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REACTION OF 3-METHYLENEDIHYDRO-(3*H*)FURAN-2-ONE WITH DIAZOALKANES. SYNTHESES AND CRYSTAL STRUCTURES OF SPIRANIC CYCLOPROPYL COMPOUNDS

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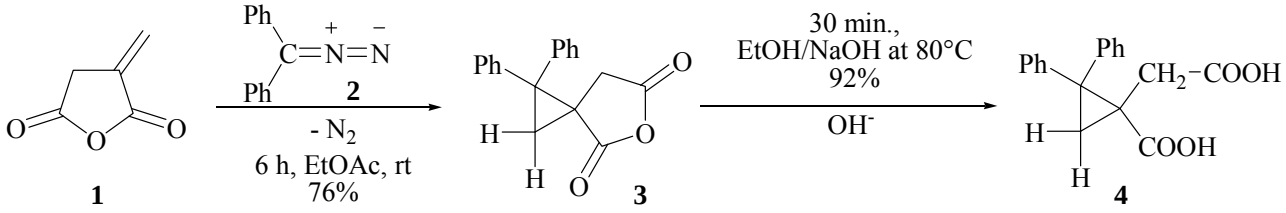
Abstract -The [3+2] cycloaddition of diphenyldiazomethane (**2**) (*1,3-dipole*) with 3-methylenedihydro-(3*H*)furan-2-one (**5**) as dipolarophile leads to the spiranic cyclopropyl derivative 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane (**8b**). Compound (**8b**) originates from an initially formed Δ^1-pyrazoline intermediate (**7**) and/or (**7'**) subsequent rearrangement after N_2 extrusion. The addition of hydroquinone to the reaction medium during the synthesis has an significant effect on the [3+2] cycloaddition yield and leads to isolation of the adduct (**8a**), in which hydroquinone bridges two 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane units through hydrogen bonds. The molecular structures of (**8a,b**) have been ascertained by X-ray crystallography. In contrast, the [3+2] cycloaddition of ethyl diazoacetate (**6**) with the dipolarophile (**5**) leads to the spiranic Δ^2-pyrazoline compound 3'-ethoxycarbonylspiro-Δ^2-pyrazolino[5':3]dihydro-(3*H*)furan-2-one (**10**) *via* a prototropic rearrangement (hydrogen shift) of an initially formed Δ^1-pyrazoline intermediate (**9**).

INTRODUCTION

α-Methylene-γ-butyrolactones constitute a class of natural compounds with potential antitumoral,

cytotoxic, allergenic, phytotoxic and antimicrobial properties.[1] Several methylene-lactones were found to act as drugs either under their native form[1] or after chemical modifications.[2a-c] The transformation of a reactive function into a five-membered heterocycle by 1,3-dipolar [3+2] cycloaddition is a widespread synthetic route.[3] For example, the use of diazomethane as reagent was found to be suitable to design specific spiranic cyclopropyl derivatives with interesting anticonvulsant properties.[2a] As shown by Peterson *et al*., employing (*Z*)- or (*E*)-2-ethylidene-γ-butyrolactone as dipolarophile, the [3+2] cycloaddition leads first to five-membered spiranic Δ^1-pyrazolines (20 °C, 2-3 days, 81-87% yield). The latter heterocycles were finally transformed to the spiranic cyclopropyl derivatives upon irradiation under UV light *via* an extrusion of dinitrogen. Note that treatment of α-methylene-γ-butyrolactone with CH_2N_2 in the presence of $Pd(OAc)_2$ as catalyst affords after 2-3 days at
20 °C, 5-oxaspiro[2.4]heptan-4-one in 49% yield,[2a] most probably via a palladium-carbene intermediate.[2c] We have examined previously the reactivity of mono- and disubstituted diazoalkanes such as ethyl diazoacetate and diphenyldiazomethane towards α-methylene-γ-butyrolactones (*i.e.* itaconic anhydride (**1**)) in the presence of hydroquinone (Scheme 1).



Scheme 1. [3+2] cycloaddition reaction of diphenyldiazomethane with itaconic anhydride.[4]

RESULTS AND DISCUSSION

The cyclopropyl compound 1,1-diphenyl-4,6-dioxo-5-oxaspiro[2.4]heptane (**3**) resulted from this [3+2] cycloaddition reaction (room temperature, 76% yield).[4] Further chemical transformation of the anhydride to its diacid form allowed an X-ray structure determination, which confirmed the spiranic cyclopropyl nature of the [3+2] adduct. As part of our research on the use of nitriloxides,[5-7] nitrones,[8,9] and diazoalkanes[4] as 1,3-dipoles in [3+2] cycloadditions with methylene-γ-butyrolactones, we report herein on the reaction and the crystal structures of 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane (**8**), cyclopropyl compounds resulting from the cycloaddition of 3-methylenedihydro-(3*H*)furan-2-one with diphenyldiazomethane. For comparison, the reaction of ethyl diazoacetate (**6**) as 1,3-dipole with the dipolarophile (**5**) was also examined, leading to the spiranic five-membered cycloadduct 3'-ethoxycarbonylspiro-Δ^2-pyrazolino[5':3]dihydro-(3*H*)furan-2-one (**10**).

Cycloaddition with diphenyldiazomethane

The [3+2] cycloaddition of 3-methylenedihydro-(3*H*)furan-2-one (**5**) with Ph_2CN_2 (**2**) in ethyl acetate solution leads at room temperature, after loss of a dinitrogen molecule, to the spirocyclopropyl compound 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane • hydroquinone (**8a**) (Scheme 2). Recently, we reported on the polymerization of methylene-γ–butyrolactone by differential thermal analysis.[8] To prevent the polymerization of the dipolarophile, the synthesis was carried out in presence of hydroquinone (2.5 mg/mL) as a free radical scavenger. The course of the reaction was followed by colorimetry. The initial red solution becomes colorless, thus indicating the complete disappearance of Ph_2CN_2 (confirmed by TLC). The ^{1}H NMR analysis of the crude oil revealed the signals pertaining to the adduct (**8a**), and other minor signals that could be attributed to (**8b**) (see below) and benzophenone azine $Ph_2C{=}N{-}N{=}CPh_2$. The latter compound results most probably from degradation of diphenyldiazomethane (see below). After precipitation in diethyl ether and recrystallisation, the product (**8a**) was isolated with 38 % yield (based on hydroquinone) in form of single crystals, suitable for an X-ray diffraction analysis.

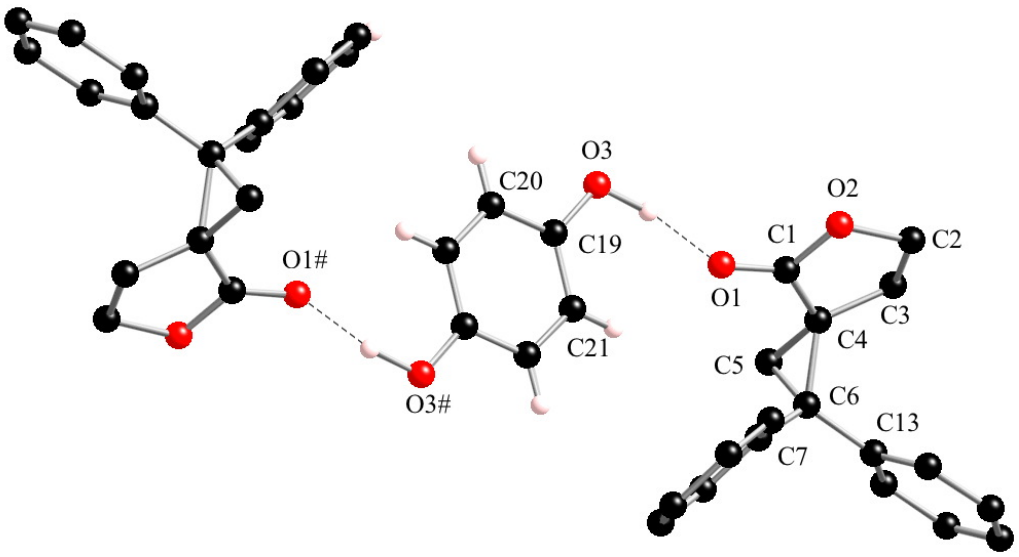
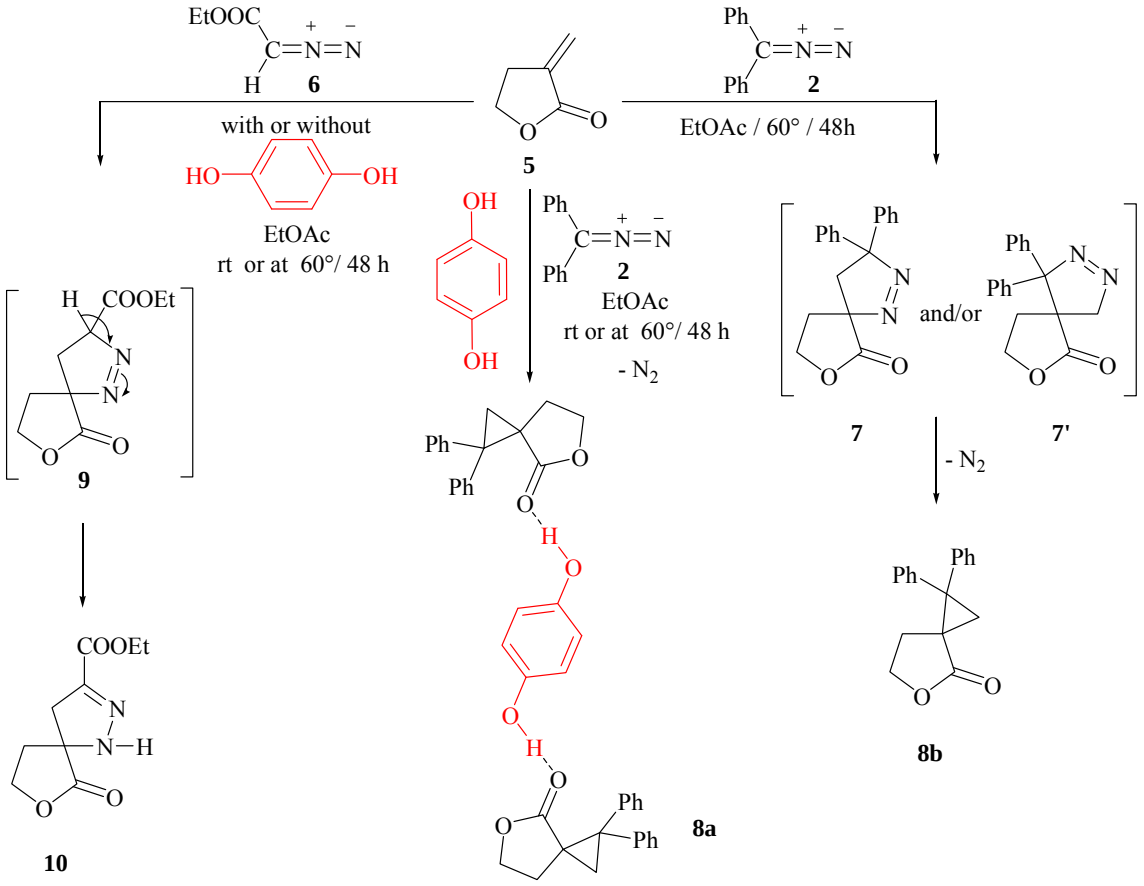


Figure 1. View of the crystal structure of (**8a**). Selected bond lengths [Å] and angles [°]: C(1)–O(1) 1.218(1), C(1)–O(2) 1.349(2), C(2)–O(2) 1.464(2), C(4)–C(5) 1.500(2), C(4)–C(6) 1.556(2), C(5)–C(6) 1.514(2), C(6)–C(7) 1.511(2), C(6)–C(13) 1.502(2); C(4)–C(5)–C(6) 62.2(1), C(5)–C(4)–C(6) 59.3(1), C(5)–C(6)–C(4) 58.5(1), O(1)–C(1)–O(2) 121.2(1).

The crystal structure of (**8a**) consists of two spirocyclopropane units, which are linked by a hydroquinone molecule through hydrogen bonds as depicted in Fig. 1. The hydroquinone molecule is placed over the symmetry centers, while the spirocyclopropane moieties have no local symmetry. There are no unusual metric parameters in both molecules. Apart from the crystal structure of 1-carboxy-2,2-diphenyl-1-

cyclopropane-ethanoic acid recently reported by us,[4] only two other examples of 2,2-diphenyl-spirocyclopropane structures have been found in the Cambridge Data Base.[10,11] The structure of (**8a**) is stabilized by a strong hydrogen bond between the hydroxyl group of hydroquinone (O3-HO3) and the terminal atom O1 of spirocyclopropane. Such a hydrogen bonding has been already observed during the co-crystallization of oxadiazole derivatives with hydroquinone.[12] The O3-HO3 and HO3•••O1 distances are equal to 1.09(1) and 1.73(2) Å, respectively. The O3••••O1 separation reaches 2.818(1) Å and the O3-HO3-O1 angle is equal to 170(1)°.

To evaluate the parameters influencing the N_2-extrusion process, the [3+2] cycloaddition was also carried out in Et_2O at room temperature. This solvent was chosen to prevent a N_2-extrusion to occur during the evaporation step. In addition, the poor solubility of the adduct (**8a**) in Et_2O should facilitate its isolation. As expected, the reaction led to precipitation of (**8a**) as the sole product, which did not reveal any presence of nitrogen (IR, ^{1}H NMR and elementary analyses, Table 1). The analyses performed on the mother liquor did not show any trace of primary adducts (**7**) and/ or (**7'**). The [3+2] cycloaddition was finally carried out in presence of hydroquinone during 48 h in ethyl acetate at 60 °C. After work-up, pure compound (**8a**) was now obtained with an improved yield of 50 % (based on hydroquinone).



Scheme 2. [3+2] Cycloaddition mechanism of the diazoalkanes (**2**) and (**6**) towards (**5**).

In order to get more information about the role of hydroquinone in this reaction, the [3+2] cycloaddition was also performed without this agent, using now ethyl acetate as solvent during 48 h at 60 °C. The reaction between (**5**) and (**2**) leads now to the spiroheterocycle 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane (**8b**), arising from the rearrangement of the Δ^1-pyrazoline intermediates (**7**) and/or (**7'**) after N_2-extrusion (Scheme 2). After recrystallisation, the product (**8b**) was isolated in 67% yield (based on 5 mmol of **5**). The melting point of the spiroheterocycle (**8b**) was found to be now 118-120 °C instead of 182-184 °C (Table 1) measured for (**8a**). The crystal structure of (**8b**), which crystallizes in the non–centrosymmetric orthorhombic *Pbc2₁* space group, was also determined. There are four independent spiranic molecules in the asymmetric unit that are divided into two (*S,R*) pairs of enantiomers. One of them is depicted in Figure 2. There are not particularly short intermolecular contacts.

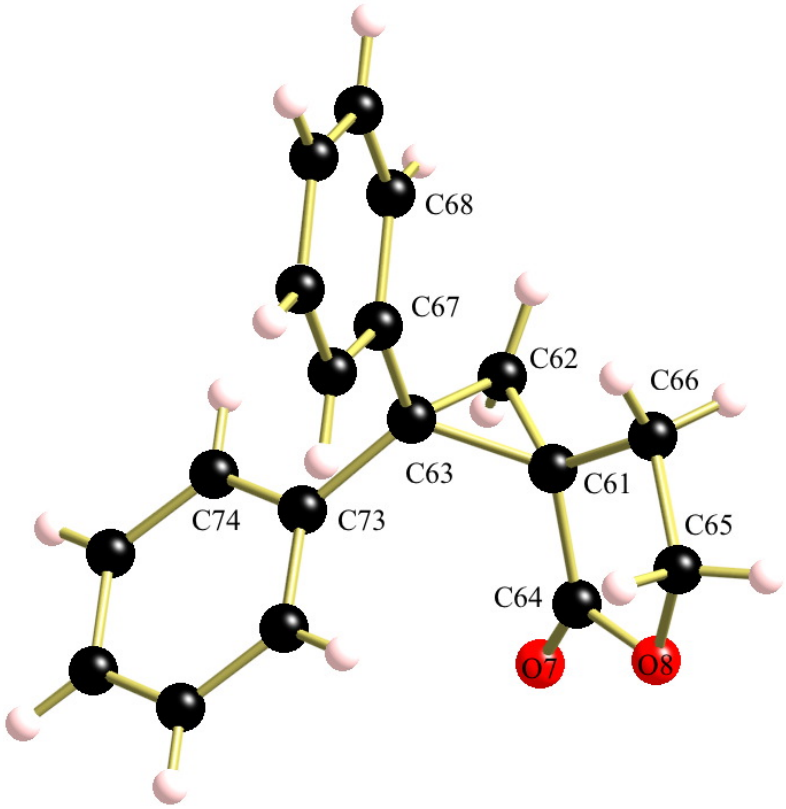
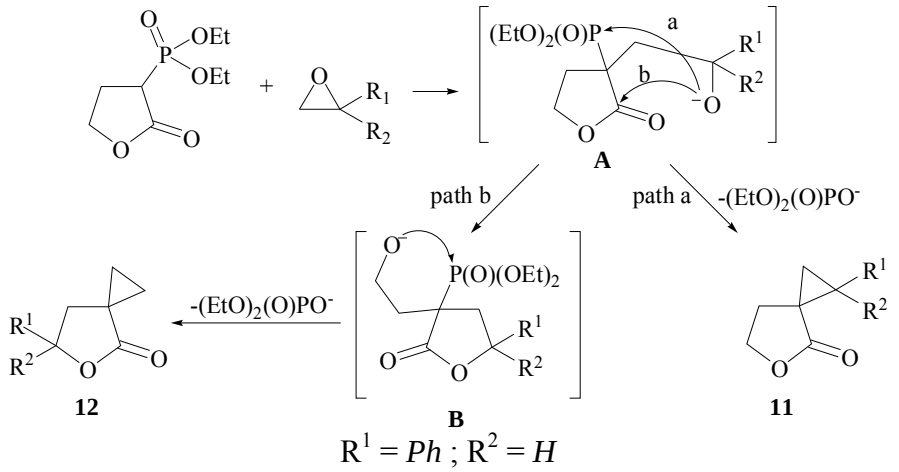


Figure 2. View of the crystal structure of (**8b**). One of the four independent molecules present in asymmetric unit is shown. The mean values of four equivalent bonds are given in square brackets. Selected bond lengths [Å]: C(61)–C(62) 1.508(3) [1.507], C(61)–C(63) 1.551(3) [1.545], C(62)–C(63) 1.504(3) [1.505], C(61)–C(64) 1.478(3) [1.481], C(61)–C(66) 1.512(3) [1.507], C(64)–O(7) 1.206(3) [1.207], C(64)–O(8) 1.356(3) [1.360].

Note that apart from our cycloaddition route, α-spirocyclopropyl-γ-butyrolactones are also accessible by treatment of an α-phosphono-γ-butyrolactone carbanion with various epoxides via elimination of

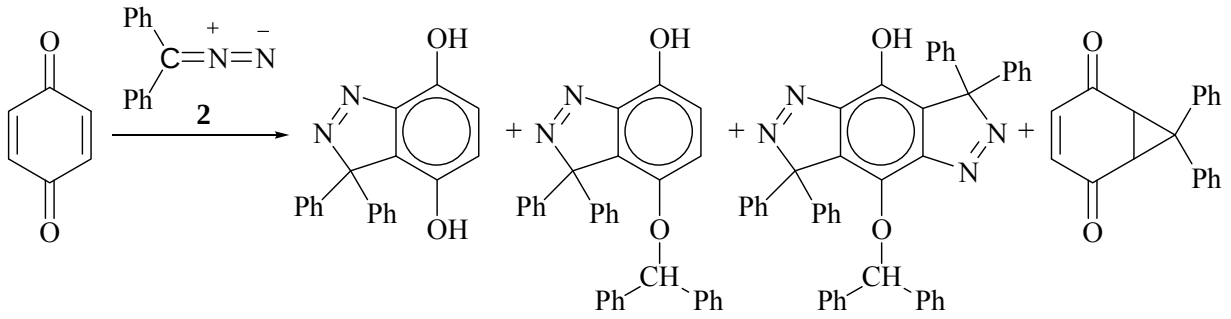
$(EtO)_2(O=)PO^-$.[2b] However, one inconvenient of this method is the competing formation of isomeric spirolactones substituted at the 6-position. For example, reaction of this α-phosphono-γ-butyrolactone carbanion with 2-phenyloxirane gave a isomeric mixture of 1-phenyl-4-oxo-5-oxaspiro[2.4]heptane (**11**) and 6-phenyl-4-oxo-5-oxaspiro[2.4]heptane (**12**) (Scheme 3).[2b]



Scheme 3. Reaction of α-phosphono-γ-butyrolactone carbanion with 2-phenyloxirane.[2b]

More recently, the transformation of an α-methylene-γ-butyrolactone derivative to a cyclopropyl spiro-compound has been accomplished by reaction with dimethyloxosulfoxonium methylide in DMSO.[13] Addition of dihalocarbenes to arglabin, a sesquiterpene incorporating an α-methylene-γ-butyrolactone motif, led also to structurally characterized spiranic cyclopropyl compounds.[14]

The presence of hydroquinone during the cycloaddition of 3-methylenedihydro-(3*H*)furan-2-one (**5**) with diphenyldiazomethane (**2**) does not only influence the structure of the isolated product**,** but was also found to have a lowering effect on the reaction yield. A side reaction involving either diphenyldiazomethane or 3-methylenedihydro-(3*H*)furan-2-one with hydroquinone and/or its oxidation product could be envisaged. For instance, the oxidation of hydroquinone by the residual oxygen present in the solution would generate another potential dipolarophile, namely benzoquinone.[15-17]
Actually, benzoquinone was found to act as a good dipolarophile towards Ph_2CN_2 (Scheme 4).[18] Note that in refluxing benzene, benzophenone azine $Ph_2C=N-N=CPh_2$ was also isolated from the crude mixture.[18] In light of these studies based on both time required for the cycloaddition to be completed (48 hours) and the reaction temperature (60 °C), the oxidation of hydroquinone could lead to benzoquinone/diphenyldiazomethane adducts.



Scheme 4. [3+2] Cycloaddition of benzoquinone and diphenyldiazomethane (in refluxing benzene).[18]

To check these hypotheses, we reacted hydroquinone (i) with 3-methylenedihydro-(3*H*)furan-2-one and (ii) with (**2**) at 60 °C for 48 h in ethyl acetate as solvent. In the first case, 3-methylenedihydro-(3*H*)furan-2-one was recovered without significant alteration (^{1}H MNR performed after solvent evaporation). In contrast, the treatment of hydroquinone with Ph_2CN_2 yield only an aromatic compound (^{1}H NMR performed after solvent evaporation) identified as benzophenone azine by X-ray analysis on some selected single crystal (data not shown) and comparison of melting point.[19] No product described in scheme 4 were identified. Indeed, the real role of hydroquinone in this reaction is still not clarified.

*Cycloaddition with ethyl diazoacetate (**6**)*

Furthermore, the reactivity of the dipolarophile (**5**) was studied towards ethyl diazoacetate (**6**) to gain information on the influence of hydroquinone on the reaction yield. In regard to our previous studies performed with itaconic anhydride,[4] this experiment should also clarify the role of the substituents attached on the 1,3-dipole on the N_2-elimination process.

The [3+2] cycloaddition of (**5**) and ethyl diazoacetate (**6**), carried out at room temperature in ethyl acetate in presence of hydroquinone (2.5 mg/mL), was completed after one week (TLC analyses). The ^{1}H NMR examination of the crude oil revealed the signals pertaining to the final product 3'-ethoxycarbonylspiro-Δ^2-pyrazolino[5':3]dihydro-(3*H*)furan-2-one (**10**) and some other minor signals resulting from partial degradation of the starting materials. After precipitation in diethyl ether and recrystallisation, compound (**10**) was isolated in 22% yield. Both NMR and IR data as well elemental analyses were in agreement with formation of a five-membered Δ^2-pyrazoline cycle, stemming from prototropic rearrangement of the spiro intermediate (**9**) (Scheme 2 and Table 1). This result is in line with previous observations reported in the literature.[4,20] When performed in ethyl acetate at 60 °C for 48 h, the same product (**10**) was now obtained with an increased overall yield of 35%. Since [3+2] cycloaddition involving Ph_2CN_2 was found to be sensitive to the presence of hydroquinone in the reaction medium (see above), we also conducted for comparison the reaction in absence of this agent.

The cycloaddition reaction performed in ethyl acetate at 60 °C led now to (**10**) in 45% yield. These experiments demonstrate that, in contrast to the reaction of 3-methylenedihydro-(3*H*)furan-2-one (**5**) with (**2**), no adduct formation with hydroquinone occurs. Note that the melting points of all samples of (**10**) synthesized in the presence or absence of hydroquinone were identical (Table1). The insignificant effect of hydroquinone noticed in our previous study on the [3+2] cycloaddition of diphenyldiazomethane with itaconic anhydride (**1**) may be explained by the fact that this reaction requires only 6 hours for completion at room temperature, thus preventing competitive reactions to occur.

CONCLUSION

It has been shown that the presence of hydroquinone added as dipolarophile stabilizing agent has a strong impact on the yield of the [3+2] cycloaddition between 3-methylenedihydro-(3*H*)furan-2-one and the two diazoalkanes under study. Whereas a weak deactivating effect is noticed with ethyl diazoacetate, a stronger decrease is observed with Ph_2CN_2. In the latter case, a structurally characterized adduct 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane • hydroquinone (**8a**) was isolated. The precise role of hydroquinone remains still unclear and other dipole/dipolarophile couples should be investigated to understand this effect more properly. We also confirmed the hypothesis presented in our previous study concerning the role of the substituent attached to the 1,3-dipole on the N_2-extrusion process.[4] In the absence of transposable protons brought by the dipolar entity, as it is the case for Ph_2CN_2, a stabilization of the [3+2] Δ^1-pyrazoline *via* its transformation into the corresponding Δ^2-pyrazoline is impossible. Therefore a N_2-loss from the [3+2] Δ^1-pyrazoline intermediate is favored, which then spontaneously leads to a spiranic cyclopropyl derivative.

EXPERIMENTAL

3-Methylenedihydro-(3*H*)-furan-2-one and ethyl diazoacetate were purchased from Aldrich. Diphenyldiazomethane was synthesized according to the literature.[21] TLC plates, DC-Alufolien Kieselgel 60 F_{254}, were from Merck. Melting points were measured on an Electrothermal IA 9200 and are not corrected. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 300 and 400 spectrometers operating at 300 and 400 MHz for ^1H, 75 and 100 MHz for ^{13}C. Chemical shifts were measured relative to TMS. IR spectra were recorded on a Bio-Rad FTS-7 spectrometer. Elementary analyses were obtained from the University of Bourgogne and gave satisfactory results (C, H, N ± 0,30 % from theoretical).

Cycloaddition reactions

The cycloadditions were carried out under nitrogen or argon atmosphere using standard Schlenk techniques. To a magnetically stirred solution of 3-methylenedihydro-(3*H*)furan-2-one (**5**) (0.49 g, 5

mmol) in EtOAc (20 mL), is added Ph_2CN_2 (**2**) (0.97 g, 5 mmol) or ethyl diazoacetate (**6**) (0.57 g, 5 mmol). The resulting mixture was stirred at 60 °C during 48 h either in presence (50 mg, 0.45 mmol) or in absence of hydroquinone. The solvent was evaporated under reduced pressure, the residual oil taken up with Et_2O. The slurry was subjected to ultrasonic irradiation leading to a crude crystalline product, filtrated and washed with Et_2O (2x20 mL) and finally recrystallised from Et_2O (Table 1).

Table 1. Physical and spectroscopic data of (**8a,b**) and (**10**)

Compound	Mp °C	Yield g (%)	IR[c] cm^{-1}	^1H NMR/$^{13}C\{^1H\}$ NMR (δ) : ppm/TMS	
white solid **8a** **8a'**	182-184 (Et_2O)	0.22 (38)[a] 0.29 (50)[a']	3420 1735	^1H NMR[d] :	1.95 (d, *J* = 5.1 Hz, 2H), 2.00 (m, 2H), 2.15 (d, *J* = 5.1 Hz, 2H), 2.30 (m, 2H), 4.40-4.50 (m, 4H), 7.10-7.60 (m, 26H, phenyl and OH).
				^{13}C NMR[d] :	23.1, 28.1, 31.4, 45.6, 65.6, 115.9-140.5, 176.4.
white solid **8b**	118-120 (Et_2O)	0.89 (67)[b]	1760	^1H NMR[d] :	2.05 (d, *J* = 5.1 Hz, 1H), 2.10 (m, 1H), 2.30 (d, *J* = 5.1 Hz, 1H), 2.40 (m, 1H), 4.50-4.60 (m, 2H), 7.30-7.50 (m, 10H).
				^{13}C NMR[d] :	23.2, 28.2, 31.4, 45.6, 65.6, 127.0-140.6, 176.4.
white solid **10a** **10a'** **10b**	109-110 [a,b] (Et_2O)	0.23 (22) [a] 0.37 (35) [a'] 0.48 (45) [b]	3290 1770 1700 1565	^1H NMR[e] :	1.30 (t, *J* = 7.0 Hz, 3H), 2.45-2.65 (m, 2H), 3.20 (d, *J* = 17.4 Hz, 1H), 3.30 (d, *J* = 17.4 Hz, 1H), 4.25 (q, *J* = 7.0 Hz, 2H), 4.30-4.60 (m, 2H), 8.10 (s, 1H).
				^{13}C NMR[e] :	14.5, 36.3, 41.8, 61.1, 65.8, 69.1, 140.1, 162.6, 177.0.

[a] : In presence of hydroquinone at rt during the synthesis.

[a'] : In presence of hydroquinone at 60°C/48h during the synthesis.

[b] : In absence of hydroquinone at 60°C/48h during the synthesis.

(**8a**) ($C_{42}H_{38}O_6$) required (%): C 78.97, H 5.99. Found (%): C 78.79, H 6.00.

(**8b**) ($C_{18}H_{16}O_2$) required (%): C 81.79, H 6.10. Found (%): C 81.58, H 6.09.

(**10a,b**) ($C_9H_{12}N_2O_4$) required (%): C 50.94, H 5.70, N 13.20. Found (%): C 51.15, H 5.67, N 13.32.

[c] as KBr pellets, [d] In $CDCl_3$ at 400 and 100 MHz. [e] In acetone d_6 at 300 and 75 MHz.

*X-Ray structural analyses of 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane (**8b**) and 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane • hydroquinone (**8a**)*

The cell and intensity measurements of colorless crystals of (**8a**) and (**8b**) were carried out on a Nonius KappaCCD diffractometer with Mo-Kα radiation (λ = 0.71073 Å) at T = 110(2) and 125(2) K, respectively. Intensity data were reduced with DENZO and SCALEPACK programs. Both structures have been solved by direct methods (SHELXS-97) and refined by least-squares based on F^2 (SHELXL-97).[22]

Table 2. Crystal data and structure refinement for (**8a**) and (**8b**)

Empirical formula	$C_{42}H_{38}O_6$[a] **8a**	$C_{18}H_{16}O_2$[b] **8b**
Formula weight	638.72	264.325
Temperature (K)	110(2)	125(2)
Wavelength (Å), (Mo-Kα)	0.71073	0.71073
Crystal system	monoclinic	orthorhombic
Space group	$P2_1/n$	$Pbc2_1$
a (Å)	8.4053(2)	13.5778(2)
b (Å)	13.5851 (5)	19.1897(2)
c (Å)	14.5443(5)	21.4387(3)
β (°)	97.674(2)	90
Volume ($Å^3$)	1645.89(9)	5585.94(13)
Z	4	16
Density (calculated) (mg/m^3)	1.289	1.257
Absorption coefficient (mm^{-1})	0.085	0.081
F(000)	664	2240
Crystal size (mm)	0.15×0.15×0.12	0.4×0.3×0.3
Theta range for data collection (°)	2.06 - 27.47	3.22 – 27.52
Index ranges	$0\leq h\leq 10$, $0\leq k\leq 17$, $-18\leq l\leq 18$	$-17\leq h\leq 17$, $-24\leq k\leq 23$, $-27\leq l\leq 27$
Reflection collected	3701	11685
Independent reflections [I>2σ(I)]	1042	11047
Completeness to theta	0.985	0.982
Absorption correction	none	none
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	3701/0/221	11685/1/721
Goodness-of-fit	0.662	1.078
Weighting scheme	$w=1/[\sigma^2F_o^2+(0.0067P)^2+0.0P]$[c]	$w=1/[\sigma^2F_o^2+(0.0583P)^2+2.0996P]$[c]
Final R indices [I>2σ(I)]	$R = 0.0370$, $wR = 0.0532$	$R = 0.0473$, $wR = 0.1184$
R indices (all data)	$R = 0.0744$, $wR = 0.0565$	$R = 0.0512$, $wR = 0.1218$
Largest diff. peak/hole, $e^-/Å^3$	0.177/-0.189	0.389/-0.221

[a] 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane • hydroquinone

[b] 1,1-diphenyl-4-oxo-5-oxaspiro[2.4]heptane . [c] $P = (F_o^2 + 2F_c^2)/3$

All non-hydrogen atoms were refined with anisotropic thermal parameters. The hydroxyl hydrogen atom HO3 of hydroquinone in (**8a**) was located from difference-Fourier map and isotropically refined. All other H atoms in (**8a**) as well as those of (**8b**) were placed in calculated positions and treated in a riding model with isotropic displacement parameters set to 1.2 and to 1.4 times of those of, respectively, the carbon sp^2 and sp^3 atoms bearing them. The asymmetric unit of (**8b**) (polar $Pbc2_1$ space group, Flack parameter equal to 0.0) contains four independent chiral molecules. Attempts to solve the structure in the centrosymmetric *Pbcm* group (same conditions for systematic extinctions), and to reduce so the number

of independent molecules in the asymmetric unit to two, were unsuccessful.

Crystallographic data for (**8a**) and (**8b**) have been deposited with the Cambridge Crystallographic Data Centre with Nos. CCDC 262382 and 602911, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk].

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REFERENCES (AND NOTES)

1. H. M. R. Hoffmann and J. Rabe, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 94.
2. a) E. M. Peterson, K. Xu, K. D. Holland, A. C. McKeon, S. M. Rothman, J. A. Ferrendelli, and D. F. Covey, *J. Med. Chem.*, 1994, **37**, 275. b) T. Minami, M. Matsumoto, H. Suganuma, and T. Agawa, *J. Org. Chem.*, 1978, **43**, 2149. c) concerning the carbene mechanism see: U. Mende, B. Raduchel, W. Skuballa, and H. Vorbruggen, *Tetrahedron Lett.*, 1975, 629.
3. A. Padwa and W. H. Pearson (Eds.), Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products, John Wiley and Sons, 2002.
4. C. Roussel, K. Ciamala, J. M. Melot, J. Vebrel, and C. Riche, *J. Chem. Res., S*, 2002, 449.
5. C. Roussel, K. Ciamala, P. Audebert and J. Vebrel, *New J. Chem.*, 1999, 2**3**, 989.
6. C. Roussel, R. Fihi, K. Ciamala, P. Audebert, and J. Vebrel, *New J. Chem.*, 2000, **24**, 471.
7. R. Fihi, K. Ciamala, J. Vebrel, and N. Rodier, *Bull. Soc. Chim. Belg.*, 1995, **104**, 55.
8. C. Roussel, R. Fihi, K. Ciamala, J. Vebrel, T. Zair, and C. Riche, *Org. Biomol. Chem.*, 2003, **1**, 2689.
9. J. C. Daran, R. Fihi, C. Roussel, N. Laghrib, M. Azrour, K. Ciamala, and J. Vebrel, *Acta Cryst.*, *Sect. E*: *Struct. Rep. Online*, 2006, E**62**, o329.
10. C. C. Chiang, C. T. Lin, A. H. J. Wang, D. Y. Curtin, and I. C. Paul, *J. Am. Chem. Soc.*,1977, **99**, 6303.
11. T. S. Cameron, A. Linden, and K. Jochem, *Acta Cryst. Sect. C: Cryst. Struct. Commun.*, 1990, C**46**, 2110.
12. Y. T. Wang, G. M. Tang, D. W. Qin, and H. D. Duan, *Acta Cryst.*, *Sect. E: Struct. Rep. Online,* 2006, E**62,** o45.

13. C. M. Yu, Y. T. Hong, and J. H. Lee, *J. Org. Chem.*, 2004, **69**, 8506.
14. a) R. I. Dzhalmakhanbetova, V. A. Raldugin, I. Yu. Bagryanskaya, Yu. V. Gatilov, M. M. Shakirov, A. T. Kulyyasov, and S. M. Adekenov, *Chem. Nat. Compounds*, 2005, **41**, 552.; b) R. I. Dzhalmakhanbetova, S. B. Akhmetova, V. A. Raldugin, Yu. V. Gatilov, G. A. Atazhanova, and S. M. Adekenov, *Chem. Nat. Compounds*, 2006, **42**, 307.
15. C. Roussel, L. Dayon, N. Lion, T. C. Rohner, J. Josserand, J. S. Rossier, H. Jensen, and H. H. Girault, *J. Am. Soc. Mass Spectrum*, 2004, **15**, 1767.
16. C. Roussel, L. Dayon, H. Jensen, and H. H. Girault, *J. Electroanal. Chem*., 2004, **570**, 187.
17. C. Roussel, T. C. Rohner, H. Jensen, and H. H. Girault, *Chem. Phys .Chem.,* 2003, **4**, 200.
18. a) T. Oshima and T. Nagai, *Bull.Chem. Soc. Jpn.*, 1988, **61**, 2507; b) T. Oshima and T. Nagai, *Bull. Chem. Soc. Jpn*., 1989, **62**, 2580.
19. a) H. Loghmani-Khouzani, M. M. M. Sadeghi, J. Safari, M. S. Abdorrezaie, and M. Jafarpisheh, *J. Chem. Res. (S)*, 2001, 80; b) A. K. Saha, M. Mahmun Hossain, D. S. Grubisha, and D. W. Bennet, *J. Chem. Cryst.*, 1995, **25**, 383; c) H. Nozaki, H. Takaya, S. Moriuti, and R. Noyori, *Tetrahedron*, 1968, **24**, 3655.
20. S. Huneck and R. Takeda, *Z. Naturforsch.* (*B*), 1992, **47b**, 842.
21. J. B. Miller, *J. Org. Chem*.,1959, **24**, 560.
22. G. M. Sheldrick, SHELXS97 and SHELXL97 1997, University of Göttingen, Germany.