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REACTIVITY OF LITHIUM CUPRATES WITH α-BROMOKETONES. A NEW SYNTHESIS OF HINDERED KETONES.

Jacques-Emile Dubois, Claude Lion and Claude Moulineau
(Laboratoire de Chimie Organique Physique, Faculté des Sciences de Paris,
Associé au C.N.R.S., 1, rue Guy de la Brosse, PARIS 5°. France)

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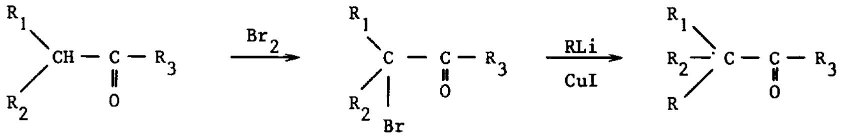
In this laboratory two reactions have been studied in depth with the synthesis of sterically hindered ketones in view : the alkylation of ketones (1) and methods involving organometallic reagents (2) [for Grignard reagents the reaction can be catalysed by cuprous salts (3)].

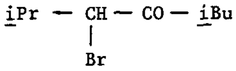
The alkylation of ketones by alkyl halides has the disadvantage of leading to a mixture of products (1). For secondary halides, moreover, the reaction proceeds with difficulty in the case of sterically hindered ketones (3). In this note we propose a new synthetic pathway leading to hindered ketones, difficult to prepare by the usual methods (4). To this end we have made use of the alkylation of α-bromoketones by lithium cuprates according to the following reaction scheme :



The lithium cuprates are relatively easily obtained (5). These compounds are capable of replacing a halogen - be it aliphatic, aromatic or vinylic - by their alkyl group (5,6) and moreover, are not reactive towards the carbonyl group (7). These distinctive properties of lithium cuprates suggested the new synthetic process given above. Thus by a stepwise procedure we have been able to prepare ketones bearing alkyl substituents of increasing steric hindrance in the first environment E_B^1 (8).

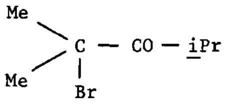
In theory this method is limited only by the availability of α-bromoketones and organolithium compounds.

We were particularly interested in the α-bromoketones 1 and 2, and the α,α'-dibromoketones 3, 4 and 5 (9)

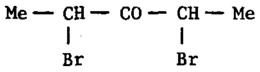


$\underline{i}\mathrm{Pr}-\underset{\mathrm{Br}}{\underset{|}{\mathrm{CH}}}-\mathrm{CO}-\underline{i}\mathrm{Bu}$

1

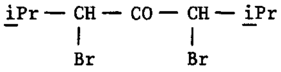


2



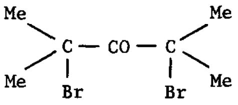
$\mathrm{Me}-\underset{\mathrm{Br}}{\underset{|}{\mathrm{CH}}}-\mathrm{CO}-\underset{\mathrm{Br}}{\underset{|}{\mathrm{CH}}}-\mathrm{Me}$

3



$\underline{i}\mathrm{Pr}-\underset{\mathrm{Br}}{\underset{|}{\mathrm{CH}}}-\mathrm{CO}-\underset{\mathrm{Br}}{\underset{|}{\mathrm{CH}}}-\underline{i}\mathrm{Pr}$

4



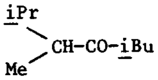
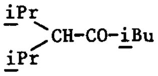
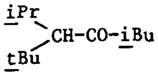
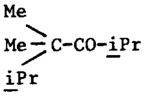
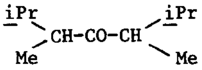
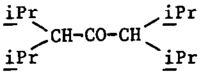
5

The action of lithium cuprates on these different ketones leads to the results shown in the table.

TABLE

Reactivity of lithium cuprates towards the

ketones **1**, **2**, **3**, **4** and **5**

Brominated Ketones	Cuprate R_2 CuLi	Reaction products	Yield % (10)	DEL (8) FO : ≯C — CO — C≮
1	Me	 $\mathrm{(iPr)(Me)CH\text{-}CO\text{-}iBu}$	63	FO(2110)(1110)
	i Pr	 $\mathrm{(iPr)_2CH\text{-}CO\text{-}iBu}$	45	FO(2220)(1110)
	t Bu	 $\mathrm{(iPr)(tBu)CH\text{-}CO\text{-}iBu}$	16	FO(2221)(1110) (11)
2	Me	tBu-CO-iPr	90	FO(3000)(2000)
	i Pr	 $\mathrm{(Me)_2(iPr)C\text{-}CO\text{-}iPr}$	33	FO(3110)(2000) (11)
3	Me	iPr-CO-iPr	22	FO(2000)(2000)
	i Pr	 $\mathrm{(iPr)(Me)CH\text{-}CO\text{-}CH(iPr)(Me)}$	8	FO(2110)(2110)
4	i Pr	 $\mathrm{(iPr)_2CH\text{-}CO\text{-}CH(iPr)_2}$	12	FO(2220)(2220)
5	Me	tBu-CO-tBu	33	FO(3000)(3000)

From the results of this preliminary study, it appears that the alkylation of α-bromoketones is possible not only with primary and secondary lithium cuprates but with tertiary as well. The reaction yields were found to decrease in the sense Me > *i*Pr > *t*Bu.

This new reaction has allowed us to obtain two new ketones [FO(3110)(2000) and FO(2221)(1110)]. By this method we have also been able to prepare the tetraisopropylacetone FO(2220)(2220) in two steps. More detailed studies are in progress in this laboratory.

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b) J.E. Dubois and F. Hennequin, *Ibid*, 3572 (1966).

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(8) In the terminology of the DARC topological system (Description and Automated Research of Correlation), a ketone is represented by its focus FO and its environment $\mathcal{E}$, divided into limited environments E_B^i, concentric with respect to the focus and each containing two rows of atoms. The topology of the limited environments E_B^i is described and indexed unambiguously by means of the descriptor DEL [J.E.Dubois, F. Hennequin and M. Chastrette, *Bull.Soc.chim.Fr.*, 3568 (1966)].

(9) These ketones have been obtained by the method of J. Colonge and J. Grenet, *Bull.Soc.chim.Fr.*, 1304 (1954) using one equivalent of bromine for the α-bromoketones **1** and **2** or two equivalents for the α,α'-dibromoketones **3**, **4** and **5**.

(10) The yields were determined by vapour phase chromatography. Along with these ketones were obtained ethylenic compounds and polymers not yet identified.

(11) These newly prepared ketones [FO(2221)(1110) and FO(3110)(2000)] exhibit the carbonyl streching frequencies $\nu_{C=O}$ 1709 and 1703 cm^{-1} respectively - in excellent agreement with values calculated by topo-frequency rules according to J.E. Dubois, A. Massat and Ph. Guillaume, *J.of Mol.Structure*, 403, (1969).