



## Intramolecular Cyclization of Aryl Substituted Iodonium Ylides with Copper(I) Chloride

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**Abstract** : Cu(I)Cl decomposition of the phenyliodonium ylides derived from *o*-, *m*- and *p*-methoxyphenyl-3-ketopentanoic acid methyl esters affords the corresponding 5-, 6- and 7-methoxy-1-carbomethoxy-2-tetralones in preparative yields. The lower homologous phenyliodonium ylides derived from *o*-, *m*- and *p*-methoxyphenyl-3-ketobutyric acid methyl esters yield the analogous 1-carbomethoxy-2-indanone only in the meta-methoxyphenyl case, and the ortho- and para-methoxyphenyl substituted iodonium ylides yield dimeric products.

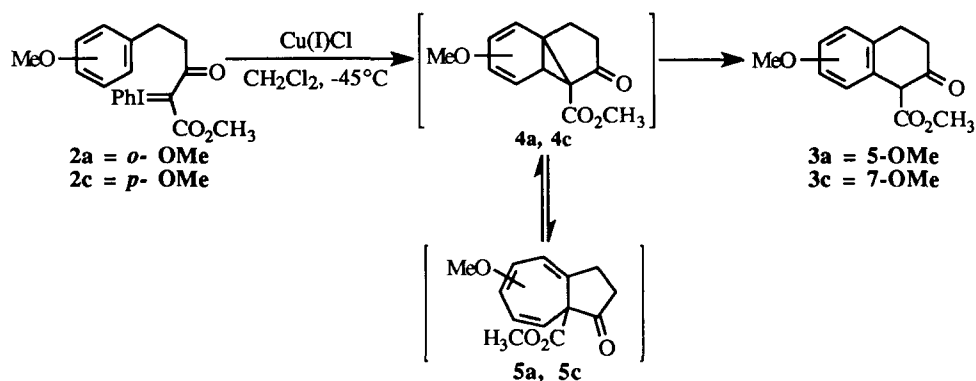
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Methyl 2-tetralone-1-carboxylates bearing methoxyl substituents on the aromatic ring are important precursors for a range of biologically active compounds. A case in point is the carbomethoxylation of 5-methoxy-2-tetralone to yield methyl 3,4-dihydro-2-hydroxy-5-methoxynaphthalene carboxylate (**3a** of the present paper) as a starting material for the synthesis of a benzidine prostacyclin.<sup>1</sup> A direct route *via* cyclization of a substituted methoxyphenyl precursor would be advantageous. Cyclization of 1-diazo-4-arylbutane-2-ones to 2-tetralones using Rh(II) catalysis has been reported.<sup>2a,b</sup> Because of our interest in organohypervalent iodine, we undertook adaptation of this methodology to the above mentioned synthetic problem.

Iodonium ylides derived from  $\beta$ -dicarbonyl are synthetically equivalent to the corresponding diazo  $\beta$ -dicarbonyl compounds in certain reactions. We have already shown that iodonium ylides derived from  $\beta$ -keto esters effect Cu(I)Cl promoted intramolecular cyclopropanation of appropriately positioned double bonds within the molecule.<sup>3a,b</sup> Thus, the C=IPh unit can be effectively substituted for the C=N<sub>2</sub> group. A similar parallel in reaction behavior has been shown by Müller *et al.* in the intramolecular C-H insertion reaction of iodonium ylides of  $\beta$ -keto esters upon decomposition with Rh<sub>2</sub>(OAc)<sub>4</sub>.<sup>4</sup> Padwa *et al.* have used iodonium ylides as an  $\alpha$ -diazo equivalent in the intramolecular cycloadditions of carbonyl ylides.<sup>5</sup> These parallels between C=N<sub>2</sub> and C=IPh led us to examine the above mentioned important syntheses of tetralones as well as indanones *via* intramolecular reactions of a  $\beta$ -keto ester with an adjacent aromatic ring. The advantages of substitution of C=IPh for C=N<sub>2</sub> resides in toxicity considerations (potential carcinogenicity of diazo compounds) and safety (the diazoketones of ref. 2a are prepared from diazomethane and the synthesis are not suitable for multigram reactions).

Aryl substituted  $\beta$ -keto esters **1a-c** were converted to the corresponding iodonium ylides **2a-c** *via* treatment with PhI(OAc)<sub>2</sub>/KOH. Iodonium ylides **2a-c** were decomposed with Cu(I)Cl in dichloromethane at -45°C to give the substituted methyl 2-tetralone-1-carboxylates **3a-c** (scheme 1). Thus, a solution of

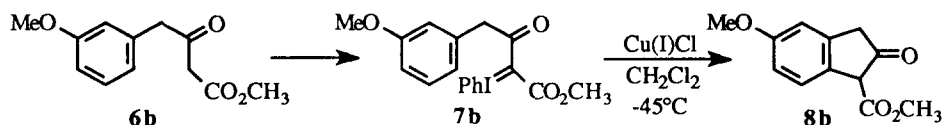
individual iodonium ylides **2a-c** (493 mg, 1 mmol) in 50 ml of dry dichloromethane at  $-45^{\circ}\text{C}$  under argon was added dropwise to a stirred suspension of  $\text{Cu(I)Cl}$  (100 mg, 1 mmol) in 250 ml of dry dichloromethane over a 60 min. period. The reaction was maintained at  $-45^{\circ}\text{C}$ , protected from light and then allowed to warm to room temperature over 2 hr. period. The crude tetralones were purified by column chromatography to yield the pure substituted methyl-2-tetralone-1-carboxylates **3a-c**; **3a**(75%), **3b**(90%) and **3c**(82%) (scheme 1).



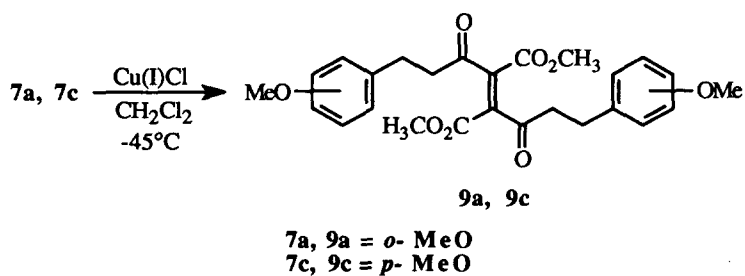
Scheme 1

A pathway for the formation of 2-tetralones **3a** and **3c** involves intramolecular cyclopropanation of the arene ring to give **4a** and **4c** which are in equilibrium with the Buchner intermediates **5a** and **5c** (scheme 1). The intermediacy of **5a** and **5c** was established by  $^1\text{H}$  NMR and TLC.<sup>6</sup> For the meta methoxyl ylide **2b**, no intermediate of this type as detected for **2a,c**  $\rightarrow$  **5a,c** was observed. The pathway of scheme 1 resembles the course of reactions proposed for the analogous decomposition for  $\alpha$ -diazoketo compounds.<sup>(2a,b)</sup>

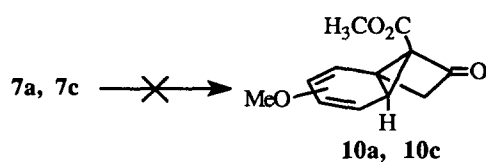
The cyclization process for 2-tetralones is not as useful synthetically for the iodonium ylides of the lower homologous *o*-, *m*- and *p*-4-methoxyphenyl-3-ketobutyric acid methyl esters **7a-c**. In the case of meta-methoxy compound **7b** the corresponding substituted 1-carbomethoxy-2-indanone **8b** is formed in 65% yield.



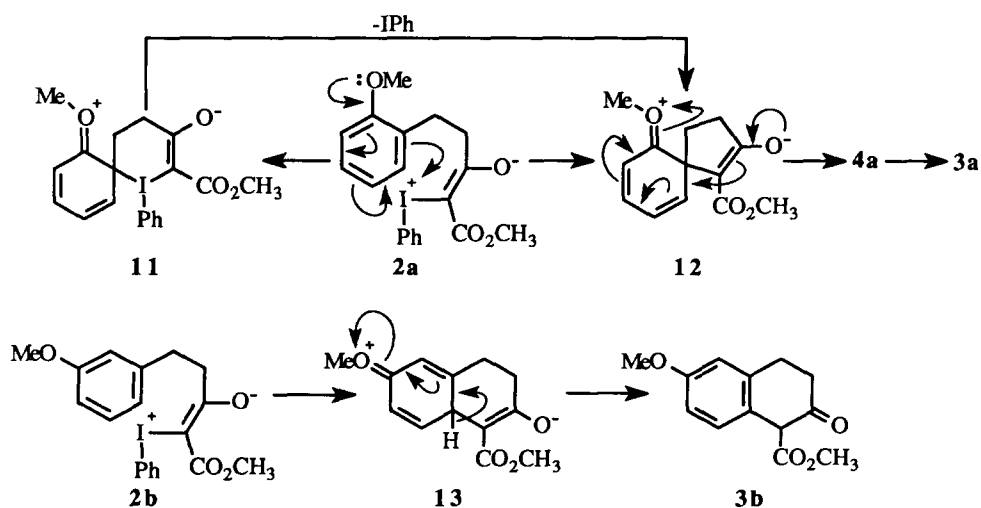
In the cases of the ortho- and para-methoxy compounds **7a** and **7c** respectively, only the corresponding trans dimers **9a** and **9c** are observed.<sup>7</sup>



Intramolecular cyclopropanation analogous to  $2a, 2c \rightarrow 4a, 4c$ , in the case of  $7a$  and  $7c$ , would generate a highly strained tricyclic butanones **10a** and **10c**.



The facts that  $2b \rightarrow 3b$  apparently occurs directly and only  $7b$  yields the cyclized product **8b** may be mechanistically connected. We propose that intramolecular cyclopropanation in the cases  $2a \rightarrow 3a$  and  $2c \rightarrow 3c$  is a stepwise process (as is shown below for  $2a$ ):



The same process as in  $2a \rightarrow 11 \rightarrow 4a$  can be drawn for  $2c \rightarrow 3c$ . Only in the meta-methoxyl cases ( $2b$  and  $7b$ ) can simple deprotonation of the initial intermediate lead directly to aromatization  $2b \rightarrow 13 \rightarrow$

**3b.** The flow of electrons in **2a** → **12** is arbitrary. Attack may be at the iodonium center with subsequent loss of PhI from the tricoordinate iodane intermediate as in **2a** → **11** → **12**. The role of Cu(I)Cl in generation of the dipolar intermediate is unknown. These points are objects of current research.

**Acknowledgements.** We wish to thank the National Science Foundation for support of this work (grant number: CHE-9520157).

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## References and Notes

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6. The dihydroazulene intermediates **5a** and **5c** were identified by comparison of <sup>1</sup>H NMR data of compounds with similar structures found in literature: **5a**<sup>2b</sup> and **5c**<sup>2a</sup>.  
**5a**: <sup>1</sup>H NMR (400Mhz, CDCl<sub>3</sub>): δ, 2.5-3.2 (4H, m, 2-H<sub>2</sub> and 2-H<sub>3</sub>), 3.55 (3H, s, -CO<sub>2</sub>CH<sub>3</sub>), 3.65 (3H, s, -OCH<sub>3</sub>), 5.68 (1H, d, J=6.9 Hz, H<sub>8</sub>), 6.3-6.4 (3H, m, H<sub>5</sub>, H<sub>6</sub> and H<sub>7</sub>).  
**5c**: <sup>1</sup>H NMR (400Mhz, CDCl<sub>3</sub>): δ, 2.5-3.2 (4H, m, 2-H<sub>2</sub> and 2-H<sub>3</sub>), 3.59 (3H, s, -CO<sub>2</sub>CH<sub>3</sub>), 3.60 (3H, s, -OCH<sub>3</sub>), 5.44 (1H, d, J=10.8 Hz, H<sub>8</sub>), 5.66 (1H, d, J=7.2 Hz, H<sub>4</sub>), 6.2-6.3 (2H, m, H<sub>5</sub> and H<sub>7</sub>).
7. The X-ray structure of **9c** was determined by Richard Gilardi, Laboratory of the Structure of Matter, Naval Research Laboratory, Washington D.C. and details will be reported in the full paper.

(Received in USA 16 April 1997; accepted 1 May 1997)