10, 1.86, 5.96. The solvent was CS_2. The peaks at τ 3.85 are each split into 2.0-Hz doublets.

[6] (a) E. O. Fischer and J. Müller, *J. Organometal. Chem.*, **1**, 464 (1964); (b) M. R. Churchill and J. Wormald, *Inorg. Chem.*, **8**, 716 (1969).

[7] Simple two-atom bridged ferrocenes are known; *cf.* H. L. Lentzer and W. E. Watts, *Tetrahedron*, **27**, 4343 (1971).

[8] The only other peaks of greater intensity than 20% of the base peaks [*m/e* 260 (100%), 261 (21%), 262 (4%)] are *m/e* 56 (Fe^+, 37%), 158 ($C_8H_6Fe^+$, 47%), and 202[2] ($C_{16}H_{10}^+$, 27%).

[9] The uv spectrum in *n*-hexane shows the following: λ_{max} 465 nm (ϵ 520), 290 (sh), 246 (9100), 217 (11,400).

[10] *Anal.* Calcd for $C_{16}H_{12}Co_2$: C, 59.65; H, 3.76; Co, 36.59. Found: C, 59.06; H, 4.04; Co, 34.80.

[11] Peaks of greater than 5% intensity at 75 eV: *m/e* 43 (8%), 59 (Co^+, 7%), 102 ($C_8H_6^+$, 9%), 161 ($C_8H_6Co^+$, 11%), 202 ($C_{16}H_{10}^+$, 6%),[1] 263 [$(C_8H_6)_2Co^+$, 11%], 264 (7%), 322 (P^+, 100%), 323 (P^+, 18.5).

[12] The visible spectrum in argon-purged benzene shows a maximum at 369 nm (ϵ 4230) and a tail out to 850 nm.

[13] The elemental analysis, like that of other cobalticinium hexafluorophosphates,[14] was poor. However, the tetraphenylborate was analyzed successfully for C and H. *Anal.* Calcd for $C_{40}H_{32}CoB$: C, 82.48; H, 5.54. Found: C, 82.88; H, 5.41. The analyst's results for Co were inconsistent: calcd, 10.12; found, 11.39, 8.09. Analyses were by Schwartzkopf Microanalytical Laboratory, Woodside, N. Y.

[14] J. E. Sheats and M. D. Rausch, *J. Org. Chem.*, **35**, 3245 (1970).

[15] In CD_3CN: AB quartet, $|J| = 5.5$ Hz at τ 2.78 and 3.04, the high-field lines split further into 1.7-Hz doublets (3.86 H) and multiplets at 4.63 (4.14 H), 5.07 (2.07 H), and 5.35 (1.93 H).