DIAZAPOLYCYCLIC COMPOUNDS XXVIII[1] . THE REACTION OF ACETYLATED TERPENOIDS WITH *DIAZAQUINONES*[2]

Fernando Gómez Contreras*, Manuel Lora-Tamayo°, and Ana Mª Sanz*

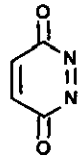
* Departamento de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense, 28040 Madrid, Spain

° Centro Nacional de Química Orgánica, C.S.I.C., Juan de la Cierva 3, 28006 Madrid, Spain

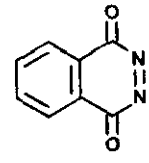
Abstract - The [4+2] cycloaddition reactions of diazaquinones 1-3 with 1,3-dienic systems obtained via the enol acetylation of carbonylic terpenoids are described.

In previous works we have been dealing with the synthesis and structural analysis of diazapolycyclic compounds obtained by [4+2] cycloaddition of pyridazine-3,6-dione (1), phthalazine-1,4-dione (2) and benzo[g]phthalazine-1,4-dione (3) with 1,3-dienes[3] . These reactions have led to otherwise not readily accessible heterocyclyc systems which could provide the framework for biologically active derivatives, since they can be considered as cyclic analogues of some enzymatic inhibitors[4] and benzo[g]phthalazine-1,4-dione adducts are also closely related to the aglycones of anthracycline antibiotics.

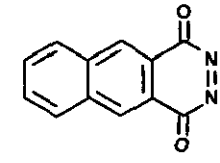
Although the diazapolycyclic skeleton is readily available from the diazaquinone, a major problem lies in the adequate functionalization of the new tetrahydropyridazine ring in order to design derivatives of potential biological interest. The range of dienes that have been used in these reactions is rather limited,



1



2



3

mainly because the unstable diazaquinone must be formed in the presence of the diene by oxidation of the corresponding cyclic hydrazide , and only simple dienes are not affected under the oxidative conditions required. Consequently, the functionalization must be achieved after the formation of the diazapolycyclic system. For this reason, we reported in a recent paper the use of terpenoid type dienes in order to obtain diazapolycycles containing unsaturated side-chains[6]. Attemps performed with neoalloocimene, alloocimene or myrcene gave good yields of the corresponding adducts, in which the double bond on the side-chain can be selectively functionalized whereas the tetrahydropyridazine ring remains unchanged.

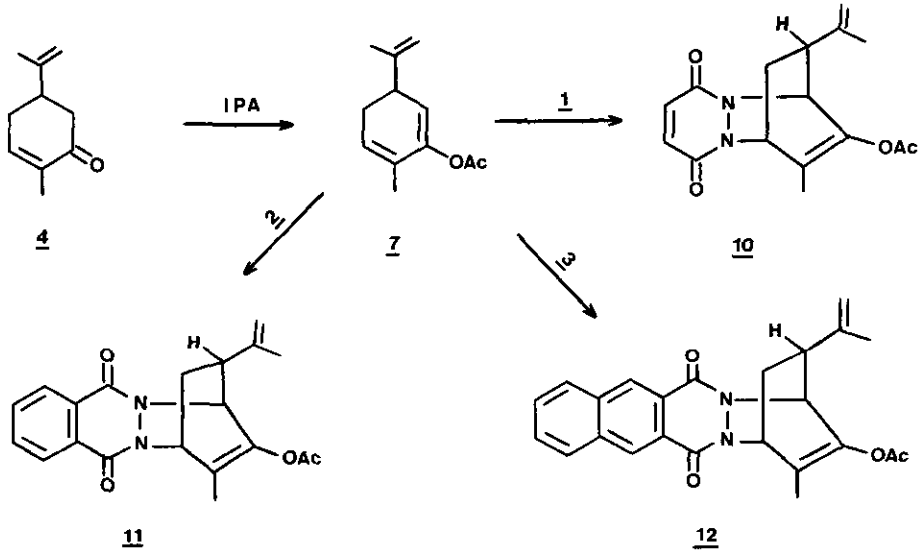
In connection with this work , we have now extended the scope of these cycloadditions to terpenoids containing an α,β-unsaturated carbonyl moiety which, by enol acetylation with isopropenyl acetate, afforded the required dienic function. Carvone (4), isophorone (5) and citral (6) were used as the starting compounds. Diazaquinones 1-3 were the dienophiles of choice. The dienic system was created as described in the experimental part. According to the usual procedures, the diazaquinones were formed "in situ" from the cyclic hydrazides. Oxidation of the 2,3-naphthalenedicarboxylic acid hydrazide to comp. 3 was performed with lead tetraacetate (LTA) in methylene dichloride at room temp, whereas tert-butyl hypochlorite (TBH) in acetone at -70 °C was used for the preparation of 1 and 2. A high degree of diene polymerization was only found for citral derivatives 9a-c. However, considerable amounts of diazaquinone polymers were detected in all the experiences performed. The most significative data concerning the cycloaddition reactions are summarized in Table I. See also Schemes 1-3.

The reaction of the carvone derivative 7 with diazaquinones 1-3 afforded 2-acetoxy-1,4-(1-isopropenyl)ethano-3-methyl-6,9-dioxo-1,4,6,9-tetrahydropyridazino-[1,2-b]pyridazine (10), 2-acetoxy-1,4-(1-isopropenyl)ethano-3-methyl-6,11-dioxo-1,4,6,11-tetrahydropyridazino[1,2-b]phthalazine (11) and 2-acetoxy-1,4-(1-isopropenyl)ethano-3-methyl-6,13-dioxo-1,4,6,13-tetrahydrobenzo[g]pyridazino[1,2-b]-phthalazine (12)[7]. In spite of the low yields obtained, analytical and preparative tlc showed that compounds 10-12 were the only products formed in amount enough for identification, the rest of the reaction mixtures mainly consisting of unreacted diene and diazaquinone polymers. This applies also to the other cycloadditions listed in Table I.

Table I. [4+2] Cycloaddition reactions

Diazaquinone	Terpenoid	Adduct	Oxidant	Time(h)	Yield(%)	mp(°C)
1	Carvone	10	TBH	3	16	166-168[a)]
2	Carvone	11	TBH	3	20	90-92[a)]
3	Carvone	12	LTA	24	36	170-172[a)]
1	Isophorone	13	TBH	3	11	234-236[b)]
2	Isophorone	14	TBH	3	13	151-152[b)]
3	Isophorone	15	LTA	24	23	156-158[b)]
3	Citral	16a/16b	LTA	24	15/12	176-178/98-99[c)]
3	Citral	16a/16c	LTA	24	8/8	176-178/120-121[c)]
3	α-Phellandrene	17	LTA	24	62	84-86[b)]

a) From acetone/H_2O. b) From ethanol. c) Rechromatographed, but not crystallised.

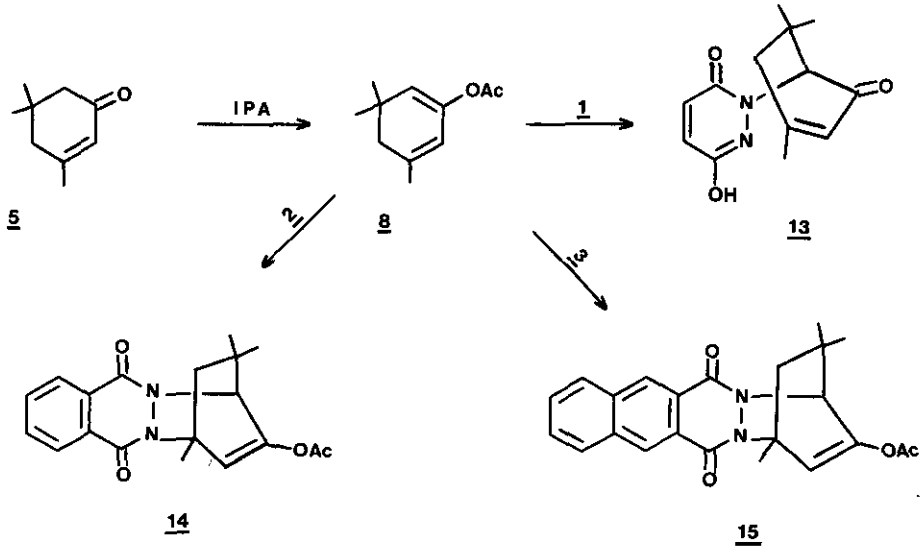


4 7 10 11 12

Scheme 1

The most relevant spectroscopic data for cycloadducts 10-17 are displayed in Tables II and III. The formation of the tetrahydropyridazine ring in compounds 10-12 is mainly supported by the ^1H nmr spectra, on the basis of the appearance of two multiplets between 5 and 6 ppm, which should be assigned to the methine hydrogens adjacent to nitrogen. The markedly low field position found in these

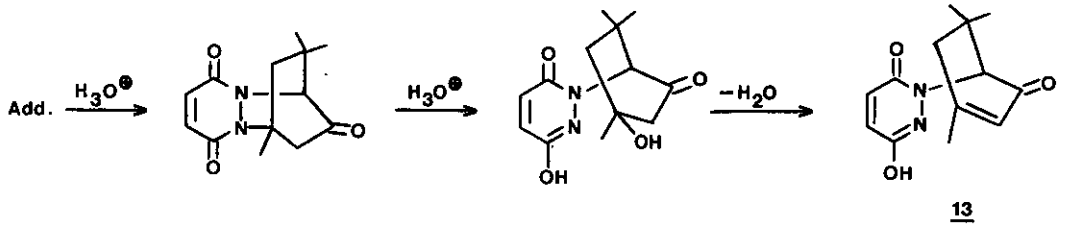
signals is due to the coplanarity of the methine hydrogens and the neighbouring carbonyl groups, compelled by the molecular geometry, and it is usually regarded as a distinctive feature of equatorial hydrogens vicinal to nitrogen in related diazapolycyclic adducts[8]. Furthermore, C_1 and C_4 appear in the off resonance ^{13}C nmr spectrum as two doublets with chemical shifts over 50 ppm, consistently deshielded with respect to the rest of the sp^3 carbon atoms.



Scheme 2

In a similar way, isophorone reacted with isopropenyl acetate to give 8, which was treated with 2 and 3 to give 3-acetoxy-1,4-(2,2-dimethyl)ethano-1-methyl-6,11-dioxo-1,4,6,11-tetrahydropyridazino[1,2-b]phthalazine (14) and 3-acetoxy-1,4-(2,2-dimethyl)ethano-1-methyl-6,13-dioxo-1,4,6,13-tetrahydrobenzo[g]pyridazino-[1,2-b]phthalazine (15) respectively. Compounds 14 and 15 exhibit in the ^1H nmr spectra a singlet at 5.24 and 5.22 ppm, referable to the only methine hydrogen adjacent to nitrogen, and indicative of the tetrahydropyridazine ring formation, whereas the low field shifts (2.02 and 2.03 ppm) found for the methyls vicinal to nitrogen can also be explained on the basis of its coplanarity with the C=O group. However, the reaction of 8 with pyridazine-3,6-dione resulted in the identification of 1-(2-oxo-4,6,6-trimethyl-3-cyclohexenyl)-3-hydroxypyridazin-6-one (13) as the only isolable reaction product. ^1H Nmr data of 13 are similar to those found in adducts 14 and 15, but the ethylenic H_3 moves downfield about 0.3 ppm, and the

methylene at C_5 is significantly more deshielded, since it is now close to a double bond. On the other hand, an allylic coupling of 1.5 Hz between the pseudo-axial hydrogen at C_5 and H_3 is observed in 13, but not in 14 or 15. Moreover, $J_{H_5H_5'}$ is larger in 13 (14.2 Hz) than in 14 or 15 (13.5 and 13.3 Hz respectively), in accordance with the well known fact that the magnitude of geminal couplings increases with the presence of vicinal double bonds[9]. The ^{13}C nmr spectrum of 13 shows a new carbonyl at 202.2 ppm, whereas the signals corresponding to C_2 and C_4 in 14 and 15 disappear, giving place to a singlet at 133.0 ppm that can be taken as if due to the ethylenic C_4. The broad absorption band at 2300-3300 cm^{-1} shown by the ir spectrum is usually indicative of tetrahydropyridazine ring opening in diazaquinone adducts[10].



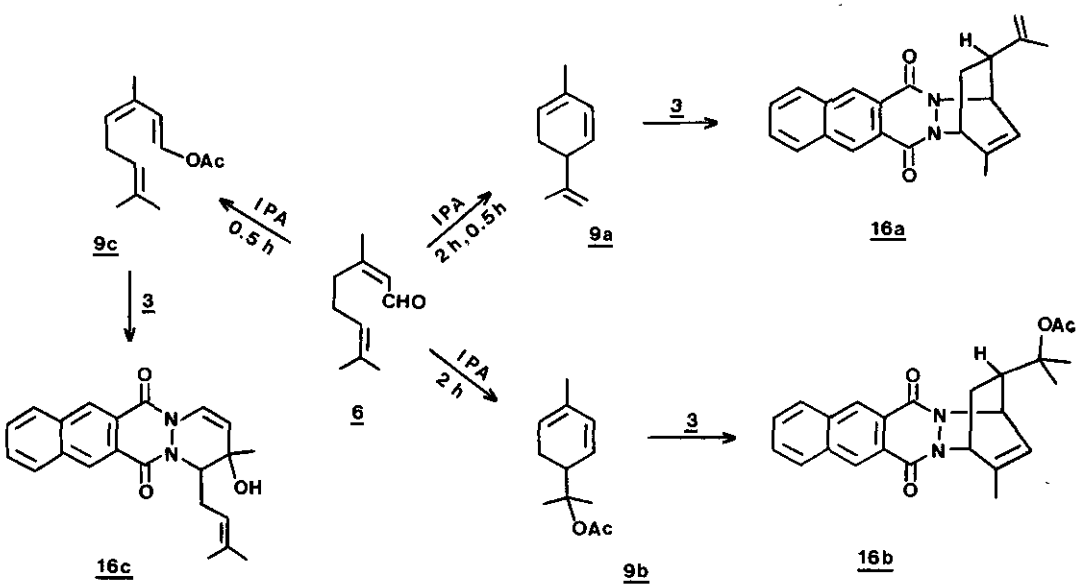
13

Scheme 3

Compound 13 should arise from the expected cycloaddition product by tetrahydropyridazine ring opening according to the sequence of Scheme 3, that involves hydrolisis of the enol acetate to the keto form and further ring opening in the acid medium to give a tertiary alcohol that is readily dehydrated to the α,β-unsaturated ketone 13. Tetrahydropyridazine ring opening of diazaquinone adducts in acid media is a side reaction previously reported for simple 1,3-butadiene derivatives[11]. On the other hand, conformational features of these and resembled heterocycles involve a very unfavourable steric interaction between the quasi-equatorial methyl at C_1 and the oxygen atom of the neighbouring amido group, that usually forces the substituents at C_1 to assume a pseudoaxial orientation[4,12]. For the same reason, cis-1,4-disubstituted adducts obtained in the reaction of trans,trans-2,4-hexadiene with diazaquinones adopt a boat-like conformation in spite of the unfavourable interactions created between both methyl groups[13]. Therefore, steric hindrance may account for the easy ring opening to 13. In fact, pyridazine-3,6-dione adducts are more readily opened than those obtained from

more conjugated diazaquinones.

Similar treatment of citral followed a more complex pattern. Acetylation under the same conditions as above (IPA, 2 h, 95 °C) and further distillation under vacuum of the crude product led to the isolation of a main fraction with features resembling those reported by Riser for the mixture of citral acetates[14]. The reaction of the acetylation product with benzo[g]phthalazine-1,4-dione under the conditions described in Table I afforded two presumable cycloadducts in 12 and 15% yields, together with a large amount of polymeric resins. After arduous purification that included several consecutive tlc separations, owing to the difficulty in removing the polymeric material, these two compounds could be isolated in purity enough for identification, and were assigned as 2-methyl-1,4-(2-isopropenyl)ethano-6,13-dioxo-1,4,6,13-tetrahydrobenzo[g]pyridazino[1,2-b]-phthalazine (16a) and 2-methyl-1,4-[2-(1-acetoxy-1-methyl)ethyl]ethano-6,13-dioxo-1,4,6,13-tetrahydrobenzo[g]pyridazino[1,2-b]phthalazine (16b)[7].



Scheme 4

Structural evidence mainly comes from the ^1H nmr spectrum, that in 16a presents five signals between 4.7 and 6.2 ppm. Two of them are singlets falling at 4.70 and 4.88 ppm, referable to the vinylic hydrogens at the isopropenyl group, and the remaining three, strongly deshielded, can be assigned as methinic vicinal to

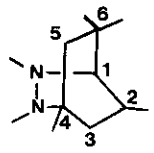
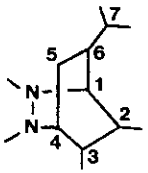


Table II. Relevant ^{1}H nmr data of cycloadducts and derivatives.

($CDCl_3$, TMS int., δ, ppm)

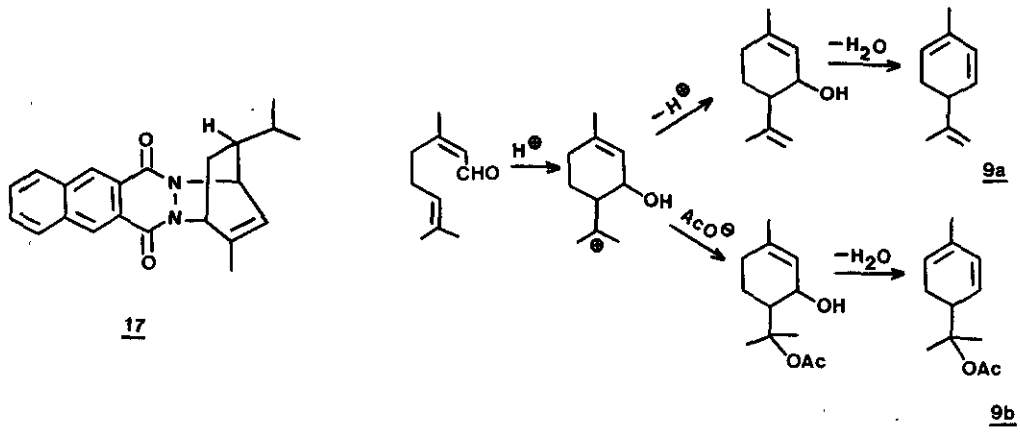


Compd.	H_1	H_2 or H_3	H_4	H_5	H_6	$Me_{C3 \text{ or } C4}$	$Me_{C6 \text{ or } C7}$		Coupling const. (Hz)
10	5.55(bs)	-	5.50(m)	2.30(o) 1.67(o)	2.72(m)	1.82(s)	4.60(s)[b] 4.82(s)[b]	1.78(s)	H_4-H_5=2.0, $H_4$$H_5$,=2.5, H_5-H_6=5.8, H_5,-H_6=5.5
11	5.80(m)	-	5.72(m)	2.36(o) 1.46(o)	2.82(m)	1.87(s)	4.70(s)[b] 4.92(s)[b]	1.82(s)	H_4-H_5=4.5, H_4-H_5,=2.3, H_5-H_6=7.2, H_5,-H_6=5.6
12	5.78(m)	-	5.72(m)	2.43(o) 1.74(o)	2.84(m)	1.83(s)	4.64(s)[b] 4.82(s)[b]	1.78(s)	H_4-H_5=4.5, H_4-H_5,=2.3, H_5-H_6=7.2, H_5,-H_6=5.6
13	5.30(s)	5.92(m)	-	2.92(q) 1.96(d)	-	1.92(s)	0.96(s)	1.18(s)	H_1-H_5=1.5, H_5-H_5,=14.2
14	5.24(s)	6.20(bs)	-	2.38(d) 1.77(d)	-	2.02(s)	1.04(s)	1.08(s)	H_5-H_5,=13.5
15	5.22(s)	6.16(bs)	-	2.45(d) 1.78(d)	-	2.03(s)	1.08(s)	1.10(s)	H_5-H_5,=13.2
16a	6.02(c)	6.18(m)	5.85(m)	2.43(o) 1.74(o)	2.93(m)	1.92(s)	4.88(s)[b] 4.70(s)[b]	1.78(s)	H_1-H_2=6.1, H_1-H_6=2.5, H_4-H_5=3.2, H_4-H_5,=1.5
16b	6.02(c)	6.14(m)	5.82(m)	2.30(o) 1.55(o)	2.68(m)	1.96(s)	1.38(s)	1.45(s)	H_1-H_2=6.1, H_1-H_6=3.2, H_4-H_5=3.3, H_4-H_5,=2.2
16c	7.60(d)	5.39(d)	4.90(t)	2.25(t)	5.29(t)	1.48(s)	1.25(s)	1.31(s)	H_1-H_2=8.1, H_4-H_5=8.3, H_5-H_6=8.3
17	5.88(c)	6.03(m)	5.62(m)	2.38(m) 1.45(m)	2.02(m)	2.05(s)	1.16(d)	1.16(d)	

a) For making easier the comparison of the chemical shifts in compounds 10-17, systematic numbering has not been followed. In the upper part of this Table there is a figure displaying the arbitrary numbering employed for ^{1}H and ^{13}C nmr data. Abbreviations: s=singlet, d=doublet, t=triplet, q=quartet , o=octet, m=multiplet, b=broad.

b) Vinylic protons.

nitrogen (H_1 , H_4) or ethylenic (H_2) hydrogens. Three more protons appear in the 1.7-3.0 range. Two of them are octets presumably belonging to a methylene group (J_{gem} = 12.0 Hz) and show couplings with H_4 (3.2 and 1.5 Hz). The third one is coupled to both (9.1 and 7.5 Hz) and to H_1 (2.5 Hz). Moreover, H_1 is also coupled to H_2 (6.1 Hz). Only two methyls linked to double bond (1.78 and 1.92 ppm) can be observed. Data found for 16b are very similar to these, the only difference being the presence of an acetoxy group and three methyls at 1.96, 1.45 and 1.38 ppm, whereas the vinylic hydrogens disappear. Definitive evidence for the proposed structures of 16a and 16b was obtained from the reaction of benzo[g]phthalazine-1,4-dione with α-phellandrene [2-methyl-5-(1-methyl)ethyl-1,3-cyclohexadiene], that afforded 1,4-[2-(1-methyl)ethyl]ethano-6,11-dioxo-1,4,6,13-tetrahydrobenzo-[g]pyridazino[1,2-b]phthalazine (17) in good yield. Spectroscopic data found for 17 are closely related to those discussed above for 16a and 16b, as can be seen in table II[7].

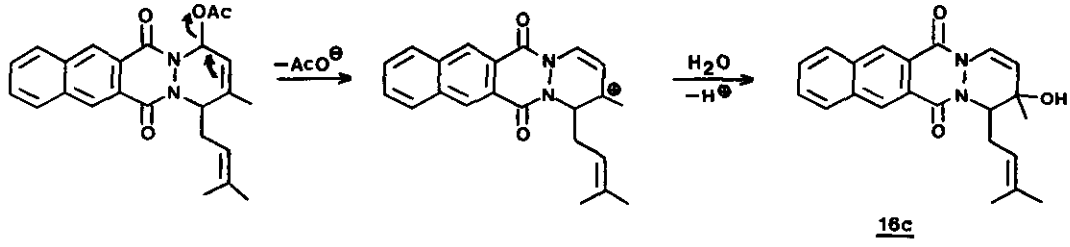


Scheme 5

Consequently, it seemed that 5-isopropenyl-2-methyl-1,3-cyclohexadiene (9a) and 5-(1-acetoxy-1-methyl)ethyl-2-methyl-1,3-cyclohexadiene (9b) were the real intervening dienes in the cycloaddition of the acetylated derivatives of citral. Reinvestigation of the acetylated mixture confirmed the presence of both 9a and 9b, together with a high percentage of p-cymene, surely formed by isomerization of 9a. These facts could be explained by considering that in the acid medium employed, cyclization of 6 to the p-menthadiene system occurs as shown in Scheme 5.

After that, dehydration of the two p-menthadiene derivatives to 9a and 9b takes place with isomerization of the double bond, in order to make trans elimination possible. A similar explanation has been proposed for the sulphuric acid catalyzed transformation of citral in p-cymene[15].

In a subsequent experience, the acetylation conditions were modified (IPA, 0.5 h, 60 °C), and a 1:1 mixture of 9a and the formerly desired diene 9c was obtained. The cycloaddition of the acetylated mixture with benzo[g]phthalazine-1,4-dione led to the isolation of 16a and a new compound which was not the expected product from 9c, but was identified as 4-(3-methyl-2-butenyl)-3-hydroxy-3-methyl-6,11-dioxo-3,4,6,13-tetrahydrobenzo[g]pyridazino[1,2-b]phthalazine (16c). Its ^{1}H nmr spectrum exhibits a doublet at very low field (7.60 ppm), usually indicative of double bond isomerization in diazaquinone adducts[16]. The expected signal at 4.90 ppm corresponding to the methine hydrogen vicinal to nitrogen is also observed. One of the three methyls is bonded to an sp^3 carbon atom (1.48 ppm), and the acetoxy group has been replaced by OH, as corroborated by ir data (Table III). According to the spectroscopic evidence, 16c appears as a sole product, and not as a mixture of diastereomers, but its stereochemistry could not be determined on the basis of the available data.



16c

Scheme 6

Compound 16c is assumed to be formed from the adduct of 3 and 9c via isomerization of the double bond towards the more conjugated 1,2 position with loss of the acetoxy group. This is an usual behaviour of diazapolycyclic adducts when treated in an acid solution[16]. Subsequently, the tertiary carbocation would be attacked by water to give 16c (Scheme 6).

Table III. Relevant spectral data of cycloadducts and derivatives

Comp.	Ms (m/z of M^+)	Ir (cm^{-1}, KBr)	^{13}C Nmr ($CDCl_3$, δ, ppm)[a]
10	302 (17%)	1750(C=O), 1650(C=O)	12: C_1=52.1, C_3=126.5, C_4=54.5, C_5=41.7, C_6=43.0, C_8=111.8, Me_{C3}=20.6, Me_{C7}=21.9
11	352 (8%)	1740(C=O), 1640(C=O)	
12	402 (12%)	1740(C=O), 1640(C=O)	13: C_1=60.6, C_2=202.2, C_3=126.5, C_4=133.0, C_5=35.7, C_6=46.4, Me_{C4}=21.9, Me_{C6}=25.2, 28.2
13	248 (32%)	2300-3500(NH)(OH), 1660(CO)	
14	340 (6%)	1740(C=O), 1640(C=O)	14: C_1=45.2, C_2=91.1, C_3=129.6, C_4=60.0, C_5=32.7, C_6=45.2, Me_{C4}=21.0, Me_{C6}=27.1, 27.4
15	391 (2%)	1740(C=O), 1640(C=O)	
16a	344 (8%)	1650(C=O), 1620(C=C)	16a: C_1=52.6, C_2=124.8, C_3=126.8, C_4=50.9, C_5=29.6, C_6=42.6, C_8=111.9, Me_{C3}=22.2.
16b	404 (23%)	1730(C=O), 1650(C=O)	
16c	362 (2%)	3400(OH), 1650(C=O)	16b: C_1=52.6, C_2=123.7, C_3=124.7. C_4=48.8, C_5=26.6, C_6=46.2, Me_{C3}=22.4, Me_{C7}=23.5, 24.5
17	346 (22%)	1645(C=O), 1620(C=C)	

a) For ^{13}C nmr numbering policies see footnote in Table II.

EXPERIMENTAL

Melting points were determined in open capillary tubes on a Gallenkamp apparatus and are not corrected. Ir spectra were recorded on a Perkin Elmer 257 instrument in potassium bromide pellets. ^1H Nmr spectra were obtained with Varian T60 and XL300 instruments, operating at 60 and 300 MHz. ^{13}C Nmr spectra were recorded either on Varian XL300 or FT80 spectrometers. TMS was used as internal standard. For mass spectra, a Hitachi Perkin Elmer RMV-6MG at 70 eV was employed. Elemental analyses were obtained by the Instituto de Química Orgánica del C.S.I.C. (Madrid) with a Perkin Elmer 240 analyzer. Analytical t.l.c. was performed on aluminium sheets coated with a 0.2 mm layer of silica gel $60F_{254}$ (Merck). Chromatographic separations were performed by preparative t.l.c. on 20×20 glass plates coated with a 2 mm layer of silica gel PF_{254} (Merck). The eluent was benzene/ethyl acetate in a 70/30 ratio for all the separations performed. Methylene dichloride was purified by sucessive washing with 5% sodium carbonate solution and water, dried over molecular sieve and then fractionated. Acetone was heated under reflux

with solid potassium permanganate, dried over anhydrous magnesium sulphate and fractionated. Lead tetraacetate was purified by crystallisation from acetic acid. tert-Butyl hypochlorite was freshly prepared from the corresponding alcohol by a standard procedure[17]. Potassium salts of the hydrazides were formed by heating the hydrazides in an aqueous solution containing equimolecular amounts of potassium hydroxide and evaporating to dryness.

General Procedure for Acetylation

To a mixture of 30 ml of isopropenyl acetate, 0.05 g of p-toluenesulphonic acid and 0.10 g of copper acetate, 0.1 mol of the terpenoid was added gradually over a period of 2 h. In the meantime, the acetone formed was distilled off continuously. When the theoretical amount of acetone had been removed, the crude product was flash distilled under vacuum (1-5 mm Hg). Redistillation of the flashed residue at 12-15 mm Hg afforded the corresponding enol acetates: 7 (bp: 60-66 °C, 6 h, 50% yield), 8 (bp: 80-82 °C, 2 h, 30% yield), 9a and 9b (bp: 65-70 °C, 2 h, 38% whole yield), 9a and 9c (bp: 62-70 °C, 0.5 h, 42% whole yield).

General Procedure for Cycloaddition

Method A: Lead Tetraacetate as the Oxidant.

To a cooled (0 °C) anhydrous methylene chloride suspension of the cyclic hydrazide (0.01 mol in 150 ml), 1 ml of acetic acid and 0.01 mol of the diene were added whilst stirring. After that, 0.01 mol of lead tetraacetate was added in small portions over a period of 1.5-2 h, and the reaction mixture was stirred at room temperature for several hours. During this addition a transient and very vivid colouration due to the formation of the diazaquinone was usually observed. The white precipitate formed was filtered off (lead acetate and diazaquinone polymer), and the filtrate was washed sucessively with aqueous 5% sodium bicarbonate and water, and dried over magnesium sulphate. The solvent was removed by rotary evaporation to give an oily residue. In order to take off the unreacted diene and part of the polymeric side-products, the residue was repeatedly washed with n-hexane. The remaining syrup was usually chromatographed under conditions that have been described above, and was crystallised from the solvents indicated in Table I.

Method B: tert-Butyl Hypochlorite as the Oxidant.

A stirred suspension of 0.01 mol of tert-butyl hypochlorite in 100 ml of anhydrous

acetone was cooled to -70 °C in a dry ice-acetone bath, and 0.001 mol of the hydrazide sodium salt was added to give a deeply coloured solution of the diazaquinone. After that, the mixture was stirred for 0.5 h and quickly filtered, while the temperature was maintained at -70 °C. A diene solution in anhydrous acetone (0.01 mol in 50 ml) was dropwise added until the solution became colourless. The resulting mixture was stirred at room temperature for several hours, and the solvent was eliminated under vacuum to give an oily residue, which was treated as described in method A.

Analytical data found (calcd) for cycloadducts and derivatives:

10 ($C_{16}H_{18}N_2O_4$): C, 63.74 (63.57); H, 6.25 (5.96); N, 9.48 (9.27)
11 ($C_{20}H_{20}N_2O_4$): C, 68.12 (68.18); H, 5.75 (5.68); N, 7.50 (7.95)
12 ($C_{24}H_{22}N_2O_4$): C, 71.81 (71.64); H, 5.54 (5.47); N, 7.30 (6.96)
13 ($C_{13}H_{16}N_2O_3$): C, 63.11 (62.90); H, 6.81 (6.45); N,11.54 (11.29)
14 ($C_{19}H_{20}N_2O_4$): C, 67.32 (67.06); H, 5.97 (5.88); N, 8.28 (8.23)
15 ($C_{23}H_{23}N_2O_4$): C, 70.94 (70.59); H, 5.88 (5.88); N, 7.21 (7.16)
16a ($C_{22}H_{20}N_2O_2$): C, 76.38 (76.74); H, 6.25 (5.91); N, 8.09 (8.14)
16b ($C_{24}H_{23}N_2O_4$): C, 71.37 (71.29); H, 6.18 (5.94); N, 6.86 (6.93)
16c ($C_{22}H_{22}N_2O_3$): C, 73.01 (72.93); H, 6.41 (6.08); N, 7.49 (7.73)
17 ($C_{22}H_{21}N_2O_2$): C, 76.72 (76.30); H, 6.27 (6.36); N, 8.32 (8.09)

ACKNOWLEDGEMENTS

Support of this work by a Grant from the Comisión Asesora de Investigación Científica y Técnica de la Presidencia del Gobierno of Spain (Project PB86-0570) is gratefully acknowledged. The authors also thank to Prof. M. Pardo Criado for helpful comments and criticism.

REFERENCES AND NOTES

1. Part XXVII of this series: L. Campayo, F. Gómez Contreras, and P. Navarro, J. Heterocyclic Chem., 1987, 24, 981.
2. Partly presented in the 11th International Congress of Heterocyclic Chemistry, Heidelberg, Germany, August 1987, Abstr. p. 47.
3. See, for example: F. Gómez Contreras and M. Lora-Tamayo, Heterocycles, 1979, 13, 389.
4. P.J. Gilbert and W.A. Thomas, J. Chem. Soc., Perkin II, 1985, 1077.

5. M. Quinteiro, C. Seoane, and J.L. Soto, Heterocycles, 1978, 9, 1771.

6. F. Gómez Contreras, M. Lora-Tamayo and A.M. Sanz, Heterocycles, 1987, 25, 193.

7. The stereochemistry of the substituents at C_5 or C_6 has been assigned in compounds 10-12, 16a-b and 17 by considering an exo addition of the dienophile. Coupling constants are not useful for this assignment, due to the geometry of the adducts. However, the ^1H nmr chemical shifts for the protons of these substituents do not show the shielding that would be expected if they were syn to the aromatic moiety (see table II, and also references cited below). They can therefore be ascribed to the anti positions, as would also be inferred from the obvious sterical preference for the diazaquinone towards a regiospecific approach from the molecular surface opposite to the isopropyl or isopropenyl group. These reasonings are in full accordance with those that can be found in the literature concerning the [4+2] cycloadditions of α-phellandrene and the menthatriene 9a. See, for example: B. Singaram and J. Verghese, J. Indian Chem. Soc., 1977, 54, 630; L.A. Paquette and R.F. Doehner, J. Org. Chem., 1980, 45, 5105; N.H. Buttrus, J. Cornforth, P.B. Hitchcock, A. Kumar, and A.S. Stuart, J. Chem. Soc. Perkin Trans. I, 1987, 851. On the other hand, optically pure (R)-(-)-carvone and (S)-(-)-α-phellandrene were used for the cycloadditions in order to prevent the formation of isomers.

8. F. Gómez Contreras and P. Navarro, J. Heterocyclic Chem., 1979, 16, 1035.

9. P. Sohar, "Nuclear Magnetic Resonance Spectroscopy", CRC Press, Florida, 1983, Vol. 1, p. 59.

10. M. Lora-Tamayo, P. Navarro, and J.L. Soto, Liebigs Ann. Chem., 1971, 748, 96.

11. M. Lora-Tamayo, P. Navarro, M. Pardo, and J.L. Soto, An. Quim., 1975, 71, 400.

12. a) G. Toth, I. Hermecz, and Z. Meszaros, J. Heterocyclic Chem., 1979, 16, 1181.
b) I. Hermecz, B. Podanyi, Z. Meszaros, J. Kokosi, G. Szasz, and G. Toth. ibid., 1983, 20, 93.

13. F.J. Lahoz, C. Foces-Foces, and F.H. Cano, Acta Cryst., 1986, C42, 467; C. Foces-Foces and F.H. Cano, ibid., 1987, C43, 1235.

14. A. Riser, Bull. Soc. Chim. France, 1953, 232, 570.

15. O. Zeitschel and H. Schmidt, J. Pr. Chem., 1932, 133, 370.

16. M.C. Cano, F. Gómez Contreras, and P. Navarro, An. Quim., 1980, 76C, 147.

17. H.M. Teeter and E.W. Bell, Org. Synth., 1952, 32, 20.

Received, 1st August, 1988