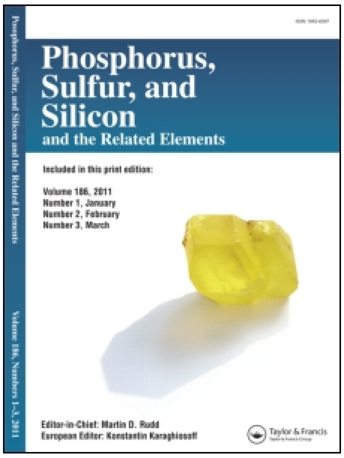

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ORGANOPHOSPHORUS COMPOUNDS, XXXIII THE REACTION OF PHOSPHITE ESTERS WITH QUINISATIN

M. M. Sidky[a]; M. R. Mahran[a]; A. A. El-kateb[a]; I. T. Hennawy[a]
[a] National Research Centre, Dokki-Cairo, Egypt

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ORGANOPHOSPHORUS COMPOUNDS, XXXIII THE REACTION OF PHOSPHITE ESTERS WITH QUINISATIN†

M. M. SIDKY, M. R. MAHRAN, A. A. EL-KATEB, and I. T. HENNAWY

National Research Centre, Dokki-Cairo, Egypt.

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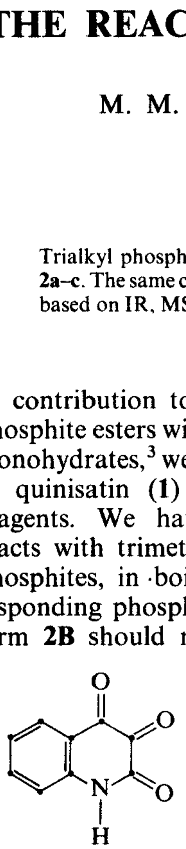
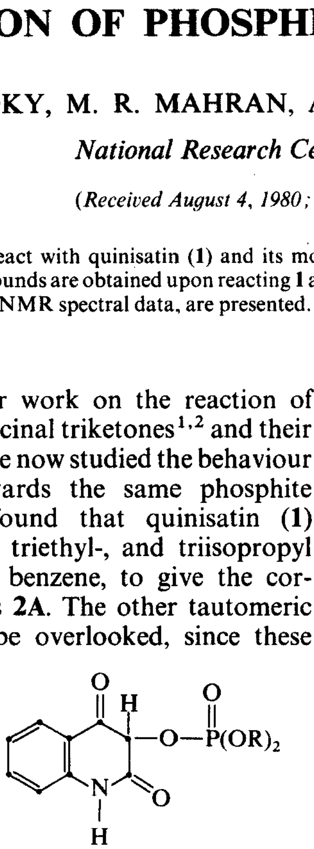
Trialkyl phosphites react with quinisatin (**1**) and its monohydrate **3** to give the corresponding phosphate derivatives **2a–c**. The same compounds are obtained upon reacting **1** and/or **3** with the proper dialkyl phosphite. Structural reasonings based on IR, MS and NMR spectral data, are presented.

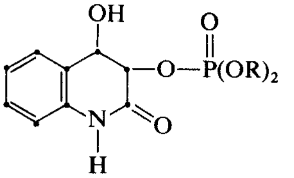
In contribution to our work on the reaction of phosphite esters with vicinal triketones[1,2] and their monohydrates,[3] we have now studied the behaviour of quinisatin (**1**) towards the same phosphite reagents. We have found that quinisatin (**1**) reacts with trimethyl-, triethyl-, and triisopropyl phosphites, in boiling benzene, to give the corresponding phosphates **2A**. The other tautomeric form **2B** should not be overlooked, since these compounds respond positively to the ferric chloride reaction giving a green colour, and dissolve freely in 10% aqueous alkali.



1



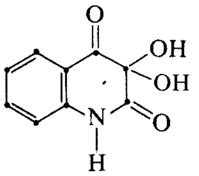
2A



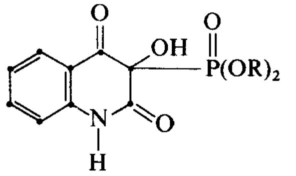
2B

a, R = CH_3
b, R = C_2H_5
c, R = C_3H_7-*i*

Structural elucidation for compounds **2** was based upon the following evidence: (i) Correct elemental analysis and molecular weight determination (MS) were obtained for all products, (ii) The IR spectrum (in KBr) of compound **2a**, taken as an example, showed bands at 3400 cm^{-1} (OH, broad), 3200 cm^{-1} (NH), 1655 cm^{-1} (C═O, amide), 1590, 1500 cm^{-1} (C═C, aromatic), 1250 cm^{-1} (P═O)[4] and at 1040 cm^{-1} (P—O—CH_3)[4], (iii) The ^{1}H NMR spectrum of **2a** (in DMSO-d_6) disclosed the presence of 6 methoxyl protons as a doublet at $\delta = 3.86$, ^{J}HP = 11.5 Hz and a multiplet at $\delta = 7.10$–7.66 (4H, due to the aromatic protons). The exchangeable (D_2O) protons (NH and OH) appeared as two broad signals at $\delta = 7.80$ and $\delta = 11.73$. Structure **2** accommodates these data more adequately than does the other possible alternative α-hydroxyphosphonate form **4**, (iv) The structure assigned for compounds **2** was also based on the δ^{31}P NMR shift (−3.70 ppm, *vs.* H_3PO_4 for **2a**) which corresponds to a phosphate and not to an α-hydroxyphosphonate.[5,6] Furthermore, the fact that compounds **2a–c** were found identical (mixture m.p. and superimposable IR spectra) with the 1 : 1 adducts formed *via* the reaction of dimethyl-, diethyl-, and diisopropyl phosphites, respectively, with quinisatin (**1**), affords additional evidence for the proposed structure **2**, (v) Treatment of compound **2a** with ethereal diazomethane solution, resulted in the formation of two different methylation products. The major product (> 70%) was assigned the dimethyl ether



3



4, R as in **2**

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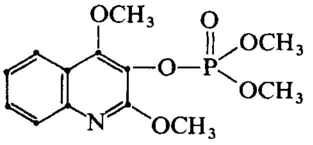
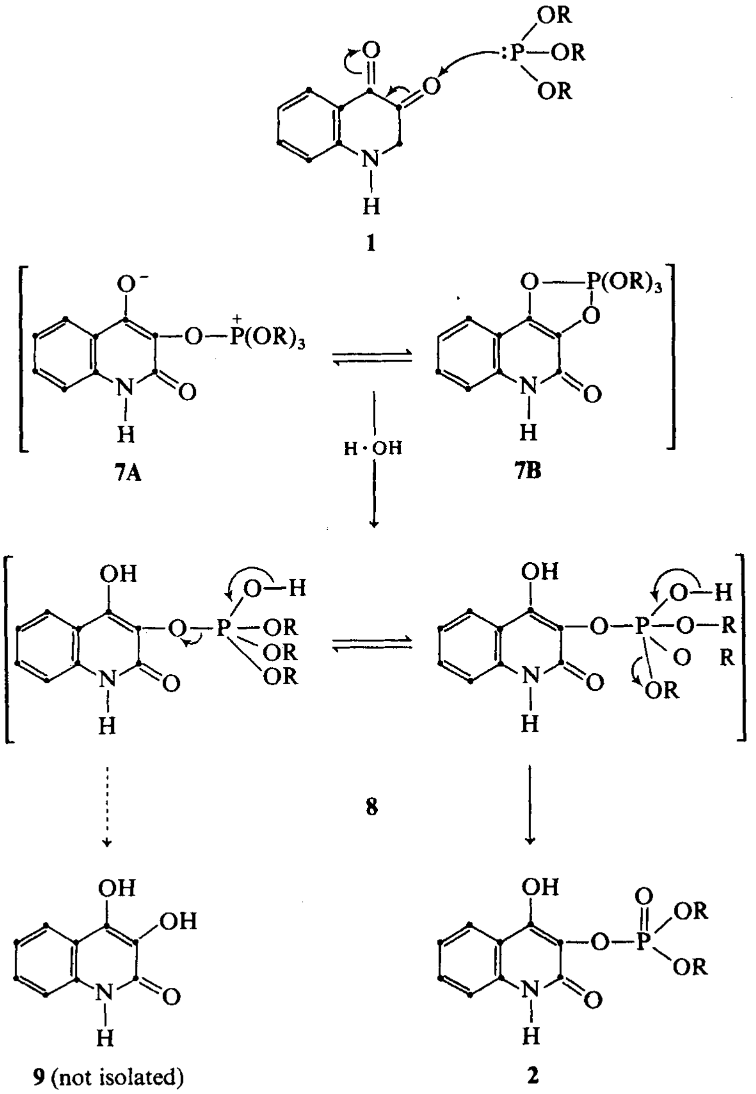
† Also known as quinoline-2,3,4-trione.



5, $\delta\ {}^{31}P = -3.20$ ppm.

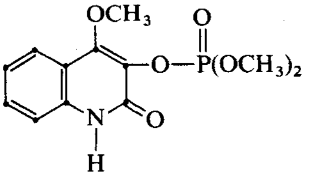
phosphate structure **5**, for the following reasons: (a) Elemental analyses and molecular weight determination (MS) for compound **5** corresponded to $C_{13}H_{16}NO_6P$. (b) Its IR spectrum, in KBr, revealed the absence of absorption bands both in the 3600–3200 cm^{-1} region (OH and NH) and in the 1700–1620 cm^{-1} region (C=O). (c) Presence of a doublet (6H, ^{3}HP = 11.5 Hz, for protons of the OCH_3 groups attached to phosphorus) at $\delta = 4.00$, singlet (3H, OCH_3) at $\delta = 4.15$ and another singlet (3H, OCH_3) at $\delta = 4.20$, were distinguishing features of the ^1H NMR spectrum of compound **5**, in $CDCl_3$.

Elemental analyses and molecular weight determination (MS) for the minor (<20%) methylation-product of **2a**, on the other hand, corresponded to a monomethyl ether-phosphate formula ($C_{12}H_{14}NO_6P$). Structures like **6A** and **6B** would satisfy presentation of this minor product since

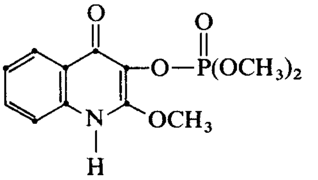


SCHEME 1

its IR spectrum contains absorption bands at 3220 cm^{-1} (NH) and 1625 cm^{-1} (C=O). Moreover, its ^1H NMR spectrum disclosed the presence



6A



6B

$\delta\ ^{31}P = -2.50$ ppm.

of signals at $\delta = 4.00$ (6H, doublet, $^JHP = 11.5$ Hz, for the OCH_3 group attached to phosphorus) and a singlet at $\delta = 4.20$ (3H, OCH_3).

Closer insight into the final structure of compound **6** is, however, beyond the scope of the present study.

A possible explanation for the course of the reaction of trialkyl phosphites with quinisatin (**1**), is shown in *Scheme* 1. This involves attack by the phosphite-phosphorus on the most reactive[7] middle carbonyl group of the trioxo-system of quinisatin (**1**) to give the dipolar structure **7A**; existing probably in equilibrium with the unsaturated 5-membered cyclic oxyphosphorane **7B**. Addition of elements of water (unavoidable moisture) to adduct **7** produces a transient intermediate (**8**) with pentacovalent phosphorus.[6,8–10] This collapses then to give the observed products (**2**). In favour of this idea is the finding that trialkyl phosphites react with quinisatin hydrate (**3**) to give the corresponding phosphate derivatives (**2a–c**) (cf. the reaction of trialkyl phosphites with vicinal triketone monohydrates).[3,6] The other alternative hydrolysis pathway to give a dihydroxy compound like **9** (not observed), is thus avoided (*Scheme* 1).

From the present study, it could be seen that the reaction of trialkyl phosphites with quinisatin (**1**) follows a course different from that observed with other heterocyclic polycarbonyl compounds.[6] Thus, quinisatin (**1**) reacts with alkyl phosphites to give the corresponding hydroxy-phosphates (**2**); simulating the behaviour of α-diketones[11–13] and *o*-quinones[11,12,14–16] with phosphite esters.

EXPERIMENTAL

All mp's were uncorrected. The benzene (thiophene-free) used was dried (Na). Triaklyl phosphites[17,18] were purified by treatment with Na followed by fractional distillation and dialkyl phosphites[19,20] were freshly distilled. The IR spectra were recorded, in KBr, with Perkin-Elmer Infracord Model 137 and Beckman Infracord Model 4220. The ^1H NMR spectra were run on Varian Spectrometers at 60 MHz and/or 90 MHz, using TMS as an internal reference. The mass spectra were recorded at 70 eV, with a Varian MAT 112 Mass Spectrometer.

The Reaction of Quinisatin (**1**) *with Trialkyl Phosphites*

A mixture of quinisatin (**1**)[7,21,22] (0.7 g, 0.004 mole) and trimethyl phosphite (2.5 g, 0.02 mole) was heated in absence of solvent at 100°C for 2 hr or refluxed in benzene (40 ml) for 48 hr. The volatile materials were evapoarated, *in vacuo*, and the residual substance triturated with benzene (10 ml). The solid product that formed was collected (1 g, 95%) and recrystallized from dry benzene to give phosphate **2a** as colourless crystals, m.p. 180–182°C (dec.). Anal. Calcd. for $C_{11}H_{12}NO$ P: C, 46.31; H, 4.21; N, 4.91; P, 10.87. Found: C, 45.77; H, 3.98; N, 4.56; P, 11.0%. Mol. Wt.: Calcd. 285. Found (MS): 285.

Similarly, the reaction of quinisatin (**1**) with triethyl-, and triisopropyl phosphites afforded phosphates **2b** and **2c**, respectively.

Compound **2b** gave colourless crystals (95%) from benzene-petroleum ether (b.r. 60–80°), m.p. 195–197°C (dec.). Calcd. for $C_{13}H_{16}NO_6P$: C, 49.52; H, 5.11; N, 4.47; P, 9.89. Found: C, 49.62; H, 4.53; N, 4.81; P, 10.05%. Mol. Wt.: Calcd. 313. Found (MS): 313. IR: Bands at 3425 cm^{-1} (OH), 3160 cm^{-1} (NH), 1670 cm^{-1} (C=O, amide), 1610, 1580, 1500 cm^{-1} (C=C, aromatic), 1260 cm^{-1} (P=O) and 1035 cm^{-1} ($P-O-C_2H_5$)[4]. ^1H NMR (DMSO-d_6): Signals at $\delta = 1.30$ (6H, triplet, $^JHH = 7.00$ Hz, due to the ethoxy-CH_3 protons), $\delta = 4.35$ (4H, quintet, for the ethoxy-CH_2 protons attached to phosphorus) and $\delta = 7.20$–8.57 (4H, multiplet, aromatics). Two exchangeable protons (OH and NH) appeared as broad singlets at $\delta = 8.90$ and $\delta = 12.00$. ^{31}P NMR (*vs.* H_3PO_4): $\delta = -3.68$ ppm.

The colourless crystals of phosphate **2c** were obtained in ca. 95% yield from benzene-petroleum ether (b.r. 40–60°), m.p. 170–172°C (dec.). Anal. Calcd. for $C_{15}H_{20}NO_6P$: C, 52.78; H, 5.86; N, 4.10; P, 9.09. Found: C, 52.99; H, 5.24; N, 4.63; P, 9.20%. Mol. Wt.: Calcd. 341; Found (MS): 341. IR: Bands at 3380 cm^{-1} (OH, broad), 3225 cm^{-1} (NH), 1640 cm^{-1} (C=O, amide), 1595, 1500 cm^{-1} (C=C, aromatic), 1260 cm^{-1} (P=O) and 1030 cm^{-1} ($P-O-C_3H_7$-*i*)[4]. ^1H NMR ($CDCl_3$): Signals at $\delta = 1.40$ (12H, doublet, $^JHH = 7$ Hz, for the isopropoxy-CH_3 protons), $\delta = 4.95$ (2H, multiplet, due to the isopropoxy-*CH* protons coupled with phosphorus) and $\delta = 7.15$–8.00 (4H, multiplet, aromatics). The exchangeable protons (OH, NH) appeared as broad singlets at $\delta = 8.10$ and 12.00.

The phosphate products **2a–c** dissolve freely in dilute aqueous sodium hydroxide solution (10%) and exhibit a green colour reaction with alcoholic ferric chloride solution.

The Reaction of Quinisatin Hydrate (**3**) *with Trialkyl Phosphites*

A mixture of quinisatin hydrate (**3**)[21] (0.77 g; 0.004 mole) and trimethyl phosphite (2.5 g, 0.02 mole) was heated in absence of solvent at 100°C for 2 hr, or refluxed in benzene (40 ml) for 72 hr. The volatile materials were evaporated, *in vacuo*, and the residual substance triturated with benzene (10 ml). The solid product that formed was collected (1 g, 90%) and recrystallized from benzene to give colourless needles proved to be phosphate **2a** (m.p., mixture m.p. and comparative IR and NMR spectra).

In the same manner, the reaction of quinisatin hydrate (**3**) with triethyl phosphite and triisopropyl phosphite afforded colourless products (yield ca. 95%) proved to be phosphate **2b** (m.p. and mixture m.p. 195–197°) and phosphate **2c** (m.p. and mixture m.p. 170–172°), respectively.

The Reaction of Quinisatin (1) *with Dialkyl Phosphites*

A mixture of quinisatin (**1**) (0.7 g, 0.004 mole) and dimethyl phosphite (2.20 g, 0.02 mole) was heated in absence of solvent at 100°C for 2 hr, or refluxed in benzene (40 ml) for 48 hr. After evaporating the volatile materials, *in vacuo*, the residual substance was treated with benzene (10 ml). The solid product that formed, was collected (1.0 g, 95%) and recrystallized from benzene to give colourless needles proved to be phosphate **2a** (m.p., mixture m.p. and superimposable IR spectra).

In a similar manner, the reaction of **1** with diethyl phosphite and diisopropyl phosphite afforded phosphate **2b** (m.p., mixture m.p. and comparative IR spectra) and phosphate **2c** (m.p., mixture m.p. and comparative IR spectra), respectively.

Action of Diazomethane on Phosphate 2a

To a suspension of compound **2a** (0.8 g) in methanol (2 ml) was added an ethreal diazomethane solution (from 5 g *N*-nitrosomethylurea) and the mixture kept for 24 hr at 10°C. The undissolved material was filtered off (*filtrate A*), recrystallized from benzene to give the monomethyl ether phosphate **6A** (or **6B**) as colourless crystals ($<20\%$), m.p. 137–139°C (dec.). Anal. Calcd. for $C_{12}H_{14}NO_6P$: C, 48.16; H, 4.71; N, 4.71; P, 10.36. Found: C, 48.52; H, 4.35; N, 5.27; P, 10.68%. Mol. Wt.: Calcd. 299. Found (MS): 299. ^{1}H NMR ($CDCl_3$): Signals at $\delta = 4.00$ (6H, doublet, ^{J}HP = 11.5 Hz, for the OCH_3 protons attached to phosphorus), $\delta = 4.20$ [3H, singlet, for the CH_3O—C(aryl) protons], $\delta = 7.15$–7.85 (4H, multiplet, aromatics) and an exchangeable broad singlet at $\delta = 11.73$ (NH). δ ^{31}P NMR (*vs.* H_3PO_4): $\delta = -2.50$ ppm.

The combined methanol-ether filtrate (*filtrate A*) was evaporated till dryness and the residual oil substance triturated with petroleum ether (b.r. 40–60°) then left to cool in the refrigerator. The precipitated material was collected ($>70\%$) and recrystallized from petroleum ether to give the dimethyl ether phosphate **5** as colourless crystals, m.p. 95–97°C (dec.). Anal. Calcd. for $C_{13}H_{16}NO_6P$: C, 49.84; H, 5.11; N, 4.47; P, 9.90. Found: C, 49.37; H, 4.92; N, 4.24; P, 9.50%. Mol. Wt.: Calcd. 313. Found (MS): 313. IR: No absorption bands in the 3600–3200 cm^{-1} region and in the 1700–1620 cm^{-1} region; bands were present at 1615, 1590, 1500 cm^{-1} (C=N and C=C, aromatic), 1260 cm^{-1} (P=O) and 1040 cm^{-1} (P—O—CH_3). ^{1}H NMR ($CDCl_3$): Signals at $\delta = 4.00$ (6H, doublet, ^{J}HP = 11.5 Hz, for the OCH_3 protons attached to phosphorus), $\delta = 4.15$ (3H, OCH_3, singlet), $\delta = 4.20$ (3H, OCH_3, singlet) and $\delta = 7.30$–8.18 (4H, aromatics). Exchangeable protons were absent. ^{31}P NMR (*vs.* H_3PO_4): $\delta = -3.20$ ppm.

REFERENCES

1. A. Mustafa, M. M. Sidky, and F. M. A. Soliman, *Tetrahedron*, **23**, 99 (1967).
2. A. Mustafa, M. M. Sidky, S. M. A. D. Zayed, and M. R. Mahran, *Liebigs Ann. Chem.*, **712**, 116 (1968).
3. M. M. Sidky, M. R. Mahran, and W. M. Abdo, *Tetrahedron*, **28**, 5715 (1972).
4. L. J. Bellamy, *The Infra-red Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, N.Y., p. 311 (1964).
5. F. Ramiez, A. V. Patwardhan, N. Ramanathan, N. B. Desai, C. V. Greco, and S. R. Heller, *J. Amer. Chem. Soc.*, **87**, 543 (1965).
6. F. Ramirez, S. B. Bhatia, and C. P. Smith, *J. Org. Chem.*, **31**, 4105 (1966).
7. A. Schönberg and E. Singer, *Tetrahedron*, **34**, 1285 (1978).
8. F. Ramirez, O. P. Madan, N. B. Desai, S. Meyerson, and L. M. Banas, *J. Amer. Chem. Soc.*, **85**, 2681 (1963).
9. F. Ramirez, O. P. Madan, and C. P. Smith, *J. Amer. Chem. Soc.*, **87**, 690 (1965).
10. F. Ramirez, A. V. Patwardhan, N. B. Desai, and S. R. Heller, *J. Amer. Chem. Soc.*, **87**, 549 (1965).
11. F. Ramirez and N. B. Desai, *J. Amer. Chem. Soc.*, **82**, 2652 (1960).
12. F. Ramirez and N. B. Desai, *J. Amer. Chem. Soc.*, **85**, 3252 (1963).
13. F. Ramirez, R. B. Mitra, and N. B. Desai, *J. Amer. Chem. Soc.*, **82**, 2651 (1960).
14. F. Ramirez, S. B. Bhatia, A. V. Patwardhan, E. H. Chen, and C. P. Smith, *J. Org. Chem.*, **33**, 20 (1968).
15. M. M. Sidky and F. H. Osman, *UAR J. Chem.*, **14**, 225 (1971).
16. M. M. Sidky, M. R. Mahran, and L. S. Boulos, *J. Indian Chem. Soc.*, **49**, 383 (1972).
17. T. Milobendzki and A. Sachnowski, *Chem. Polski.*, **15**, 34 (1917); *Chem. Abstr.*, **13**, 2865 (1919).
18. A. H. Ford-Moore and B. J. Perry, *Organic Syntheses*, **31**, 111 (1951).
19. P. W. Gann and R. L. Heider, U.S., 2,692,890 (1954); *Chem. Abstr.*, **49**, 12529 (1955).
20. H. McCombie, N. C. Saunders, and G. J. Stacey, *J. Chem. Soc.*, 380 (1945).
21. B. Eistert and P. Donath, *Chem. Ber.*, **106**, 1537 (1973).
22. Th. Kappe, E. Lender, and E. Ziegler, *Monatsh. Chem.* **99**, 990, 2157 (1968).