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[3+2]-Cycloaddition Reactions of 2-Phenyliodonio-1,3-dioxacyclohexanemethylide: Facile Synthesis of Fused Dihydrofuran Derivatives.

Amalia Asouti,[#] Lazaros P. Hadjiarapoglou,[*]

Section of Organic Chemistry, Department of Chemistry, University of Ioannina, 45110 Ioannina, GREECE.

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Abstract:

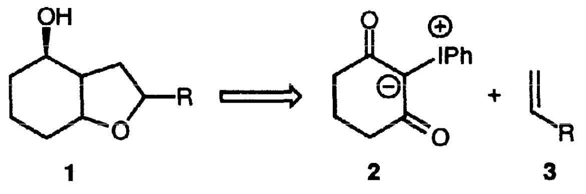
Iodonium ylide **2**, derived from 1,3-cyclohexadione, undergoes thermal [3+2]-cycloaddition with acetonitrile, carbon disulfide and *p*, *p*'- dimethoxythiobenzophenone with Cu(acac)$_2$ catalysis to form the corresponding 5-membered heterocycles and alkene respectively. Photochemically **2** reacts with various alkenes and dienes to form dihydrofuran derivatives, key intermediates for paniculide A, B and pentalene synthesis.

Keywords : Iodonium Ylide; [3+2]-Cycloaddition; Dihydrofuran.

The decomposition of diazo compounds in the presence of transition-metal catalysts has a remarkable potential in organic synthesis.[1] These catalysts mediate the formation of metallo carbenoids *in situ*, and transfer the carbene moiety to a suitable acceptor providing a wide range of synthetic transformations such as cyclopropanation, C-H and C-X insertion, and ylide formation. The intermediate metallo carbenoids often show high levels of stereoselectivity despite their high reactivity. But the major drawback of these reactions is the need for diazo compounds, which are potentially explosive, toxic, or/ and carcinogenic.

Presumably, the use of diazo compounds might be avoided if it was possible to generate the metallo carbenes from other precursors. Such alternatives could be iodonium ylides, a class of hypervalent iodonium compounds,[2] the photochemical and metal-catalysed decomposition[3] of which afford products typically of carbenoid reactions,[4] although the involvement of carbenes (or carbenoids) in these reactions has been questioned.[5]

Our interest in the chemistry of iodonium ylides stems from our anticipation that the 7-oxabicyclo[4.3.0]



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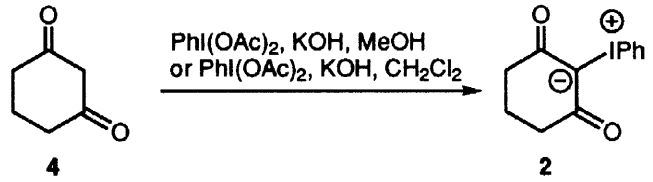
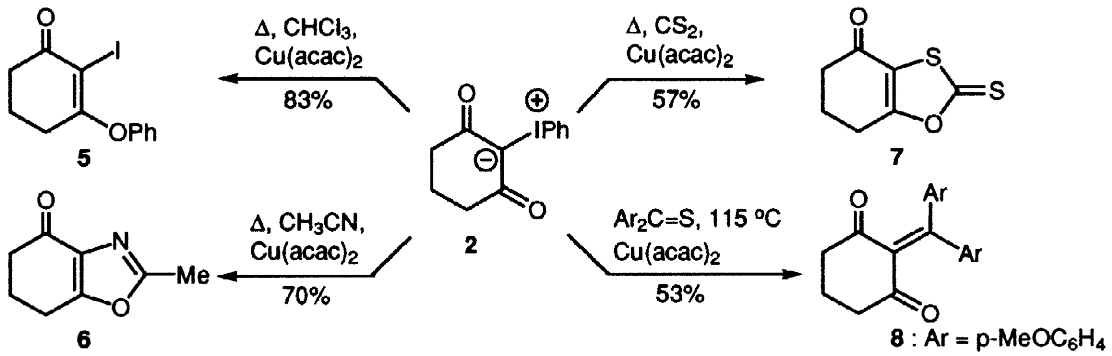
ring system, naturally occurring in paniculide A[6] and B,[7] temisin,[8] eriolanin,[9] etc. could be easily obtained via the reaction of an iodonium ylide with a suitable acceptor. We reasoned that the iodonium ylide **2** might be an ideal starting material to arrive at these ring systems. We have extended this work and report here the results of a series of systematic investigations leading into this valuable transformation.

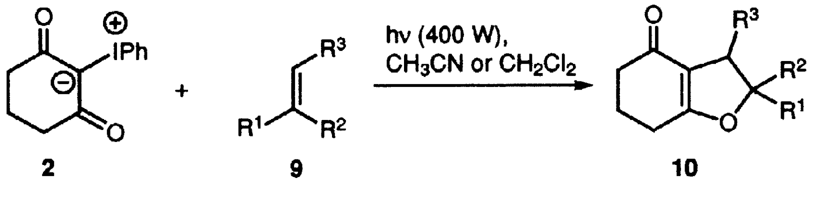
Iodonium ylide **2** was isolated as a stable white solid from the reaction of 1,3-cyclohexadione **4** and diacetoxyiodobenzene under classical Schank's conditions[10] (83% yield) or by the simpler Koser's method[11] (60% yield).



Although ylide **2** is stable at - 30 °C for a few months, it converted into the iodo ether **5** (83% yield) upon heating as a $CHCl_3$ solution in the presence of catalytic amounts of $Cu(acac)_2$. This iodo ether is a by-product of all the thermal Cu- or Rh-catalysed reactions of **2**. When acetonitrile was used as a solvent, the iodo ether **5** was again produced (18% yield) but the major product was now oxazole **6** (70% yield). By employing carbon disulfide, oxathiole **7** was isolated (57% yield) along with the iodo ether **5** (30% yield). Alkene **8** was isolated in moderate yield (53%) by simply heating a mixture of **2**, *p, p*'-dimethoxythiobenzophenone, and $Cu(acac)_2$ at 115 °C for 5 min. It is crucial to perform this reaction without a solvent, since the use of a solvent leads to the oxidation of the thiobenzophenone to benzophenone by the hypervalent iodonium compound.

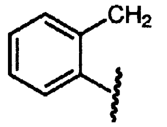
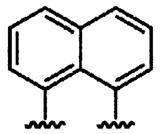


Next, we turned our attention into the reaction of **2** with alkenes and dienes for which, by analogy to the diazo chemistry,[12] dihydrofurans were expected to be formed. The Cu- or Rh- catalysed reactions gave the desired dihydrofurans, but the oily products were heavily contaminated by the iodo ether **5**. Thus, alternative photochemical conditions were investigated and a series of substituted dihydrofurans **10** were prepared in moderate to good yields (cf. Table 1) by the reaction of **2** with various alkenes and dienes.



The simple protocol[13] employed consisted of the irradiation [400 W medium pressure mercury lamp] of a suspension of **2** and the alkene **9** (excess) in the appropriate solvent for 30-240 min. The solvent and the

Table 1. Photochemical Reaction of Iodonium Ylide **2** with Alkenes **9**.

Entry	Alkene	Substituents			Reaction Conditions		Product	Yield (%)
		R^1	R^2	R^3	Solvent	Time (min)		
1	**9a**	Ph	H	H	CH_3CN	90	**10a**	58
2	**9b**	$PhCH_2$	H	H	CH_3CN	90	**10b**	22
3	**9c**	Ph	Me	H	CH_3CN	70	**10c**	37
4	**9d**	EtO	H	H	-	120	**10d**	86
5	**9e**	H	$CH_2CH_2CH_2$		CH_2Cl_2	120	**10e**	60
6	**9f**	H			CH_3CN	50	**10f**	70
7	**9g**	H	$CH{=}CHCH_2$		CH_3CN	40	**10g**	74
8	**9h**	H	OCH_2CH_2		CH_3CN	30	**10h**	68
9	**9l**	H			CH_3CN	240	**10l**	40
10	**9j**	H	$CH_2CH_2CH_2CH_2$		CH_2Cl_2	45	**10j**	26
11	**9k**	H	$OCH_2CH_2CH_2$		CH_3CN	00	**10k**	60

excess alkene were then removed to yield the dihydrofurans **10** as oils after flash column chromatography. In general, the best yields were obtained by using 5-membered cyclic alkenes and enol ethers. Styrene yielded dihydrofuran **10a** in 58% yield (entry 1) and the reaction with allylbenzene and α-methyl styrene afforded dihydrofurans **10b,c** in 22% and 37% yield respectively. 5-Membered cyclic alkenes and dienes **9e-g,i** provided the corresponding dihydrofurans **10e-g, i** in good yields, while cyclohexene gave the desired dihydrofuran **9j** only in 26% yield. Other alkenes, such as cyclooctene, *trans*-stilbene, norbornylene, camphene etc. either failed to react under these reaction conditions or gave complex reaction mixtures. The yield of the cycloaddition was improved when enol ethers were employed, as is shown for ethyl vinyl ether **9d** (86% yield; entry 4), dihydrofuran **9h** (68%; entry 8) and surprisingly dihydropyran **9k** (60% yield; entry 11). This indicates that an electrophilic carbene might be formed in the above photochemical decompositions of iodonium ylide **2**.

In summary, we have demonstrated that iodonium ylides are serving as a convenient and efficient "carbene" transfer agent for the formation of a variety of 5-membered heterocycles. We are presently examining the optimization and application of these reactions towards the synthesis of paniculide A, B and pentalene and our results will be presented in due course.

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[#] Undergraduate Research Participant, Spring 1997.

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13. All new compounds were fully characterized. Selected data for **10d** : ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, *J*= 7.1 Hz, 3H), 2.00-2.09 (m, 2H), 2.33 (t, *J*= 6.5 Hz, 2H), 2.44-2.45 (m, 2H), 2.63-2.67 (m, 1H), 2.92 (dd, J = 7.4, 15.8 Hz, 1H), 3.62-3.68 (m, 1H), 3.85-3.91 (m, 1H), 5.74 (dd, *J*= 3.3, 7.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8, 21.4, 23.7, 32.7, 36.2, 64.9, 108.4, 127.0, 175.6, 195.0.