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Direct Preparation of Monoarylidene Derivatives of Aldehydes and Enolizable Ketones with DIMCARB

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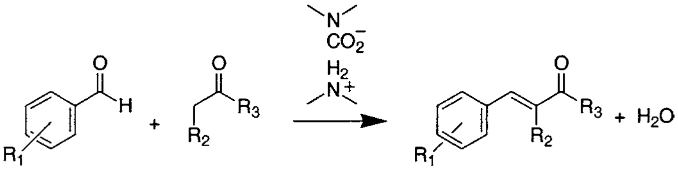
ABSTRACT



Aryl α,β-unsaturated ketones and aldehydes were synthesized, in moderate to excellent yields, with use of dimethylammonium dimethyl carbamate (DIMCARB) as a recyclable reaction medium and as a catalyst.

For other research, we required mono-2-arylidene derivatives of ketones, particularly of cyclohexanone and cyclopentanone. Direct access to these compounds from the parent ketones and aryl aldehydes by Claisen−Schmidt condensations[1] was not straightforward. Several publications,[2,1b] including from our laboratory,[3] have demonstrated that typically, such reactions proceed beyond mono-condensation. Diadducts such as *E*,*E*-2,6-dibenzylidenecyclohexanone or *E*,*E*-2,5-dibenzylidenecyclopentanone can be formed exclusively, even when the molar ratio of starting aldehyde to ketone is substantially below 1:1.[2a] Consequently, preparation of the monoarylidene adducts usually requires at least two steps, i.e. aldol addition followed by a separate elimination.[4] Aldol addition is readily reversible[5] and to avoid this, the Mukaiyama approach starting from the trimethylsilyl enol ether of the ketone[6] has gained favor.[7] Silylation of the ketone introduces another step and lowers the atom economy.[8] We now report that in or with DIMCARB (*N*,*N*-dimethylammonium *N*′,*N*′-dimethylcarbamate),[9] the monoarylidene derivatives of ketones and enolizable aldehydes can be prepared directly, with high selectivity, in moderate to excellent yields.

DIMCARB is an adduct of CO_2 and Me_2NH, both of which are gases under ambient conditions. It is a relatively stable liquid up to 50 °C and can be produced in bulk, readily and inexpensively.[9] It has substantial ionic character and can dissolve salts such as LiCl, NaCl, NaBr, KCl, and KI at levels between 2 and 5% w/v.[10] While lower than that of water and higher than that of hydrophobic organic solvents, such polarity is comparable with that of ionic liquids,[11] which have

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[1] (a) Le Gall, E.; Texier-Boullet, F.; Hamelin, J. *Synth. Commun.* **1999**, *29*, 3651. (b) Toda, F.; Tanaka, K.; Hamai, K. *J. Chem. Soc., Perkin Trans. 1* **1990**, *28*, 3207. (c) Noyce, D. S.; Pryor, W. A. *J. Am. Chem. Soc.* **1955**, *77*, 1397.

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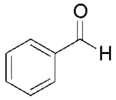
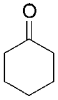
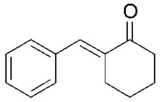
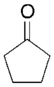
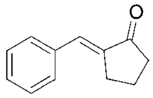
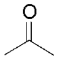
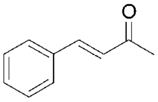
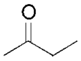
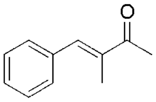
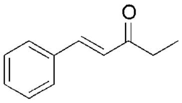
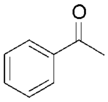
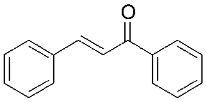
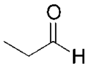
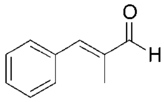
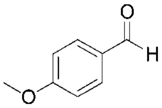
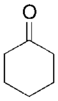
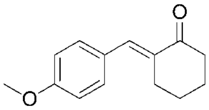
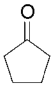
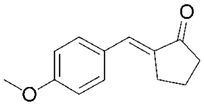
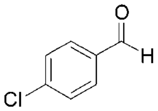
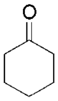
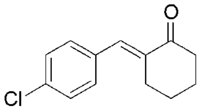
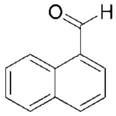
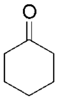
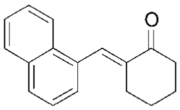
Table 1. Synthesis of Aryl α,β-Unsaturated Ketones[a]

entry	aryl aldehyde	aliphatic carbonyl compound	product	temperature (°C)	time (h)	yield (%)	comments
1				50	8	57	a,c,e
				22	31.5	69	b,c,e
				50	5.25	76	c,e,g
2				50	3	74	b,c,e
				22	3	64	c,e
3				50	3	43	a,c,e
				22	3	75	c,e,f
4				50	24	54	b,c,e
						16	
5				22	48	65	b,c,e,f
6				50	25	61	b,c,e
7				50	24	73	b,c,e
8				22	3	78	c,e
				22	2	77	d
9				50	28	48	a,c,e
10				50	18	80	c,e

[a] Conditions: DIMCARB removed by (a) distillation under CO_2 atmosphere, (b) in vacuo, (c) after acidification with 0.5 M H_2SO_4. Workup by (d) extraction into 1:1 hexane/EtOAc and adsorption onto silica gel and (e) extraction with organic solvent. (f) Yield determined by NMR. (g) 1.2 mol equiv of ketone used.

attracted interest as synthetic media through their negligible vapor pressure, solvent properties, and lack of flammability.[12] The isolation of nonvolatile products from ionic liquids can be difficult. In contrast, at 60 °C, DIMCARB dissociates to CO_2 and Me_2NH, which can be condensed and reassociated.[9] Thus, since DIMCARB can be recycled during reactions or recovered afterward for reuse, in many respects it could be considered as a self-associated, "distillable" ionic medium.

First, condensations were carried out in DIMCARB as solvent at temperatures up to 50 °C for times ranging from 2 to 32 h. Yields, usually on the order of 60−80%, were obtained almost routinely (see Table 1). Under these conditions a range of enolizable ketones and an enolizable aliphatic aldehyde afforded monoarylidene products. Methods for workup included recovery of DIMCARB by distillative dissociation−reassociation in vacuo or under an atmosphere

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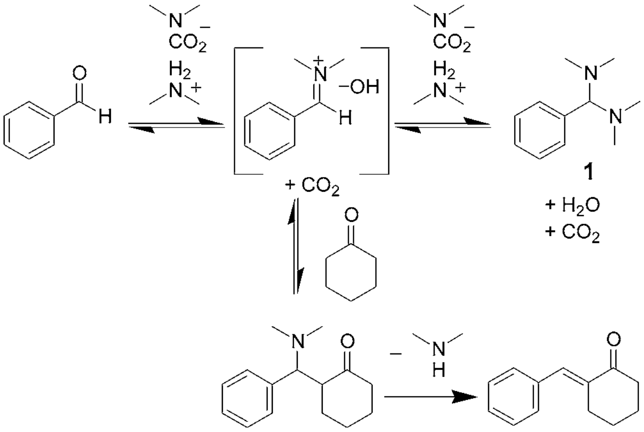
of CO_2. An acidic workup was effective when base-labile monoarylidene products were formed.

The novel one-pot processes in Table 1 were convenient, but empirical efforts to increase the yields were unsuccessful. Investigations into mechanistic aspects revealed that competing pathways can come into play. A aminal **1**,[13] which appears to have a key role, is formed through reaction of 2 equiv of dimethylamine with 1 equiv of the arylaldehyde (see Scheme 1). Elimination of a dimethylamino moiety from the aminal affords a putative, transient iminium species that can undergo Mannich reaction with the ketone. Subsequent elimination of dimethylamine from the Mannich adduct is facile and affords the 2-arylidene derivative.

Scheme 1. Suggested Reaction Pathway of Benzaldehyde and Cylohexanone in DIMCARB



As evidenced by the evolution of CO_2, in DIMCARB, aminals were formed more rapidly from the aryl aldehydes than were enamines from the ketones. Although the latter processes were observed to a minor extent on occasions, enamine chemistry was not significant in the present context. This conclusion was supported by the failure of benzene-1,2-dicarboxaldehyde to react with cyclohexanone under the conditions. A cis and trans mixture of the bis-dimethylamino ether **2**[14] was formed instead (see Scheme 2).

Apparently, the aminal does not react directly with the ketone. We considered that a vast excess of DIMCARB (up to 12 mol equiv were used for experiments in Table 1) may have helped to stabilize the aminal and could have accounted, at least in part, for the moderate yields of arylidene monoadducts reported in Table 1. The reactions summarized in Table 2 were performed in one pot and employed DIMCARB in lower levels (about 5 mol equiv) as a reagent/catalyst/cosolvent. Indeed, improved yields, between 74 and 91%, were obtained. Preparations of monoarylidene cyclopentanones were particularly convenient. After removal of the reaction medium, aqueous workup and solvent extraction, no further purification was required. The hydroxy- and carboxyarylaldehydes employed herein were insoluble in the cosolvent (in this case CH_2Cl_2) alone. DIMCARB facilitated their dissolution, presumably owing to the large number of coordinating centers in a relatively small molecule. To the best of our knowledge, all compounds in Table 2 were obtained in higher yields than by all other reported methods or were new.

Scheme 2. Reaction of Benzene-1,2-dicarboxaldehyde with DIMCARB in the Presence of Cyclohexanone

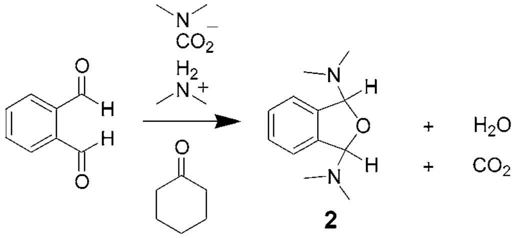
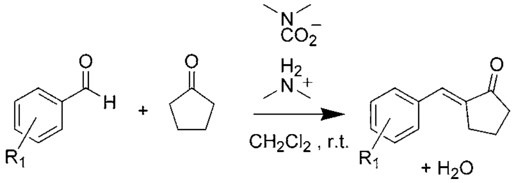


Table 2. Synthesis of Aryl α,β-Unsaturated Cyclopentanones



entry	R_1	time (h)	yield (%)	ref
1	H	18	85	15
2	*p*-OCH_3	17	91	16, 15a
3	*o*-OCH_3	17	87	15a
4	*p*-OH	18	86	
5	*p*-Cl	60	91	
6	*p*-Br	60	82	
7	1-naphthaldehyde[a]	24	83	
8	*p*-CO_2H	13	74	

[a] Represents aldehyde, not R_1 group.

Although the present reactions could be perceived as mono-Claisen–Schmidt condensations, the pathway involves Mannich reactions and elimination. As will be discussed elsewhere, the reactions do not proceed by mixing the reactants alone, in the presence of either an amine or a carboxylic acid alone.

Acknowledgment. We thank the Australian Research Council for funding the establishment and continuation of

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Supporting Information Available: Experimental procedure for the α,*β*-unsaturated carbonyl compounds in Tables 1 and 2 and spectral data for novel compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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