Synthesis of Heterocyclic Propellanes *via* 1,3-Dipolar Cycloaddition Reactions to Bicyclo[5.3.0]dec-1(7)-en-2-one [1]

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The synthesis of several heterocyclic propellanes *via* 1,3-dipolar cycloaddition reactions of arylnitrile oxides, diarylnitrilimines and arylazides with bicyclo[5.3.0]dec-1(7)-en-2-one is described and the spectral properties of the obtained propellanes are discussed. The cycloadditions are also examined on the basis of frontier molecular orbitals (FMO) of the reacting species.

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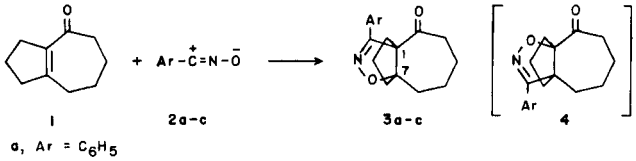
Although 1,3-dipolar cycloaddition is a generally useful method for five membered heterocyclic ring synthesis, it has not been used for the synthesis of heterocyclic propellanes, an interesting class of compounds [2]. To the best of our knowledge, until recently, only one 1,3-dipolar cycloaddition reaction of phenyl azide with a norbornene derivative leading to a heterocyclic propellane was referred in the literature [3], whereas the use of the analogous Diels-Alder type reactions is the fundamental synthetic approach for the preparation of alicyclic propellanes. In connection with our former studies [4,5] on 1,3-dipolar cycloaddition reactions, this kind of reaction was examined as a possible synthetic route for heterocyclic propellanes.

Recently, in our previous paper [6] we have reported the synthesis of propellanes *via* 1,3-dipolar cycloaddition of nitrile oxides to bicyclo[5.3.0]dec-1(7)-en-2-one (**1**). In this paper we give the details with some additional data confirming the proposed structures and we also report some new reactions of ketone **1** with diaryl nitrilimines and aryl azides.

Arylnitrile oxides **2a-c** reacted with ketone **1** to give 10-aryl-8,9-oxaza[5.3.3]propell-9-en-2-ones **3a-c** in moderate yields (25-32%).



1 2a-c 3a-c 4

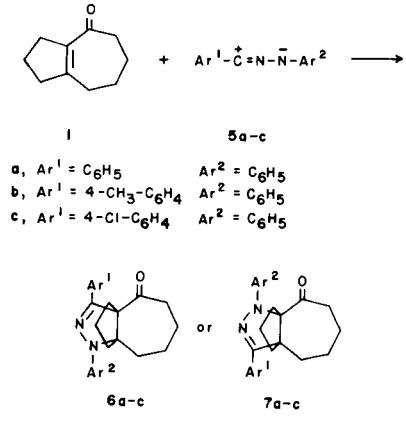
a, Ar = C_6H_5
b, Ar = 2, 4, 6-$(CH_3)_3$-C_6H_2
c, Ar = 2, 6-Cl_2-C_6H_3

On the basis of data for the regiochemistry of cycloaddition of nitrile oxides with cycloalkenones [7] and on FMO considerations [6] the isolated propellanones were considered as the regioisomers of type **3** instead of the possible regioisomers of type **4**.

A further supporting evidence for the proposed structure **3** was the ^{13}C-nmr spectrum of **3b** in which the C_1 and C_7 resonated at 79.1 and 98.7 respectively [8]. The chemical shifts for C_1 and C_7 of the regioisomer **4** should be at ~110 and 50-60 ppm respectively, according to the chemical shifts of analogous compounds [9,10].

The proposed structure **3** was finally confirmed from the X-ray crystallographic analysis [11] carried out on compound **3c**. The clinographic projection of the propellanone **3c** is given in Figure 1. Compound **3c** crystallizes in space group monoclinic $P2_{1/c}$ with z = 4 and cell constants α = 6.8944(8), b = 10.941(1), c = 20.431(6) Å, β = 95.59(2)°. The structure was refined to a final R = 0.073 value.

Ketone **1** reacts also with diaryl nitrilimines, resulting one of the two possible regioisomeric propellanones 8,10-diaryl-8,9-diaza[5.3.3]propell-9-en-2-one (**6**) or 8,10-diaryl-9,10-diaza[5.3.3]propell-8-en-2-one (**7**) in moderate yields (38-57%). The reactions took place in benzene solution by refluxing for 48 hours. The isolated propellanones give



1 5a-c

a, Ar^1 = C_6H_5 Ar^2 = C_6H_5
b, Ar^1 = 4-CH_3-C_6H_4 Ar^2 = C_6H_5
c, Ar^1 = 4-Cl-C_6H_4 Ar^2 = C_6H_5

6a-c 7a-c

satisfactory elemental analyses and spectroscopic data (ir, nmr, ms) which are summarized in Table. Thus, in the ir they give the carbonyl absorption at 1700-1705 cm^{-1}, whereas in the mass spectra the molecular ion is in all cases the base peak. There is also a series of common peaks $(M-28)^+$, $(M-57)^+$, $(M-71)^+$, $(M-83)^+$ resulting mainly from the fragmentation of the cycloheptanone ring.

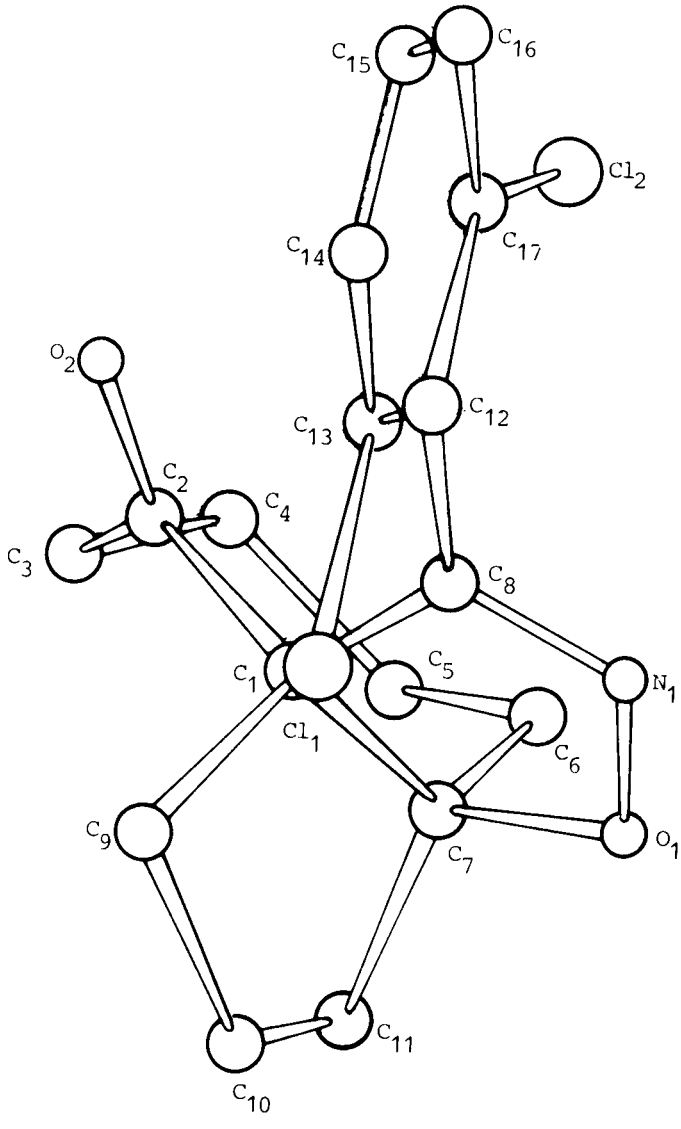


Figure 1

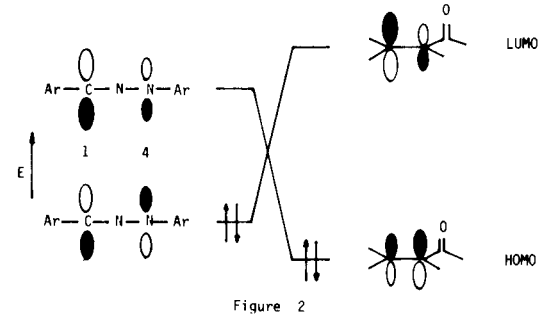
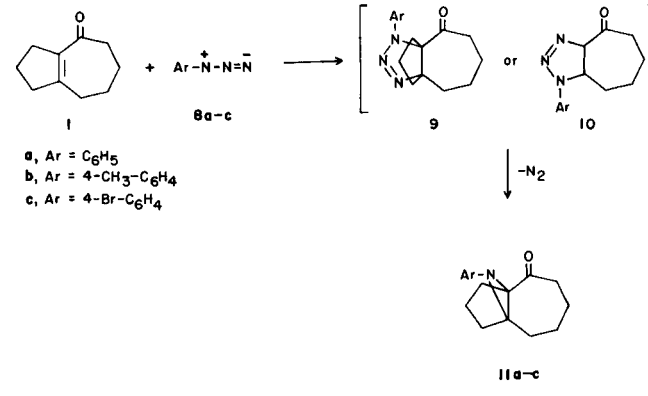


Figure 2

Reactions of ketone **1** with arylazides **8** lead to the formation of 11-aryl-11-aza[5.3.1]propellan-2-ones **11** in moderate yields (20-29%). The reactions took place in benzene solution after prolonged heating for 130 hours. The isolated propellanones are considered to be formed through thermal decomposition of the initial cycloaddition product **9** or **10**. Formation of aziridines through nitrogen abstraction is a common thermal or photochemical decomposition path of triazoles formed by cycloaddition of



1 8a-c 9 10

a, Ar = C_6H_5
b, Ar = 4-CH_3-C_6H_4
c, Ar = 4-Br-C_6H_4

11a-c

The present experimental data do not permit any unambiguous assignment between the two possible regioisomers. Predictions from FMO theory for the regiochemistry of the reactions are not very clear in the case of nitrilimines because of the uncertainty about the relative magnitude of ^{C}N and the ^{C}C at the HOMO of the nitrilimines. Taking into account the more recently accepted view that ^{C}C is slightly bigger than ^{C}N [7,12] and according to Houk's approximations [13] the diagram of frontier molecular orbital interaction for **1** and **5** must be as in Figure 2. From Figure 2 the reaction is probably HOMO, LUMO dipole controlled because both interactions correspond to almost equal energy differences. Since each interaction leads to a different regioisomer the formation of both regioisomeric propellanones **6** and **7** is possible.

azides [14,15]. The analytical and spectral data of propellanones **11**, summarized in Table, are in accordance with the proposed structure. In the ir they give the carbonyl absorption at 1685 cm^{-1}. In the mass spectra the molecular ion is the base peak in all cases. There is also a series of common peaks formed by fragmentation of cycloheptanone and cyclopentane ring resulting in the $ArNH_2^{+\cdot}$ fragment.

From the above presented results it seems that 1,3 cycloaddition is a rather promising reaction pathway for the formation of heterocyclic propellanes. The extension of the scope of the reaction with other dipoles and other bicyclic unsaturated compounds is under further consideration.

Table

Analytical and Spectral Data of **3**, **6-7** and **11**

Compound	Mp (°C) Recrystallization solvent	Yield %	IR (Nujol, cm^{-1}) ν C=O	^1H NMR (Deuteriochloroform, δ)	MS, m/z (RI %)	Molecular Formula (MW)	Analysis % Calcd./Found C	H	N
3a	80-83 (ethyl ether)	25	1705	0.97-3.27 (m, 14H), 7.08-7.72 (m, 5H)	269 (97) M+, 259 (9), 103 (17), 77 (100), 41 (56), 39 (52)	$C_{17}H_{19}NO_2$ (269.63)	75.81 75.68	7.11 6.98	5.20 4.99
3b	115-117 (ethyl ether)	30	1700	1.07-2.93 (m, 23H), 6.65 (broad singlet, 2H)	311 (80) M+, 294 (35), 161 (55), 150 (35), 41(100), 39 (92)	$C_{20}H_{25}NO_2$ (311.41)	77.13 76.99	8.09 8.09	4.50 4.28
3c	135-137 (ethyl ether)	32	1710	1.17-2.93 (m, 14H), 7.17-7.48 (m, 3H)	341/339/337 (1,5) M+ 324/322/320 (4), 191/189/187 (27), 150 (52), 41 (89), 39 (100)	$C_{17}H_{17}Cl_2NO_2$ (338.23)	60.36 60.06	5.07 4.95	4.14 3.98
6a-7a	139-140 (petroleum ether)	38	1700	1.03-3.00 (m, 14H), 6.75-8.00 (m, 10H)	344 (100) M+, 316 (60), 287 (19), 273 (33), 261 (20), 77 (31)	$C_{23}H_{24}N_2O$ (344.44)	80.20 79.98	7.02 7.03	8.13 8.08
6b-7b	Oil	57	1705 [a]	0.90-2.92 (m, 17H), 6.42-7.90 (m, 9H)	358 (100) M+, 330 (58), 301 (18), 287 (37), 275 (31), 91 (35), 77 (53)	$C_{24}H_{26}N_2O$ (358.46)	80.41 80.53	7.31 7.47	7.82 7.58
6c-7c	Oil	42	1705 [a]	0.63-3.41 (m, 14H), 6.30-8.11 (m, 9H)	380/378 (100) M+, 352/350 (25), 323/321 (10), 309/307 (19), 297/295 (20), 256/254 (40), 139 (29), 137 (53)	$C_{23}H_{23}ClN_2O$ (378.89)	72.90 73.01	6.13 5.98	7.39 7.29
11a	60-62 (ethanol)	20	1685	0.76-3.26 (m, 14H), 6.51-7.45 (m, 5H)	241 (100) M+, 186 (71), 172 (74), 130 (90), 93 (42), 77 (99)	$C_{16}H_{19}NO$ (241.32)	79.63 79.74	7.94 8.03	5.80 5.88
11b	86-87 (ethanol)	29	1685	0.78-3.28 (m, 14H), 2.27 (s, 3H), 6.66 & 7.04 (two d, J = 9 Hz, 4H)	255 (100) M+, 200 (57), 186 (52), 144 (48), 107 (32), 91 (34)	$C_{17}H_{21}NO$ (255.35)	79.96 80.09	8.29 8.36	5.49 5.25
11c	117-118 (ethanol)	21	1685	1.01-3.21 (m, 14H), 6.64 and 7.35 (two d, J = 9 Hz, 4H)	321/319 (100) M+, 266/264 (57), 252/250 (49), 210/208 (47), 173/171 (22), 157/155 (29)	$C_{16}H_{18}BrNO$ (320.23)	60.00 59.88	5.66 5.50	4.37 4.21

[a] Neat.

EXPERIMENTAL

All melting points are uncorrected and they were obtained with a Kofler hot stage apparatus. The ir spectra were obtained with a Perkin-Elmer Model 297 spectrophotometer. The nmr spectra, reported in δ units, were obtained with a Varian A-60A spectrometer with tetramethylsilane as internal standard. The mass spectra were measured with a Hitachi-Perkin-Elmer Model RMU-6L spectrometer, with an ionization energy of 70 eV. Elemental analyses were performed with a Perkin-Elmer analyzer Model 240-B.

Preparation of Starting Materials.

Bicyclo[5.3.0]dec-1(7)-en-2-one (**1**) was prepared from cyclodecane-1,6-dione by treating with formic acid [16]. Mesitonitrile oxide (**2b**) and 2,6-dichlorobenzonitrile oxide (**2c**) were prepared according to known procedures [17] from the corresponding aldoximes with *N*-bromosuccinimide and triethylamine. Benzonitrile oxide (**1a**) and nitrilimines **5a-c** were prepared *in situ* with triethylamine from benzhydroximic acid chloride [18] and the corresponding *N*-phenylarylhydrazidoyl chloride [19] respectively. Arylazides **8** were prepared from the corresponding arylhydrazines by a known procedure [20].

General Procedure for the Reactions.

In the reactions of ketone **1** with the stable 1,3-dipoles **2b, 2c, 8a, 8b** and **8c**, a solution of **1** (1 mmole) and of the 1,3-dipole (2 mmoles) in chloroform (reactions with **2b, 2c**) or benzene (reactions with **8a, 8b, 8c**) is refluxed for 48 hours (reactions with **2b, 2c**) or 130 hours (reactions with **8a, 8b, 8c**). After the evaporation of the solvent the reaction mixture is chromatographed on a silica gel column with benzene (reactions with **2b, 2c**) or a mixture of hexane ethyl acetate 9:1 (reactions with **8a, 8b, 8c**) as eluant.

In the reactions of ketone **1** with the unstable dipoles **2a, 5a, 5b** and **5c**, the 1,3-dipole is liberated *in situ* during the reaction. Thus, in the case of **2a** an ether solution of **1** (1 mmole) and benzhydroxamoyl chloride (2 mmoles) in the presence of triethylamine is allowed to stay at room temperature for 3 days whereas in the case of **5a, 5b** and **5c** a benzene solution of **1** (1 mmole) and the corresponding *N*-phenylarylhy-

drazidoyl chloride (2 mmoles) in the presence of triethylamine (2 mmoles) is refluxed for 48 hours. After the removal of the precipitated triethylamine hydrochloride by filtration and evaporation of the solvent, the residue is chromatographed on a silica gel column with benzene as eluant.

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