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ALKYLATIONS IN NEUTRAL MEDIA. REACTIONS OF NICKEL(II) bis-2,4-PENTANEDIONATO WITH ALKYL HALIDES

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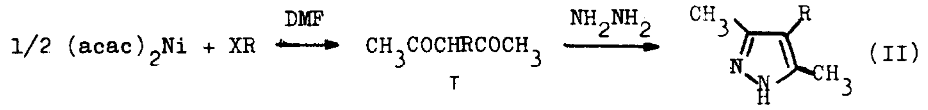
C-alkylation of β-dicarbonyl compounds, as their alkali metal salts, is a useful synthetic reaction, its scope being sometimes limited by the possibility of side reactions (C-dialkylation, O-alkylation, cleavage, etc.), and by the sensitivity of the reacting products to the strong alkaline media. The use of thallium(I) salts was claimed to yield only C-monoalkylation products in nearly quantitative yield[1], but a contradictory report appeared later[2]. Since the regioselectivity for C-alkylation seems to depend on the covalent character of the oxygen-metal bond of the chelate, and/or on the heterogeneous nature of the reaction mixture[1,3], it is surprising that few reports have appeared dealing with the use of fully covalent chelates of β-dicarbonyl compounds. The reactions of the copper(II) chelates of 2,4-pentanedione and of ethyl acetoacetate with 1-bromo-3-methylprop-2-ene, in the presence of K_2CO_3, have been reported to yield both normal and allylic substitution products[4]. The reaction of the silver chelate of ethyl acetoacetate with methyl iodide has also been described[5]. The reactions with other alkyl halides were not successful[4,6].

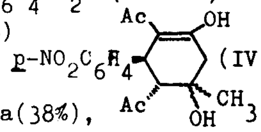
We wish to report that nickel(II) bis-2,4-pentanedionato ($(acac)_2Ni$), reacts with primary alkyl halides in DMF to give mainly C-monoalkylation products. Only when benzylic or allylic halides were used, C-dialkylation products could be isolated (see table). In no case materials from O-alkylation were detected; however, in run 5, Ib was contaminated with a small amount of another unidentified product. As solvent media, we have found DMF to be far superior to DMSO, $HCCl_3$ and acetonitrile, and, as cation, Ni(II) gave much better results than Cu(II), Fe(III), Cr(III) and Al(III). When DMSO was used as the solvent, oxidation products were formed in addition to those of the expected alkylation.



a (R= p-$NO_2C_6H_5CH_2$)	-----	mp. 86-9°
b (R= $C_6H_5CH_2$)	bp. 97-102°/0.3torr	-----
c (R= n-Bu)	bp. 104-6°/15torr	mp. 42.5-43.5°(Lit[9] 44-5°)
d (R= n-Pr)	bp. 85-8°/14torr	mp. 79-80°(Lit[10] 78°)
e (R= CH_3OCOCH_2)	bp. 134-7°/13torr	mp. 41-3°
f (R= CH_3COCH_2)	bp. 87-9°/0.7torr	-----
g (R= $CH_3OCOCH{=}CHCH_2$)	bp. 109-13°/0.5torr	-----

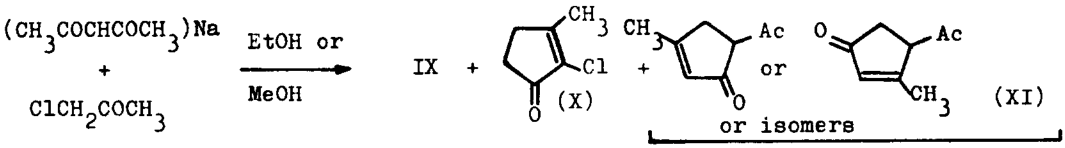
Products Ia through Ig were keto-enol mixtures. III (mp. 88-9°, lit[7] 90-1°) and IV (mp. 177-9°) (runs 1 and 2) were independently prepared by reaction of excess 2,4-pentanedione with p-nitrobenzaldehyde in the presence of piperidine and acetic acid. V and VI (run 3) were unambiguously characterized by nmr. They were also prepared by Knoevenagel condensation of n-butanal with 2,4--pentanedione followed by careful column chromatography in silica gel. VII (runs 4 and 5) had mp. 112-4° (Lit[8] 113°). Ig (E isomer) (mass spec.: m/e 198 (M^+, 6%), 180(16), 156(22), 125(34), 124(38), 123(28), 121(20), 113(35), 109 (19), 95(32), 81(38), 53(15), and 43(100)) showed a second small peak in glc, attibuted to the Z isomer. VIII (run 11) (mp. 126-30°) showed a second faint spot in tlc, also attributed to the E,Z isomer.

Runs 10 and 11 are noteworthy in that, as far as we know, the reactions of the corresponding XR with alkali metal salts of 2,4-pentanedione (the conventional alkylation method), have never been described. In our hands, reaction of sodium 2,4-pentanedionato with chloroacetone, both by direct and reverse additions, gave a mixture of about 25 products (glc) from which 2,5-hexanedione (IX) was isolated and converted into N-phenyl-2,5-dimethylpyrrole, mp. 49-50° (Lit[11] 52-3°). A combined glc-mass spectrometry analysis allowed the detection of two products of M^+ C_6H_7ClO and $C_8H_{10}O_2$, consistent with structures X and XI arising respectively from initial aldol condensation of chloroacetone and of If, which however could not be detected (glc).

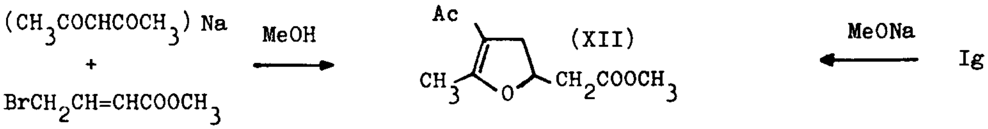
Run	XR	$(acac)_2Ni/XR$	Conditions	Products
1+	p-$NO_2C_6H_4CH_2Cl$	1:2	DMSO, 100°, 8h	p-$NO_2C_6H_4CHO$(XIII, 2%), p-$NO_2C_6H_4CH_2OH$(traces, XIV p-$NO_2C_6H_4CH=C(COCH_3)_2$ (III, 6%) Ia(52%)  (IV)
2+	p-$NO_2C_6H_4CH_2Cl$	1:6	DMSO, 100°, 8h	XIII(8%), XIV(22%), III(6%), Ia(38%), IV(traces), recovered XR
3+	$CH_3CH_2CH_2CH_2Br$	1:1	DMSO, 100°, 8h	$CH_3CH_2CH_2CH=C(COCH_3)_2$ (V), $CH_3CH_2CH=CHCH(COCH_3)_2$ (VI) (42% overall)
4	$C_6H_5CH_2Br$	1:2	DMF, 75°, 68h	Ib (69%), $(C_6H_5CH_2)_2C(COCH_3)_2$ (VII, 4%)
5	$C_6H_5CH_2Cl$	1:2	DMF, 100°, 70h	Ib (32%), VII (2%)
6	$CH_3CH_2CH_2CH_2Br$	1:2	DMF, 95°, 65h	Ic (17%)
7	$CH_3CH_2CH_2I$	1:2	DMF, 100°, 68h	Id (8%), $CH_3COCH_2COCH_3$ (traces)
8	CH_3OCOCH_2Br	1:2	DMF, 90°, 40h	Ie (53%)
9	$CH_3CHBrCH_3$	1:2	DMF, 95°, 68h	$CH_3COCH_2COCH_3$ and $CH_2=CHCH_3$ were characterized
10	CH_3COCH_2Cl	1:2	DMF, 100°, 65h	If (30%)
11	$CH_3OCOCH=CHCH_2Br$ (E:Z ca. 80:20)	1:2	DMF, 100°, 21h	Ig (mainly E, 65%), $(CH_3OCOCH=CHCH_2)_2C(COCH_3)_2$ (VIII, mainly E,E, 7%)

No efforts were made to improve the yields, which are based on pure (glc) distilled liquids and isolated crystalline materials. All new compounds gave correct elemental analysis and showed spectroscopic behaviour as expected.

+ In all runs but 1,2 and 3, anhydrous $(acac)_2Ni$ (by azeotropic distillation of water with toluene) was used. Comercial dihydrated $(acac)_2Ni$ was used in these three runs.



Similar conventional reactions with methyl 4-bromobut-2-enoate (*E*:*Z* *ca*. 87:13), gave, contrary to the nickel method, no *C*-monoalkylation product. Instead, the reverse addition gave 3-acetyl-4,5-dihydro-5-methoxycarbonylmethyl-2-methylfuran (XII, bp. 115-6°/0.7-0.8torr; mass spec.: m/e 198(M^+, 9%), 125 (26), 109(10), 59(13), and 43(100)) as the major product in *ca*. 50% yield. The direct addition procedure gave the same XII in lower yield together with several unidentified products. Ig could be converted into XII by boiling in methanol with a catalytic amount of sodium methoxide.



Preliminary experiments reveal that the nickel(II) chelate of ethyl acetoacetate behaves similarly. Details will be published elsewhere.

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