The Behavior of 1,7,7 – Trimethyl Bicyclo [2.2.1] Heptane -2,3- Dione And 3-(2-Phenylhydrazono) -1,7,7- Trimethyl Bicyclo [2.2.1] Heptane -2- one Toward Organophosphorus Reagents.

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Abstract: heptanedione 1 reacts with tris(dialkylamino) phosphines (3a,b) to give dipolar product 6a,b. Phosphate product of type 9 are produced upon reacting phenylhydrazone 2 with trialkylphosphites 4a-c. Also, reaction of phenylhydrazone 2 with Lawesson's reagent (LR, 5) gave adducts 10 and 11. Structural elucidation for the new products was based upon compatible analytical and spectral data.


Kew Words: Heptanedione, phenylhydrazone heptanone, tris(dialkylamino) phosphines, trialkyl phosphites and Lawesson's Reagent.

1. Introduction

Heptanone derivatives 1 and 2 (camphorquinones) are reported to possess a variety of pharmacological importance such as dentin bonding agents [1], dental cements [2], and in root canal filling materials [3]. This together with our interest in organophosphorus chemistry [4-12] enhanced the synthesis of new phosphorus compounds. The present investigation has aimed to study the reaction of 1,7,7 -trimethyl- bicyclo [2.2.1] heptane -2,3- dione (1) with tris (dialkylamino) phosphines (3a,b) and 3-( phenyl hydrazone) -1,7,7- trimethyl bicyclo [2.2.1] heptane-2-one (2) with trialkyl phosphate (4a-c) and 1,3,2,4-dithiadiphosphetane - 2 , 4 - disulfide (LR) (5) (Scheme 1).

2. Experimental

Melting points were determined in open glass capillaries using an Electrothermal IA 9000 series digital melting point apparatus (Electrothermal, Essex, UK) and were uncorrected. The IR spectra were measured in KBr pellets with a Perkin-Elmer Spectrophotometer model 157(Grating). The 1H and 13C-NMR spectra were recorded in CDC13 as solvent on a Joel-500 MHz spectrometer, and the chemical shifts were recorded in δ values relative to TMS. The 31P-NMR (125 MHz) spectra were taken with a Varian CFT-20 (vs. external 85% H3PO4 standard). The mass spectra were performed at 70 eV on a Shimadzu GCS-OP 1000 Ex spectrometer provided with a data system. Elemental analyses were performed using an Elmenter Varu EL Germany Instrument.

Reaction of tris(dimethylamino)phosphine (3a) with 1,7,7- trimethyl-bicyclo [2.2.1] hepane -2,3-

dione (1) An excess of amino phosphate 3a (≈ 3ml) was added to 1 (0.16 g, mmol) and was heated for 5h. The reaction mixture was evaporated under reduced pressure and the residue was chromatographed on a silica gel column to give product 6a,7,7 trimethyl-3- (tris (dimethylamino) phosphoniooxy) bicyclo [2.2.1] hept-2-en-olate, using methanol / chloroform as an eluent (5 / 95 , v/v), product 6a was separated as colorless crystals, yield 3% and m.p. 221-222°C (methanol / chloroform). IR [υ [cm-1, KBr ]: 1590 (C=C), 1490 (enolate, carbonyl), 1310 and 870 [ P-N (CH2CH3)2]. 1H-NMR (500 MHz , δ ppm, CDC13) : 0.99 ( s, 3H , CH3), 1.38 - 1.43 (m, 6H, 2CH3), 1.62 - 1.86 (m, 2H, CH2), 2.33 (m, H, CH), 4.71 - 4.93 (m, 3H, CH3), 6.10 - 6.20 (s, 2H, CH2). 13C-NMR (125 MHz, δ ppm, CDC13) : 18.32 (CH3), 19.91 (2CH3), 26.95, 29.96 (2CH2), 39.75 (CH), 46.03 (C(CH3)2), 49.25 (C=CH3), 37.83 (N (CH3), 101.01 (C=O), 189.03 (C=O-P). 31P-NMR (δ, ppm, CDC13) : +38.73. MS m/z (%) 329 [M +](50). Anal. Calcd for C16H32N3O2P (329.22) : C , 58.34 ; H, 9.79 ; N, 12.76 ; P, 9.82. Found : C, 58.53 ; H, 9.43 ; N, 12.42 ; P, 9.82.

Similarly, 1,7,7 - trimethyl- bicyclo [2.2.1] heptane -2,3 - dione (1) react with tris(diethylamino)phosphine (3b) to give product 6b with 1,7,7- trimethyl-3- tris(diethylamino)phosphoniooxy bicyclo [2.2.1] hept-2-en-2-olate, using methanol / chloroform (5/95 , v/v). product 6b was separated as colorless crystals yield 67 % and m.p 234-235 °C (methanol / chloroform) . IR [υ [cm-1, KBr ]: 1585 (C=C), 1489 (enolate , carbonyl) 1312 and 875 (P-N (CH2CH3)2). H-NMR (500 MHz, δ ppm, CDC13) : 0.99 ( s, 3H , CH3 ), 1.03 ( s, 6H, 2CH3), 1.25 -1.43 (m, 2H, 2CH2), 1.62 – 1.86 (m, 2H, 2CH2), 2.33 (m, H, CH), 4.71 - 4.93 (m, 3H, CH3), 6.10 - 6.20 (s, 2H, CH2). 13C-NMR (125 MHz, δ ppm, CDC13) : 18.32 (CH3), 19.91 (2CH3), 26.95, 29.96 (2CH2), 39.75 (CH), 46.03 (C(CH3)2), 49.25 (C=CH3), 37.83 (N (CH3), 101.01 (C=O), 189.03 (C=O-P). 31P-NMR (δ, ppm, CDC13) : +38.73. MS m/z (%) 329 [M+](50). Anal. Calcd for C16H32N3O2P (329.22) : C , 58.34 ; H, 9.79 ; N, 12.76 ; P, 9.82. Found : C, 58.53 ; H, 9.43 ; N, 12.42 ; P, 9.82.
Reaction of trimethyl phosphate 4a with 3-(2-phenyldiazono) - 1,7,7 - trimethyl bicyclo[2.2.1] hept-2-en-ylphosphate (2c) - hept -2-one (2) 

Trimethyl phosphate (4a) (0.12 g, 1 mol) was added drop wise to a solution of compound 2 (0.25 g, 1 mol) in dry toluene (30 mL), and the reaction mixture was refluxed for 5 h. After evaporation the residue was applied to a silica gel column chromatography to give product 9a. 

1.86 (m, 2H, CH2), 2.35 (m, H, CH), 0.95, 1.35 (2t, 18H, P[N(CH2CH3)3]3), 2.85, 3.25 (m, 12H, P[N(CH2CH3)3]3). MS m/z (%) 413 [M'] (90), corresponding to the molecular formula C22H44N3O2P. Anal. Calcd: for C22H44N3O2P (413.58) : C, 63.89; H, 11.11; N, 10.49; P, 7.58. Found: C, 60.53; H, 8.21; N, 7.33; P, 7.93.

Similarly, 3-(2-phenyldiazono) -1,7,7 - trimethyl bicyclo [2.2.1] heptane -2 - one (2) reacted with triisopropyl phosphite (4c) to give 9c. Diisopropyl 1,7,7-trimethyl-3-(2-phenyldiazinyl)bicyclo[2.2.1] hept-2-en-ylphosphate (9c, C22H44N3O2P). Eluent: Petroleum ether / ethyl acetate (95/5, v/v). 

Product 9c was separated as colorless crystals, yield 65% and m.p 175 - 176°C. IR [v, cm-1, KBr]: 3325 (NH), 3269 (NH), 1600 (C=C) and 1255 (P=O). 1H-NMR (500 MHz, δ ppm, CDCl3): 0.98 (6H, 2CH3), 1.12 (s, 6H, 2CH3), 1.22 - 1.40 (m, 2H, CH2), 1.55 - 1.65 (m, 2H, CH2), 2.55 (m, H, CH), 2.13 [m, 12H (O)P(O–CH (CH3)2}], 3.43 - 4.73 [2m, 2H, (O)P(O–CH (CH3)2)], 7.25 - 7.42 (m, 5H, aromatics) and 11.10 (s, 1H, NH), 11.75 (s, 1H, NH). MS m/z (%) 422 [M'] (40). Anal. Calcd: for C22H44N3O2P (422.50): C, 60.54; H, 8.35; N, 6.63; P, 7.55.

Reaction of Lawesson's reagent (5) with 3-(2-phenyl hydradono) -1,7,7 - trimethyl bicyclo [2.2.1] heptane -2-thione (2c) - hept -2-one (2) 

A mixture of 5 (0.4 g, 1 mol), and 2 (0.25 g, 1 mol) in dry toluene (40 mL) was refluxed for 15 h. The reaction mixture was evaporated under reduced pressure and the residue was applied to a silica gel column chromatography, using petroleum ether/ethyl acetate as eluent to give products 10 and 11, respectively. The product 10, 1,7,7-trimethyl - 3 - (2- phenylhydrazono) bicyclo [2.2.1] heptane -2-thione (10, C16H30N2S). Eluent: petroleum ether/ethyl acetate (98/2, v/v). It was separated as yellow crystals yield 35% and m.p 75 - 76°C. IR [v, cm-1, KBr]: 3327 (NH), 3275 (NH), 1603 (C=C) and 1260 (P=O). 1H-NMR (500 MHz, δ ppm, CDCl3): 0.99 (6H, 2CH3), 1.15 (s, 6H, 2CH3), 1.22 – 1.40 (m, 2H CH2), 1.55 – 1.65 (m, 2H CH2), 2.56 (m, H, CH), 2.46 - 2.67 (m, 5H, aromatics) and 11.16 (s, 1H, NH), 11.76 (s, 1H, NH). MS m/z (%) 380 [M'] (55). Anal. Calcd for C16H30N2S (366.17): C, 70.55; H, 7.40; N, 10.28; S, 11.77. Found: C, 70.55; H, 7.42; N, 10.59; S, 11.65.
When heptanedione 1 is allowed to react with tris(dimethylamino)phosphate (3a) [8] without solvent was heated 5h to gave the open dipolar adduct 4,7,7 trimethyl -3-(2-phenylhydrazono) bicyclo [2.2.1] hept-2-en-2-olate (6a). Compound 6a were chromatographically pure and possess sharp melting point. The structure of compound 6a was identified for the following reasons: Elemental and mass spectral analyses for compound 6a corresponded to empirical formula of C_{16}H_{32}N_{3}O_{2}P. The IR of 6a (KBr, cm⁻¹) exhibited strong absorption bands at 1310,870 cm⁻¹ (P≡N) and absence of band at 1700 (C=O) camphor. The ¹H-NMR spectrum (in CDCl₃) of the adduct showed doublet centered at δ= 2.65 ppm (J_{HP} = 10.50 HZ) due to 18 H of the dimethylamino group attached to the phosphorus atom of the [N(CH₃)₂]₃ moiety [14]. The ³¹P-NMR spectrum of 6a exhibited signal at δ=+38.73 ppm (85% H₃PO₄). The formation of the open dipolar ion 6a might arise [15] by the nucleophilic attack of the phosphorus of 3a on the carbonyl carbon in heptanequinone 1. Our results rule out the possibility of the formation of compounds having the cyclic structure 7 since the latter would predict a negative value for the signal of ³¹P-NMR corresponding to the structure 7 (Scheme 2).

Similarly, the reaction of 1 with tris(diethylamino)phosphine (3b) proceeded without solvent to give chromatographically pure adduct 6b. Structure elucidation for compound 6b was attested by analytical and spectral data (cf. Experimental).

Next, the study was extended to include the behavior of 3-(2-phenylhydrazono) -1,7,7'-trimethyl bicyclo [2.2.1] heptane-2- one (2) toward trimethyl phosphite (3a) [16] in dry toluene proceeded at the reflux temperature to give a chromatographically pure 1:1 adduct formulated as dimethyl-1,7,7'-trimethyl-3-(2-phenylhydrazinyl) bicyclo [2.2.1] hept -2-en-2-ylphosphate (9a) (Scheme 3), was deduced from its elemental analysis, IR ¹H, ¹³C, ³¹P-NMR, and mass spectral data (cf. Experimental). Similarly 4b and 4c reacted with 2 to give dialkyl phosphate 9b and 9c respectively, in good yields (scheme 3). Structure assignments for 9b and 9c were substantiated on the basis of their elemental analysis and spectral data. (cf. Experimental)

A possible explanation for the course of the reaction of trialkylphosphites 3a-c with 2 was shown in Scheme 3. The reaction was assigned to proceed through an initial attack of the phosphorus reagents 3a-c at the most reactive center in 2 and led to the formation of the dipolar adduct 8. The reaction was accompanied with rapid hydrolysis by the presence of unavoidable moisture and elimination of one molecule of alcohol under the applied reaction conditions to afford the dialkyl phosphate products (9a-c) (Scheme 3).

Furthermore, this study was extended to include the reaction of Lawessen's reagent 5[7,11] with 2. It was found that, when one mole of 2 was allowed to react with one equivalent of 5 in refluxing toluene for 15 h. A mixture of 10 and 11 were obtained. Compounds 10 and 11 are chromatographically pure and possess sharp melting points. Compound 10 (yield 35%) was formulated as 1,7,7 trimethyl -3-(2-phenylhydrazono) bicyclo [2.2.1] heptane -2-thione based upon analytical and spectroscopic arguments (cf. Experimental). The second product 11 (yield 55%) was formulated as the thiated cyclic 2'(4-methoxyphenyl) - 4,7,7 - trimethyl -3'- (phenylamino)- 3H - spiro [ bicyclo [2.2.1] heptane -2,4 - [1,3,2] thiazaphosphodimine] - 3'-thione , for the following reasons: Elemental and mass spectral analyses for compound 11 corresponded to an empirical formula of C_{23}H_{27}N_{2}OPS_{3}. The structure assigned for compound 11 was based on the ³¹P-NMR shift at δ = +89.99 ppm (85% H₃PO₄), which corresponded to a cyclic structure [7, 17]. The IR spectrum of 11 (KBr, cm⁻¹) showed absence of bands at 1700 cm⁻¹ (C=O) and at 3480 cm⁻¹ (C≡N) of phenylhydrazone heptanone of compound 2. The ¹H-NMR spectrum of 11 (CDCl₃, δ ppm) revealed the presence of signals at 7.15 -7.95 ppm (m, 9H) corresponding to the aromatic protons and at 3.85 ppm (s, 3H, OCH₃). The ¹³C-NMR (CDCl₃, δ ppm) revealed absence of a signal of carbonyl group of the starting material 2 at 204.83 ppm (C≡O) and appear signal at 243.21 ppm (C≡S). The mass spectrum of 11 contained a prominent peak of M⁺ at m/z 474 (85%) which supported the thiated, cyclic structure 11. Compound 11 was formed via the thiation by usual manner and the addition of LR 5 to the carbonyl group (C≡O) and (C≡N) group of hydrazone of the starting material 2 (Scheme 4).
Scheme 1

Scheme 2
Scheme 3

Scheme 4
Conclusion

From the present study, it was shown that 1,7,7-trimethyl bicyclo[2.2.1]heptane-2,3-dione (1) reacted with tris(diarylaminophosphines) 3a,b to give the dipolar adducts 6a,b. On the other hand, 3-(2-phenylhydrazone)-1,7,7-trimethyl bicyclo[2.2.1]heptane-2-one(2) reacted with trialkylphosphite 4a-c to give phosphate 9a-c. Also, 2 reacted with LR 5 to give thiated product 10 and led to new thiated cyclic adduct 11. The different adducts whose structures vary according to the nature of the phosphorus reagents as well as on the stability of the addition products.

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Reference

12/12/2011