139276-32-7; $EtOOCCH_2C{\equiv}N$, 105-56-6; $CH_3C{\equiv}N$, 75-05-8; $EtOOCCH_2COOEt$, 105-53-3; CH_3COOEt, 141-78-6; CH_3COCH_2COOEt, 141-97-9; $CH_3COCH_2COCH_3$, 123-54-6; $PhCOCH_2COPh$, 120-46-7; CH_3COPh, 98-86-2; $PhCOCH_2CH_3$, 93-55-0; $EtOOCCH_2Ph$, 101-97-3; 2,3-dichlorobenzaldehyde, 6334-18-5; (*E*)-*N*-[2-(2,3-dichlorophenyl)-1-tosylethenyl]formamide, 139276-33-8; valeraldehyde, 110-62-3; (*E*)-*N*-(1-tosyl-1-hexenyl)formamide, 139276-34-9.

Chemistry of *N,P*-Acetals: Application to the Synthesis of 20-Ketosteroids

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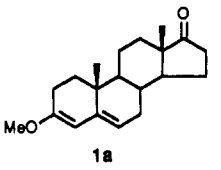
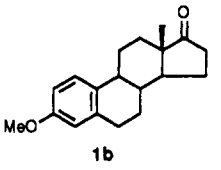
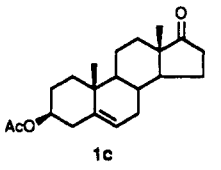
A series of new derivatives of α-(isocyanomethyl)phosphonates (**6a,b,c** and **9**) is described, which are formed by methylation of (*E*)-17-[(diethylphosphono)isocyanomethylene] steroids **5a,b,c** and 17β-[(diethylphosphono)isocyanomethyl] steroid **8**. It proved possible to hydrolyze these compounds under relatively mild conditions to 20-ketosteroids **7a,b,c** and **10**, showing for the first time that geminal N- and P-substituted carbon compounds do react as *N,P*-acetals.

Acetals contribute valuable functionality to organic synthesis.[2,3] *O,O*-Acetals are particularly useful as protected aldehydes and ketones, which are deprotected by mild acid hydrolysis.[2a,b] *S,S*-Acetals are important acyl anion equivalents ("reversal of polarity"), and are hydrolyzed to carbonyl compounds under oxidative conditions.[2c,d] Acid hydrolysis of other types of acetals (e.g., *O,S*-,[3a-e] *N,S*-,[3a,b,f-l,14] *N,N*-,[3a,b,m,n] and *N,O*-acetals[3a,b,o]) has been described also. Remarkably, compounds with geminal N and P substituents attached to carbon have so far not been recognized as acetals. It is the purpose of this paper to demonstrate *N,P*-acetal behavior of such compounds.

We have synthesized a series of new derivatives of α-(isocyanomethyl)phosphonates starting with compounds **5**. These compounds are converted by allylic alkylation to *N,P*-acetals **6** (Scheme I) and by reduction followed by alkylation to *N,P*-acetal **9** (Scheme II). With aqueous $HClO_4$, compounds **6** and **9** proved to hydrolyze to the corresponding ketones **7** and **10**, showing for the first time that *N,P*-acetal behavior is feasible indeed. So far, derivatives of α-(aminomethyl)phosphonates, carrying masked amino groups, have been hydrolyzed to stages no further than amino phosphonate esters or acids,[4] which, in the present context, means a conversion of one type of *N,P*-acetal into the other. In 1984, Diel and Maier[4e] stated with respect to the hydrolysis of esters of 1-isocyanocyclopropane-1-phosphonic acid and 1-(benzylideneamino)cyclopropane-1-phosphonic acid that "by *complete* (italics by J.S. et al.) hydrolysis with concentrated hydrochloric acid at 100 °C one obtains...in quantitative yield 1-aminocyclopropane-1-phosphonic acid."[5]

We have applied the *N,P*-acetal chemistry to steroid derivatives **5**, which were needed for other synthetic applications.[6] Basically known chemistry was used to develop a practical synthesis of the formal Knoevenagel condensation products **5** from 17-oxosteroids **1** and diethyl (isocyanomethyl)phosphonate[7] (**2**). Schöllkopf et al.[7] have reported that the formation of oxazolines of type **3** is possible only with aldehydes and with acetone, using copper(I) oxide in benzene. However, by using KH in

Table I. Yields of Compounds 4a–c to 7a–c Depicted in Scheme I and Derived from Steroids 1a–c

steroids 1	yield[a] (%) of compds 4	5	6	7	overall
 **1a**	70	98	92	86[b]	54
 **1b**	70	84	90	76	40
 **1c**	76	60	95	71[c]	31

[a] Yields of isolated purified materials based on **1** in the case of **4**, and further on the next lower compound numbers. [b] 3,5-Dienol ether group was hydrolyzed to 4-en-3-one. [c] 3β-Acetoxy group was hydrolyzed to 3β-hydroxy.

(1) Gist-brocades N.V., Delft, The Netherlands.

(2) For reviews, see: (a) Meskens, F. A. J. *Synthesis* **1981**, 501–522. (b) Schmitz, E.; Eichhorn, J. G. In *The Chemistry of the Ether Linkage*, Patai, S., Ed.; Interscience: New York, 1967; pp 309–351. (c) Gröbel, B.-T.; Seebach, D. *Synthesis* **1977**, 357. (d) Cussans, N. J.; Ley, S. V.; Barton, D. H. R. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1654.

(3) (a) Methoden der Organischen Chemie, *Houben-Weyl*; Borrman, B., Ed.; Georg Thieme Verlag: Stuttgart, 1968; Vol. 7/4, p 340. (b) *Umpoled Synthons*; Hase, T. A., Ed.; Wiley-Interscience: London, 1987. (c) Trost, B. M.; Miller, C. H. *J. Am. Chem. Soc.* **1975**, *97*, 7182. (d) Mandai, T.; Takeshita, M.; Kawada, M.; Otera, J. *Chem. Lett.* **1984**, 1259. (e) Mandai, T.; Moriayam, T.; Nakayama, N.; Sugino, K.; Kawada, M.; Otera, J. *Tetrahedron Lett.* **1984**, *25*, 5913. (f) Miyashita, M.; Kumazawa, T.; Yashikoshi, A. *J. Org. Chem.* **1980**, *45*, 2945. (g) Possel, O.; van Leusen, A. M. *Heterocycles* **1977**, *7*, 77. (h) Possel, O.; van Leusen, A. M. *Tetrahedron Lett.* **1977**, 4229. (i) van Leusen, D.; van Leusen, A. M. *Tetrahedron Lett.* **1977**, 4233. (j) Moskal, J.; van Leusen, A. M. *Tetrahedron Lett.* **1984**, 2585. (k) van Leusen, A. M.; Oosterwijk, R.; van Echten, E.; van Leusen, D. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 50. (l) van Hemert, A. W.; van Leusen, A. M. To be published. (m) Baldwin, J. E.; Bottaro, J. C. *J. Chem. Soc., Chem. Commun.* **1981**, 1121. (n) Doleschall, G. *Tetrahedron Lett.* **1975**, 1889. (o) Meyers, A. J. *Pure Appl. Chem.* **1979**, *51*, 1255.

(4) (a) Rachon, J.; Schöllkopf, U.; Wintel, T. *Liebigs Ann. Chem.* **1981**, 709. (b) Schöllkopf, U.; Hoppe, I.; Thiele, A. *Liebigs Ann. Chem.* **1985**, 555. (c) Costisella, B.; Gross, H. *Tetrahedron* **1982**, *38*, 139. (d) Rachon, J. *Chimia* **1982**, *36*, 462. (e) Diel, P. J.; Maier, L. *Phosphorus Sulfur Relat. Elem.* **1984**, *20*, 313.

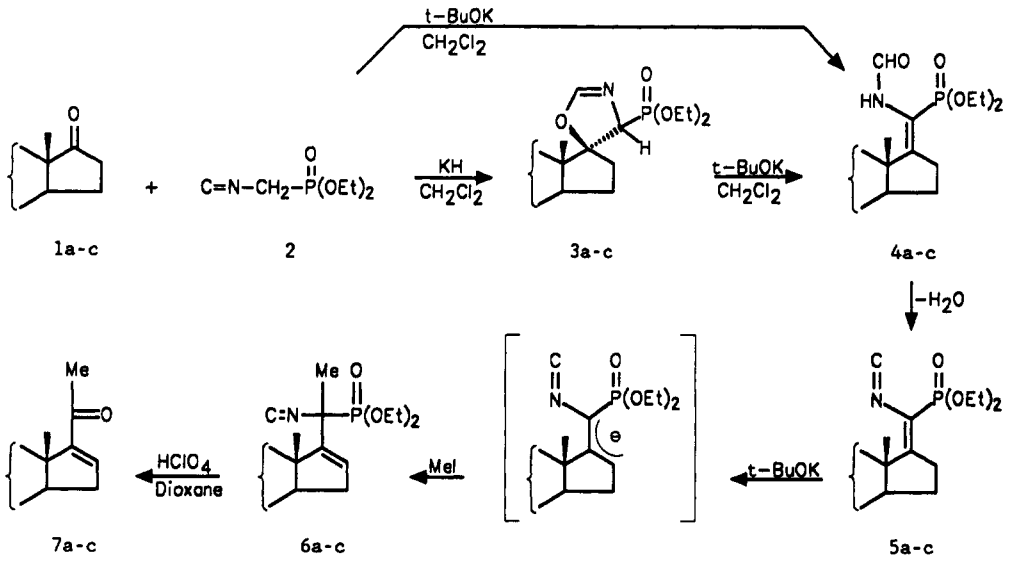
(5) Translated from German by the authors.

(6) Compounds **5** and **8** are versatile intermediates in steroid side-chain construction reactions using Wittig–Horner–Emmons methodology: Stoelwinder, J.; van Leusen, A. M. To be published.

(7) (a) Schöllkopf, U.; Schröder, R.; Stafforst, D. *Liebigs Ann. Chem.* **1974**, 44. (b) Schöllkopf, U.; Wintel, T. *Synthesis* **1984**, 1033.

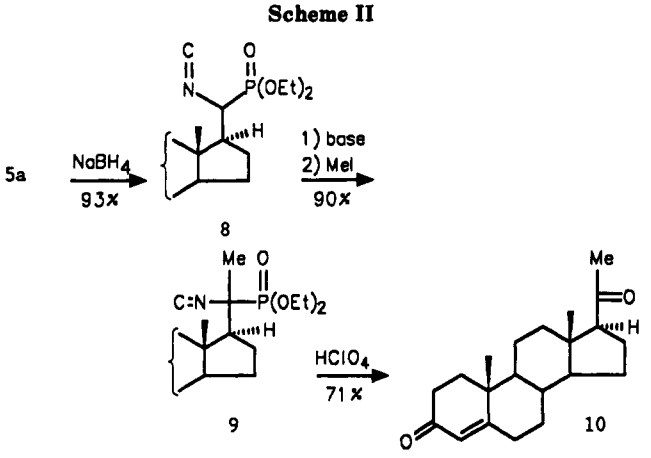
0022-3263/92/1957-2249$03.00/0

Scheme I[a]



[a] See Table I for structural definitions of a–c.

Scheme II



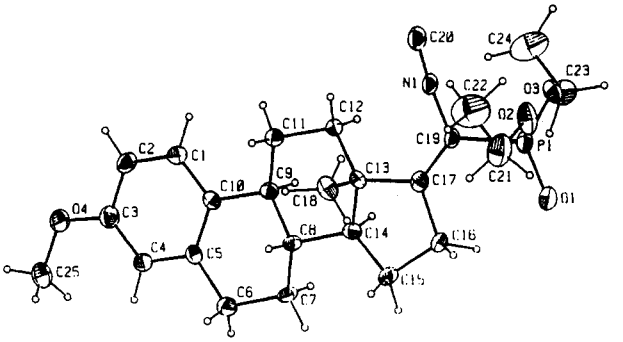


Figure 1. ORTEP plot of (*E*)-17-[(diethylphosphono)isocyanomethylene]-3-methoxy-19-norandrosta-1,3,5(10)-triene (**5b**). Steroid **5b** crystallizes in the $P2_1$ space group with two crystallographically independent molecules in the unit cell, both with a C17,C19 *E* configuration, as was determined by Dr. A. Meetsma.[21] The diethylphosphono group assumes two slightly different conformations. One of these arbitrarily chosen conformations is depicted in this figure.

dichloromethane, we were able to synthesize 2-oxazolines **3** from the more elaborate 17-oxosteroids also. Subsequently, the electrocylic ring opening[7a] of **3** to (*E*)-17-[(diethylphosphono)formamidomethylene] steroids **4** was effected with *t*-BuOK. A more attractive procedure was worked out, next, in which the 17-oxosteroids **1** are converted in one operation into compounds **4** using *t*-BuOK in dichloromethane (Table I). Dehydration of the formamide group of **4** under standard conditions,[8] using *i*-$Pr_2NH/POCl_3$, gave (*E*)-17-[(diethylphosphono)isocyanomethylene] steroids **5** in high yield. Compounds of type **5** (which have not been reported previously), just as compounds **4**, are both unsaturated derivatives of α-aminomethylphosphonates as well as ketene *N,P*-acetals. According to ^{13}C NMR compounds **5** are formed as single stereoisomers; the C17, C20 double bond has *E* stereochemistry as determined by single-crystal X-ray analysis of **5b** (Figure 1). Compounds **4** are therefore assumed to have the *E* configuration also. Compounds **5** were easily deprotonated (*t*-BuOK) at C16, and the resulting allylic anions were selectively methylated at C20 in high yield (Scheme I and Table I).

As the overall result so far the methylene group of diethyl (isocyanomethyl)phosphonate (**2**) has been alkylated twice to give compounds **6** and **9**. As was discussed above, **6** and **9** are a type of compound of which the acid hydrolysis to amino phosphonates and amino phosphonic acids was worked out previously.[4] After much experimentation, we now find that **6a** is hydrolyzed to 16-dehydroprogesterone (**7a**) in 86% yield, using 5% $HClO_4$ in refluxing 1,4-dioxane (the A-ring protection is removed concomitantly). Similar results were obtained from 20ξ-(diethylphosphono)-20ξ-isocyano-3-methoxy-19-norpregna-1,3,5(10),16-tetraene (**6b**) and 3β-acetoxy-20ξ-(diethylphosphono)-20ξ-isocyanopregna-5,16-diene (**6c**, Scheme I and Table I). In a related series of reactions **5a** was converted in 59% overall yield to progesterone (**10**, obtained as a mixture of C17 epimers,[9] β/α (6:1), Scheme II) when the C17, C20 double bond of **5a** was reduced[10]

(8) Obrecht, R.; Herrmann, R.; Ugi, I. *Synthesis* **1985**, 400.

(9) Partial racemization at C17 most likely is due to acid-catalyzed enolization. In a separate experiment, we have treated a commercial sample of progesterone[12] under the same conditions used for the hydrolysis of **9**, which resulted in partial epimerization at C17. Previously, partial epimerization of isoprogesterone using HCl/EtOH was reported by Butenandt et al.[13]

(10) Selective hydrogenation of the C17, C20 double bond in **5a** took place by attack from the α-side of the steroid,[11] yielding (20ξ)-17β-[(diethylphosphono)isocyanomethyl]-3-methoxyandrosta-3,5-diene (**8**) in 93%, which was confirmed by NOESY NMR.

(11) Fieser, L. F. *Experientia* **1950**, *6*, 312.

(12) Purchased from Sigma.

(13) Butenandt, A.; Schmidt-Thomé, J.; Paul, H. *Chem. Ber.* **1939**, *72*, 1112.

($NaBH_4$) prior to methylation (at C20).

We thus have established that (isocyanomethyl)-phosphonate **2** is able to fulfill a role similar to tosylmethyl isocyanide (TosMIC) in introducing carbon-20 in 17-oxo-steroids[14] and that geminal *N,P*-derivatized carbon compounds do react as *N,P*-acetals under the proper conditions. At this stage of our investigations it is not yet established whether amino phosphonic acids are intermediates in the conversion of **6** to **7** (and **9** to **10**).

Experimental Section

The synthesis of **4**, **5**, and **6** was performed in a N_2 atmosphere. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 300 and at 75.43 MHz, respectively, unless stated otherwise. Whenever possible, purification of products and intermediates was achieved by crystallization, followed by microanalyses.[15] Otherwise, intermediates were purified by column chromatography, followed by HRMS. Diethyl (isocyanomethyl)phosphonate (**2**), although commercially available (Fluka), was prepared according to ref 7. Steroid **1a** was donated by Gist-brocades N.V., Delft, The Netherlands; steroids **1b** and **1c** were purchased from SIGMA.

(*E*)-17-[(Diethylphosphono)formamidomethylene]-3-methoxyandrosta-3,5-diene (4a). *t*-BuOK (5.55 g, 50 mmol) was added to a stirred solution of 3-methoxyandrosta-3,5-dien-17-one (**1a**, 7.50 g, 25 mmol) in CH_2Cl_2 (200 mL) at −15 °C. After the solution was stirred for 10 min at this temperature, diethyl (isocyanomethyl)phosphonate (**2**, 4.50 g, 25 mmol) in CH_2Cl_2 (50 mL) was added. Stirring was continued for 1 h at 0 °C, and then water (100 mL) was added. The organic layer was washed once with brine and dried (Na_2SO_4). The solvent was removed to give 11.07 g of crude **4a**, which was purified by chromatography over Al_2O_3 (150 g, neutral, act. II/III). The first fraction eluted with CH_2Cl_2/NEt_3 (100:1) was discarded.[16] The main fraction was obtained with CH_2Cl_2/MeOH (2:1) to give 7.72 g (70%) of **4a**, mp 90 °C dec: IR (KBr) 3220 (NH), 1690 (C=O), 1660, 1638 (C=C), 1220, 1030 cm^{-1} ($P(O)(OEt)_2$); ^1H NMR ($CDCl_3$, 60 MHz) δ 0.9–3.3 (m) with 1.02 (br s, together C(18)H_3 and C(19)H_3), 1.38 (t, CH_3CH_2), 3.55 (s, CH_3O), 4.16 (m, CH_3CH_2), 5.12 (s, C(4)*H*), 5.21 (m, C(6)*H*), 7.4–7.7 (m, N*H*), 7.8–8.2 (m, C*H*O); exact mass calcd for $C_{28}H_{40}NO_5P$ *m/e* 477.264, found 477.264.

(*E*)-17-[(Diethylphosphono)formamidomethylene]-3-methoxy-19-norandrosta-1,3,5(10)-triene (4b) was prepared analogously to **4a** using estrone methyl ether (**1b**, 0.57 g, 2.0 mmol). The product was obtained after column chromatography as a yellow solid (0.62 g, 70%), mp 110–120 °C. Pure **4b** was obtained by two crystallizations from acetone/petroleum ether (bp 40–60 °C), mp 116–120 °C: IR (Nujol) 3190 (NH), 1661 (C=O), 1614 (C=C), 1243, 1027 cm^{-1} ($P(O)(OEt)_2$); ^1H NMR ($CDCl_3$) δ 0.97, 0.98 (2s, together C(18)H_3), 1.36 (m, CH_3CH_2), 1.4–2.4 (m), 2.85 (m), 3.77 (s, CH_3O), 4.17 (m, CH_3CH_2), 6.6–7.3 (m, 3*H*(arom) + N*H*), 7.92, 8.20 (d, s, together C*H*O, amide rotamers); exact mass calcd for $C_{25}H_{36}NO_5P$ *m/e* 461.233, found 461.233.

(*E*)-3β-Acetoxy-17-[(diethylphosphono)formamidomethylene]androst-5-ene (4c) was prepared analogously to **4a** using 3β-acetoxy-5-androsten-17-one (**1c**, 0.66 g, 2.0 mmol). After column chromatography **4c** was obtained as a solid, 0.77 g (76%), mp 82–83 °C: IR (Nujol) 3195 (NH), 1735, 1694 (C=O), 1628 (C=C), 1239, 1023 cm^{-1} ($P(O)(OEt)_2$); ^1H NMR ($CDCl_3$) δ 0.82 (2s, together C(18)H_3), 0.88 (s, C(19)H_3), 1.20 (m, CH_3CH_2), 1.4–2.7 (m), 3.89–4.01 (m, CH_3CH_2), 4.42–4.45 (m, C(3)*H*), 5.18–5.27 (m, C(6)*H*), 7.74–8.01 (m, N*H*C*H*O); exact mass calcd for $C_{27}H_{42}NO_6P$ *m/e* 507.276, found 507.275.

(*E*)-17-[(Diethylphosphono)isocyanomethylene]-3-methoxyandrosta-3,5-diene (5a). To a stirred solution of **4a** (6.90 g, 15 mmol) in 100 mL of THF at −30 °C were added subsequently *i*-Pr_2NH (4.55 g, 45 mmol) and $POCl_3$ (2.53 g, 16.5 mmol). After stirring for 1 h at −30 °C a saturated aqueous solution of Na_2CO_3 (8 mL) was added while the temperature was maintained below −5 °C. Stirring was continued for 5 min at this temperature. After addition of water (100 mL), extraction with CH_2Cl_2 (2 × 100 mL), and drying (Na_2SO_4) of the organic layer, the solvents were removed to give 7.28 g of crude product **5a**. The crude material was purified by elution over a short column of Al_2O_3 (neutral, act. II/III) to give 6.74 g (98%) of **5a** as a yellow solid. Analytically pure **5a** was obtained by one crystallization from hexane, mp 127–128 °C: IR (KBr) 2107 (N=C), 1649, 1625 (C=C), 1244, 1036 cm^{-1} ($P(O)(OEt_2)$; ^1H NMR ($CDCl_3$) δ 0.98 (s, C(19)H_3), 1.04 (s, C(18)H_3), 1.38 (t, CH_3CH_2, *J* = 9 Hz), 1.4–2.9 (m), 3.55 (s, CH_3O), 4.16 (m, CH_3CH_2), 5.05 (s, C(4)*H*), 5.15 (m, C(6)*H*). Anal. Calcd for $C_{26}H_{38}NO_4P$ (459.57): C, 67.94; H, 8.34; N, 3.05; P, 6.74. Found: C, 68.18; H, 8.37; N, 3.06; P, 6.71.

(*E*)-17-[(Diethylphosphono)isocyanomethylene]-3-methoxy-19-norandrosta-1,3,5(10)-triene (5b) was prepared according to the procedure given for **5a** from **4b** (0.40 g, 0.87 mmol). After chromatography 0.33 g (84%) of **5b** was obtained as a solid. Analytically pure **5b** was obtained after two crystallizations from Et_2O/petroleum ether (bp 40/60 °C), mp 96–97 °C: IR (Nujol) 2108 (N=C), 1610, 1500 (C=C, Ar), 1282 (OMe), 1256, 1022 cm^{-1} ($P(O)(OEt)_2$); ^1H NMR ($CDCl_3$) δ 1.0 (s, C(18)H_3), 1.38 (t, CH_3CH_2), 1.4–3.0 (m), 3.77 (s, CH_3O), 4.17 (m, CH_3CH_2), 6.6–7.2 (m, 3*H*(arom)); ^{13}C NMR ($CDCl_3$) shows a 31-line spectrum with δ 168.5 (s, N=C) and double signals for C(13), C(16), C(17), C(18) and C(19) due to ^{13}C–^{31}P coupling. Anal. Calcd for $C_{25}H_{34}NO_4P$ (443.52): C, 67.70; H, 7.73; N, 3.16. Found: C, 67.58; H, 7.73; N, 3.11.

(*E*)-3β-Acetoxy-17-[(diethylphosphono)isocyanomethylene]androst-5-ene (5c) was prepared analogously to **5a** from **4c** (1.53 g, 3.0 mmol). After purification by chromatography 0.88 g (60%) of **5c** was obtained as a slowly solidifying solid, mp 106–107 °C: IR (neat) 2108 (N=C), 1735 (OAc), 1611 (C=C), 1246, 1022 cm^{-1} ($P(O)(OEt)_2$); ^1H NMR ($CDCl_3$) δ 0.94 (s, C(19)H_3), 0.97 (s, C(18)H_3), 1.33 (t, CH_3CH_2, *J* = 11 Hz), 1.4–3.0 (m), 1.98 (s, OAc), 4.1–4.2 (m, CH_3CH_2), 4.5–4.6 (m, C(3)*H*), 5.33 (d, C(6)*H*). Anal. Calcd for $C_{27}H_{40}NO_5P$ (489.59): C, 66.24; H, 8.23; N, 2.86. Found, C, 66.25; H, 8.17; N, 2.81.

20ξ-(Diethylphosphono)-20ξ-isocyano-3-methoxypregna-3,5,16-triene (6a). *t*-BuOK (0.22 g, 2 mmol) was added to a solution of **5a** (0.46 g, 1.0 mmol) in THF (10 mL) at −40 °C. After the solution was stirred for 10 min, MeI (130 μL, 2.0 mmol) was added. Stirring was continued for 15 min at −40 °C, after which the temperature was raised to 0 °C. The suspension was poured in water (50 mL), and the mixture was extracted with two portions of CH_2Cl_2 (25 mL). The combined extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated to give 0.55 g (94%) of **6a**, mp 109–116 °C: IR (Nujol) 2124 (N=C), 1653, 1628 (C=C), 1234, 1169 cm^{-1} ($P(O)(OEt)_2$); ^1H NMR ($CDCl_3$) δ 0.96 (s, C(19)*H*), 1.05 (s, C(18)*H*), 1.38 (m, CH_3CH_2), 1.4–2.5 (m), 1.75, 1.80 (2s, C(21)H_3), 3.55 (s, CH_3O), 4.20 (m, CH_3CH_2), 5.10 (s, C(4)*H*), 5.20 (br s, C(6)*H*), 5.80, 6.20 (2 br s, together C(16)*H*); exact mass calcd for $C_{27}H_{40}NO_4P$ *m/e* 473.269, found 473.269.

20ξ-(Diethylphosphono)-20ξ-isocyano-3-methoxy-19-norpregna-1,3,5(10),16-tetraene (6b) was prepared according to the procedure given for **6a**, using **5b** (0.29 g, 0.66 mmol). After workup and purification by crystallization from Et_2O, 0.28 g (92%) of **6b** was obtained, mp 133–134 °C: IR (Nujol) 2127 (N=C), 1609 (C=C, Ar), 1254, 1162 cm^{-1} ($P(O)(OEt)_2$); ^1H NMR ($CDCl_3$) δ 1.05 (s, C(18)H_3), 1.38 (m, CH_3CH_2), 1.81, 1.86 (2s, together C(20)H_3), 2.85 (m), 3.78 (s, CH_3O), 4.10–4.35 (m, CH_3CH_2), 5.82, 6.20 (2 br s, together C(16)*H*), 6.60–7.20 (m, 3*H*(arom)); exact mass calcd for $C_{26}H_{36}NO_4P$ *m/e* 457.208, found 457.208.

3β-Acetoxy-20ξ-(diethylphosphono)-20ξ-isocyanopregna-5,16-diene (6c) was prepared according to the procedure given for **6a** using **5c** (0.25 g, 0.50 mmol). After workup 0.24 g (95%) of **6c** was obtained, mp 129–133 °C: IR (neat) 2127 (N=C), 1735 (OAc), 1669 (C=C), 1248, 1025 cm^{-1} ($P(O)(OEt)_2$); ^1H NMR

(14) (a) van Leusen, D.; van Leusen, A. M. *Synthesis* **1991**, 531. (b) van Leusen, D.; van Leusen, A. M. *Recl. Trav. Chim. Pays-Bas* **1991**, *110*, 393.

(15) Crystallization of compounds **4**, **6**, **8**, and **9** was difficult to achieve, probably as a result of rotamers in case of **4** and diastereomers in case of **6**, **8**, and **9**. Although partial purification was achieved by chromatography, no satisfactory microanalyses were found due to problems in the determination of the contents of phosphorous.

(16) This material consists mainly of a mixture of (*E*)- and (*Z*)-17-(isocyanomethylene)-3-methoxyandrosta-3,5-diene, which is formed by an unwanted Wittig–Horner–Emmons side reaction of **2** with 17-oxo-steroids **1**. An application of this reaction to steroids is described by Barton et al.[17]

(17) Barton, D. H. R.; Motherwell, W. B.; Zard, S. Z. *J. Chem. Soc., Chem. Commun.* **1981**, 774.

($CDCl_3$) δ 1.0 (s, C(18)H_3), 1.02 (s, C(19)H_3), 1.38 (m, CH_3CH_2), 1.72, 1.79 (2s, together C(21)H_3), 2.0 (s, OAc), 1.2-2.4 (m), 4.2 (m, CH_3CH_2), 4.55 (m, C(3)H), 5.35 (br s, C(6)H), 5.8, 6.15 (2 br s, together C(16)H); exact mass calcd for $C_{28}H_{42}NO_5P$ m/e 503.280, found 503.280.

Pregna-4,16-diene-3,20-dione (7a). An aqueous solution of 5% $HClO_4$ (2 mL) was added to a stirred solution of crude **6a** (0.24 g, 0.50 mmol) in 1,4-dioxane (6 mL) at rt. The mixture was refluxed for 12 h. After the solution was cooled a saturated aqueous solution of Na_2CO_3 (5 mL) was added. The residue was dissolved in 25 mL of CH_2Cl_2, and the organic layer was washed with water (10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated to give 0.164 g of a slowly solidifying yellow oil. Pure **7a** was obtained by column chromatography (silica, CH_2Cl_2) followed by one crystallization from ether/acetone, in a yield of 0.134 g (86%), mp 185-188 °C: $[\alpha]^{20}_D$ +156° (c 1, EtOH) [lit.[18] mp 186-188 °C, $[\alpha]_D$ +155° (c 1, EtOH)]. This material was identical with a commercial sample according to IR and ^1H NMR.

3-Methoxy-19-norpregna-1,3,5(10),16-tetraen-20-one (7b) was prepared analogously to the procedure given for **7a**, using **6b** (0.137 g, 0.30 mmol). Pure **7b** (0.071 g, 76%) was obtained by chromatography, mp 194-195 °C: $[\alpha]^{20}_D$ +118 (c = 1, $CHCl_3$) [lit.[19] mp 193-194 °C, $[\alpha]^{15}_D$ +115° (c 1, $CHCl_3$)]. This material was identical by IR and ^1H NMR with a commercial sample.

3β-Hydroxypregna-5,16-dien-20-one (7c) was prepared analogously to the procedure given for **7a** using **6c** (0.22 g, 0.44 mmol). After purification by filtration over a short column of silica and crystallization from EtOAc 0.098 g (71%) of **7c** was obtained, mp 211-212 °C. This material was identical by IR and ^1H NMR with an authentic sample,[20] mp 212-214 °C.

(20ξ)-17β-[(Diethylphosphono)isocyanomethyl]-3-methoxyandrosta-3,5-diene (8). A mixture of **5a** (0.56 g, 1.0 mmol) and $NaBH_4$ (0.04 g, 1.0 mmol) in THF (10 mL) and 96% EtOH (10 mL) was stirred at 20 °C for 3 h. The solvents were removed, and the resulting residue was dissolved in 25 mL of water and extracted with two portions of 25 mL of CH_2Cl_2. The combined extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated to yield 0.43 g (93%) of **8**, mp 59-62 °C: IR (neat) 2137 (N=C), 1654, 1629 (C=C), 1256, 1022 cm^{-1} (P(O)(OEt)$_2$); ^1H NMR ($CDCl_3$) δ 0.78, 0.80 (2s, together C(18)H_3), 0.95 (s, C(19)H_3), 1.35 (m, CH_3CH_2), 1.4-2.4 (m), 3.52 (s, CH_3O), 3.70 (dd, C(17)H, J = 13, 17 Hz), 3.92 (d, C(20)H, J = 22 Hz), 4.20 (m, CH_3CH_2), 5.10(s, C(4)H), 5.20 (t, C(6)H); exact mass calcd for $C_{26}H_{40}NO_4P$ m/e 461.269, found 461.269.

20ξ-(Diethylphosphono)-20ξ-isocyano-3-methoxypregna-3,5-diene (9). t-BuOK (0.24 g, 2.0 mmol) was added to a solution of **8** (0.92 g, 2.0 mmol) in THF (20 mL) at -40 °C. After the solution was stirred for 10 min, MeI (150 μL, 2.4 mmol) was added. Stirring was continued for 15 min at -40 °C, and then the temperature was raised to 0 °C. The suspension was poured into 50 mL of water, and the mixture was extracted with two portions of 25 mL of CH_2Cl_2. The combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated to give 0.86 g (90%) of **9**, mp 127-129 °C: IR (neat); 2125 (N=C), 1654, 1628 (C=C), 1255, 1025 cm^{-1} (P(O)(OEt)$_2$); ^1H NMR ($CDCl_3$) δ 0.94 (2s, together C(18)H_3 and C(19)H_3), 1.38 (m, CH_3CH_2), 1.60, 1.65 (2s, together C(21)H_3), 2.55 (2t, C(17)H, J = 15 Hz), 3.55 (s, CH_3O), 4.20 (m, CH_3CH_2), 5.10 (s, C(4)H), 5.20 (br s, C(6)H); exact mass calcd for $C_{27}H_{42}NO_4P$ m/e 475.285, found 475.285.

Progesterone (10) was prepared analogously to the procedure given for **7a**, using **9** (0.176 g, 0.37 mmol). After chromatography (silica, CH_2Cl_2) 0.083 g (71%) of **10** was obtained as a 1:6 mixture of 17α- and 17β-progesterone **10** (mp 126-129 °C), as established by ^1H NMR integration of the C18 and C19 signals: ^1H NMR ($CDCl_3$) δ 0.65 (s, C(18)-β), 0.90 (s, C(18)-α), 1.10 (s, C(19)-α), 1.18 (s, C(19)-β), 2.07 (s, C(20)-α), 2.12 (s, C(20)-β), 2.55 (C(17)-β), 2.75 (C(17)-α), 5.70 (s, C(4)).

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Supplementary Material Available: ^1H NMR spectra of compounds **4**, **5**, **6**, **8**, **9**, and **10** (14 pages). Ordering information is given on any current masthead page.

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1,2,3-Triazol-1-imines. 1. The Synthesis and Lead Tetraacetate Oxidation of Biacetyl Benzoylhydrazone Arylhydrazones to the Novel 2-Aryl-*N*-benzoyl-4,5-dimethyl-1,2,3-triazol-1-imines

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The synthesis and the $Pb(OAc)_4$ oxidation of the mixed bishydrazones of biacetyl **7** was studied. The formation of the novel *N*-benzoyl-1,2,3-triazol-1-imines **9** from the oxidation of **7** provided support to the proposed in the past mechanism for the oxidation of bis-aroylhydrazones of α-dicarbonyl compounds **4**. Thermolysis and photolysis of **9a** in DMSO was carried out. The results suggested that benzoylnitrene was formed in the photochemical reaction, and therefore compounds such as **9** could serve as non-azide aroyl nitrene precursors. For **9a** the results of the X-ray analysis were correlated with charge densities and bond orders gleaned by the MNDO method. Product **9d** was alternatively synthesized by the addition of photochemically generated benzoylnitrene to the 1,2,3-triazole **21**.

The oxidation of bis-arylhydrazones of 1,2-dicarbonyl compounds **1** with a variety of oxidants generally leads to the formation of the corresponding bis-areneazoethylenes **2**[1-7] (Scheme I). Compounds **2** exist in dynamic equilibrium with the isomeric *N*-aryl-1,2,3-triazol-1-imines **3**. The presence of the form **3** has been correctly inferred from

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