# THE ADDITION REACTION OF DIALKYL CARBONATES TO KETONES (*)

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Summary — The reaction of benzyl phenyl ketone with dimethyl carbonate gives methyl benzoate and methyl phenylacetate; diethyl carbonate gives the corresponding ethyl esters. The reaction takes place at high temperature (about 200 °C) and in the presence of potassium carbonate as a catalyst. Other benzyl ketones react similarly. Aliphatic ketones yield a less selective addition. Accordingly, cyclohexanone with dimethyl carbonate gives dimethyl pimelate. The reaction is a *retro*-Claisen condensation, which occurs through the intermediate formation of the alkoxycarbonyl derivative.

It has already been reported[1,2] that a highly selective mono-methylation of arylacetonitriles, lactones and malonic esters with dimethyl carbonate (DMC) takes place according to eq. *1*.

$$ArCH_2X + DMC \xrightarrow{\text{base}} ArCH(CH_3)X + \\ + CH_3OH + CO_2 \qquad 1$$

$$X = CN, COOCH_3$$
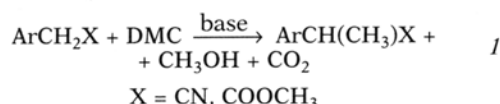
In an attempt to selectively alkylate other CH-acidic compounds with dialkyl carbonates and particularly methylene-active compounds with DMC, benzyl phenyl ketone has now been reacted with DMC.

Although the methylene group of benzylic ketones is more acidic than that of arylacetonitriles (thus the carbanion generated under basic conditions may more easily give nucleophilic displacements according to a $B_{Al}2$ mechanism[1a]), the main reaction observed was the cleavage of the -CH$_2$-CO- bond and the formation of two esters, according to eq. *2a*.

$$PhCH_2COPh + CH_3OCOOCH_3 \rightarrow PhCOOCH_3 + \\ + PhCH_2COOCH_3 \qquad 2a$$

RESULTS

Reactions *2* were carried out at high temperature (about 200 °C), in a mixture of ketone, dialkyl carbonate and K_2CO_3 in the molar ratio of 1:20:2, respectively.

Methyl esters were produced by DMC in high yields and without any intermediates detectable by gas-chromatography. As reported in table 1, this reaction seems to be a general one: it can be applied to benzylic ketones and, although with lower selectivity, to aliphatic ketones, both linear and alicyclic.

Also diethyl carbonate (DEC) reacts with benzylic and aliphatic ketones in a similar way; the reaction

provides ethyl esters, according to eq. *2b*. The results are shown in table 2.

$$PhCH_2COPh + C_2H_5OCOOC_2H_5 \rightarrow PhCOOEt + \\ + PhCH_2COOEt \qquad 2b$$
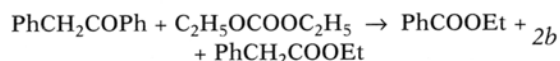
The main difference between DMC and DEC (compare tables 1 and 2) does not concern the respective addition rate to the ketones (eqs. *2*), but rather the rate of the subsequent alkylation reaction of the esters with the dialkyl carbonate[2b]; for example, eq. *3* shows the alkylation with DMC of the ester produced from reaction *2a*.

$$PhCH_2COOCH_3 + DMC \rightarrow PhCH(CH_3)COOCH_3 + \\ + CH_3OH + CO_2 \qquad 3$$
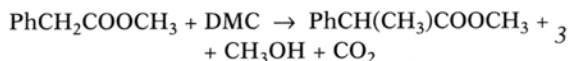
The higher steric hindrance of the ethyl group, compared to that of the methyl group, can justify the observation that the addition of DEC to ketones gives rise to a smaller amount of alkylation by-products; this is in accordance with the fact that nucleophilic attack to DEC, according to eq. *1*, was remarkably slower than to DMC[1].

Furthermore, it is unlikely that esters produced in reaction *2* may derive from a direct alkylation of the ketones followed by the C-CO bond cleavage, because when the alkylated derivatives of the ketones were reacted with DMC (entries 7 and 8, table 1; *vide infra*, eqs. *11* and *12*), they prefer by far to undergo a subsequent slower alkylation (at the already alkylated carbon), rather than cleavage.

DISCUSSION

REACTION MECHANISM

Some preliminary tests were carried out in order to investigate the mechanism of this reaction.

a) The addition of dialkyl carbonates to ketones does not take place in the absence of the base: under the conditions of table 1, after 5 h at 200 °C, no reaction occurs if a base is not present; therefore, the process has carbanionic species as intermediates.

TABLE 1 - REACTIONS OF DIMETHYL CARBONATE WITH BENZYLIC AND ALIPHATIC KETONES[a]

| ENTRY	SUBSTRATE	TEMPERATURE (°C)	REACTION TIME (h)	CONVERSION[b] (%)	PRODUCTS (mol % referred to converted ketone)
1	$PhCH_2COCH_3$	195	6.4	88	$PhCH_2COOCH_3$ (71)[c]
2	$PhCH_2COPh$	200	6.5	71	$PhCOOCH_3$ (99) $PhCH_2COOCH_3$ (66)[d]
3	$p\text{-}CH_3PhCOCH_2Ph$	200	5.8	78	$p\text{-}CH_3PhCOOCH_3$ (99) $PhCH_2COOCH_3$ (65)[e]
4	$(CH_3CH_2CH_2)_2CO$	200	6.7	99	$CH_3CH_2CH_2COOCH_3$ (34)
5	Cyclopentanone	200	4.0	80	$(CH_2)_4(COOCH_3)_2$ (14)
6	Cyclohexanone	200	11.4	88	$(CH_2)_5(COOCH_3)_2$ (11)
7	$PhCH(CH_3)COPh$	200	6.2	98	$PhC(CH_3)_2COPh$ (70)[f]
8	$PhCH(C_4H_9)COCH_3$	200	7.6	38	$PhCH(CH_3)(C_4H_9)COCH_3$ (32)

(a) Molar ratio ketone : DMC : K_2CO_3 = 1:20:2. (b) Conversions were determined by GC. All products were identified by comparison with authentic samples. (c) Other identified products were $PhCH(CH_3)COOCH_3$ and $PhCH(CH_3)COCH_3$ (4% and 11%, respectively). (d) Other identified products were $PhCH(CH_3)COOCH_3$ and $PhC(CH_3)(COOCH_3)_2$ (5% and 11%, respectively). (e) Other identified products were $PhCH(CH_3)COOCH_3$ and $PhC(CH_3)(COOCH_3)_2$ (5% and 10%, respectively). (f) Other identified products were $PhCOOCH_3$ and $PhCH(CH_3)COOCH_3$ (9% and 8%, respectively).

b) The reaction of benzyl phenyl ketone with ethylene carbonate, carried out under the conditions of table 1, does not give the product which would be expected if the addition mechanism consists of a C-CO bond cleavage with the simultaneous insertion of the carbonate molecule into the ketone skeleton, eq. 4.

$$PhCH_2COPh + \text{(ethylene carbonate)} \not\longrightarrow$$
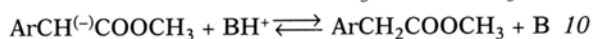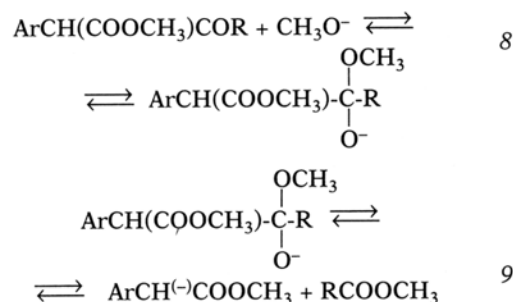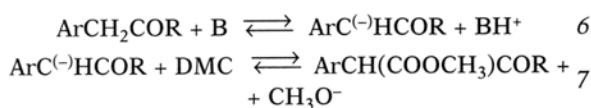$$\not\longrightarrow PhCH_2COO(CH_2)_2OCOPh \qquad 4$$
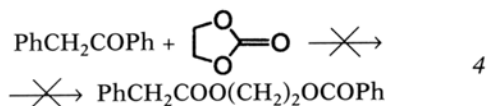
Instead, polymerization products were almost exclusively formed during reaction 4 and not even traces of the mixed ethylene glycol diester were observed.

c) Under the conditions of table 1 (200 °C, 5 h, using either K_2CO_3 or t-BuOK as catalysts), no reaction takes place between methyl benzoate and methyl acetate; thus, the addition product of the classical Claisen condensation (eq. 5) does not form under such conditions.

$$PhCOOCH_3 + CH_3COOCH_3 \not\longrightarrow$$
$$\not\longrightarrow PhCOCH_2COOCH_3 + CH_3OH \qquad 5$$
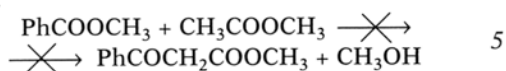
From these results, it might be concluded that the mechanism, at least as far as the reaction between benzylic ketones and DMC is concerned, involves equilibria 6-10.

$$ArCH_2COR + B \rightleftarrows ArC^{(-)}HCOR + BH^+ \qquad 6$$
$$ArC^{(-)}HCOR + DMC \rightleftarrows ArCH(COOCH_3)COR + \; + CH_3O^- \qquad 7$$

$$ArCH(COOCH_3)COR + CH_3O^- \rightleftarrows$$
$$\rightleftarrows ArCH(COOCH_3)\text{-}\underset{\underset{O^-}{|}}{\overset{\overset{OCH_3}{|}}{C}}\text{-}R \qquad 8$$

$$ArCH(COOCH_3)\text{-}\underset{\underset{O^-}{|}}{\overset{\overset{OCH_3}{|}}{C}}\text{-}R \rightleftarrows$$
$$\rightleftarrows ArCH^{(-)}COOCH_3 + RCOOCH_3 \qquad 9$$

$$ArCH^{(-)}COOCH_3 + BH^+ \rightleftarrows ArCH_2COOCH_3 + B \quad 10$$

Reaction 7, which is a condensation between DMC and the benzylic ketone, has been already reported in the case of alicyclic ketones[3,4]; equilibria 8 and 9 represent a reverse Claisen reaction, by which the β-keto ester produced in 7 is split.

The driving force shifting equilibria 6-10 towards the C-CO bond cleavage rather than towards its formation (as occurs in the Claisen reaction), seems to be influenced by the weak base used (potassium carbonate) and the high temperature; the latter may alter the value and the sign of the free energy, ΔG, during the sequence of reactions 6-10[a].

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(a) The reaction of benzyl phenyl ketone with a 20 molar excess of DMC (b.p. 90 °C) or DEC (b.p. 124 °C) was carried out at the reflux temperature (atmospheric pressure) in the presence of CH_3ONa/CH_3OH or EtONa/EtOH, respectively. Both reactions successfully proceeded according to eqs. 2a and 2b but, while the former showed only 20% conversion after 15 h, the latter gave 96% conversion after 3 h. The faster reaction with DEC may be easily explained by the higher reaction temperature.

TABLE 2 - REACTIONS OF DIETHYL CARBONATE WITH BENZYLIC KETONES[a]

ENTRY	SUBSTRATE	TEMPERATURE (°C)	REACTION TIME (h)	CONVERSION [b] (%)	PRODUCTS (mol % referred to converted ketone)
1	$PhCH_2COCH_3$	200	3.25	5	–
		210	2.0	11	–
		220	2.75	98	$PhCH_2COOEt$ (87) [c]
2	$PhCH_2COPh$	200	3.2	8	–
		210	5.1	98	$PhCOOEt$ (99) [d]
					$PhCH_2COOEt$ (61)
3	$p\text{-}CH_3PhCOCH_2Ph$	200	1.3	2	–
		210	7.5	96	$p\text{-}CH_3PhCOOEt$ (95) [e]
					$PhCH_2COOEt$ (88)

(a) Molar ratio ketone : DEC : K_2CO_3 = 1:20:2. (b) Conversions were determined by GC. All products were identified by comparison with authentic samples. (c) Other identified products were $PhCH(CH_3)COOEt$, $PhCH(COOEt)_2$ and $PhC(Et)(COOEt)_2$ (2.4%, 2.4% and 8.7%, respectively). (d) Other identified products were $PhCH(Et)COOEt$, $PhCH(COOEt)_2$ and $PhC(Et)(COOEt)_2$ (4.2%, 3.4% and 20.0%, respectively). (e) identified products were $PhCH(COOEt)_2$ and $PhC(Et)(COOEt)_2$ (2.6% and 2.2%, respectively).

However, as regards reaction 2, there are still some important aspects which cannot be taken for granted: unexpectedly, the addition reaction of the dialkyl carbonates with the alkylated derivatives of the ketones took place only to a very small extent even in the case of the relatively small methyl group, as reported in eq. *11*.

$$ArCH(CH_3)COAr' + DMC \xrightarrow{\quad\times\quad}$$
$$\xrightarrow{\quad\times\quad} ArCH(CH_3)COOCH_3 + Ar'COOCH_3 \qquad 11$$
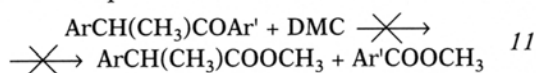
Indeed, these compounds underwent a slow ketone alkylation that, in the case of DMC, produced the dimethyl derivative (eq. *12*):

$$ArCH(CH_3)COAr' + DMC \xrightarrow{\qquad\qquad}$$
$$\xrightarrow{\qquad\qquad} ArC(CH_3)_2COAr' + CO_2 + CH_3OH \qquad 12$$
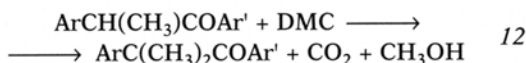
This result may indicate that little differences in carbanion stability, induced by alkyl groups, strongly influence equilibria *7-10*.

CONCLUSIONS

The addition of dialkyl carbonates to ketones and the simultaneous formation of two esters coming from the C-CO bond cleavage of the ketone, have never been reported although, as regards condensation reactions, the single mechanistic steps here suggested, are well established since long time.

Being methyl (ethyl) esters the final products, the overall reaction results in the oxidation of ketones, so that it might also be classified as a possible alternative to the Baeyer-Villiger reaction.

The reaction of ketones or arylacetonitriles with DEC, under normal conditions of temperature, produces β-keto esters or β-cyano esters, respectively. In our case, in spite of the high temperature (or because of this), the reactions of dialkyl carbonates

with arylacetonitriles or ketones are highly selective in producing alkyl derivatives (eq. *1*) or addition products (eqs. *2a* and *2b*), respectively.

Also alicyclic ketones, when reacted according to eq. *2*, produce esters of α,ω-dicarboxylic acids (entries 5 and 6, table 1); these compounds are of interest for the production[5a,b] of polyesters and polyamides. In this way, the addition reaction of DMC (DEC) to ketones produces dimethyl (diethyl) esters of dicarboxylic acids, while the carbon atom chain of the molecule becomes longer by one unit. In industrial processes, α,ω-dicarboxylic acids are prepared by oxidation of alicyclic ketones[6].

EXPERIMENTAL

GENERAL PROCEDURES FOR REACTIONS CARRIED OUT IN AUTOCLAVE

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