Tetrahedron Vol. 43, No 6, pp. 1161 to 1168, 1987
Printed in Great Britain.

0040-4020/87 $3.00+.00
Pergamon Journals Ltd.

THE REACTION OF SEVERAL TERPENE 1,3-DIENES WITH 4-METHYL-1,2,4-TRIAZOLINE-3,5-DIONE

BY ROLAND RIENÄCKER,[a] PNINA ASHKENAZI,[b] MOSHE KAPON,[b]
REINHARD BENN,[a] AND DAVID GINSBURG[b]

a) Max-Planck-Institut für Kohlenforschung, D-4330 Mülheim/Ruhr, BRD.
b) Department of Chemistry, Israel Institute of Technology,
Haifa 32000, Israel.

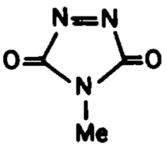
(*Received in UK* 3 *February* 1987)

Abstract.- Several 1,3-dienic terpenes of various structural types are attacked by the title dienophile from the less hindered side.

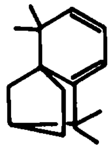
The regiospecificity of attack by methyl triazolinedione(MTAD), 1, upon 1,3-conjugated dienes belonging to the [2.2.2]bicyclooctane or the norbornane families has been shown to occur mainly from the more hindered side and explained by means of secondary interaction within the σ-π frame.[1] In view of the work of Gleiter, Paquette et al we studied a system containing the α-pinene skeleton and found the absence of any such interactions, i.e. nopadiene reacts with MTAD and PTAD from the less hindered side.[2] We now report results of other 1,3-dienic terpenes which all indicate that here too Diels-Alder attack occurs from the less hindered side. These are accompanied, in some cases, by products of the -ene reaction.

Seven terpenic substrates were investigated but results are reported for five of them 2-6.

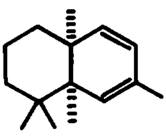
9,10-Dehydroisolongifolene 2 afforded with 1 at least four isolable products, 7-10. The MTAD reaction is relatively slow and is over after 3 min. The structures of 7-10 are shown.



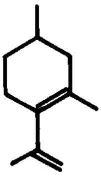
1



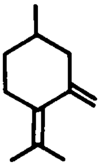
2



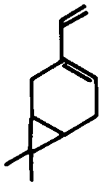
3



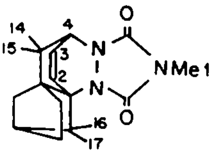
4



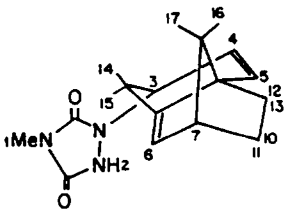
5



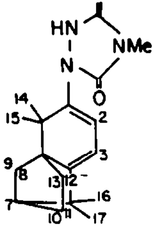
6



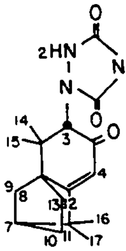
7



8



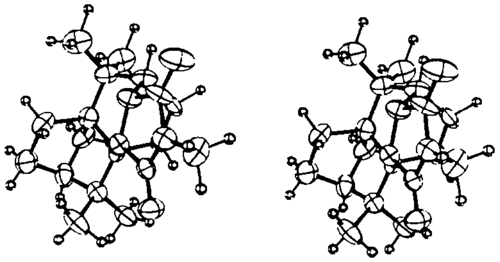
9



10

The Diels-Alder adduct 7 was the major product isolated (46%). The by-products were those of ene-reactions, 9 and 10 and 8, a rearrangement -ene product with the neoisolongifolane structure.

The ORTEP projections of 7, 8, and 10 are given below. The additional data obtainable from their NMR spectra are also given.

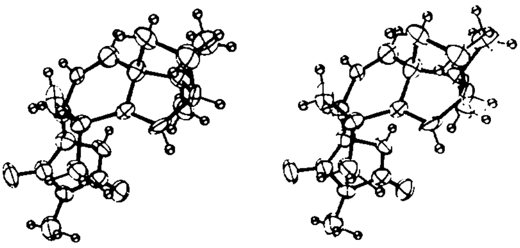


ORTEP of 7

No.	$\delta(^1H)$	
1	2.96	
2	6.66	
3	6.15	
4	4.16	
14	1.44	Bracketed assignment throughout can be mutually exchanged
15	1.28	
16	1.25	
17	0.86	

400 MHz NMR of 7

The numbering (see formula 7) is arbitrary for this and other products (cf formulae). Even the 400 MHz spectrum was too complex with insufficient material for a ^{13}C spectrum (within reasonable time). Only some structural elements are given in the above table. No NOE study was carried out because not all methylene protons were assigned.



ORTEP of 8

No.	δ(^{1}H)	J(H,H)			NOE
1	3.08				
2	6.47				
3	4.60	$J_{3,4}$ = 5.2			3 ⟶ 4,14,15
4	5.71	$J_{4,5}$ =10.1			
5	6.05	$J_{3,5}$ = -1.5			5 ⟶ 13,4
6	5.73	$J_{6,7}$ = 3.3			
7	2.40	$J_{7,10}$ =3.6	$J_{7,11}$ ≈0		7 ⟶ 10,6,16 or 17
10	1.95	$J_{10,11}$ =11.3	$J_{10,12}$ =3.4	$J_{10,13}$ = 8.9	10 ⟶ 11,7,16, or 17
11	1.09	$J_{11,12}$ = 9.1	$J_{11,13}$ =3.6		
12	1.18	$J_{12,13}$ = -11.7			
13	1.78				13 ⟶5!,12, no 3
14	1.18				
15	1.10				
16	0.93				
17	0.92				

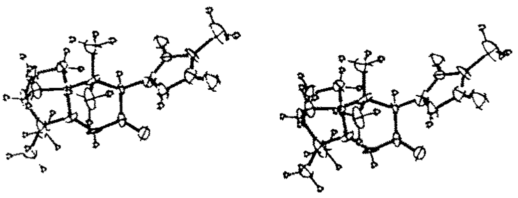
NMR of <u>8</u>

All ^{1}H assignments are unambiguous except for possible mutual exchange of 14 with 15 and 16 with 17. The argumentation for the stereochemistry (substituent at C adjacent to H-3 is quasi axial) is indirect. Since there are no NOE interactions of H-3 either with H-16 and H-17 or H-12 and 13, H-3 must point away from these methylene groups. In line with this interpretation is $^3J_{3,4}$ = 5.2 Hz, ruling out orthogonality of these protons. Yet, the argumentation is not unambiguous for from the spectrum of <u>10</u> one would expect an NOE from H-3 to H-12 if the other stereoisomer were present (see below).

Product <u>9</u> could unfortunately not be studied by X-ray crystallography because it was an oil. Although it was pure no stereochemical assignment could be performed since the NMR spectrum was too complex even at 400 MHz. It is fortunate however that a study of models does not leave much doubt as to the structure (cf. formula) of a substituted dehydroneoisolongifolene.

No.	δ(^{1}H)		NOE
1	3.10		1 ⟶ no effect
2	6.11	$J_{2,3}$ =5.8	2 ⟶ 3
3	5.49		3 ⟶ 2
7	1.92	$J_{7,10}$ =4.2	
8	1.28		
9	1.80		
10	1.48		
11	1.64		
12	1.23		
13	1.70		
14	1.05		
15	1.03		
16	1.13		
17	1.15		

NMR of <u>9</u>



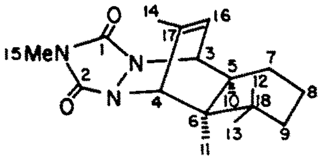
ORTEP of 10

No.	$\delta(^1H)$	J(H,H)
1	3.12	
2	7.49	
3	5.12	
4	5.80	
7	2.03	J(7,8) =1.6 J(7,9) =1.8; J(7,10) =4.0; J(7,11) =0
8	1.42	J(8,9) = -10.2
9	1.77	J(9,11) =2.7; J(9,12) =2.4
10	1.68	J(10,11) = -12.8; J(10,12) =5.2; J(10,13) =12.3
11	1.83	J(11,12) =9.0; J(11,13) =3.7
12	1.55	J(12,13) = -12.2
13	2.13	
14	1.17	
15	1.13	
16	1.12	
17	1.09	

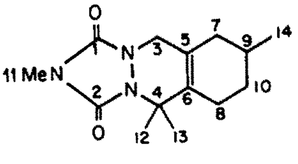
NMR of 10

Stereochemistry is unambiguous since clear NOE found for H-3 with H-12. This also has a connection to the assignment of the stereochemistry of 8 in solution where the corresponding NOE could not be observed.

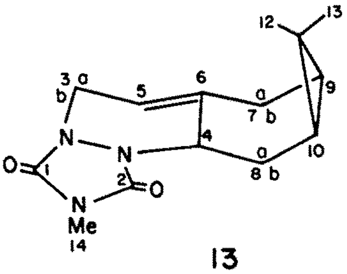
Thujopsene isomerizate 3,[4] reacts with 1 during 2 minutes and affords the Diels-Alder adduct 11 as an oil whose NMR data are given:



11



12



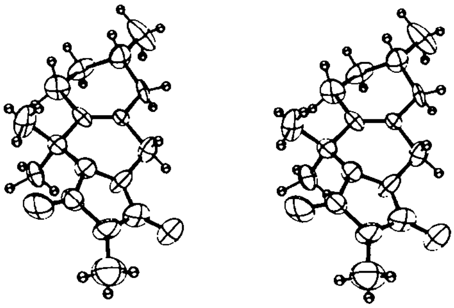
13

No.	(^{13}C)	Multiplicity	$^1J(C,H)$	$\delta(^1H)$	J(H,H)	NOE
1	159.49	s	—	—		
2	158.20	s	—	—		
3	64.99	d	152	4.10	$^3J_{3,16}$ ≈6.0	3 ⟶ 16
4	62.98	d	149	4.29	$^4J_{4,16}$ = -2.0	4 ⟶ 16
5 ⎫	43.95	s	—	—		
6 ⎭	40.14	s	—	—		
7 ⎫	32.60	t	127	1.1 and 1.2		
8 ⎬	16.16	t	130	1.2 and 1.3		
9 ⎭	31.70	t	128	1.3,1.3		
10	25.66	q	127	1.23		
11	20.27	q	127	1.16		
12 ⎫	29.63	q	125	0.97		
13 ⎭	28.05	q	120	0.97		12,13 ⟶ 14
14	20.69	q	127	1.94		14 ⟶ 16,4,12,13
15	25.40	q	142	2.99		
16	121.34	d	168	5.88	$^4J_{16,14}$ = -1.7	16 ⟶ 3
17	138.72	s	—	—		
18	35.94	s	—	—		

NMR of 11

^{13}C and ^1H assignments performed via 2D ^1H, ^{13}C shift correlation diagram. Brackets indicate that mutual exchange of the assignments is possible. Stereochemistry is assigned through NOE's. No NOE's exist between H-16 and 10, nor between H-14 and 11, which one would expect for alternative structure with angular methyls and boat shown in formula of 11 above reversed.

Although 3-methyl-mentha-3,8-diene. 4, gave a mixture of products which was not separated into its components, its isomer 5, isopropylidene-2-methyleno-4-methylcyclohexane gave the product 12 whose X-ray and NMR data are given. The former, 4, reacted within 5 minutes whilst the latter, 5, underwent instantaneous reaction with MTAD.



ORTEP of 12

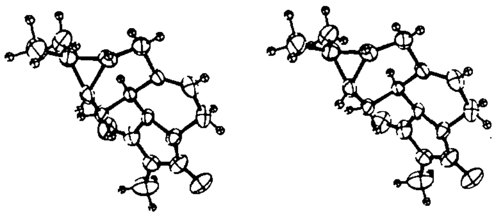
No.	(^{13}C)	(multip)	$^{1}J(C,H)$	$\delta(^{1}H)$
1	154.14	s	—	
2	153.94	s	—	
3	46.12	t	140	3.91 3.68 ^{2}J =15.6
4	61.49	s	—	
5	132.30	s	—	
6	121.41	s	—	
7	35.80	t	~124	
8	30.99	t	~126	from 1.0
10	25.91	t	~125	until 2.0
9	28.15	d	126	
11	24.90	q	141	3.06
12	23.24	q	129	1.64
13	22.30	q	128	1.43
14	21.44	q	123	0.99

NMR of 12

Numbers in brackets can be mutually exchanged.

The stereochemistry of reaction cannot be solved since in solution the molecule is more or less flat. Too many conformers need to be considered. Nevertheless the data obtained for 12 appears above. No detailed assignment has been made since only little of 12 was available.

We were able to isolate a product only of one out of three examples of a bicyclic substrate containing fused cyclohexane and cyclopropane rings. Although all three reacted instantaneously with MTAD, the isomeric 2-isopropenyl-2-carene and 4-isopropenyl-3-carene gave mixtures containing also rearranged products and were not separated. However, 7,7-dimethyl-3-vinyl-bicyclo[4.1.0]hept-3-ene, 6, gave the product of Diels-Alder reaction 13 whose X-ray and NMR data are given below.



ORTEP of 13

No.	(^{13}C)	multip	$^1J(CH)$	$\delta(^1H)$	J(H-H)	NOE
1 }	154.49	s	—	—		
2 }	152.93	s	—	—		
3	43.16	t	142	4.15, 3.81	^2J =-15.9	
4	53.02	d	140	4.12	$J_{4,8b}$ =10.3 $J_{4,8a}$ =7.1	
5	112.01	d	163	5.58	$J_{3a,5}$ =4.5	
6	135.49	s	—	—		
7	28.42	t	128	2.03, 2.68	^2J = -15.2 $J_{7a,9}$ =3.8	
8	26.74	t	130	1.74, 2.59	$J_{8a,10}$ =0	
9	22.19	d	158	0.91	$J_{9,10}$ =9.3	9 ⟶ 7b, 10
10	20.58	d	160	0.71	$J_{10,8b}$ =7.9 $^2J_{10a,10b}$ = -13.7	10 ⟶ 8b
11	17.95	s	—	—		
12	15.81	q	124	1.10	$J_{9,7b}$ =10.0	12 ⟶ 4, 8a, 7a
13	28.81	q	123	1.02		13 ⟶ 9, 10
14	25.00	q	140	3.08		

NMR of 13

Assignments of 1,2 could be reversed but all other ^1H and ^{13}C assignments are unambiguous. They were performed via a 2D ^1H, ^{13}C shift correlation diagram using the $^1J(C,H)$ couplings. The cyclopropane ring and H-4 are mutually cis. This is indicated both by J(H,H) couplings and by the NOE's. In particular, H-4 and H-8b are nearly antiparallel ($^3J_{4,8b}$ =10.3!) and H_{8a} and H_{10} are orthogonal ($J_{8a,10}$ ~ 0). Using NOE's, assignments for H-12 and H-13 can be performed unambiguously. However H-12 shows NOE interactions with H-4, clearly indicating that the cyclopropane ring and H-4 point to one another. The structure in solution is in complete agreement with the above ORTEP projection of 13.

Observation of the above ORTEP projections, readily shows that no secondary orbital interactions may be invoked in these substrates for their mode of reaction with MTAD, in contrast to the cases studied by Paquette and Gleiter.[1]

Experimental

Infrared spectra were measured using a Perkin-Elmer 298 spectrophotometer. ^1H NMR spectra were measured using a Bruker 400 MHz instrument. Mass spectra were measured using a Varian MAT 711 spectrometer. M.p.'s are uncorrected.

Reaction of 2 with MTAD.- A solution of 2, 98.4% purity, $[\alpha_D^{20}]$ -433.6°, n_D^{20} 1.5100, d_4^{20} 0.9386 (650 mg) in CH_2Cl_2 (20 ml) was treated with a solution of MTAD (364 mg) in CH_2Cl_2 (30 ml) The color of the dienophile disappeared after 3 min at r.t. After removal of solvent the solid soluble in benzene-hexane (81%) was purified on prep silica plates with acetone (15): hexane(85) as eluent. The mixture (824 mg) gave fractions of 7 (384 mg; 46.6%), 8 (264 mg; 32%), 9 (130 mg; 15.8%), and 10 (46 mg; 5.6%).

Compound 7 had m.p. 110-111° (pentane). IR($CHCl_3$): 1775, 1720, 1470 cm^{-1}. MS: 315 (M^+, 100); 201 (19); 179 (7); 159 (44); 157 (22); 155 (26); 145 (82); 131 (22). M.W. $C_{18}H_{25}N_3O_2$ Calc 315.1946, found 315.1933. Sample for X-ray analysis crystallized from cyclohexane.

Compound 8 had m.p. 170-171° (benzene). IR($CHCl_3$): 1340, 1780, 1715, 1480 cm^{-1}. MS: 315 (1); 201 (36); 173 (12); 159 (21); 157 (7); 145 (100); 131 (6); 115 (6). M.W. Found 315.1817.

Compound 9 was an oil. IR($CHCl_3$): 3380, 1780, 1720, 1480 cm^{-1}. MS: 315 (M^+, 100); 300 (23); 272 (20); 258 (22); 246 (11); 244 (50); 232 (55); 201 (18); 159 (29); 157 (26); 145 (64); 144 (22). M.W. Found 315.1965.

Compound 10[3] had m.p. 188-190° (CH_2Cl_2-hexane, red color at m.p.). IR($CHCl_3$): 3340, 1800, 1780, 1720, 1680, 1480, 1380 cm^{-1}. MS: 331 (M^+, 100); 316 (22); 260 (10); 219 (16); 217 (16); 203 (34); 201 (15); 161 (34). M.W. $C_{18}H_{25}N_3O^3$. Calc 331.1895, found 331.1884.

Reaction of 3 with MTAD.- A CH_2Cl_2 (20 ml) solution of diene 3, purity ~99%, $[\alpha]_D^{20}$-177.4°, n_D^{20} 1.5074, (545 mg) was treated with MTAD (302 mg) in CH_2Cl_2 (30 ml). The color disappeared after 2 min. The benzene-hexane soluble fraction gave 11 (677 mg; 80%). It was crystallized for X-ray analysis, m.p. 130-132° (hexane). 11: IR($CHCl_3$): 1770, 1715, 1480 cm^{-1}. MS: 317 (M^+, 11); 179 (100); 133 (18); 119 (23); 115 (3). M.W. $C_{18}H_{27}N_3O_2$ Calc 317.2103 found 317.2102.

Reaction of 5 with MTAD.- A CH_2Cl_2 (20 ml) solution of 5, purity 97.7%, n_D^{20} 1.4832, d_4^{20} 0.8434 (616 mg) instantaneously decolorized a solution of 1 (464 mg) in CH_2Cl_2 (30 ml). An oil was obtained. Elution with hexane (85)-acetone (15) from a prep silica plate gave a product, 12, which had m.p. 54-56°. 12: IR($CHCl_3$): 1770, 1715, 1470 cm^{-1}. MS: 263 (M^+, 40); 248 (100); 191 (19); 163 (7); 149 (11); 115 (2). M.W. $C_{14}H_{21}N_3O_2$ Calc 263.1633 found 263.1619.
12 was obtained in 87% yield but was accompanied by one by-product whose structure was not determined.

Reaction of 6 with MTAD.- 6, purity 99.1%, $[\alpha]_D^{20}$, -12.3°, n_D^{20} 1.5088, d_4^{20} 0.8939 (547 mg) and 1 (418 mg) in CH_2Cl_2 (20 and 30 ml, respectively) reacted instantaneously (96%). The product, 13, was purified on a silica column using hexane(9)-ethyl acetate(1) and was crystallized (hexane), m.p. 106-107°. IR($CHCl_3$): 1780, 1715, 1480, 1460, 1410, 1030 cm^{-1}. MS: 261 (M^+, 100); 218 (7); 204 (5); 192 (4); 179 (73); 146 (15). M.W. $C_{14}H_{19}N_3O_2$ Calc 261.1476 found 261.1453.

The full crystallographic data will be published elsewhere.[5]

References

1. For review see D. Ginsburg, *Tetrahedron, 39, 2095* (1983) and references to many papers by R. Gleiter and L.A. Paquette *et al.* cited therein.
2. P. Ashkenazi, R. Benn, and D. Ginsburg, *Helv. Chim. Acta, 67, 583* (1984).
3. *Cf.* R.M. Wilson, K.A. Schnapp, R.K. Merwin, R. Ranganathan, D.L. Moats, and T.T. Conrad, *J. Org. Chem., 51,4028*(1986), and refs. 11 and 12 therein.
4. A new sesquiterpene, obtained by K/Al_2O_3 - catalyzed isomerization of thujopsene, R. Rienäcker, unpublished results.
5. M. Kapon, unpublished results.