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SYNTHESIS OF 2-PHENYLPHOSPHOLENO[3,4-d]TROPONE 2-OXIDE. A NEW METHOD FOR SYNTHESIS OF 4,5-ANNELATED TROPONES

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2-Phenylphospholeno[3,4-d]tropone 2-oxide has been synthesized starting with 3,4-bis(methylene)-7,7-dibromobicyclo[4.1.0]heptane. This has opened a new short synthetic route to 4,5-annelated tropones.

Recently, 1- and 2-phosphaazulene derivatives have been attracting interest[1,2] but there has never been reported the synthesis of their derivatives without substituent on ring carbons. Our interest in such derivatives has been focused on their synthesis starting with 3,4-bis(methylene)-7,7-dibromobicyclo-[4.1.0]heptane (1). Here we wish to report a synthesis of 2-phenylphospholeno-[3,4-d]tropone-2-oxide (2), which is thought to be a key intermediate for the synthesis of many useful and interesting derivatives of 2-phosphaazulene, in a short route.

The diene (1) was prepared as follows. anti-4,4-Dibromo-9-oxatricyclo-[5.3.0.$0^{3,5}$]decane[3] was treated with triphenylphosphine dibromide[4] to give anti-[cis-3,4-bis(bromomethyl)]-7,7-dibromobicyclo[4.1.0]heptane (3),[5] mp 98-98.5 °C, in 91% yield. This compound was bisdehydrobrominated[6] with potassium t-butoxide in tetrahydrofuran to give 1[7] in 46% yield.

The diene (1) was converted to tricyclic phospholene P-oxide (4 and 5) in 99% yield via a chlorophospholenium chloride by McCormack reaction.[8] The oxide mixture (anti:syn= 3:2) was easily separated by silica gel chromatography and their structures were assigned by ^{1}H NMR spectra with use of the Sievers' shift reagent. The anti-P-oxide (5),[9] mp 191-192 °C, showed a larger down-field shift of the hydrogen signal on three-membered ring relative to the same shift of the aromatic meta- and para-proton signals ($a = \Delta\delta H_5/\Delta\delta H_{Ar} = 0.79$) than that of the syn-isomer (4)[9] ($a = 0.70$), mp 220-223 °C, in agreement with the fact that the oxygen, which would interact with the shift reagent, of the former is located nearer to the hydrogen on three-membered ring than one of the latter.

The both P-oxides were treated with m-chloroperbenzoic acid (mCPBA) to give the corresponding epoxides in quantitative yields. At room temperature, 4 gave mainly one isomer (6),[10] with a trace amount of 7, while 5 gave 9:1 mixture of two epoxides (8 and 9) which were separated by column chromatography. The selectivity of the oxidation was improved by lowering the reaction temperature (0 °C; 20:1). Quin et al. reported that the epoxidation of 3-phospholene P-oxide usually occurs at the anti-side to the oxygen, though the stereochemistry is

sensitive to the environment of the reaction center.[11] Based on this fact, it is reasonable to assign 6 as the anti-epoxide both to the three-membered ring and oxygen on P in line with the assignment of structure 4. In the ^{1}H NMR spectrum of 6, two proton signals of phenyl group showed down field shift compared with those of 4, which suggested the effect of the neighboring epoxide.[12] The same down field shift of the proton signal was observed in the minor product of oxidation of 5, which was assigned as 9 (anti-epoxide to P-oxide),[13] mp 190-192 °C, and consequently the main product must be 8,[13] mp 173-175 °C. In the epoxidation of 5, the blocking ability of the dibromomethylene group is clearly surpassing that of P-oxide.

In order to obtain seven-membered ring by opening the three-membered ring of 6 or 8, we treated the epoxide (6) with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene and obtained 2-phospholenol P-oxide (10),[14] mp 213-215 °C, in 96% yield. Likewise, epoxide (8) gave 11,[14] mp 224-225 °C, in 90% yield. When compound (11) was refluxed with trifluoroacetic acid (TFA), a tropone (2),[15] mp 189-191 °C, was unexpectedly obtained in 86% yield. On treatment of 6 or 8 with refluxing TFA gave directly 2 (60-79%). The reaction might have started with dehydration to a norcaradiene (12) then proceeded successively via a tropylium bromide (13)[16] and a cycloheptatriene (14) followed by the elimination of RBr as shown in the scheme. This opened a new route to the synthesis of 4,5-annelated tropones as follows.

The diene (1) was stirred with maleic anhydride in ether to give a mixture of the adduct (15) in 91% yield.[17] These were oxidized with mCPBA to a mixture of epoxides (16), and it was, without further purification, refluxed with 9 equiv. molar excess of TFA in chloroform. The concentrated reaction mixture was dissolved in 5% aq. sodium hydrogencarbonate and acidified after washing with dichloromethane. The acid thus obtained was directly treated with ethereal diazomethane to give the tropone cis-diester (17),[18] mp 162-163 °C, in 65% overall yield from 15. Similarly, starting from the adduct of 1 to dimethyl fumarate, the trans-diester (18), mp 124-125 °C, was obtained. The utilization and limitation of this reaction to the synthesis of several useful tropones are now under extensive investigation. All compounds obtained above gave satisfactory analytical data. We are grateful to Mr. Jun-Ichi Gohda of our University for the elementary analysis.

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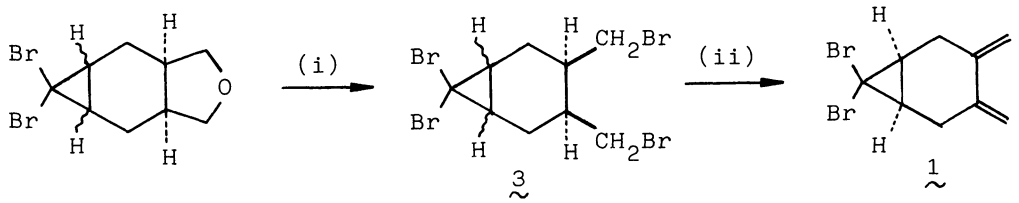
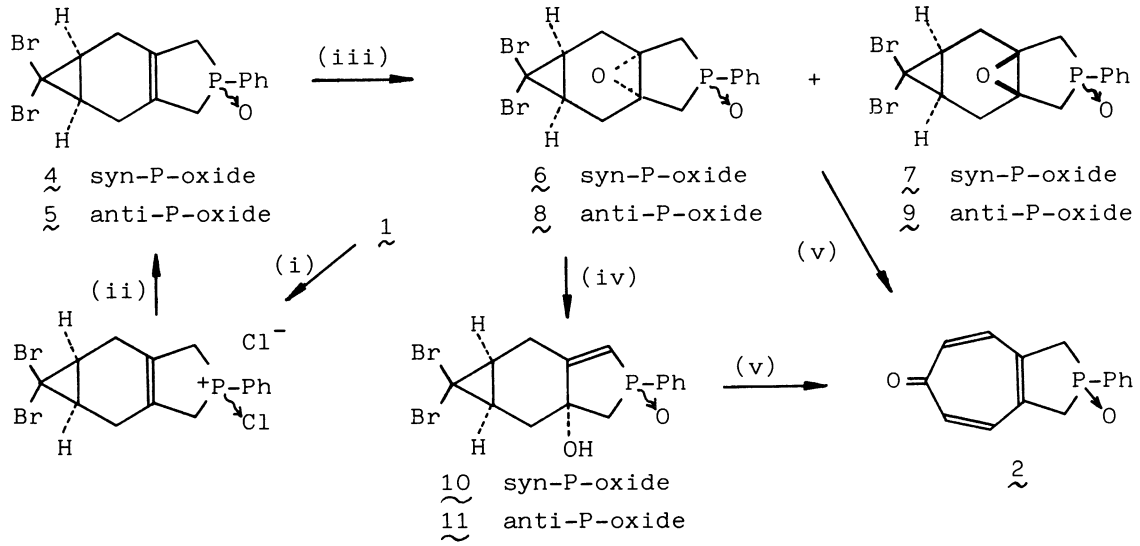
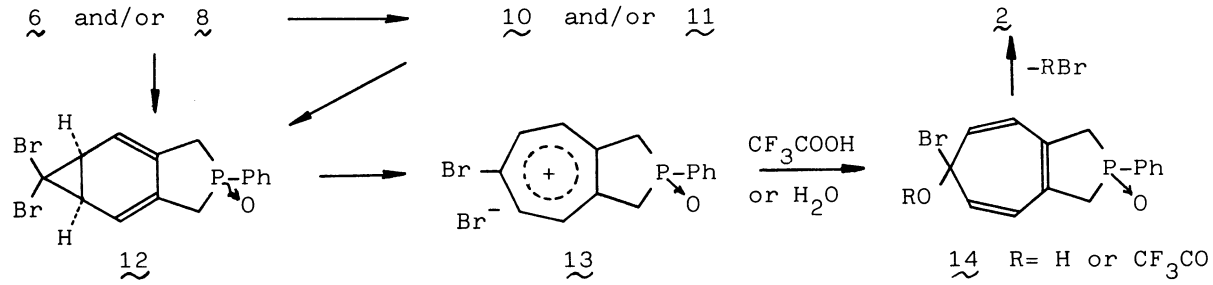
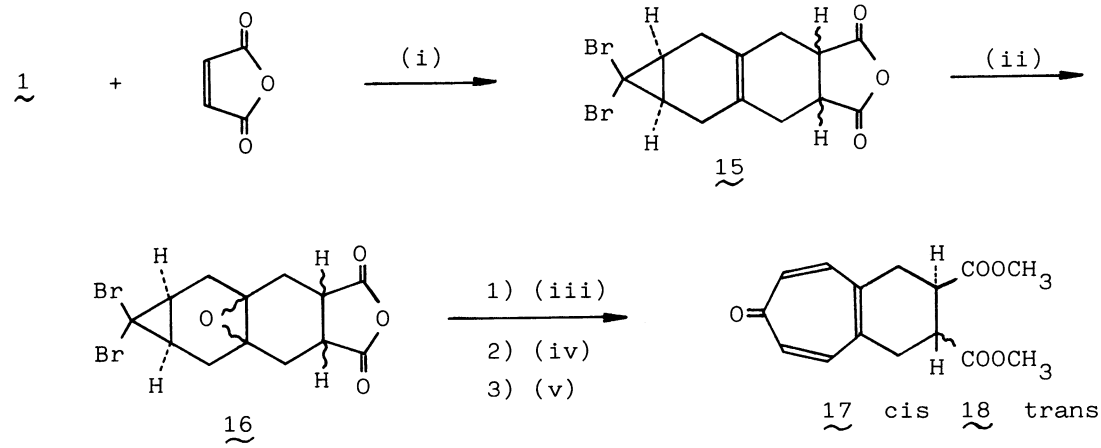


(i) 2 equiv. Ph_3PBr_2/C_6H_5Cl(25 mL/1.04 g), 120 °C, 2 h
(ii) 2.6 equiv. t-BuOK/THF(80 mL/8.33 g, 3), r.t., 2.5 h.



(i) 1.1 equiv. $PhPCl_2$/hexane(2.5 mL/1.0 g, 1/10 mg, Cupric stearate), r.t., 2 weeks (ii) H_2O-CH_2Cl_2(10 mL, 1:1 v/v), r.t., 2.5 h
(iii) 1.1 equiv. mCPBA/CH_2Cl_2(2 mL/0.2 g, 4 or 5), r.t., overnight
(iv) 2.5 equiv. DBU/benzene(4 mL/0.21 g, 6), reflux, 6 h
(v) TFA(0.3 mL/25.8 mg, 11 or 2 mL/0.47 g, 6), reflux, 1-2 d.





(i) Et_2O(13 mL/0.35 g, 1), r.t., overnight (ii) 1.05 equiv. mCPBA/CH_2Cl_2(10 mL/0.85 g, 15), r.t., 3 h (iii) 10 equiv. TFA/$CHCl_3$(10 mL/0.41 g, 16), reflux, 5 h (iv) aq. $NaHCO_3$ (v) excess CH_2N_2/ether

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4) A. G. Anderson, Jr. and F. J. Freenor, J. Am. Chem. Soc., 86, 5037 (1964).
5) 3: ^{1}H NMR ($CDCl_3$, δ, TMS): 3.2-3.5 (4H, m) and 1.6-2.4 (8H, m).
6) Similarly, 1 was obtained starting from syn-4,4-dibromo-9-oxatricyclo-[5.3.0.$O^{3,5}$]decane in a yield similar to that of the anti-isomer.
7) 1: Colorless liquid; purified by column chromatography. ^{1}H NMR: 5.25 (2H, bs), 4.82 (2H, bs), 2.89 (2H, d,d, J= 18.5; 6.0 Hz), and 1.8-2.2 (4H, m).
8) L. D. Quin, J. Peters, and T. B. Barket, J. Org. Chem., 33, 1034 (1968).
9) anti-P-Oxide (5): ^{1}H NMR: 7.2-7.6 (5H, m) and 1.9-2.8 (10H, m). ^{13}C NMR ($CDCl_3$, δ_{CDCl_3} = 77.1 ppm): 25.1 (J_{PC}= 14.7 Hz), 26.6 (1.8), 37.2, 38.0 (68.3), 126.9 (9.8), 128.6 (11.6), 129.6 (9.8), 131.9 (2.5), and 137.3 (84.8). syn-P-Oxide (4): ^{1}H NMR: 7.3-7.7 (5H, m) and 2.0-2.9 (10H, m). ^{13}C NMR: 25.1 (J_{PC}= 14.7 Hz), 25.7 (1.8), 36.4, 37.7 (68.3), 127.1 (10.4), 128.7 (11.6), 129.4 (9.8), 132.0 (3.1), and 134.0 (93.4).
10) 6: ^{1}H NMR: 7.7-8.0 (2H, m), 7.3-7.6 (3H, m), and 1.7-2.8 (10H, m). ^{13}C NMR: 24.4, 25.2 (J_{PC}= 12.2 Hz), 36.1 (67.2), 62.4 (4.9), 128.5 (12.2), 131.1 (11.0), 131.9 (2.5); the signal due to the IPSO carbon was not detected.
11) L. D. Quin, C. Symmes, Jr., E. D. Middlemas, and H. F. Lawson, J. Org. Chem., 45, 4688 (1980).
12) L. A. Paquette, J. W. Fischer, A. R. Browne, and C. W. Doecke, J. Am. Chem. Soc., 107, 686 (1985), and references cited therein.
13) 9: ^{1}H NMR: 7.7-8.0 (2H, m), 7.4-7.7 (3H, m), and 1.8-2.8 (10H, m). 8: ^{1}H NMR: 7.3-7.8 (5H, m) and 1.8-2.8 (10H, m). ^{13}C NMR: 24.5, 25.0 (J_{PC}= 12.2 Hz), 36.8 (68.4), 38.5, 64.0 (2.4), 128.7 (12.0), 129.8 (11.0), 131.6 (2.4), and 133.2 (94.0).
14) 10: ^{1}H NMR: 7.3-7.8 (5H, m), 6.19 (1H, d, J_{PH}= 21.0 Hz), 2.6-3.2 (5H, m), and 1.9-2.3 (3H, m). ^{13}C NMR: 25.5, 27.0 (J_{PC}= 20.7 Hz), 28.7, 37.4, 37.9 (8.6), 40.4 (68.4), 78.2 (13.6), 118.6 (94.0), 127.0 (109.9), 130.1 (13.4), 130.8 (12.3), 134.7 (3.7), and 171.1 (19.6). 11: ^{1}H NMR: 7.4-7.8 (5H, m), 6.29 (1H, d, J_{PC}= 21.0 Hz), and 1.8-3.3 (8H, m). ^{13}C NMR: 25.5, 26.9 (J_{PC}= 20.8 Hz), 28.6, 37.7, 38.0, 40.4 (69.6), 78.0 (13.4), 118.8 (97.7), 127.2 (109.9), 130.0 (13.4), 130.7 (12.2), 134.5 (3.7), and 170.6 (19.5).
15) 2: ^{1}H NMR (400 MHz, $CDCl_3$, δ, TMS): 7.70-7.77 (2H, m), 7.58-7.64 (1H, m), 7.49-7.55 (2H, m), 7.08 (2H, d, J= 12.1 Hz), 6.96 (2H, d, J= 12.1 Hz), 3.57 (2H, d,d, J= 18.2, J_{PH}= 16.4 Hz), and 3.41 (2H, d,d, J= 18.2, J_{PH}= 7.6 Hz). $\lambda_{max}^{C_2H_5OH}$ (log ε): 228 (4.42), 266 (3.44), 274 (3.48), and 320 nm (4.07). ^{13}C NMR: 40.8 (J_{PC}= 67.4 Hz), 128.8 (11.7), 129.7 (10.3), 131.3 (97.7), 132.5 (2.9), 136.1 (13.2), 140.2, 140.9 (8.8), and 186.
16) We detected 1-bromo-5-isopropyl-2-methyltropylium cation when 2,3-epoxy-7,7-dibromo-3-isopropyl-6-methylbicyclo[4.1.0]heptane was treated with TFA in deuteriochloroform (unpublished work).
17) 15 (10:1 mixture): major product: mp 191 °C. ^{1}H NMR: 3.15 (2H, m) and 2.5-1.65 (10H, m). ^{13}C NMR: 25.9(d), 26.9(t), 28.4(t), 37.1(s), 40.1(d), 125.9(s), and 174.2(s) (Off-resonance technique).
18) 17: ^{1}H NMR: 6.86 and 6.80 (AB-q, J= 12.8 Hz), 3.72 (6H, s), 3.9-3.6 (2H, m), and 3.35-2.9 (4H, m). ^{13}C NMR: 33.4(t), 39.4(d), 52.2(q), 138.5(d), 139.4(s), 140.6(d), 172.4(s), and 187.0(s). $\lambda_{max}^{C_2H_5OH}$ (log ε): 228.5 (4.39), 232 (4.39), and 319 nm (4.10).

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