Photochemistry of triazolopyridinium ylides

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(received 12 Mar 00; accepted 20 Aug 00; published on the web 28 Aug 00)
DOI: http://dx.doi.org/10.3998/ark.5550190.0001.312

Abstract
Triazolopyridinium, -quinolinium, and isoquinolinium ylides were photolysed in the presence of acetylenic esters, no products of 1,3-dipolar cycloaddition were found. Some different products, for example quinolizine 26a, were obtained on photolysis compered thermolysis.

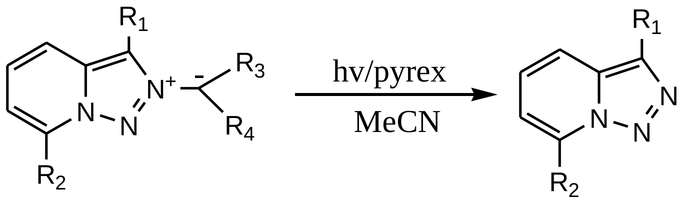
Keywords: Cycloimmonium ylides, photolysis, quinolizines, dimethylacetylenedicarboxylate

Introduction

The photochemistry of cycloimmonium ylides is a topic that has received considerable attention. Nevertheless, to the best of our knowledge, there are no studies on the photochemistry of triazolopyridinium ylides and their benzologues. We present here our results on the photoreactions of some triazolopyridinium, triazoloquinolinium and triazoloisoquinolinium ylides.

Results and Discussion

The photoreaction of stable dicyanomethylides 1a, 2, 3a and 4a, results in the cleavage of the N^+-C^- ylide bond with formation of the heterocycles 5, 6, 7 and 8 respectively, and probably the corresponding disubstituted carbene (Equations 1,2,3). This is usually the main process in similar reactions reported in the literature.[1]



1a R_1=CH_3; R_2=H; R_3=R_4=CN

b R_1=CH_3; R_2=R_3=H; R_4=COPh

c R_1=CH_3; R_2=R_3=H; R_4=COOMe

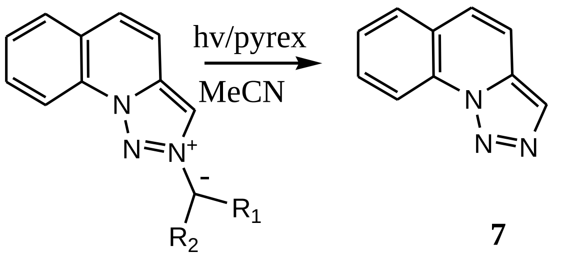
d R_1=CH_3; R_2=R_3=H; R_4=COOEt

2 R_1=H; R_2=CH_3; R_3=R_4=CN

5 R_1=CH_3; R_2=H

6 R_1=H; R_2=CH_3

Equation 1



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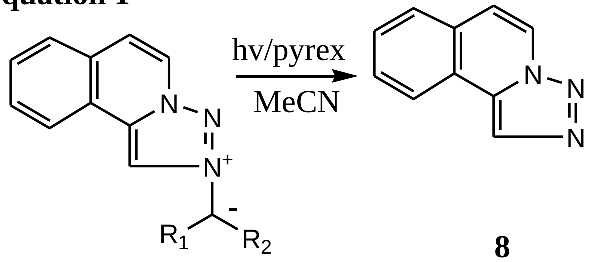
3a R_1=R_2=CN

b R_1=H; R_2=COPh

Equation 2



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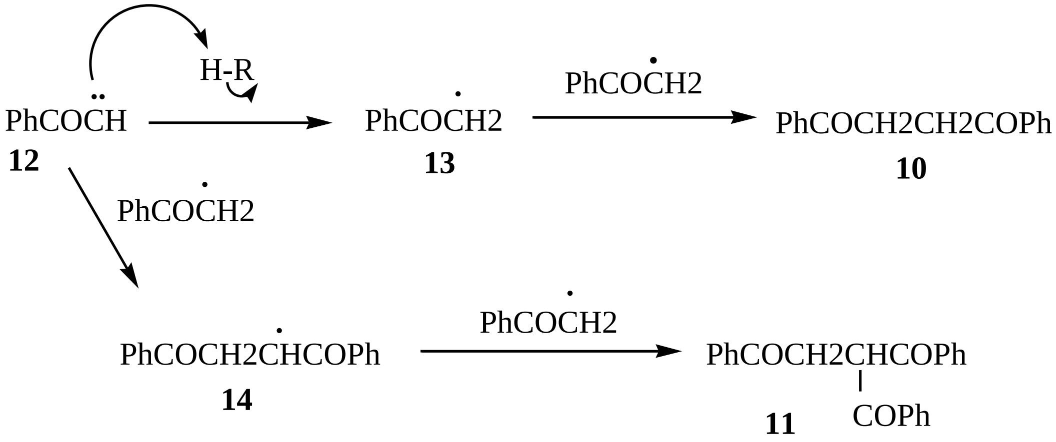
4a R_1=R_2=CN

b R_1=H; R_2=COPh

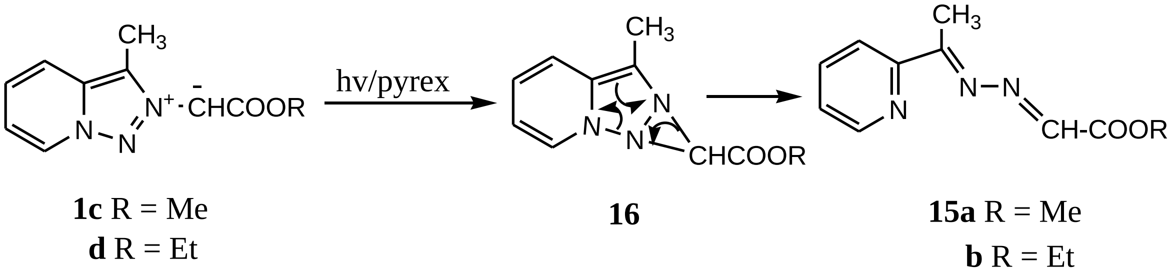
Equation 3

When the unstable monosubstituted triazolopyridinium 1b, triazoloquinolinium 3b and triazoloisoquinolinium 4b ylides were irradiated, similar results were found and compounds 5, 7 and 8 respectively were isolated. Furthermore, in all casesa mixture of two side products, identified as compounds 10 and 11, were formed. The formation of these compounds can be explained by invoking the corresponding carbene 12, which abstracts a hydrogen radical from the solvent, leading to the formation of a new radical 13 dimerisation of which would give 10. The carbene 12 could also react with radical 13, in which case radical 14 would be formed, and combination with 13 would then give 11 (Scheme 1).



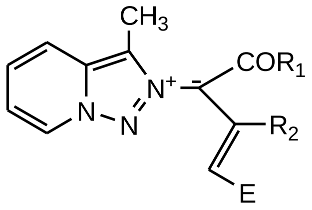
Scheme 1

Different results were found when the substituent in the ylides was a methoxy- or ethoxycarbonyl group. Irradiation of compounds 1c-d produced the alkylidene hydrazones 15a,b which were identified by their analytical and spectroscopic data. To account for the formation of these open-chain isomers we propose a photochemical electrocyclic reaction. This process involves four π-electrons, in a 1,3-dipolar species, forming a transient diaziridine 16. Further light-induced rearrangement would then give the isolated compounds (Scheme 2).

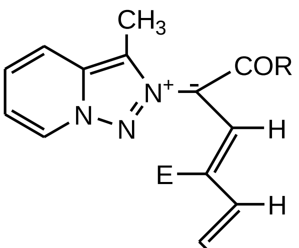


Scheme 2

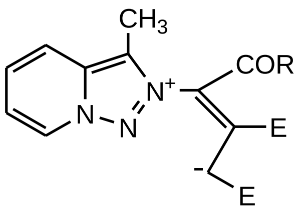
1,3-Dipolar addition to nitrogen ylides is an attractive approach to the synthesis of five membered heterocycles. Looking for new tricyclic or tetracyclic compounds we had studied the reaction of some triazolopyridinium, triazoloquinolinium and triazoloisoquinolinium ylides, as potential 1,3-dipoles, with acetylenic esters as 1,3-dipolarophiles, and we reported that compounds 1-4 thermally react with methyl propiolate (MP) and dimethyl acetylenedicarboxylate (DMAD) giving different adducts, depending on the solvent and the type of ylide,[2-7] but we have never found a 1,3-dipolar cycloaddition product, probably due to lack of enough energy to form a covalent C-N bond. Considering the likely formation of diaziridines 16 as intermediates we thought it might be possible to change the reaction course of those ylides with acetylenic dipolarophiles, by carring out the reaction photochemically, because light-initiated reactions could generate intermediates with high reactivity towards C-N covalent bond formation.



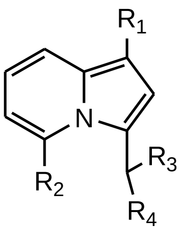
17b R_1=Ph, R_2=H
c R_1=OMe, R_2=H
d R_1=OEt, R_2=H
e R_1=Ph, R_2=E



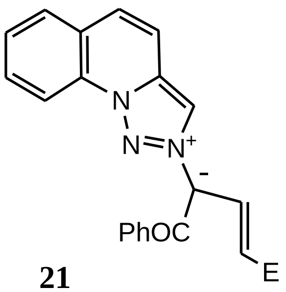
18c R=OMe
d R=OEt



19c R=OMe
d R=OEt



20a R_1=CH_3, R_2=H, R_3=R_4=CN
b R_1=CH_3, R_2=R_3=H, R_4=COPh
c R_1=CH_3, R_2=R_3=H, R_4=CO_2Me
d R_1=CH_3, R_2=R_3=H, R_4=CO_2Et
e R_1=H, R_2=CH_3, R_3=R_4=CN



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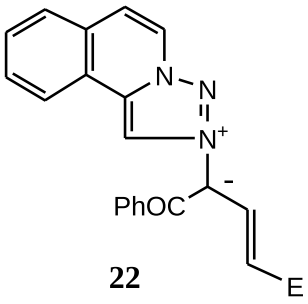

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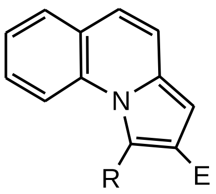
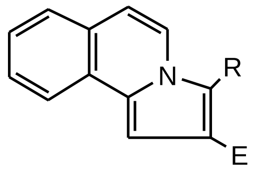
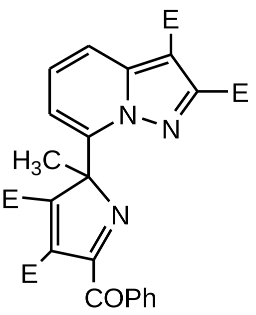


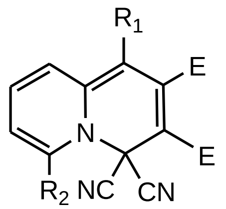
23a R=$CH(CN)_2$
b R=CH_2COPh
c R=E



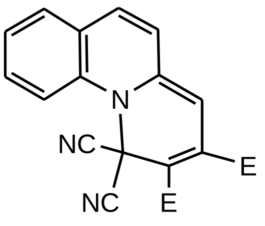
24a R=$CH(CN)_2$
b R=CH_2COPh
c R=E



25b R=Ph
c R=OMe
d R=OEt



26a R_1=CH_3, R_2=H
b R_1=H, R_2=CH_3



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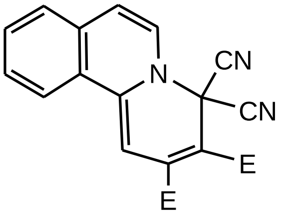

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Photochemical reactions of ylides 1-4 with MP and DMAD were studied using acetonitrile as solvent. The results of these experiments are detailed in full in Tables 1 and 2, in which are also collected the thermal reaction results previously published.

Table 1. Reactions of ylides 1-4 with methyl propiolate

Compd.	Reaction type	Solvent	Time	Temp.	Products	Yield %	Ref.
1a	Photo	CH_3CN	3h	r.t.	5	54	-
1a	Thermal	CH_3CN	4 days	reflux	20a	73	4
1b	Photo	CH_3CN	2h	r.t.	5, 17b, 20b	15, 68, 3	-
1b	Thermal	CH_3CN	8h	r.t.	17b	43	7
1b	Thermal	Toluene	overnight	r.t.	20b	65	5
1c	Photo	CH_3CN	2h	r.t.	5, 17c, 18c, 20c	14, 59, 1, 22	-
1c	Thermal	CH_3CN	8h	r.t.	17c, 18c	65, 16	7
1c	Thermal	Toluene	overnight	r.t.	20c	82	5
1d	Photo	CH_3CN	2h	r.t.	5, 17d, 18d, 20d	30, 46, 2, 5	-
1d	Thermal	CH_3CN	8h	r.t.	17d, 18d	82, 6	7
1d	Thermal	Toluene	overnight	r.t.	20d	82	5
2	Photo	CH_3CN	3h	r.t.	6	81	-
2	Thermal	CH_3CN	7 days	reflux	20e, 2	58, 29	4
3a	Photo	CH_3CN	3h	r.t.	7	80	-
3a	Thermal	CH_3CN	2 days	reflux	23a, 3a	56, 26	3
3b	Photo	CH_3CN	2h	r.t.	21, 23b	60, 5	-
3b	Thermal	CH_3CN	overnight	r.t.	21	52	3
3b	Thermal	Toluene	overnight	r.t.	23b	64	3
4a	Photo	CH_3CN	3h	r.t.	8	64	-
4a	Thermal	CH_3CN	2 days	reflux	24a	48	3
4b	Photo	CH_3CN	2h	r.t.	22, 24b	48, 39	-
4b	Thermal	CH_3CN	overnight	r.t.	22, 24b	48, 11	3
4b	Thermal	Toluene	overnight	r.t.	24b	54	3

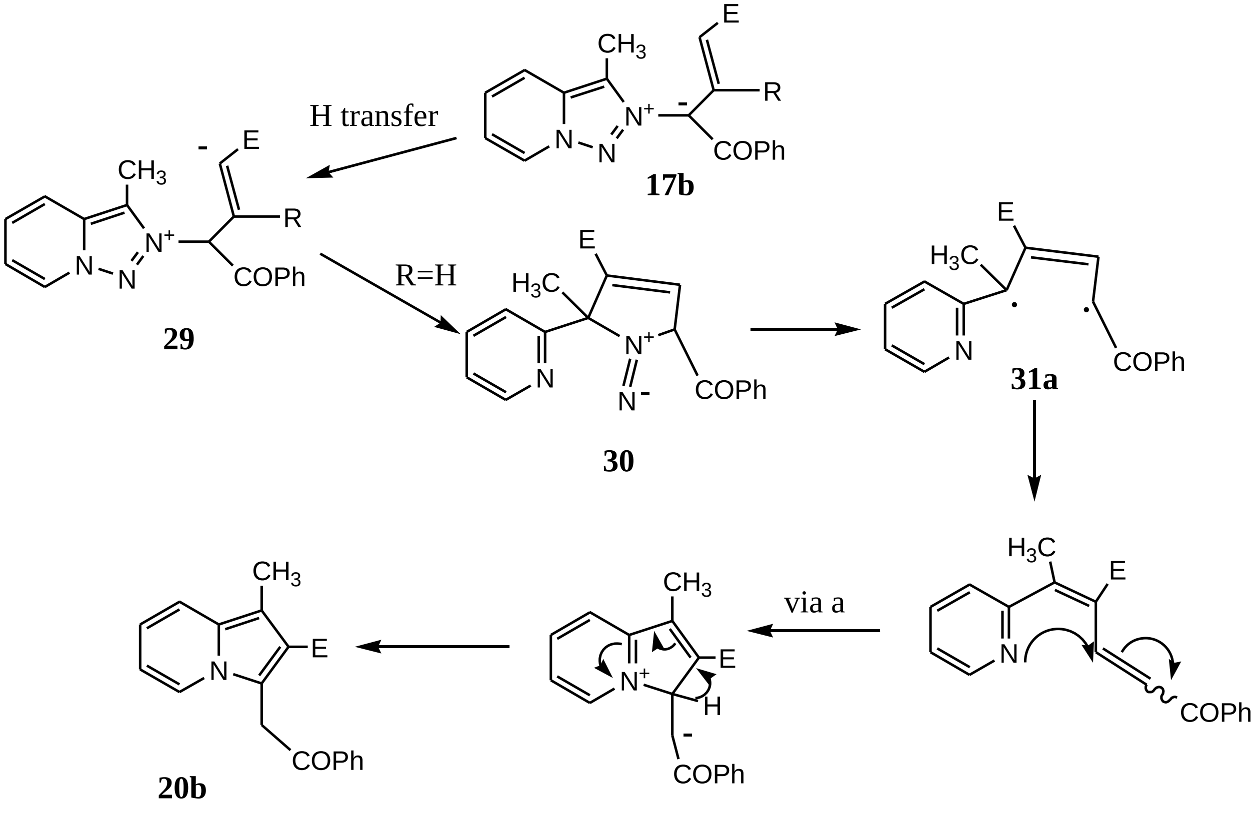
Table 2. Reactions of ylides 1-4 with dimethyl acetylenedicarboxylate

Compd.	Reaction type	Solvent	Time	Temp.	Products	Yield %	Ref.
1a	Photo	CH_3CN	3h	r.t.	26a	52	-
1a	Thermal	CH_3CN	various	various	none	----	4
1b	Photo	CH_3CN	2h	r.t.	5	91	-
1b	Thermal	CH_3CN	8h	r.t.	17e	70	7
1b	Thermal	Toluene	overnight	r.t.	25b	73	6
1c	Photo	CH_3CN	2h	r.t.	5	76	-
1c	Thermal	CH_3CN	8h	r.t.	19c	52	7
1c	Thermal	Toluene	overnight	r.t.	25c	82	6
1d	Photo	CH_3CN	2h	r.t.	5	69	-
1d	Thermal	CH_3CN	8h	r.t.	19d	61	7
1d	Thermal	Toluene	overnight	r.t.	25d	65	6
2	Photo	CH_3CN	3h	r.t.	26b	39	-
2	Thermal	CH_3CN	90m	reflux	26b	62	4
3a	Photo	CH_3CN	2h	r.t.	27	51	-
3a	Thermal	CH_3CN	48h	reflux	27	61	2
3b	Photo	CH_3CN	2h	r.t.	7	73	-
3b	Thermal	CH_3CN	overnight	r.t.	7	54	2
3b	Thermal	Toluene	overnight	r.t.	7, 23c	59, 13	2
4a	Photo	CH_3CN	2h	r.t.	8	59	-
4a	Thermal	CH_3CN	42h	reflux	28, 24c	59, 12	2
4b	Photo	CH_3CN	2h	r.t.	8	77	-
4b	Thermal	CH_3CN	overnight	r.t.	8	61	2
4b	Thermal	Toluene	overnight	r.t.	8, 24c	63, 9	2

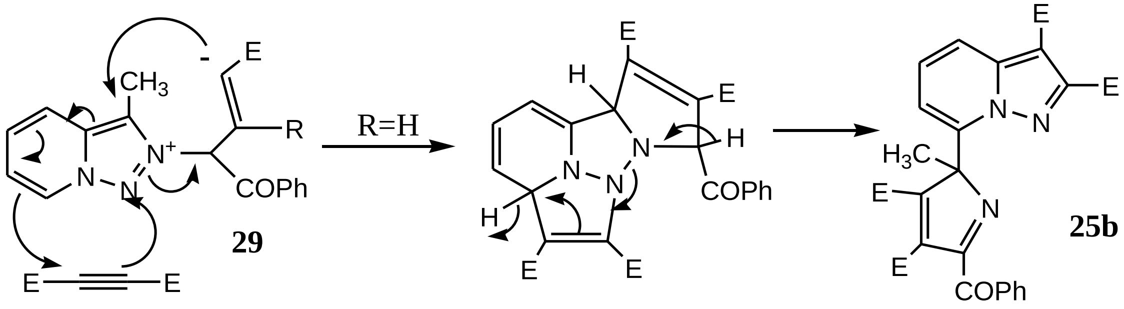
In these photochemical experiments we found different results, depending on the acetylenic ester and the ylide used, but in no case were we able to isolate 1,3-dipolar cycloadducts. The products obtained are of similar type to those found in the thermal reactions, but are produced in different solvents, reaction times, temperatures and with different yields.

The photo formation of compounds 20, 23 and 24, the quinolizine 26a, and the parent heterocycles 5, 6, 7 and 8 in acetonitrile as solvent, are the most important differences between the photo and thermal reactions of the studied ylides with acetylenic esters. The parent heterocycles could be formed by cleavage of the N^+-C^- ylide bond directly from the starting ylides or from the new ylides 17, 21 or 22 generated after irradiation. To test this last possibility, we irradiated compound 17c and obtained triazolopyridine 5, in good yield, as the only product.

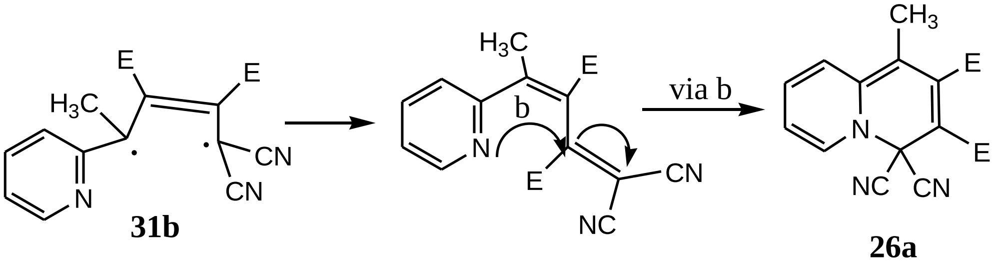
To account for the formation of 20, 23 and 24 we believe that light-initiated reactions start like heat-initiated reactions by a nucleophilic Michael addition, as we exemplify for 1b, giving the betaine 29. In the previously published reactions, this betaine evolved in different ways depending on the conditions (Scheme 3). In a protic solvent 1:1 adduct 17b is formed by rapid hydrogen transfer,[3-7] in a non-polar solvent and MP as co-reagent, indolizine 20b[3-5] is the isolated product, formed *via* a slower nucleophilic attack on C3 with cleavage of the N1-N8 bond, giving the diazene intermediate 30 which loses nitrogen forming a diradical 31a, finally giving the indolizine skeleton *via* route a. A change of co-reagent to DMAD (Scheme 4) produced the addition of a second molecule of DMAD and a remarkable rearrangement giving pyrazolo[1,5-*a*]pyridine 25.[6] Probably in the light-activated reactions the intermediate betaine is highly reactive and has the ability to react rapidly with C3 competing with the hydrogen transfer, forming in the reaction with MP, the mixture of compounds 17b and 20b. The formation of 26a from 1a and DMAD could be explained similarly by formation of a similar diradical 31b from the corresponding betaine, affording a 1.4-diene which would give the quinolizine, *via* route b, as we have explained in reference 4 (Scheme 5).



Scheme 3



Scheme 4



Scheme 5

Experimental Section

General Procedures. Mps were determined on a Kofler heated stage and are uncorrected. NMR spectra were determined on Bruker 250MHz or Varian 400MHz spectrometers. HRMS (EI) determinations were made using a VG Autospec Trio 1000 (Fisons) instrument. Photochemical reactions were carried out in a water-cooled quartz glass vessel equipped with a medium-pressure Hg lamp. All experiments were carried out in argon purged solutions of acetonitrile. The compounds 1a, 2,[4] 1b-d,[7] 3a, 3b, 4a, 4b,[3] were prepared as described in the literature.

General procedure for photoreactions of ylides 1-4

Pyrex tubes containing a solution of the corresponding ylides in dry acetonitrile were fixed to the external part of the quartz vessel. After irradiation, the mixture was filtered and the filtrate evaporated. Purification was performed by flash column chromatography on silica gel using hexane/ethyl acetate as eluent.

Photoreaction of ylides 1a, 2, 3a and 4a. Ylides 1a, 2, 3a and 4a (0.25 mmol)were irradiated for 3 h. Compounds 5, 6, 7 and 8 were formed in 90, 88, 95 and 83% yield respectively.

Photoreaction of ylides 1b, 3b and 4b. Ylides 1b, 3b and 4b (0.25 mmol)were irradiated for 3 h. Compounds 5, 7 and 8 were formed in 88, 91 and 90% yield respectively. In all cases, two side products were also isolated after further elution. 1,4-Diphenyl-1,4-butanedione 10, yellow oil(2%). ^{1}H NMR (400 MHz), $CDCl_3$, δ 7.97 (d, J = 8.7 Hz, 4H), 7.53-7.39 (m, 6H), 3.40 (s, 4H). ^{13}C NMR, $CDCl_3$, δ 198.7 (CO), 136.8 (C), 133.2 (CH), 128.6 (CH), 128.1 (CH), 32.6 (CH_2). $\nu_{max.}$/cm^{-1} 1677. HRMS (EI) calcd. for $C_{16}H_{14}O_2$ = 238.0993, found 238.0993. 1,5-**Diphenyl-3-benzoyl-1,5-pentanedione (11),** yellow oil (3%). ^{1}H NMR (400 MHz), $CDCl_3$, δ 8.03 (d, J = 7.5 Hz, 2H), 7.85 (d, J = 8.8 Hz, 4H), 7.50-7.33 (m, 9H), 4.69 (m, 1H), 3.44 (dd, J_{ab} = 18.04 Hz, J_{ax}= 6.45 Hz, 2H), 3.25 (dd, J_{ba} = 17.82 Hz, J_{bx} = 6.52 Hz, 2H). ^{13}C NMR, $CDCl_3$, δ 202.4 (CO), 197.6 (CO), 136.4 (C), 135.9 (C), 133.4 (CH), 133.2 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.1 (CH), 40.3 (CH_2), 37.0 (CH). $\nu_{max.}$/cm^{-1} 1679. HRMS (EI) calcd. for $C_{24}H_{20}O_3$ = 356.1412, found 356.1362.

Photoreaction of ylide (1c). Ylide 1c (0.060 g, 0.29 mmol) was irradiated for 2 h. A yellow oil was isolated after chromatography and identified as methyl 2-[1-(2-pyridyl)ethylidenehydrazono]acetate 15a (73%). ^{1}H NMR (250MHz), $CDCl_3$, δ 8.58 (ddd, J_{ab} = 4.8Hz, J_{ac} = 1.6 Hz, J_{ad} = 0.8 Hz, 1H), 8.04 (dd, J_{dc} = 8.0 Hz, J_{db} = 1.1 Hz, 1H), 7.68 (ddd, J_{cd} = 8.0 Hz, J_{cb} = 7.6 Hz, J_{ca} = 1.8 Hz, 1H), 7.40 (s, 1H), 7.27 (ddd, $J_{b\,c}$= 7.6 Hz, J_{ba} = 4.9 Hz, J_{bd} = 1.1 Hz, 1H), 3.87 (s, 3H), 2.35 (s, 3H). ^{13}C NMR, $CDCl_3$, δ 163.2 (CO), 161.5 (C), 154.5 (C), 148.9 (CH), 144.2 (CH), 136.4 (CH), 124.8 (CH), 121.5 (CH), 52.7 (CH_3), 14.4 (CH_3).$\nu_{max.}$/cm^{-1} 1720. HRMS (EI) calcd. for $C_{10}H_{11}N_3O_2$= 205.0851, found 205.0847.

Photoreaction of ylide (1d). Ylide 1d (0.060 g, 0.2 mmol) was irradiated for 3.5 h. A yellow oil was isolated after chromatography and identified as ethyl 2-[1-(2-pyridyl)ethylidenehydrazono]acetate 15b (59%). ^{1}H NMR (250 MHz), $CDCl_3$, δ 8.58 (ddd, J_{ab} = 4.3 Hz, J_{ac} = 1.6 Hz, J_{ad} = 0.7 Hz, 1H), 8.04 (d, J_{ac} = 8.0 Hz, 1H), 7.68 (ddd, J_{cd} = 8.0 Hz, J_{cb} = 7.60 Hz, J_{ca} = 1.8 Hz, 1H), 7.38 (s, 1H), 7.27 (ddd, J_{bc} = 7.4 Hz, J_{ba} = 4.7 Hz, J_{bd} = 1.16 Hz, 1H), 4.33 (q, J = 7.3 Hz, 2H), 2.35 (s, 3H), 1.33 (t, J = 7.3 Hz, 3H). ^{13}C NMR, $CDCl_3$, δ 162.8 (CO), 161.3 (C), 154.6 (C), 148.9 (CH), 144.5 (CH), 136.4 (CH), 124.8 (CH), 121.5 (CH), 61.9 (CH_2), 14.5 (CH_3), 14.2 (CH_3). $\nu_{max.}$/cm^{-1} 1700. HRMS (EI) calcd. for $C_{11}H_{13}N_3O_2$= 219.1007, found 219.1001.

General procedure for photoreactions of ylides 1a-b, 3a-b, 4a-b with acetylenic esters

Pyrex tubes containing a solution of the corresponding ylides (0.25 mmol) in dry acetonitrile were fixed to the external part of the quartz vessel, the corresponding acetylenic ester (10% excess) was added, the mixture was irradiated and filtered, the filtrate evaporated and the crude purified by chromatography. Time of irradiation, temperature, compounds formed and yields are given in tables 1 and 2. The only new compound formed is 4H-4,4-dicyano-2,3-dimethoxycarbonyl-1-methylquinolizine 26a. mp 183-185 ºC (hexane). ^{1}H NMR (400 MHz) δ ($CDCl_3$), 9.33 (dt, J_1 = 7.3 Hz, J_2 = 1.1 Hz, 1H), 7.46 (dt, J_1 = 8.7 Hz, J_2 = 1.1 Hz, 1H), 7.04 (ddd, J_1 = 8.3 Hz, J_2 = 6.9 Hz, J_3 = 1.1 Hz, 1H), 6.84 (ddd, J_1 = 7.1 Hz, J_2 = 6.9 Hz, J_3 = 1.44 Hz, 1H), 3.95 (s, 3H), 3.87 (s, 3H), 2.32 (s, 3H). ^{13}C NMR δ ($CDCl_3$), 167.3 (C=O), 160.9 (C=O), 135.0

(C), 127.1 (CH), 126.9 (C), 121.6 (CH), 117.5 (CH), 114.0 (CH), 109.9 (C), 77.2 (C), 52.4 (CH_3), 51.5 (CH_3), 8.8 (CH_3). ^{13}C NMR δ (DMSO-d_6), 168.0 (C=O), 160.9 (C=O), 159.9 (C), 153.2 (C), 135.0 (C), 126.6 (CH), 125.9 (C), 122.4 (CH), 118.3 (CH), 115.0 (CH), 109.8 (C), 79.4 (C), 52.5 (CH_3), 51.7 (CH_3), 8.6 (CH_3). $\nu_{máx}$ /cm^{-1} (KBr), 2254, 1728, 1687. HRMS (EI) calcd. for $C_{16}H_{13}N_3O_4$ = 311.0906, found 312.0981 (MH^+).

Acknowledgements

Our thanks to the Comisión Interministerial de Ciencia y Tecnologia (CICYT, project PB98-1422) for its financial support.

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