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Friedel-Crafts Coordinated Processes: 1-Oxoindanes from Aromatic β-Dicarbonyl Compounds and Aldehydes

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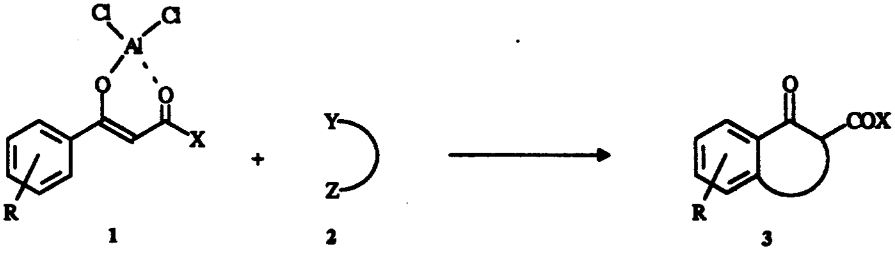
Key Words: 1-Oxoindanes; β-dicarbonyl chelates; vicinal bis-alkylation.

Abstract: Variously substituted 1-oxoindanes were synthesized by highly selective bis-alkylation of aromatic β-dicarbonyl compounds with non enolizable aldehydes.

In the course of our studies on the metal-template electrophilic reactions of ambidental substrates[1] we have examined the reactivity of dichloroaluminium chelates of aromatic β-dicarbonyl compounds 1 toward multireactive electrophiles 2.

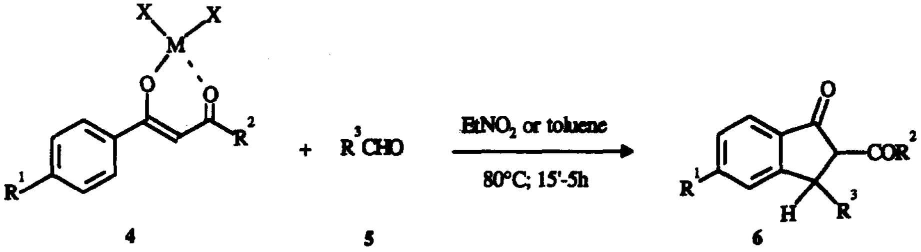


As a result of these studies we have reported a new, highly selective route for building up bicyclic derivatives 3 such as indan-1,3-diones[2] and hydroxynaphthoquinones[3] by selective electrophilic bis-acylation of substrates 1. Following this strategy we have also found a synthesis of 1-oxoindane derivatives[4] by reaction of substrates 1 with methoxyacetyl chloride previously reported by McKillop as a simple and efficient chloromethylating reagent[5].

Despite the easy of experimental technique, good yields and excellent selectivities, the above reaction suffers from one limitation. In fact this process only allows synthesis of 1-oxoindanes unsubstituted on the cyclopentanone ring.

Focussing our previous experience with the regioselective bis-alkylation of magnesium phenolates with aliphatic[6] and aromatic[7] aldehydes, we have studied the reaction of bromomagnesium and dichloroaluminium chelates **4** with not enolizable aldehydes.

Here, we report our preliminar results of the synthesis of 1-oxoindanes **6**[8] including some 3-substituted derivatives by reaction of the easily accessible aromatic β-dicarbonyl compounds **4**[9] with formaldehyde and aromatic aldehydes.



M = MgBr(OEt$_2$); AlCl$_2$

R^1 = H, Me, OMe

R^2 = OEt, Me

R^3 = H, Ar, CH=CH-Ar

Table. Electrophilic bis-alkylation of aromatic β-dicarbonyl compounds.

Entry	R¹	R²	R³	Yield (%)	Selectivity (%)	Method
a	H	OEt	H	72	(93)	A
b	Me	"	"	78	(92)	"
c	OMe	"	"	65	(85)[a]	"
d	H	Me	H	66	(87)	"
e	"	OEt	C_6H_5	72	(88)	B
f	"	"	p-ClC_6H_4	58	(87)	"
g	"	"	p-$OMeC_6H_4$	70	(89)	"
h	OMe	"	C_6H_5	82	(90)	"
i	H	"	CH=CH-C_6H_5	63	(78)	"
l	OMe	"	"	68	(77)[b]	"
m	H	Me	C_6H_5	48	(78)[b]	"

[a] Reaction time: 15 minutes.

[b] Reaction time: 1 hour

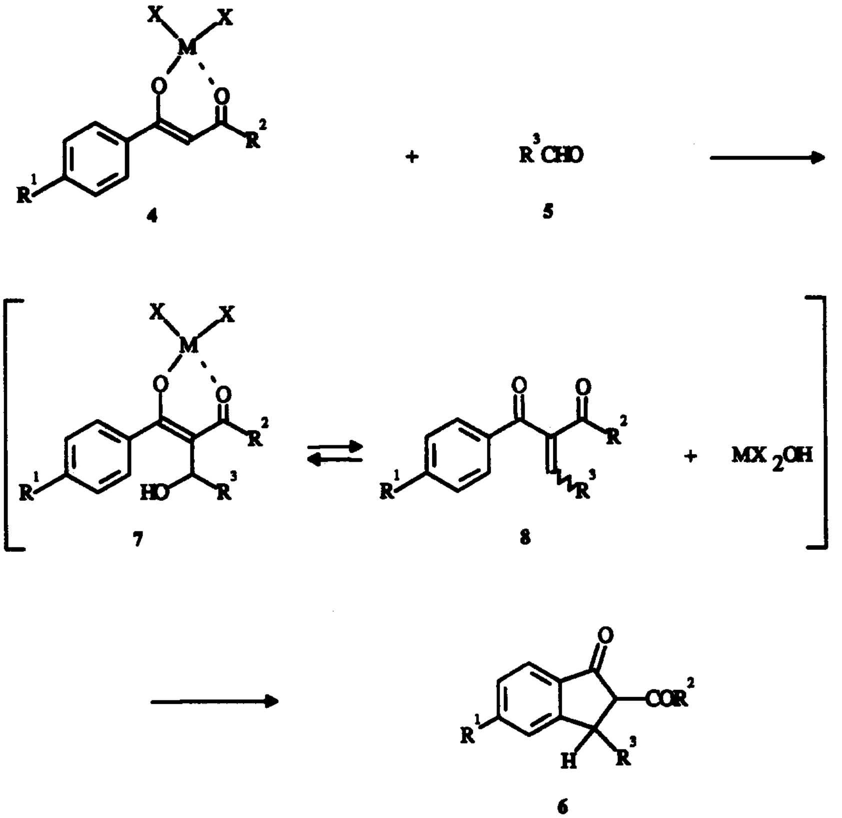
Method A: EtMgBr (0.01 mol) in dry ether was added dropwise to a solution of the selected β-dicarbonyl compound (0.01 mol) under nitrogen. Ether was removed and dry toluene replaced. Paraformaldehyde (0.3 g, 0.01 mol) was added and the mixture was heated at 80°C for 5 hours. After normal workup, products **6a-d** were separated by flash chromatography (hexane-ethyl acetate 5-20%).

Method B: to a solution of $AlCl_3$ (2.66 g, 0.02 mol) and the β-dicarbonyl compound (0.01 mol) in dry nitroethane, the selected aromatic aldehyde (0.01 mol) was added and the mixture was heated at 100°C for 5 hours. Products **6e-m** were obtained as described in Method A.

This was achieved by following two methods depending on the nature of the aldehyde **5**. Bromomagnesium chelates in toluene (Method A) were utilized with formaldehyde, whereas dichloroaluminium chelates in nitroethane (Method B) were employed with the less reactive aromatic aldehydes including cinnamic aldehyde. Compounds **6** represent versatile synthons for the preparation of various biologically active products[10] as well as indanones[11] and azulenes[12].

Synthetic results reported in the table indicate that the present method is of general applicability with respect to the β-dicarbonyl compound **4** as well as the aromatic and aliphatic not enolizable aldehydes[13]. Moreover the efficiency of the reaction slightly depends on the electronic effect of the substituent R^1.

These results and our previous experience with the reaction of magnesium phenolates with aromatic aldehydes[6] and formaldehyde[7] allow the formulation of a plausible mechanism as that shown in the Scheme.



The reaction of the metal chelate **4** [MX_2 = MgBr(OEt$_2$) or AlCl$_2$: see synthetic Method A or B] at the active methylene carbon with the aldehyde **5**, produces the intermediate **7** which could be converted into the enedione **8** *via* an elimination process. An easy cycloalkylation alternatively involving the intermediate **7** or **8** gives the 1-oxoindane **6**[14].

In conclusion, we have shown that bromomagnesium and dichloroaluminium chelates of aromatic β-dicarbonyl compounds undergo highly selective bis-alkylation with not enolizable aldehydes affording variously 3-substituted 1-oxoindane derivatives.

Acknowledgements

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References and notes

1. a) Casnati, G.; Casiraghi, G.; Pochini, A.; Sartori, G.; Ungaro, R. *Pure Appl. Chem.* **1983**, *55*, 1677; b) Sartori, G.; Casnati, G.; Bigi, F.; Predieri, G. *J. Org. Chem.* **1990**, *55*, 4371; c) Sartori, G.; Maggi, R.; Bigi, F.; Casnati, G. *J. Chem. Soc. Perkin Trans. I*, **1991**, 3059; d) Sartori, G.; Maggi, R.; Bigi, F.; Arienti, A.; Casnati, G. *ibid.*, **1993**, 39.
2. Sartori, G.; Bigi, F.; Maggi, R.; Baraldi, D.; Casnati, G. *J. Chem. Soc. Perkin Trans. I*, **1992**, 2985.
3. Sartori, G.; Bigi, F.; Canali, G.; Maggi, R.; Casnati, G.; Tao, X. *J. Org. Chem.*, **1993**, *58*, 840.
4. Sartori, G.; Bigi, F.; Tao, X.; Casnati, G.; Canali, G. *Tetrahedron Lett.*, **1992**, *33*, 4771.
5. McKillop, A.; Madjadabadi, F.A.; Long, D.A. *Tetrahedron Lett.*, **1983**, *24*, 1933.
6. Casiraghi, G.; Casnati, G.; Cornia, M.; Sartori, G.; Ungaro, R. *J. Chem. Soc. Perkin Trans. I*, **1974**, 2077.
7. Casiraghi, G.; Casnati, G.; Cornia, M.; Pochini, A.; Puglia, G.; Sartori, G.; Ungaro, R. *J. Chem. Soc. Perkin Trans. I*, **1978**, 318
8. Compounds 4 were previously prepared by cycloacylation of the corresponding 3-arylpropionic acid derivatives: a) Sethna, S. "Cycliacylation" in Olah, G.A. *Friedel-Crafts and Related Reactions*; Interscience Publishers: New York, **1964**, Vol. III, Part 2, pp 911-1002; b) Premasagar, V.; Palaniswamy, V.A.; Eisenbraun, E.J. *J. Org. Chem.* **1981**, *46*, 2974.
9. a) Spraue, J.M.; Beckham, L.J.; Adkins, H. *J. Am. Chem. Soc.* **1934**, *56*, 2665; b) Wallingford, V.H.; Homeyer, A.H.; Jones, M. *ibid.*, **1941**, *63*, 2252; c) *Org. Synth. Coll.* Vol. IV, **1963**, 415.
10. Trost, B.M.; Fleming, I. *Comprehensive Organic Synthesis*; Semmelhack, M.F. Ed.; Pergamon Press: Oxford, **1991**, Vol. 4, p. 230 and references therein.
11. a) House, H.O.; Hudson, C.B. *J. Org. Chem.* **1970**, *35*, 647; b) House, H.O.; McDaniel, W.C. *J. Org. Chem.*, **1977**, *42*, 2155.
12. Herz, W. *J. Am. Chem. Soc.*,**1958**, *80*, 1243.
13. The reaction carried out with propionic aldehyde gave the Ethyl-1-oxo-3-ethyl-2-indancarboxylate in 30% yield and 42% selectivity.
14. Taylor, R. *Electrophilic Aromatic Substitution*; J. Wiley & Sons Ed.; New York, **1990**, pp 209-214.

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