Tetrahedron Letters, Vol.31, No.47, pp 6781-6784, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

SYNTHESIS OF o-ACYLARYLCARBOXYLIC ESTERS : A NEW REPLACEMENT OF PHENOLIC HYDROXYL BY A CARBONYL GROUP

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Abstract: *A wide variety of the title esters are prepared in good yields via a new two step replacement of phenolic hydroxyl by an ethoxycarbonyl group.*

Unsubstituted and N-substituted hydrazones are useful precursors for heterocycles.[1] Recently, 1,2-diacyl- and 1,2,3-triacyl-benzenes have been prepared[2,3] in high yields by a novel oxidative cleavage reaction of acylhydrazones of o-hydroxyaryl ketones with lead tetraacetate (LTA). The reactivity of LTA has been the subject of extensive research and several excellent reviews of LTA chemistry have been published.[4]

To further explore the above reaction and to extend its synthetic potential, we investigated the reactivity of ethoxycarbonyl hydrazones **2** towards LTA. The hydrazones **2** were prepared by treatment of the readily available o-acylphenols **1** with ethyl carbazate. We now report that the LTA oxidation of **2** does indeed lead to the formation of the desired o-ketoesters **3**, most of them previously unreported, in good yields (Table 1). Classical methods to approach such structures often result in ring-closed phthalan derivatives.[5]

This oxidation process further generalizes the replacement of phenolic hydroxyl by a substituted carbonyl group. The mechanism of the reaction is currently under investigation. Moreover, the simplicity of the experimental procedure gives this reaction considerable synthetic value. Of the o-ketoesters prepared, only ethyl o-acetylbenzoate **3a** has previously been reported in the literature.[5] Even in this case, o-acetylbenzoic acid is less readily available than the present starting material o-hydroxyacetophenone.

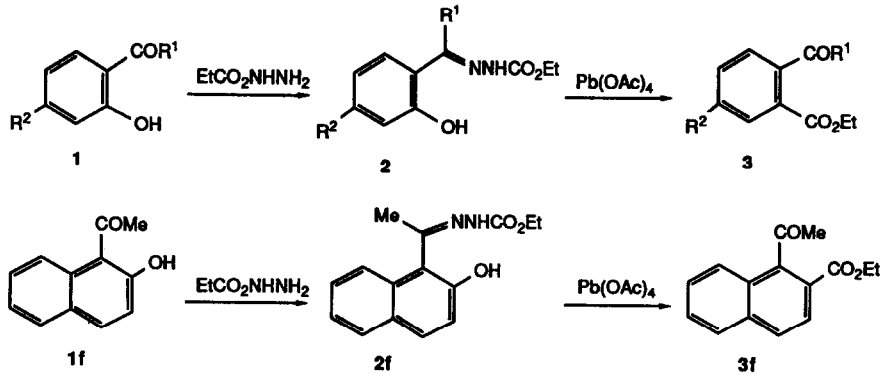
In a typical oxidation procedure, LTA is added to a solution of hydrazone **2** in tetrahydrofuran and the mixture is stirred at room temperature for 2 hs. The oily product, obtained after filtration of LTA and condensation of the filtrate, is purified by column chromatography to give **3** (Table 1). The products **2** and **3** were characterized by elemental analysis and by their ^{1}H (Table 1) and ^{13}C NMR spectra (Table 2).

Table 1. Preparation and ^1H NMR Data of the Ethoxycarbonyl Hydrazones and o-Ketoesters 3.

Prodt	Yld (%)	m.p. (°C)	Molecular Formula [a]	^1H-NMR [b] δ, J (Hz)						
				R^1	Aromatics	R^2	NH (s, 1H)	OH (s, 1H)	—— OEt —— (t, 3H)[c]	(q, 2H)[c]
2a	75	144	$C_{11}H_{14}N_2O_3$	2.38(s, 3H)	6.8-7.6(m, 4H)	——	9.6	12.6	1.45	4.3
2b	79	160-62	$C_{12}H_{16}N_2O_4$	2.28(s, 3H)	6.46-7.78(m, 3H) 7.0(d, 2H, J=7)	3.77 (s, 3H)	10.67	13.23	1.5	4.21
2c	83	140	$C_{12}H_{16}N_2O_3$	1.1(t, 3H, J=8) 2.27(q, 2H, J=8)	6.84-7.59(m, 4H)	——	10.25	13.09	1.31	4.25
2d	76	183-85	$C_{18}H_{21}N_2O_4$	——	6.7(dd, 1H, J=9) 6.95(m, 2H) 7.72(m, 2H) 7.99(m, 3H)	4.17(s, 3H)	10.28	——	1.64	4.56
2e	98	229	$C_{10}H_{12}N_2O_3$	8.3(s, 1H)	6.92(m, 2H) 7.28(m, 1H) 7.47(d, 1H, J=8)	——	11.2	11.4	1.28	4.23
2f [d]	95	81-83	$C_{15}H_{16}N_2O_3$	2.34(s, 3H) 2.43(s,3H)	7.1-7.8(m, 6H)	——	——	——	1.21 1.34	4.12 4.3
3a	87	oil	$C_{11}H_{12}O_3$	2.47(s, 3H)	6.8-7.8(m, 4H)	——	——	——	1.28	4.38
3b	76	oil	$C_{12}H_{14}O_4$	2.42(s, 3H)	6.7-7.8(m, 4H)	3.78(s, 3H)	——	——	1.38	4.28
3c	90	oil	$C_{12}H_{14}O_3$	1.12(t, 3H, J=7) 2.73(q, 2H, J=7)	7.0-7.87(m, 4	——	——	——	1.28	4.26
3d	71	oil	$C_{18}H_{19}O_4$	——	5.65(dd, 1H, J=7) 6.12(m, 1H) 7.37(m, 5H) 7.76(dd, 1H, J=9)	3.7(s, 3H)	——	——	1.3	4.3
3e	60	oil	$C_9H_{10}O_3$	10.8(s, 1H)	6.7-7.22(m, 4H)	——	——	——	1.3	4.25
3f	65	oil	$C_{15}H_{14}O_3$	2.62(s, 3H)	7.19-8.0(m, 6H)	——	——	——	1.35	4.35

[a] Satisfactory microanalyses were obtained for solids and correct accurate molecular masses were obtained for oils by MS.
[b] DMSO/TMS for the compounds **2** and $CDCl_3$/TMS for the compounds **3**.
[c] J=8 Hz for **2b** and 7 Hz for all other.
[d] ^1H NMR signals due to two isomers.

Hydrazone **2f** was obtained as a mixture of cis and trans isomers. ^1H and ^{13}C NMR analysis clearly showed a ratio of about 1:1. The mixture of the two isomers was further oxidized by LTA to give the expected product **3f**. The mass spectra of **3** showed prominent peaks corresponding to the molecular ions together with fragment ions for $[M\text{-}CO]^+$, $[M\text{-}COR^1]^+$ and $[M\text{-}R^1]^+$, characteristic of the proposed structures.



1-3	R¹	R²
a	Me	H
b	Me	OMe
c	Et	H
d	Ph	OMe
e	H	H

Table 2. ^{13}C-NMR Chemical Shifts (δ) for Ethoxycarbonyl Hydrazones 2 and o-Ketoesters 3.

Product	R^1	C_1-C_6	R^2	C=N	R^1C=O	CO_2Et	OEt
2a	14.6	117.8, 118.6, 119.3, 127.4, 131.0, 136.4	—	151.9	—	158.8	14.4, 62.5
2b	13.5	101.6, 105.3, 112.9, 129.1, 129.3, 154..1	55.2	160.2	—	161.3	14.6, 61.1
2c	11.0 18.9	117.4, 118.1, 118.5, 127.5, 130.5, 154.1	—	157.0	—	158.8	14.4, 61.2
2d		101.7, 105.6, 107.1, 11.9, 128.3, 128.4, 128.7, 129.2, 129.6, 130.8, 130.9, 134.6	52.2	153.7	—	160.2	14.4, 61.1
2e	—	119.2, 119.5, 119.8, 129.3, 130.9, 145.5	—		—	157.4	14.9, 61.2
2f[b]	18.8 23.4	112.8, 118.6, 118.7, 122.8, 123.0, 123.7, 124.1 126.5, 127.6, 128.2, 128.7, 128.9, 129.5, 129.8, 131.2, 131.6, 150.8, 151.1		152.0 152.1	—	154.3 154.4	14.2, 14.3 61.8, 62.5
3a	30.1	118.8, 120.2, 126.3, 129.6, 129.9, 131.9	—	202.9	154.9	13.7, 61.6	
3b	28.9	109.2, 111.5, 114.1, 115.8, 129.8, 133.5	55.6	—	199.3	161.6	13.8, 61.7
3c	14.0 36.1	125.8, 126.3, 129.2, 129.8, 131.7, 148.5	—	206.4	166.6	14.6, 61.5	
3d		102.1, 123.3, 128.7, 128.8, 129.3, 130.0, 131.1, 133.7, 150	55.8	—	182.8	169.8	13.8, 61.7
3e	—	117.0, 117.5, 119.3, 130.4, 131.3	—	—	199.0	158.0	14.4, 62.4
3f	32.7	123.1, 125.1, 125.7, 126.1, 127.5, 128.3 128.4, 128.8, 135.4, 144.0, 135.4, 144.1		199.0	166.0	14.1, 61.7	

[a]DMSO/TMS for the 2 and $CDCl_3$/TMS for the compounds 3.
[#]Mixture of isomers.

Experimental

Melting points were determined on a hot stage apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR 300MHz spectrometer. $CDCl_3$ or $DMSO_{d6}$ were used as solvents and TMS as the internal standard.(abbreviations used: s=singlet; d=doublet; t=triplet; q=quartet; m=multiplet and dd= doublet of doublets). Mass spectra were recorded on AEI MS-30 spectometer.

A General Procedure for Ethoxycarbonyl Hydrazones 2:

The carbonyl compounds **1** (0.01 mol) and ethyl carbazate (0.01 mol) were stirred at room temperature in ethanol (50 ml) for 24 hs. For the preparation of **2b**, benzene was used as the solvent and the reaction time was 48 hs. Furthermore, **2d** was formed upon reflux in propanol-1. The precipitated solid was filtered off to give the pure hydrazones **2** (Tables 1 and 2).

A General Procedure for Ethyl o-Acylarylcarboxylates 3:

Hydrazone **2** (0.005 mol) was dissolved in tetrahydrofuran (30 ml) and LTA (0.005 mol) was gradually added. A mild effervescence (evolution of N_2) was observed upon addition of the oxidant. The mixture was stirred at room temperature 2 hs. Filtration of lead diacetate and evaporation of the solvent gave an oil which was subjected to column chromatography (silica gel 70-230 ASTM) eluted with hexane/chloroform 1/1 to give the o-ketoesters **3** (Tables 1 and 2).

References and Notes

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1. See *"Comprehensive Heterocyclic Chemistry"*, A. R. Katritzky and C. W. Rees, Editors, 1984, Pergamon Press, Vol. 3, p. 41; Vol. 4, p. 334, 337; Vol. 7, p. 75 and references therein.
2. A. Kotali and P. G. Tsoungas, *Tetrahedron Lett.*, 1987, **28**, 4321.
3. A. Kotali, U. Glaveri, E. Pavlidou and P. G. Tsoungas, *Synthesis*, 1990, in press.
4. R. N. Butler, *Chem. Rev.*, 1984, **84**, 249.
5. a) D. Tobia and B. Rickborn, *J. Org. Chem.*, 1986, **51**, 3849; b) Beilstein, *Handbuch der Organische Chemie*, Spring Verlag, **10**, 692.

(Received in USA 29 August 1990)