Effect of Ultrasound on the Arylation of Methylene-Active Compounds with 4-Iodotoluene

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Ultrasound slightly accelerates the arylation of malonodinitrile and ethyl cyanoacetate with 4-iodotoluene under CuI and K_2CO_3 catalysis. Sonochemical reactions gave reasonable yields of the products even at 40 °C for 3—4 h, while the silent reactions had to be performed at 120 °C for 20—40 h. Reactions with other methylene-active compounds were also examined.

Thermal arylation of ethyl cyanoacetate by different iodoarenes under CuI catalysis was recently described [1]. It was postulated that reaction was going *via* anion radical intermediate. On the other hand, a hypothesis was published [2, 3] that ultrasound should promote only such homogeneous reactions which are going *via* a SET mechanism. The main aim of this work was to test the validity of this hypothesis on the above-mentioned reaction.

Our preliminary results [4] revealed that arylation of methylene-active compounds with different iodoarenes gave satisfactory results with malonodinitrile and ethyl cyanoacetate. We decided therefore to investigate thoroughly the reaction of these two and some other methylene-active compounds with 4-iodotoluene. The course of reaction is shown in Scheme 1 and the results we achieved are summarized in Table 1.

For comparison we decided to perform some experiments at the conditions given in Ref. [1]. To our surprise, we found that stirring the reaction mixture of 4-iodotoluene (*I*) with malonodinitrile (*IIa*) and ethyl cyanoacetate (*IIb*), respectively for 3 h at 120 °C in DMSO afforded resonable yields of the products *IIIa* and *IIIb*. The long reaction time given in [1] is not necessary.

From the results given in Table 1 it follows that reactions under ultrasound conditions afforded the desired products *IIIa* and *IIIb* but the yields of the products were not satisfactory. To exclude the possibility that this could be caused by the low reaction temperature an experiment at 100 °C was performed. The product was isolated in a very low yield in spite of the fact that conversion of 4-iodotoluene was very high, similar to that determined in experiment performed at 40 °C. We assume that these unsatisfied yields of the desired products are caused by a competitive dehalogenation of iodoarene affected by ultrasound. There are some indirect proofs for this hypothesis. First of all dechlorination of carbon tetrachloride by ultrasound in water was described [5] and secondly at some unsuccessful experiments we isolated the side products, which are formed just from the methylene-active component (no aromatic protons in NMR spectrum), but structure of this material was not yet fully determined.

To exclude the possibility that the low yields of the products at sonochemical experiments are just results of thermal reaction at the lower temperature a silent experiment at 40 °C was conducted, but no products were either isolated or detected by GC-MS technique. To prove that reaction is going *via* a SET (single electron transfer) mechanism (Scheme 2) an experiment without CuI was also conducted and just starting materials were detected and isolated from the reaction mixture.

The fact that just slight effect of ultrasound was observed indicates that the SET mechanism postulated for this reaction is questionable.

In spite of the fact that no reaction of other methylene-active compounds with iodoarenes was described [1], we decided to examine also acetylacetone (*IIc*), dibenzoyl methane (*IId*), and diethyl malonate (*IIe*) as reagents.

From our results it follows that no arylation was observed either at silent or sonochemical reactions. In sonochemical reaction with dibenzoyl methane (*IId*)

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Table 1. Results of the Arylation of Methylene-Active Compounds with *p*-Iodotoluene

	$CH_2Z^1Z^2$	Φ/°C	t/h	Type of reaction	Product	Yield/%
1	*IIa*	120	3	silent	*IIIa*	57.6
2	*IIa*	90	3	)))	*IIIa*	10.7
3	*IIa*	40	3	silent		
4	*IIa*	40	3	)))	*IIIa*	12.8
5	*IIa*	40	3	)))*		
6	*IIa*	40	0.5	)))	*IIIa*	6.0
7	*IIb*	120	3	silent	*IIId*	56.6
8	*IIb*	90	3	)))	*IIId*	17.2
9	*IIb*	40	3	)))	*IIId*	28.7
10	*IIb*	40	0.5	)))	*IIId*	2.1
11	*IIc*	120	4	silent	*IIIe*	10.4
12	*IIc*	40	3	)))	*IVa*	< 1
13	*IId*	120	20	silent		–
14	*IId*	120	3	silent		–
15	*IId*	90	3	)))	*IVb, IVc*	< 1
16	*IId*	40	3	)))	*IVb, IVc*	< 1
17	*IIe*	120	20	silent		
18	*IIe*	120	3	silent		
19	*IIe*	90	3	)))		
20	*IIe*	40	3	)))		

*Experiment without catalyst CuI.

Table 2. Characterization of Compounds *IVa*—*IVc*

Compound	Formula M_r	w_i(calc.)/% w_i(found)/% C	H	S	Yield/%	M.p./°C
IVa	$C_6H_{10}O_2S$	49.29	6.89	21.93	< 1	Oil
	146.20	49.68	7.08	22.76		
IVb	$C_{16}H_{14}O_2S$	71.08	5.22	11.86	< 1	80—85
	270.33	71.54	5.25	11.79		
IVc	$C_{31}H_{24}O_4$	80.85	5.25		< 1	165—170
	460.50	80.07	4.95	–		

Table 3. ^{1}H NMR Spectra of Compounds *IVa*—*IVc*

Compound	Chemical shift, δ
IVa	1.85 (s, 3H, S—CH_3), 2.36 (s, 6H, 2 × CH_3), 3.33 (s, 1H, CH)
IVb	2.20 (s, 3H, S—CH_3), 5.76 (s, 1H, CH), 7.26—8.05 (m, 10H_{arom})
IVc	2.77 (t, 2H, J = 7.0 Hz, CH_2), 5.75 (t, 2H, J = 7.0 Hz, 2 × CH), 7.26—8.20 (m, 20H_{arom})

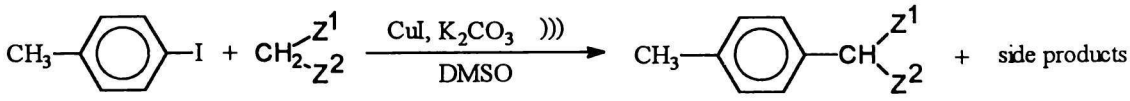
just very low yields of the side products (*IVa*—*IVc*) were isolated (Table 2). The structure of the side product was determined by ^{1}H NMR spectra (Table 1) as well as MS – M^+ = 146 (*IVa*), M^+ = 270 (*IVb*), M^+ = 460 (*IVc*).

Formation of the side products *IVa*—*IVc* (Tables 3 and 4) is a result of the reactions of methylene-active compounds with radicals formed from the solvent. DMSO is decomposed by ultrasound to form radicals [6]. No products *IVa*—*IVc* were isolated or detected in the silent reactions.

As it follows from Table 1 there were no products isolated or detected after the reactions of 4-iodotoluene with *IId* and *IIe*. Possible explanation of these results is given in Table 4. The ionization potentials of the C-anions of *IId* and *IIe* (keto) are higher than the values of ionization potential of the C-anions of *IIa* and *IIb*. There is a possibility for *IIc* and *IId* to exist as enol- or keto-tautomeric forms and as it follows from values of the heat of formation for anions of *IIc* and *IId* the keto forms of them are more stable structures.

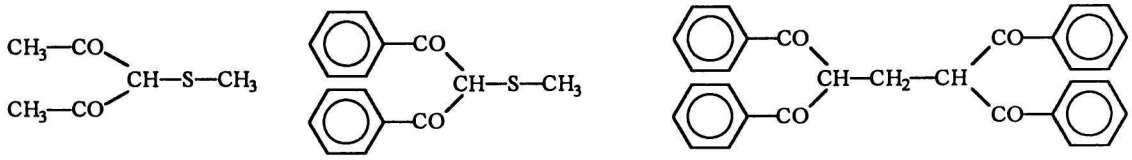
EXPERIMENTAL

4-Iodotoluene (Avocado) was used without purifi-



I *II* *III* *IV*

	Z^1	Z^2
a	CN	CN
b	COOEt	CN
c	$COCH_3$	$COCH_3$
d	COPh	COPh
e	COOEt	COOEt



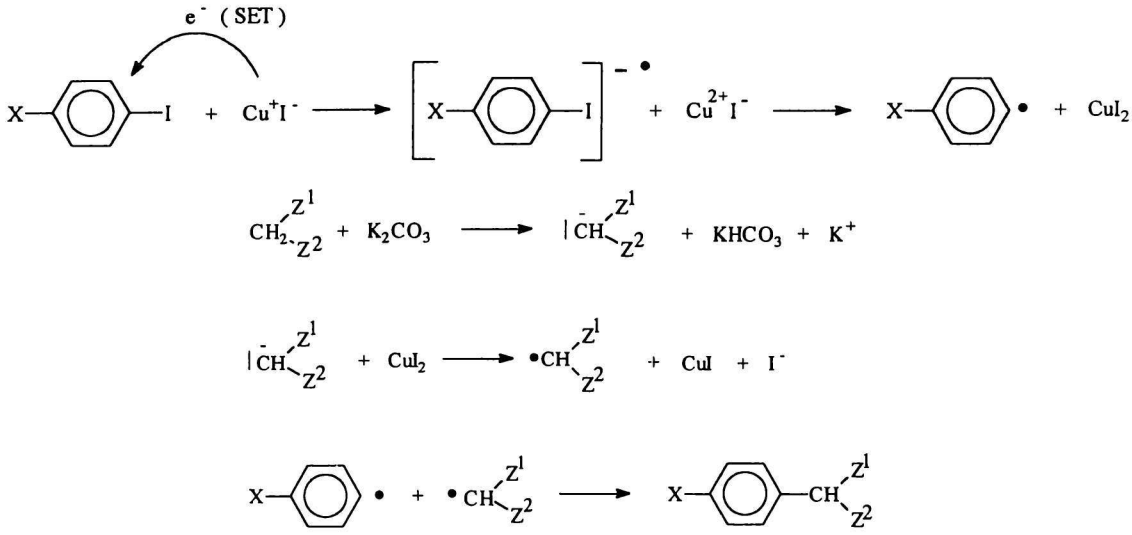
IVa *IVb* *IVc*

Scheme 1

cation. The methylene-active compounds were obtained from Aldrich and Fluka, respectively. ^{1}H NMR spectra (δ, J/Hz) of the samples were recorded in $CDCl_3$ on a Tesla BS 487 (80 MHz) instrument with tetramethylsilane as internal standard. GC-MS measurements were performed on a HP 5890 Series II gas chromatograph. Sonochemical experiments were performed in an ultrasonic horn reactor UUA 001 ULTRAGEN (20 kHz, 300 W) that worked in a 50 % cycle under N_2 atmosphere. Efficiency of sonication was characterized by the KI $\rightarrow$ KI_3 test [8]. Sonication of 50 cm^3 of 1 M-KI for 3 min gave 4.7×10^{-6} mol dm^{-3} of KI_3. Melting points were measured on a Kofler hot plate apparatus. Quantum chemical results have been obtained by the AM1 semiempirical method with full optimization and standard parametrization [9].

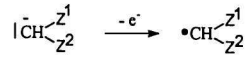
Sonochemical Arylation of Methylene-Active Compounds with 4-Iodotoluene

A mixture of 4-iodotoluene (*I*) (470 mg; 2.0 mmol), methylene-active compound (*IIa—IIe*) (4.0 mmol), and CuI (38 mg; 0.2 mmol) in DMSO (5 cm^3) was irradiated by ultrasonic horn reactor (20 kHz, 300 W) for 4 h under nitrogen. The reaction mixture was then poured into diluted (5 cm^3 HCl in 50 cm^3 H_2O) hydrochloric acid, extracted with diethyl ether. Ethereal



Scheme 2. SET mechanism of the reaction shown in Scheme 1.

Table 4. AM1 Values of the Ionization Potential (IP) and Heat Formation (ΔH_f) of the Anions of the Methylene-Active Compounds



Compound	Tautomeric form	IP/eV	w(Enol)/% [7]	ΔH_f/(kJ mol^{-1})
IIa	keto	2.836		–
IIb	keto	3.365	0.25	
IIc	keto	3.297		−463.48
IIc	enol	1.777	80	−167.00
IId	keto	3.819		−180.03
IId	enol	2.562	> 90	+71.73
IIe	keto	3.760	0.0077	

solution was dried over sodium sulfate and the solvent was evaporated. Products of the reactions were isolated by column chromatography on silica gel using isohexane—ethyl acetate (φ_r = 5 1, 10 1, respectively) as eluent.

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