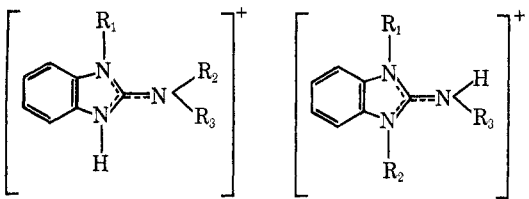
azole (244 and 283 nm) and 1-methyl-2-dimethylaminobenzimidazole (255 and 287 nm). The similarity in the spectra of the latter two compounds strongly suggests that 2-aminobenzimidazole exists principally in the form of the primary amine **1** rather than as the tautomeric imine **2** ($R_1 = R_2 = R_3 = H$).[3] When protonated, all three compound should exhibit guanidinium-type resonance (**3** and **4**) and, as expected, they show similar absorption in acid solution.

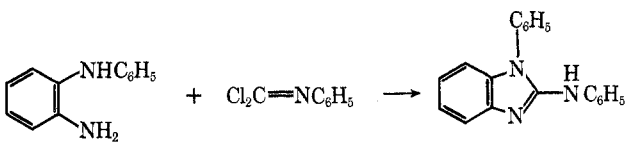


3

4

2-Anilinobenzimidazole also undergoes methylation of both ring nitrogens, yielding 1,3-dimethyl-2-phenyliminobenzimidazole, as evidenced by the higher melting point, more complex uv spectrum, and completely different ir spectrum, compared with those of authentic 1-methyl-2-(*N*-methylanilino)benzimidazole.[2b] Again, the differences in the uv spectrum largely disappear in acid solution.

In the course of this work, the previously unreported compound 1-phenyl-2-anilinobenzimidazole was prepared by the reaction of *N*-phenyl-*o*-phenylenediamine with phenyl carbonimidoyl dichloride.



Experimental Section[4]

2-Aminobenzimidazole.—A mixture of 0.24 g of benzimidazole-2-sulfonic acid[5] and 1 ml of 28% aqueous NH_3 was heated in a sealed tube at 160° for 6 hr. After recrystallization from alcohol and water, the product melted at 222° (lit.[6] 222°): λ_{max}^{EtOH} 244 nm (ε 6300), 283 (7950); $\lambda_{max}^{0.1\ N\ HCl}$ 276 nm (ε 9200).

1-Methyl-2-dimethylaminobenzimidazole.—A mixture of 0.2 g of 1-methyl-2-chlorobenzimidazole[2b] and 1.6 ml of 3.7 *N* dimethylamine in ethanol was heated 4 hr in a sealed tube at 150°. The mixture was evaporated, treated with Na_2CO_3 solution, and extracted with $CHCl_3$. The extract was dried ($MgSO_4$) and treated with a solution of dry HCl in $CHCl_3$. Chilling afforded crystals of the hydrochloride: mp 236–238° (lit.[2b] 238–239); $\lambda_{max}^{0.1\ N\ NaOH}$ 250 nm (ε 7500), 255 (7550), 287 (9800); $\lambda_{max}^{0.1\ N\ HCl}$ 281 nm (ε 9250), 288 (9400); ir (Nujol) 6.08, 12.2, 12.95, 13.1 μ.

1-Methyl-2-(*N*-methylanilino)benzimidazole was prepared in 43% yield by heating 0.214 g of redistilled *N*-methylaniline, 0.64 g of 22% BuLi in hexane, and 0.200 g of 1-methyl-2-chlorobenzimidazole under reflux in benzene for 2.5 hr. The solution was evaporated *in vacuo*, and the residue was taken up in ether. The ether solution was washed once with H_2O, dried ($MgSO_4$), and evaporated, leaving an oil which soon solidified. The crystals were sublimed *in vacuo* and then recrystallized from petroleum ether (bp 60–70°): mp 131–131.5° (lit.[2b] mp 128–129°); λ_{max}^{EtOH} 258 nm (ε 10,700), 294 (18,700); $\lambda_{max}^{0.1\ N\ HCl}$ 244 nm (ε 11,200), 288 (19,950); ir (Nujol) 6.22, 6.31, 6.58, 7.82, 8.06, 12.62, 13.22, 13.48, 13.78, 14.42 μ.

Methylation of 2-Aminobenzimidazoles.—Methylation was carried out according to the method described by Herbst, *et al.*, for the methylation of 1-ethyl-5-aminotetrazole.[7] From 0.133 g (0.001 mol) of 2-aminobenzimidazole and 0.441 g (0.0035 mol) of $(CH_3)_2SO_4$ was obtained 0.08 g of white, waxy crystals of 1,3-dimethyl-2-methyliminobenzimidazole, mp 62–64°, after purification by sublimation: λ_{max}^{EtOH} 250 nm (sh) (ε 10,700), 284 (22,800); $\lambda_{max}^{0.1\ N\ HCl}$ 277 nm (22,450), 283 (22,400).

Anal. Calcd for $C_{10}H_{13}N_3$: C, 68.57; H, 7.43. Found: C, 68.50, H, 7.40.

The hydrochloride melted at 253–255°: ir of hydrochloride (Nujol) 5.8, 5.9, 6.0, 13.4, 13.7 μ.

Treatment of 0.209 g (0.001 mol) of 2-anilinobenzimidazole[8] with 0.441 g (0.0035 mol) of $(CH_3)_2SO_4$ gave 0.18 g of 1,3-dimethyl-2-phenyliminobenzimidazole, which was recrystallized five times from EtOH–H_2O: mp 197–198°; λ_{max}^{EtOH} 247 nm (ε 16,600), 257 (20,000), 263 (21,000), 294 (28,700), 302 (30,500); $\lambda_{max}^{0.1\ N\ HCl}$ 246 nm (ε 17,200), 286 (25,000).

Anal. Calcd for $C_{15}H_{15}N_3$: C, 75.95; H, 6.33; N, 17.72. Found: C, 75.64; H, 6.05; N, 17.67.

The hydrochloride melted at 235–237°: ir (Nujol) 6.25, 6.6 6.7, 8.1, 11.7 w, 13.0 w, 13.4 sh, 1.5 s, 14.4 μ.

1-Phenyl-2-anilinobenzimidazole.—To a solution of 2.76 g (0.015 mol) of *N*-phenyl-*o*-phenylenediamine in 25 ml of 1,2-dichloroethane was added 2.61 g (0.015 mol) of phenyl carbonimidoyl dichloride.[8] Crystals appeared after a short time, and after several days a total of 2.91 g (60%) of purple, matted crystals separated, mp 218°. After several recrystallizations from H_2O, the hydrochloride was obtained as white crystals, mp 236–240°.

Anal. Calcd for $C_{19}H_{16}N_3Cl$: C, 70.91; H, 5.02; N, 13.06. Found: C, 70.70; H, 5.13; N, 13.20.

Addition of dilute NaOH to a solution of the hydrochloride precipitated 1-phenyl-2-anilinobenzimidazole: mp 160–165°; λ_{max}^{EtOH} 302 nm (ε 22,600), 296 (22,950), 256 (20,225), 245 sh (18,600); $\lambda_{max}^{0.1\ N\ HCl}$ 285 (ε 21,250), 280 (20,875); ir (Nujol) 6.13, 6.22, 6.35, 13.5, 14.4 μ.

Registry No.—**1** ($R_1 = R_2 = R_3 = H$), 934-32-7; **1** ($R_1 = R_2 = R_3 = Me$), 6595-23-9; **1** ($R_1 = Me$; $R_2 = Ph$; $R_3 = Me$), 31413-78-2; **1** ($R_1 = Ph$; $R_2 = Ph$; $R_3 = H$) HCl, 31413-79-3; **1** ($R_1 = R_2 = Ph$; $R_3 = H$), 31413-80-6; **2** ($R_1 = R_2 = Me$; $R_3 = Ph$), 29290-31-1; **2** ($R_1 = R_2 = Me$; $R_3 = Ph$) HCl, 31413-82-8; **2** ($R_1 = R_2 = R_3 = Me$), 19363-66-7; **2** ($R_1 = R_2 = R_3 = Me$)·HCl, 31413-84-0.

(3) A. R. Katritzky and J. M. Lagowski in *Advan. Heterocycl. Chem.*, **2**, 71 (1963).

(4) Melting points were determined on a calibrated Thomas-Hoover apparatus. Ultraviolet spectra were obtained using a Bausch and Lomb Spectronic 505. The infrared spectra were determined as Nujol mulls, using a Perkin-Elmer 137 spectrophotometer. Microanalyses by Schwartzkopf Microanalytical Laboratory, Woodside, N. Y.

(5) J. G. Everett, *J. Chem. Soc.*, 2406 (1930).

(6) I. G. Farbenindustrie, German Patent 612,544 (1935); *Chem. Abstr.*, **30**, 733 (1936).

(7) R. M. Herbst, C. W. Roberts, and E. J. Harvill, *J. Org. Chem.*, **16**, 139 (1951).

(8) D. B. Murphy, *ibid.*, **29**, 1613 (1964).

Isomeric Steroidal Isoxazolines by 1,3 Dipolar Cycloaddition

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Dipolar addition of nitrile oxides to unsaturated systems affords a simple method of preparing isoxazoline derivatives and has been used extensively to prepare 4,5-dihydro-1,2-oxazoles.[1] It was long believed that such cycloaddition to an asymmetric ene system resulted in only one of the two possible isomers, namely that in which the oxygen of the nitrile oxide is bonded to the

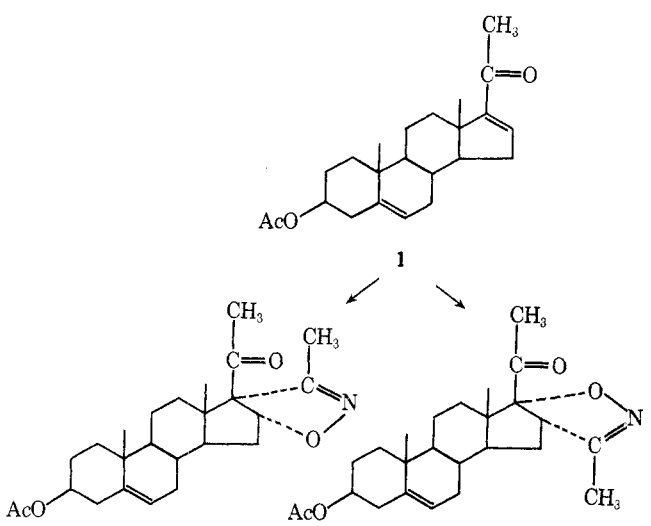
(1) C. Grundmann and P. Grünanger, "Nitrile Oxides," Springer Verlag, New York, N. Y., and Heidelberg, 1971.

most heavily substituted carbon atom of the asymmetric double bond ("normal addition"). Recently, however, a few instances in which the other possible isomer (arising from "inverse addition") was also formed have been reported.[2,3]

This "inverse" addition has been interpreted by Huisgen[4a] as arising from a concerted dipolar mechanism as a consequence of the steric requirements of a four-center intermediate, or, alternatively, from an inversion of the polarity of the dipole or of the dipolarophile. Firestone, however, suggests that it is due to a biradical mechanism, and the relative merits of these two mechanisms have been discussed in the literature.[4b,c]

The general biological interest in the steroidal adducts of the isoxazoline type is evident by the number of reported syntheses by 1,3 dipolar addition,[5] and recently we have been studying the addition of nitrile oxides to ene steroidal systems; the results of such addition to 20-oxopregna-5,16-dien-3β-yl acetate (1) is reported here.

This reaction has been studied by Culbertson, *et al.*,[5a] and they reported only one reaction product (2) derived from "normal" addition of the CH_3CNO to the C_{16}–C_{17} double bond, whereas we have isolated also another isomer arising from "inverse" addition (3).



Experimental Section

Melting points were obtained using a Kofler hot-plate microscope and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 237 spectrophotometer using the Nujol mull technique. Proton nmr spectra were recorded on a Perkin-Elmer R12 spectrometer at 60 MHz, and the reported chemical shifts are on the δ scale in parts per million downfield from internal TMS. Mass spectra were obtained using a Perkin-Elmer 270 mass spectrometer, the potential being 80 ev, and the samples were directly introduced at 200°. The specific rotations were measured with a Perkin-Elmer 141 polarimeter.

Optical rotatory dispersion curves and uv spectra were obtained using a Jasco ORD/UV-5 spectrometer, and circular dichroism curves with a Cary 60 spectrometer. The uv data for dioxane solutions were obtained using a Beckman DU2 spectrometer. The purity of the products was determined at each stage by tlc on silica gel G using the eluent systems *n*-hexane–acetone (3:1) and chloroform–ethyl acetate–*n*-hexane (94:5:1).

Acetylhydroxamoyl Chloride.—The method of Casnati and Ricca[6] was used but modified to reduce risk of explosion by using chloroform as solvent.

Addition of Acetonitrile Oxide to 20-Oxopregna-5,16-dien-3β-yl Acetate (1).—A solution of 90 ml of triethylamine in 850 ml of dry ethyl ether was added to 10 g of 1 and 8 g of acetylhydroxamoyl chloride in 800 ml of dry ether over a period of 15 hr at room temperature. The ethereal solution was then dried (Na_2SO_4) and evaporated to dryness. Recrystallization of the crude reaction product from methanol yielded a mixture of the two isomers **2** and **3**, with physical–chemical data reported by Culbertson, *et al.*[5a]

Tlc of the crude reaction product, however, showed the presence of three compounds, the two isomeric adducts (of closely comparable R_f value) and dimethylfuroxan (4,5-dimethyl-1,2,5-oxadiazole *N*-oxide).

These were separated by column chromatography on a column, 7-cm inner diameter, 80-cm height, containing 1800 g of silica gel–Celite 535 (1:1), activated for 1 hr at 110° and eluted first with petroleum ether to remove dimethylfuroxan and then with *n*-hexane–acetone (98:2) to separate the two isomeric adducts. After recrystallization from methanol these gave the following physiochemical characteristics.

Isomer 2: mp 243–244°; $[\alpha]^{20}D$ +22° (*c* 0.5, dioxane); ir 1730, 1710, 1635, 1245 cm^{-1}; ORD (*c* 5.0 mg/ml, dioxane, 390–250 mμ) $[\Phi]_{390}$ +990°, $[\Phi]_{323}$ +8680°, $[\Phi]_{301}$ ±0°, $[\Phi]_{276-279}$ −9760°, $[\Phi]_{250}$ −6120°; CD (*c* 4.98 mg/ml, dioxane, 335–250 mμ) $[\theta]_{335}$ ±0°, $[\theta]_{304-305}$ +14,870°, $[\theta]_{299}$ +16,030°, $[\theta]_{250}$ +580°; uv max 291 mμ (ε 145); nmr ($CDCl_3$) δ 0.71 (s, 3, 18-CH_3), 1.02 (s, 3, 19-CH_3), 1.91 (s, 3, 3-CH_3 isoxazoline), 2.05 (s, 3, 3-OAc), 2.25 (s, 3, 21-CH_3), 3.84 (m, 1, 16-CH), 4.6 (m, 1, 3-CH), 5.4 (m, 1, 6-CH); mass spectrum *m/e* (rel intensity) 372 (2), 371 (14), 370 (55), 355 (1), 354 (8), 353 (33), 343 (0.5), 342 (1.5), 312 (3), 311 (13), 310 (60), 105 (19), 91 (21), 81 (25), 68 (100), 57 (22), 55 (28), 43 (60), 41 (24).

Anal. Calcd for $C_{25}H_{35}NO_4$: C, 72.61; H, 8.53; N, 3.39. Found: C, 72.54; H, 8.60; N, 3.35.

Isomer 3: mp 190–191°; $[\alpha]^{20}D$ +235° (*c* 0.51, dioxane); ir 1730, 1715, 1615, 1255 cm^{-1}; ORD (*c* 5.0 mg/ml, dioxane, 400–270 mμ) $[\Phi]_{400}$ +4130°, $[\Phi]_{330}$ +28,530°, $[\Phi]_{324}$ +25,230°, $[\Phi]_{320}$ + 26,050°, $[\Phi]_{306}$ ±0°, $[\Phi]_{276-278}$ −33,500°, $[\Phi]_{270}$ −32,670°; CD (*c* 4.58 mg/ml, dioxane, 345–247 mμ) $[\theta]_{345}$ ±0°, $[\theta]_{314}$ +40,540°, $[\theta]_{312}$ +40,270°, $[\theta]_{305}$ +45,870°, $[\theta]_{256}$ ±0°; uv max 235 mμ (ε 2100) and 304 (205); nmr ($CDCl_3$) δ 0.83 (s, 3, 18-CH_3), 1.02 (s, 3, 19-CH_3), 2.01 (s, 3, 3-CH_3 isoxazoline), 2.05 (s, 3, 3-OAc), 2.25 (s, 3, 21-CH_3), 4.6 (m, 1, 3-CH), 5.4 (m, 2, 6-CH and 16-CH); mass spectrum *m/e* (rel intensity) 413 (0.5), 398 (0.5), 370 (0.5), 355 (0.5), 354 (4), 353 (17), 352 (0.5), 339 (1), 338 (4), 336 (0.5), 335 (0.5), 326 (0.5), 312 (0.5), 311 (1), 310 (2), 229 (19), 228 (100), 215 (16), 214 (18), 213 (37), 145 (25), 143 (20), 139 (16), 126 (40), 120 (20), 108 (18), 107 (15), 105 (27), 91 (26), 81 (22), 43 (92), 41 (20).

Anal. Calcd for $C_{25}H_{35}NO_4$: C, 72.61; H, 8.53; N, 3.39. Found: C, 72.61; H, 8.59; N, 3.43.

Results and Discussion

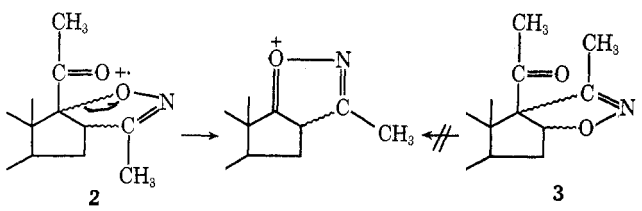
Comparison of the ir spectra of **1**, **2**, and **3** shows that on adduct formation the double bond between C_{16} and C_{17} is removed. The absorption at 1590 cm^{-1} in **1**, due to the conjugation of the carbonyl group with the double bond, disappears on adduct formation and the removal of this conjugation is also indicated by the shift in the carbonyl frequency from 1670 cm^{-1} in **1** to 1710 cm^{-1} in **2** and 1715 cm^{-1} in **3**. Further confirmation of the new ring formation is the appearance of the weak absorption at 1635 cm^{-1} in **2** and 1615 cm^{-1} in **3**, attributable to vibration of the isoxazoline ring,[5a,b]

(2) M. Christl and R. Huisgen, *Tetrahedron Lett.*, 5209 (1968).
(3) P. Grünanger, personal communication.
(4) (a) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 633 (1963); (b) R. A. Firestone, *J. Org. Chem.*, **33**, 2285 (1968); (c) R. Huisgen, *ibid.*, **33**, 2291 (1968).
(5) (a) T. P. Culbertson, G. W. Moersch, and W. A. Neuklis, *J. Heterocycl. Chem.*, **1**, 280 (1964); (b) W. Fritsch, G. Seidl, and H. Ruschig, *Justus Liebigs Ann. Chem.*, **677**, 139 (1964); (c) U. Stache, W. Fritsch, and H. Ruschig, *ibid.*, **685**, 228 (1965); (d) G. W. Moersch, E. L. Wittle, and W. A. Neuklis, *J. Org. Chem.*, **30**, 1272 (1965); (e) *ibid.*, **32**, 1387 (1967).
(6) G. Casnati and A. Ricca, *Tetrahedron Lett.*, 327 (1967).

and also by the disappearance of the band of **1** at 240 mμ in the ultraviolet spectrum.[5a]

That the isoxazoline rings formed have differing substitution patterns is indicated by their nmr spectra. That of **2** has signals at δ 3.84, attributable to the proton on C_{16} (*i.e.*, in position 4 of the isoxazoline ring), and at δ 5.4, both of integrated intensity one, whereas the spectrum of **3** has a signal at δ 5.4 of intensity two, due to the protons on C_6 and C_{16} (*i.e.*, position 5 of the isoxazoline ring), but no signal at δ 3.48.[7,8] The results can only be explained by the fact that during the reaction the oxygen of the reactant attaches to both C_{17} and C_{16} of the steroid to form two different isoxazoline rings.

Further evidence of this is the results of the mass spectra study. While the relative abundance of the mass peaks due to M − CH_3CO and M − CH_3CO_2H − CH_3CO in the spectrum of compound **2** can be easily

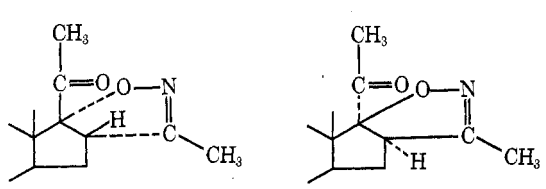


2 **3**

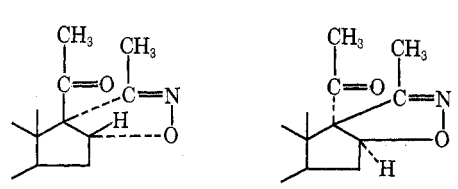
rationalized,[9] the analogous mechanism cannot arise from the structure (**3**), thus giving confirmation to the structures assigned to the two isomers.

However, while the addition of nitrile oxides to ene systems leads to isoxazoline rings of the substitution pattern shown, there still remains in this case the stereospecificity of the addition. While the cis stereospecificity of the addition necessarily restricts the number of possible configurations,[1,4a] there still remains two for each isomer, namely 16α,17α (**2** and **3**) or 16β, 17β (**2a** and **3a**) addition.

Here **2** and **3** have the acetyl group on C_{17} β and **2a** and **3a** have the acetyl group α. The configuration of



2 **2a**



3 **3a**

the acetyl side chain in position 17 has been determined by ORD and CD studies.

In studies of compounds of similar structures it has been found that if the acetyl group on C_{17} in steroids is β, the ORD curves and CD generally show a positive Cotton effect, attributable to the n → π* transition of the carbonyl group at C_{20}, whereas for an α orientation the Cotton effect is negative.[10a-d] We attribute the absorptions at 291 mμ for **2** and 304 mμ for **3** to n → π* transitions of the carbonyl groups. Besides, within the wavelength range of our study, no Cotton effect attributable to the >C=N- chromophore of the isoxazoline ring has been reported.[10d,e] Since both isomers exhibit strong positive Cotton effects at these frequencies (especially **3**), we thus conclude that the configuration of the acetyl group at C_{17} is β, so that attachment occurs α–α at C_{16}–C_{17} to form the isoxazoline ring.

That the values of the molecular ellipticity, molecular rotation, and the bathocromic shift of the Cotton effect due to the isoxazoline ring in compound **3** compared with the values obtained for 20-oxopregn-5-en-3β-yl acetate again gives confirmation to the assigned structures of the products. In **3** the >C=N- group is β–γ with respect to the C_{20} carbonyl, whereas in **2** it is γ–δ, and the higher values of molecular ellipticity and molecular rotation of the isomer assigned the structure **3** is in accord with reported data for β–γ unsaturated carbonyl systems.[11,12] The spectra also show some fine structure, especially that of **3**, as is generally found when the chromophore is conjugated or partially conjugated.

These proposed structures are also supported by the uv spectra. The spectra of the isomer given the structure **2** are very similar to that of the 20-oxopregn-5-en-3β-yl acetate, whereas the isomer given the structure **3** shows a bathochromic shift with respect to 20-oxopregn-5-en-3β-yl acetate, in keeping with the β–γ unsaturation of the proposed structure.[13-17]

While we cannot absolutely exclude the possibility in our case of an overlap of an n → π* transition of the >C=N- group with that of the carbonyl group, this >C=N- transition, if it exists, most probably has a very small ε value.

In fact, in reported studies of >C=N–containing compounds the absorption maxima are at rather low wavelengths,[10e,18,19] and on the basis of their ε values we think they must be attributed to π → π* transitions of the >C=N- group.

In any case neither Cotton effects nor uv absorption bands at wavelengths above 220 mμ have been reported for nonconjugated oximes, while for conjugated oximes

(7) A. Perotti, G. Bianchi, and P. Grünanger, "Convegno sulle risonanze magnetiche," Pavia, 1966.

(8) M. C. Aversa, G. Cum, and M. Crisafulli, *Gazz. Chim. Ital.*, **96**, 1046 1966).

(9) A. M. Duffield and O. Buchardt, *Org. Mass Spectrom.*, **3**, 1043 (1970).

(10) (a) C. Djerassi, *Bull. Soc. Chim. Fr.*, 741 (1957); (b) W. A. Struck and R. L. Houtman, *J. Org. Chem.*, **26**, 3883 (1961); (c) P. Crabbé, F. Mc Capra, F. Comer, and A. I. Scott, *Tetrahedron*, **20**, 2455 (1964); (d) G. Snatzke and J. Himmelreich, *Tetrahedron*, **23**, 4337 (1967); (e) P. Crabbé and L. Pinelo, *Chem. Ind. (London)*, 158 (1966).

(11) P. Sunder-Plassman, P. H. Nelson, P. H. Boyle, A. Cruz, J. Iriarte, P. Crabbé, J. A. Zderic, J. A. Edwards, and J. H. Fried, *J. Org. Chem.*, **34**, 3779 (1969).

(12) P. Crabbé, "Applications de la Dispersion Rotatoire Optique et du Dicroisme Circulaire Optique en Chimie Organique," Gauthier-Villars, Paris, 1968, p 492, and references cited therein.

(13) R. C. Cookson and J. Hudec, *J. Chem. Soc.*, 429 (1962).

(14) Z.-Y. Kyi and W. Wilson, *ibid.*, 798 (1953).

(15) H. C. Barany, E. A. Braude, and M. Pianka, *ibid.*, 1898 (1949).

(16) E. S. Stern and C. J. Timmons, "Electronic Absorption Spectroscopy in Organic Chemistry," E. Arnold, Ed., London, 1970, pp 41, 42, and references cited therein.

(17) C. N. R. Rao, "Ultra-violet and visible spectroscopy," Butterworths, London, 1967, pp 27, 28, and references cited therein.

(18) H. Ley and H. Wingchen, *Ber.*, **67**, 501 (1934).

(19) G. W. Perold, A. P. Steyn, and F. V. K. von Reiche, *J. Amer. Chem. Soc.*, **79**, 462 (1957).

the uv absorption and Cotton effect are in the region 230–240 mμ[14,15,18] and no absorption at longer wavelengths corresponding to n → π* transitions of the >C=N- group have been reported.

As well as the low intensity long wavelength bands which we have attributed to n → π* transitions of the carbonyl groups, our uv spectra also show for **3** a maximum at 235 mμ and for **2** a shoulder at approximately 220 mμ.

While it proved impossible to obtain the relative proportions of the two isomers formed from the chromatographic separation due to partial overlap of dimethylfuroxan, we have obtained the relative proportions from the nmr spectrum of the crude reaction product. Since both **2** and **3** contribute to the signal at δ 5.4 (in the ratio of 1:2) while only **2** contributes to the signal at δ 3.84, from the relative intensities of these two signals we calculated the product ratio of **2**:**3** as 9:1.

Registry No.—**1**, 979-02-2; **2**, 1057-99-4; **3**, 1253-19-6.

Preparation of 1,6-Diarylhexatrienes by a Modified Wittig Reaction

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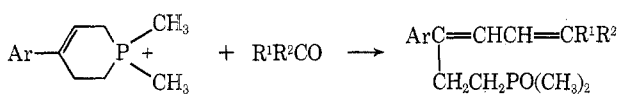
Received March 22, 1971

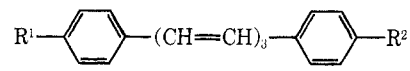
Recently we showed that reaction of cyclic phosphonium salts such as **1** with strong base followed by treatment of the resulting ylide with carbonyl compounds afforded a series of phosphorus-containing dienes.[1]



1 **2**

Prompted by the availability of a good method for the preparation of 1-methyl-3-phospholene,[2] we decided to investigate the behavior of the corresponding methiodide under the conditions of the Wittig reaction. Initial attempts to translate directly the reaction conditions used in the earlier work were not promising. When, however, a mixture of the salt and benzaldehyde was treated with 2 equiv of *tert*-butoxide in THF there was obtained on work-up an extremely insoluble crystalline compound. The absence of any PCH_3 bands in the nmr suggested that this was not a product analogous to **2**. The mass and uv spectra of the crude product both indicated this to be a mixture of isomeric 1,6-diphenylhexatrienes. Recrystallization afforded a pure sample of the polyolefin whose properties are in agreement with those recorded in the literature.[3] By carefully adjusting conditions it proved possible to obtain this product in 26% yield by direct crystallization. Table I records results of this condensation employing several aldehydes.

TABLE I

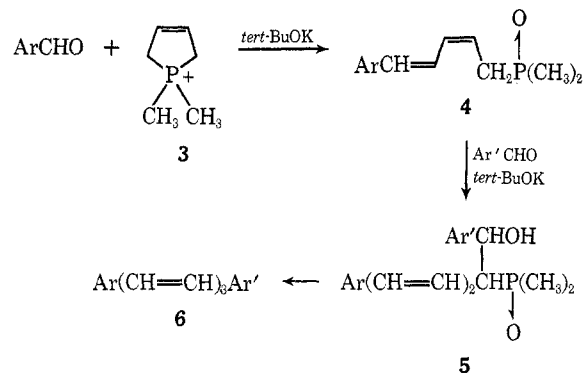


R^1	R^2	Registry no.	Mp, °C	Lit mp, °C	Yield, %
H	H	1720-32-7	194–197	199–201[a]	26
CH_3	CH_3	31382-31-7	229–231		10[b]
OCH_3	OCH_3	31382-32-8	250–250.5	247–248[c]	17

[a] See ref 3. [b] *Anal.* Calcd for $C_{20}H_{20}$: C, 92.26; H, 7.74. Found: C, 92.69; H, 7.70. [c] K. Friedrich and W. Hartmann, *Chem. Ber.*, **94**, 840 (1961).

The overall transformation can be rationalized by some scheme such as that shown in Scheme I. The

SCHEME I



first step is simply analogous to the overall reaction demonstrated in the earlier work. The product **4** in this case, however, contains an active methylene group which should undergo an aldol condensation with a second mole of aldehyde to form the corresponding triene.[4]

In order to test the validity of Scheme I, the quaternary salt **3** was treated with a single equivalent of base and tolualdehyde. The product was carefully worked up and chromatographed to afford a small amount of triene and a very polar gummy fraction. The mass spectrum (*m/e* 234.1175) and nmr (Ar H, 4 H at δ 7.2; vinyl protons 4 H δ 6–7; $ArCH_3$, 3 H at δ 2.3; PCH_3, 6 H, multiplets at δ 1.3 and 1.5) of the gum are in accord with a mixture of isomers of the intermediate **4**. Exposure of the gum to 1 equiv of potassium *tert*-butoxide and benzaldehyde gave the mixed triene, albeit in low yield (**6**, Ar = C_6H_5; Ar′ = *p*-$CH_3C_6H_4$), as the sole identifiable product. This then in broad outline provides evidence for the above scheme.

Experimental Section[5]

1-Methyl-3-phospholene Methiodide (3).—Methyldichlorophosphine (50 g) was added to a solution of 23 g of butadiene in

(1) D. Lednicer, *J. Org. Chem.*, **35**, 2307 (1970).
(2) L. D. Quin and J. A. Peters, *Tetrahedron Lett.*, 3689 (1964).
(3) R. Kuhn and A. Winterstein, *Helv. Chim. Acta*, **11**, 87 (1928).
(4) See, for example, T. H. Kinstle and B. Mendanas, *Chem. Commun.*, 1699 (1968).
(5) Melting points are uncorrected and recorded as obtained on a Thomas-Hoover capillary melting point apparatus. Nmr spectra were determined in deuteriochloroform on a Varian A-60 spectrometer. The author is indebted to the Department of Physical and Analytical Chemistry of The Upjohn Co. for elemental and spectral determinations.