Transformation of phenolic hydroxyl into acyl group: a new tool in organic synthesis

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Abstract
The progress that has been made in organic synthesis *via* the transformation of a phenolic hydroxyl into the acyl group is presented in this review. This transformation involves the formation of a new C-C bond.

Keywords: Transformation, phenol, hydroxyl, acyl group, formation of C-C bond

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1. Introduction

Interconversion of functional groups has always played an important role in organic synthesis. There have been many developments in the last decade regarding this area and two excellent editions "*Comprehensive Organic Functional Group Transformations I*" and recently "*Comprehensive Organic Functional Group Transformations II*" have presented the vast subject of organic synthesis in terms of the introduction and interconversion of all known functional groups, providing thus a unique information source documenting all methods of efficiently performing a particular transformation.[1,2]

During recent years our research has been focused on an unexpected new transformation of phenolic hydroxyl to a carbonyl group that we first found[3] in our laboratory in 1987. This transformation involves oxidation of *o*-hydroxy aryl ketones with lead tetraacetate (LTA) and allows the preparation of carbonyl compounds, formally unavailable, in high yields and in an easy experimental way.

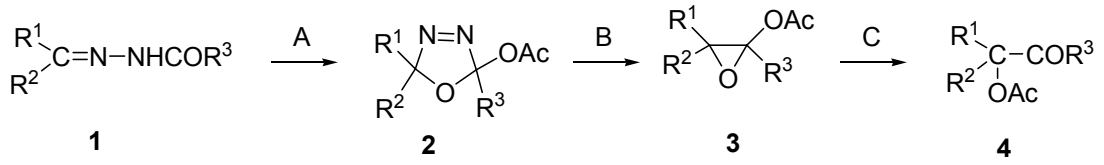
The purpose of this review is to present all the findings regarding the transformation of phenolic hydroxyl into an acyl group as well as the progress that has been made in organic synthesis based on this transformation. The presentation will begin with a discussion of the substrates and the oxidants that have been used as well as of the suggested mechanism. The papers dealing with the oxidation of aryl ketones which are not substituted at *ortho*-position as well as of *o*-amino aryl ketones will also be covered. Finally, some of the applications and the importance of the derived products will be presented. It is hoped that this review will demonstrate the synthetic potential of the above transformation and generate some new ideas in this area.

2. Transformation of Phenolic Hydroxyl into Carbonyl Group

2.1. Cyclisation reactions of *o*-unsubstituted arylketone *N*-acylhydrazones

It has been known[4-7] since 1966 that *N*-acylhydrazones of aryl ketones **1** which are not substituted at the *ortho*-position readily undergo cyclization to 1,3,4-oxadiazolines **2**, which yield epoxides **3** with elimination of nitrogen on heating. Further heating at higher temperature leads to acetates **4**. A characteristic example is given in Scheme 1.

In 1986, Alexandrou *et al.* reported[8] that the oxidation of bis-aroylhydrazones of isophthalaldehyde and terephthalaldehyde with LTA afforded the oxadiazoles **6** and **8** in 30-95%, as shown in Scheme 2.



A: $Pb(OAc)_4/CH_2Cl_2$/-15 to-50°C/44-75%

B: 0-50°C/CCl_4/44-65%

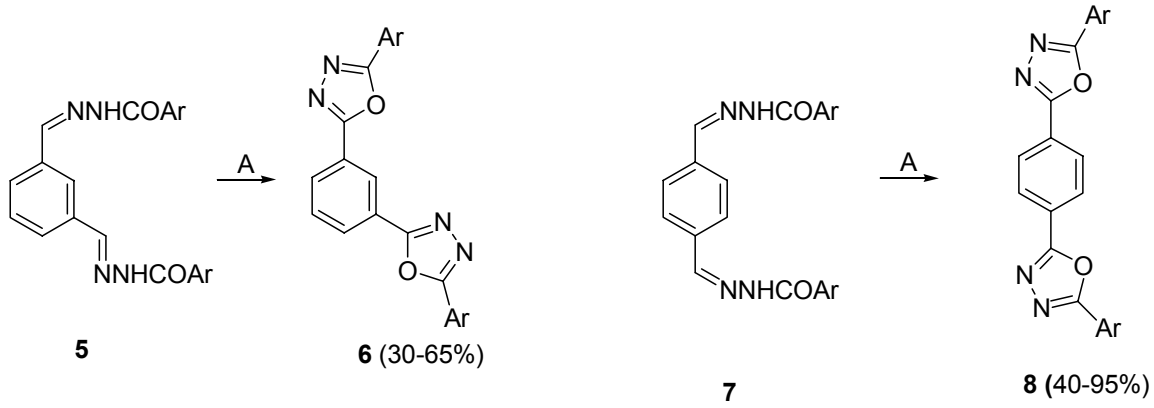
C: 170°C/96-98%

a: R^1=Ph, R^2=Me, R^3=Ph; b: R^1=R^2=Ph, R^3=Ph; c: R^1-R^2 =$(CH_2)_5$, R^3=Ph; d: R^1=R^2=Et R^3=Ph

B: $Pb(OAc)_4/CH_2Cl_2$/r.t./31-61%

e: R^1=R^2=Me, R^3=CH_2Ph; f: R^1=R^2=Me, R^3=*p*-$MeOC_6H_4CH_2$; g: R^1=R^2 =Me, R^3=*p*-$O_2NC_6H_4CH_2$

Scheme 1. LTA oxidation of *N*-carbonylhydrazones of *o*-unsubstituted arylketones.[4-7]



A: $Pb(OAc)_4$ /$CHCl_3$/25°C/or AcOH/reflux

a: Ar =Ph; b: Ar =*p*-MeC_6H_4; c: Ar =*p*-$MeOC_6H_4$; d: Ar =*p*-ClC_6H_4; e: Ar =*p*-$O_2NC_6H_4$

Scheme 2. Formation of di(oxadiazolyl)benzenes.[8]

2.2. Transformation reactions of *o*-hydroxy arylketone *N*-acylhydrazones. The initial reaction. Synthesis of 1,2-diacylbenzenes

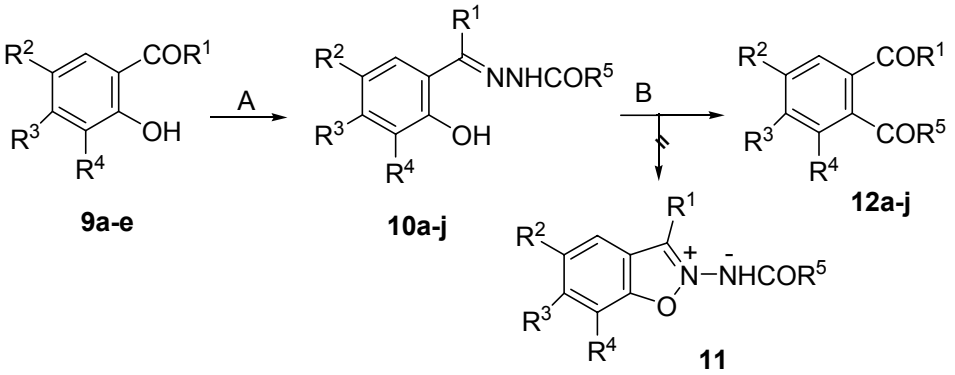
It was in 1987 when we attempted to cyclize *N*-acylhydrazones of *o*-hydroxy aryl ketones **10** to 1,2-benzisoxazole *N*-imines **11** by treatment with lead tetraacetate.[3]

o-Hydroxyarylketones are very interesting molecules both because of their potential to serve as starting materials in organic synthesis as well as because of their applications.[9] The presence

of a hydroxyl and a carbonyl group at *ortho* positions to each other at the benzene ring allows the formation of novel heterocycles as well as other non-heterocyclic aromatic compounds.[9]

Furthermore, it is well known that lead tetraacetate reactions of hydrazones of carbonyl compounds lead to a variety of synthetically useful products.[10]

Thus, we thought that the hydroxyl group could interact with the hydrazone moiety to lead to the formation of 1,2-benzisoxazole *N*-imines **11**. However, we found that monoacylhydrazones of type **10** do not yield *N*-imines **11** or the corresponding 1,3,4-oxadiazolines that would be formed if the reaction proceeded according to the literature data[4-7] about the unsubstituted hydrazones (Scheme 1), but instead they undergo a rearrangement resulting in "replacement" of the phenolic hydroxyl with an acyl substituent to give[3] 1,2-diacylbenzenes **12**, in excellent yields 70-90%, Scheme 3.



A: $R^5CONHNH_2$ /propanol/reflux, 24h/65-91%

B: $Pb(OAc)_4$ /THF/25°C, 2h/68-95%

9: a: R^1 =Me, R^2 =R^3 =R^4=H; b: R^1=Me, R^2 =H, R^3=OMe, R^4 =H;
c: R^1 =Me, R^2 =Br, R^3 =H, R^4=Br; d: R^1 =Ph R^2 =R^3 =R^4=H
e: R^1 =Ph R^2 =H, R^3=OMe, R^4=H

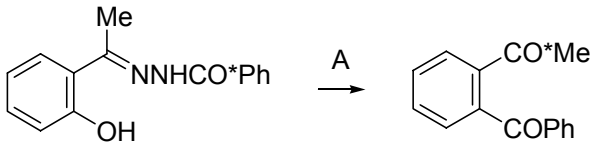
10,**12**: a: R^1 =Me, R^2 =R^3 =R^4=H, R^5=Me; b: R^1 =Me, R^2 =R^3 =R^4 =H, R^5 =Ph
c: R^1 = R^2 =Me, R^3=R^4=H, R^5=Ph; d: R^1=Me, R^2=R^4=H, R^3=OMe, R^5=Ph
e: R^1 =Me, R^2 =R^4 =Br, R^3 =H, R^5 =Ph; f: R^1 =Me, R^2 =R^3 =R^4 =H, R^5 =*p*-$O_2NC_6H_4$
g: R^1 =Me, R^2 =R^3 =R^4 =H, R^5 =4-pyridyl; h: R^1 =Ph R^2 =R^3 =R^4 =H R^5 =4-pyridyl
i: R^1 =Ph, R^2 =R^3 =R^4 =H, R^5 =Ph; j: R^1 =Ph R^2 =R^4 =H, R^3 =OMe, R^5 =Ph

Scheme 3. Synthesis of 1,2-diacylbenzenes.[3]

o-Diacylbenzenes have been of interest primarily as fluorescence reagents for both qualitative and quantitative high sensitivity analyses for amines and amino acids.[11] Having the two acyl substituents at *ortho*-positions they could also serve as precursors in the synthesis of several heterocycles. However, there were no general methods for their synthesis and only in isolated cases they have been prepared in many steps and low yields.[12]

3. The Mechanism

Since no analogous transformations had been previously reported, the mechanism of this novel reaction was investigated.[13] Crossover experiments demonstrated that the reaction is intramolecular. Furthermore, treatment of *o*-hydroxyacetophenone benzoyl-^{18}O-hydrazone **13** with LTA resulted in incorporation of ^{18}O at the acetyl position of the labeled 2-acetylbenzophenone **14** (Scheme 4).



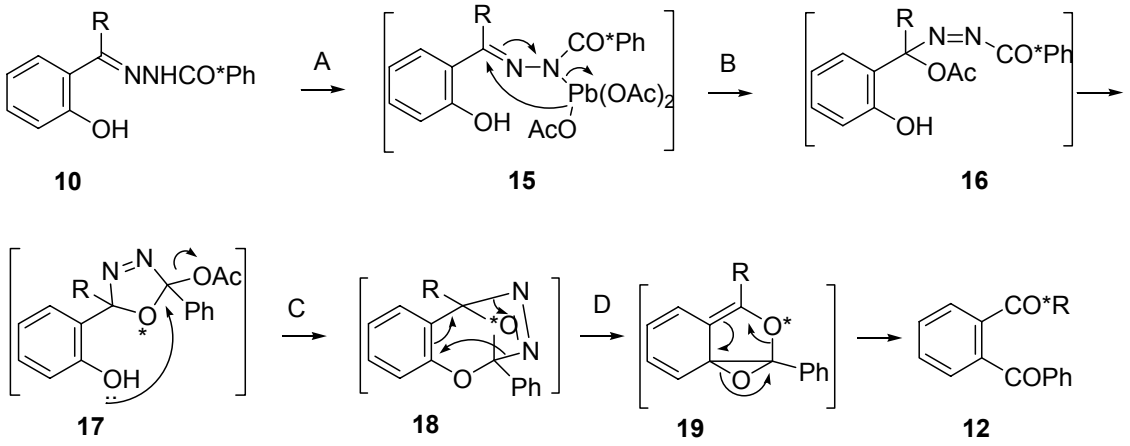
13 **14**

A: $Pb(OAc)_4$ /THF/25^{o}C, 2h/68-98%

Scheme 4. Synthesis of labeled 2-acetylbenzophenone.[13]

Based on this oxygen-labeling evidence we have suggested a possible reaction mechanism that is presented in Scheme 5.

Thus, the formation of the expected organolead intermediate **15**, followed by acetoxy migration to the hydrazone carbon gives initially azoacetate **16** and subsequently 1,3,4-oxadiazoline **17**. Intermediate **17** is indeed the final product obtained[4-7] by LTA reactions with *o*-unsubstituted *N*-acylhydrazones as hydrazones **1** in Scheme 1. The presence of the hydroxy group seems to be crucial to the mechanism of the reaction. And at this stage we suggested that the *o*-hydroxyl group reacts with the oxadiazoline to give the 1,3-dioxane species **18**. Elimination of nitrogen leads to the formation of epoxide **19**, which can undergo electrocyclic rearrangement to form 1,2-diacylbenzene **12**.

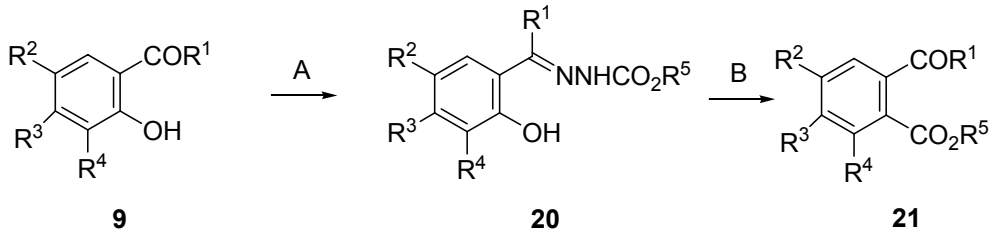


A: $Pb(OAc)_4$/ -AcOH; B: -$Pb(OAc)_2$; C: -AcOH; D: -N_2

Scheme 5. Mechanism of the transformation of hydroxyl into a carbonyl group.[13]

4. The Transformation of Hydroxyl into a Carbonyl Group in Benzene Derivatives *via* Lead Tetraacetate Oxidation

The reaction was further applied to *N*-ethoxycarbonyl hydrazones **20** and **23** which led to the synthesis of a series of *o*-acylarylcarboxylic esters **21** and **24** in good yields.[14] The results are presented in Schemes 6 and 7. The simplicity of the experimental procedure gives this reaction a considerable synthetic value. Moreover, classical methods to approach such structures often result in ring-closed pthalan derivatives.[15]



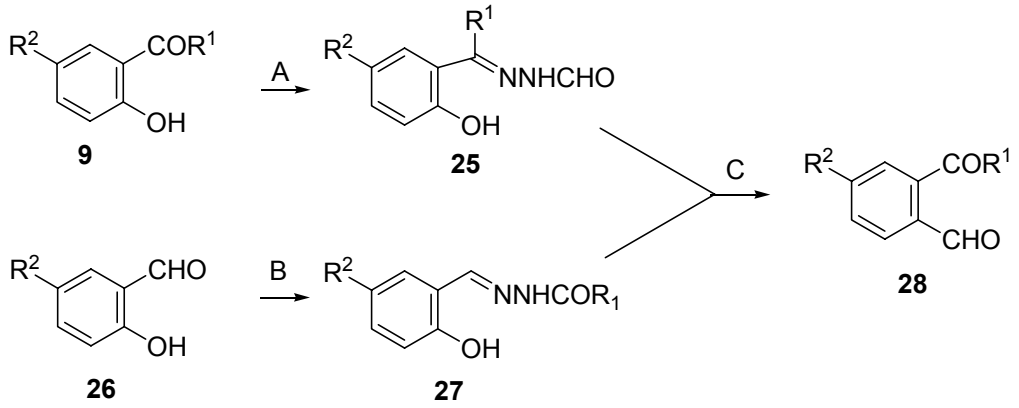
A: $R^5CO_2NHNH_2$ /ethanol/25°C, 24h/75-98%

B: $Pb(OAc)_4$ /THF/25°C/2h/ 60-90%

21: a: R^1 =Me, R^2 =R^3 =R^4 =H, R^5 =Et; b:R^1 =Me, R^2 =R^3 =OMe, R^4 =H, R^5=Et; c: R^1 =Et, R^2 =R^3 =R^4 =H, R^5 =Et; d: R^1 =Ph, R^2 =OMe, R^3 =R^4 =H, R^5 =Et; e: R^1 =R^2 =R^3 =R^4 =H, R^5 =Et

Scheme 6. Transformation of phenolic hydroxyl to carboethoxylate.[14]

Extension of the rearrangement led to the synthesis of *o*-acylbenzaldehydes as shown in Scheme 8. *N*-Formylhydrazones of *o*-hydroxyaryl ketones **25** as well as *N*-carbonylhydrazones of salicylaldehyde **27** both served as precursors to *o*-acylbenzaldehydes **28**.[16] Analogously, salicylaldehyde *N*-formylhydrazone **29** afforded phthalaldehyde **30** in 67% yield, Scheme 9. Recently, Einhorn *et al.* applied this transformation to hydrazones **27**, functionalized at the hydrazide aromatic moiety by nitro or iodo groups at any of the *para*, *meta*, or *ortho* positions to get the corresponding ketoaldehydes in good yields, 51-87% and subsequently use them as precursors to an interesting regiospecific synthesis of functionalized 1,3-diarylisobenzofurans.[17]



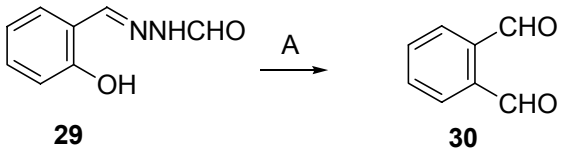
A: $HCONHNH_2$/propanol/reflux/24h/68-87%

B: $R^1CONHNH_2$/propanol/reflux/24h/92-99%

C: $Pb(OAc)_4$ /THF/25°C, 2h/77-82%

a: R^1 =Me, R^2 =H; b: R^1 =Et, R^2 =H; c: R^1 = *o*-OHC_6H_4, R^2 =H; d: R^1 =Ph, R^2 =Me; e; R^1 =Ph, R^2 =H

Scheme 8. Synthesis of *o*-acylbenzaldehydes.[16]

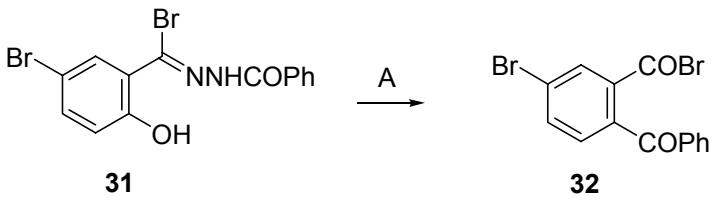


A: $Pb(OAc)_4$ /THF/25°C, 2h/67%

Scheme 9. Synthesis of phtalaldehydes.[16]

Interestingly, the transformation of a phenolic hydroxyl to a carbonyl group was also successful when 5-bromo-2-hydroxybenzoyl bromide *N*-benzoylhydrazone **31** was treated with LTA.[14] The result was the formation of 5-bromo-2-benzoylbenzoyl bromide **32** in 75% yield,

and the reaction is presented in Scheme 10. It is worthy to note that there is only one prior available preparative procedure for *o*-acylbenzoyl bromides.[18]



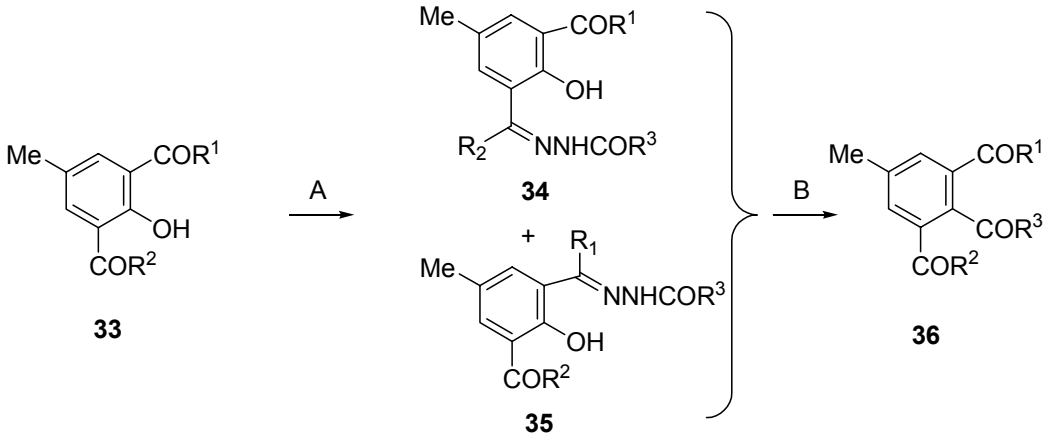
31 **32**

A: $Pb(OAc)_4$ /THF/25°C, 2h/75%

Scheme 10. Synthesis of 5-bromo-2-benzoyl bromide.[16]

Our desire to further extend the unusual transformation which was found in our laboratories, led us to use ketones bearing two acyl groups and one hydroxyl *ortho* to each other, as starting substrate.[19] Thus, the starting ketones **33** were initially treated with the appropriate hydrazide, in 1:1 ratio to give monohydrazones **34** either as a single isomer (when R^1=R^2) or as a mixture of two isomers **34** and **35** (when R^1#R^2), Scheme 11. It was not necessary to separate the isomeric mixtures of **34** and **35** for the conversion to **36**. LTA oxidation of the mixture afforded 1,2,3-triacylbenzenes **36** in very good yields.

Later, this methodology was further extended to the preparation of 1,3-dibenzoyl-2,4-diacetyl- and 1,5-dibenzoyl-2,4-diacetylbenzenes **42** and **43** in good yields, 73% and 55% respectively.[20] The transformation is presented in Scheme 12.

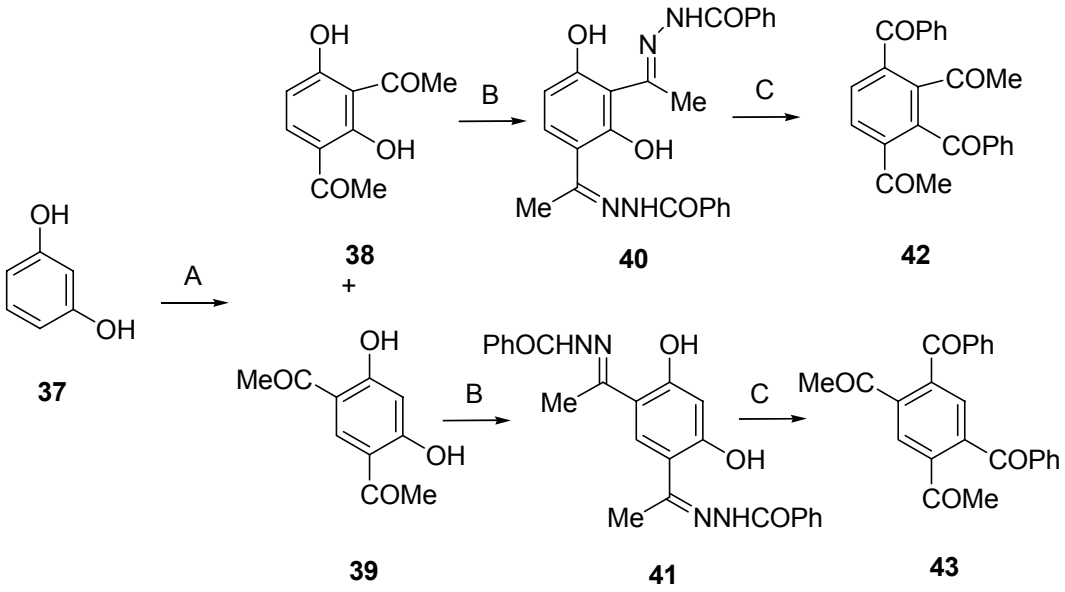


A: $R^3CONHNH_2$ /propanol/reflux, 24h/68-90%

B: $Pb(OAc)_4$ /THF/25°C, 2h/ 63-92%

a: R^1=Me, R^2=Ph, R^3=Me; b: R^1=Me, R^2=Ph, R^3=4-pyridyl; c: R^1=Me, R^2=Ph, R^3=*p*-$NO_2C_6H_4$;
d: R^1=Me, R^2=R^3=Ph; e: R^1=R^2=R^3=Ph; f: R^1=R^2=Ph, R^3=Me

Scheme 11. Synthesis of 1,2,3-triacylbenzenes.[19]



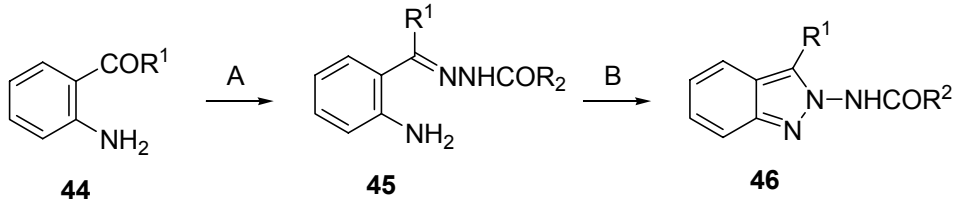
A: $AlCl_3$/MeCOCl/120°C/2h/40% for **38**, 24% for **39**

B: $PhCONHNH_2$/propanol/ reflux/24h/ 88% for **40**, 82% for **41**

C: $Pb(OAc)_4$ /THF/25°C/2h/ 73% for **42**, 55% for **43**

Scheme 12. Synthesis of tetraacylbenzenes.[20]

In contrast with *N*-acylhydrazones of *o*-hydroxyaryl ketones, *o*-aminoaryl ketones *N*-acylhydrazones **45** underwent oxidative cyclization under treatment with LTA to give 2-acylaminoindazoles **46** in very good yields, 60-80%, Scheme 13.[21]



A: $R^2CONHNH_2$/propanol/reflux/ 69-95%

B: $Pb(OAc)_4$/THF/25°C/2h/68-95%

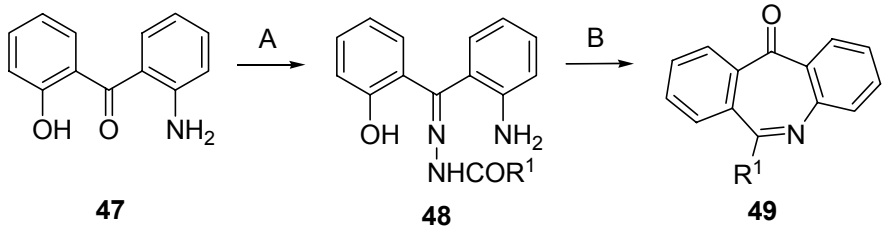
a: R^1 = Me, R^2 = Ph; b: R^1 = Me, R^2 = Me; c: R^1 = Me, R^2 = *o*-HOC_6H_4

d: R^1 = R^2 = Ph; e: R^1 = Me, R^2 = OEt; f: R^1 = Me, R^2 = OCH_2Ph

Scheme 13. Oxidative cyclisation of *o*-aminoarylketone *N*-acylhydrazones.[21]

Having shown that *o*-hydroxyaryl ketones yield the LTA induced transformation whereas, aminoaryl ketones yield LTA cyclisation reactions, we examined which pathway would be

followed if both functionalities were present.[22] Thus, *N*-acylhydrazones of 2-amino-2′-hydroxybenzophenone **48** were treated with LTA and afforded dibenz[*b,e*]azepin-11-ones **49**, in overall satisfactory yields, Scheme 14. We suggested that the reaction resulted to the hydroxyl replacement to give 2-acetyl- and 2-aroyl-2′-aminobenzophenone intermediates **50**, which without isolation, readily underwent dehydrative cyclization to the dibenz[*b,e*]azepin-11-ones **49**, Scheme 15. Intermediates **50** were probably formed according to the findings of our earlier mechanistic study.[9]



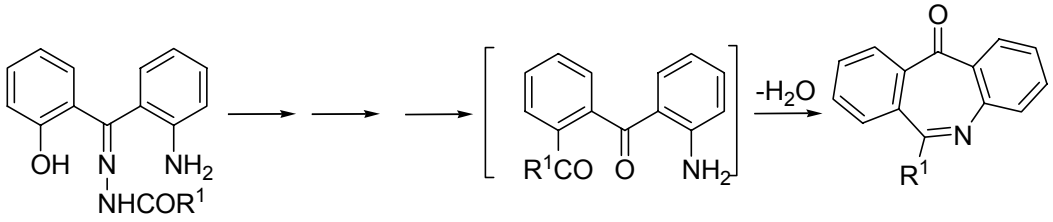
47 **48** **49**

A: $R^1CONHNH_2$ /propanol/reflux, 24h/77-87%

B: $Pb(OAc)_4$ /THF/25°C/2h/ 38-74%

a: R^1 =Ph; b: R^1 =*o*-HOC_6H_4; c: R^1 =*o*-$O_2NC_6H_4$; d: R^1 =*p*-$O_2NC_6H_4$; e: R^1 =Me

Scheme 14. Synhesis of 6-substituted dibenzazepin-11-ones.[22]



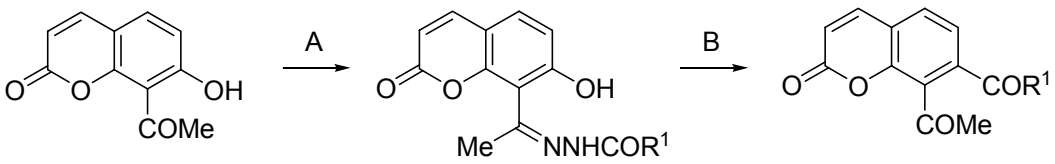
48 **50** **49**

Scheme 15. Proposed mechanism for the LTA cyclisation of *o*-amino arylketones *N*-acylhydrazones.[22]

5. The Transformation of Hydroxyl into a Carbonyl Group in Heterocycles

Our continuous interest in the potentialities of the above "replacement" in organic synthesis led us to design the synthesis of 7,8-diacylcoumarins **53** applying this transformation in the coumarin substrate **51** that bears hydroxyl ana acetyl groups at ortho positions (Scheme 16). 7-Hydroxy-8-acetylcoumarin *N*-acylhydrazones **52** were treated with LTA. The transformation of phenolic hydroxy to a carbonyl group worked out smoothly and 7,8-diacylcoumarins **53** were formed in very good yields, 73- 90%.[23,24] The transformation was also successfully applied to 7-

hydroxy-8-acetylcoumarin *N*-ethoxycarbonyl hydrazone **52l** and led to the formation of the corresponding angular 8-acetylcoumarin-7-ethoxycarboxylate **53l**.[23]



51 **52** **53**

A: $R^1CONHNH_2$ /propanol/reflux/24h/ 90-98%

B: $Pb(OAc)_4$ /THF/r.t./2-24h/ 65-90%

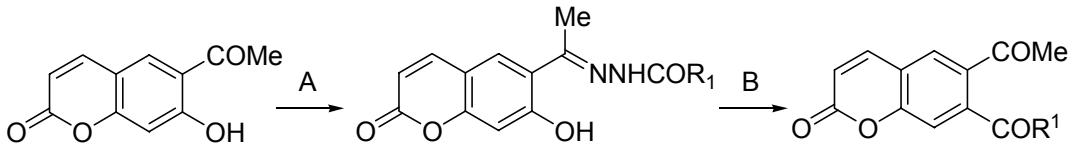
a: R^1=Ph; b: R^1=*p*-MeC_6H_4; c: R^1=*p*-HOC_6H_4; d: R^1=*o*-HOC_6H_4; e: R^1=*o*-$O_2NC_6H_4$

f: R^1=2'-furyl; g: R^1= 2'-thienyl; h: R^1=*p*-$O_2NC_6H_4$; i: R^1=4'-pyridyl; j: R^1=CH_2Ph

k: R^1=Me; l:R^1=OEt

Scheme 16. Transformation of hydroxyl into a carbonyl group in coumarins.[23,24]

It is well known that coumarin is a biologically active compound and its derivatives have been extensively used for the treatment of a variety of diseases.[25] Because the pharmacological and biochemical properties and therapeutic alterations in the structures of coumarins depend[26] upon substitution pattern, we synthesized[27] linear 6,7-diacylcoumarins **56** (Scheme 17).



54 **55** **56**

A: $R^1CONHNH_2$ /propanol/reflux/24h/ 75-92%

B: $Pb(OAc)_4$ /THF/r.t./2-24h/ 60-73%

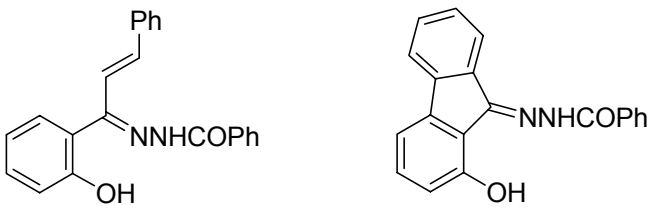
a: R^1=Ph; b: R^1=*o*-HOC_6H_4; c: R^1=*o*-$O_2NC_6H_4$; d: R^1=2'-furyl; e: R^1= 2'-thienyl; f: R^1=Me

Scheme 17. Synthesis of 6,7-diacylcoumarins.[27]

6. Limitations

Treatment of *o*-hydroxyphenyl-1-propenyl ketone benzoylhydrazone[28] **57** as well as the 1-hydroxy-9*H*-fluoren-9-one benzoylhydrazone **58** led to very complicated mixtures.[29] Both

hydrazones **57** and **58** possess a double bond at the α-carbon of hydrazonyl group that possibly influences the mechanism of the reaction.

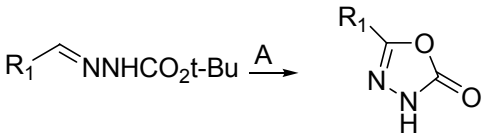


57 **58**

Figure 1

7. The Transformation of Hydroxyl into a Carbonyl Group *via* Phenyliodoso Diacetate Oxidation

It is well known that phenyliodoso diacetate (PID) is a mild oxidizing agent and a very useful reagent in organic synthesis. It shows reactivity similar to LTA and it is less hazardous, and toxic than lead(IV)compounds.[30] However, although it is a mild oxidizing agent it has been not so often used for oxidations of hydrazones. In 1986 it has been reported that the PID oxidation of aldehyde carbo-t-butoxyhydrazones **59** affords 5-substituted-1,3,4-oxadiazolin-2-ones **60** in good yields as shown in Scheme 18.[31]



59 **60**

A: $PhI(OAc)_2$/MeOH/reflux/ N_2/ 25-30min /47-67%

a: R^1=Ph; b: R^1=4-pyridyl

Scheme 18. Cyclisation of aldehyde *N*-carbonylbutoxy hydrazones.[31]

In 1990 the initial transformation of hydroxyl into a carbonyl group which is shown in Scheme 3 was performed using phenyliodoso diacetate (PID) instead of LTA and results analogous to those with LTA were obtained.[32] It was suggested that the mechanism of this reaction should be analogous to the LTA mechanism.[32,9] Alternatively, cross-linked [polystyrene(iodoso diacetate)] has been successfully used as an oxidative agent.[33]

Later, PID was also successfully used as an alternative oxidative agent for the synthesis of several substituted *o*-ketoaryl esters[34] **21** from hydrazones **20**, of tetraacylbenzenes[20] **42** and **43**, of indazoles **46**, of 7,8-diacylcoumarins[24] **53** as well as of 6-carbonylthienyl-7-acetyl-coumarin[27] **56e**. The transformation was successful and the yields were good and comparable with those obtained by the LTA oxidations. The products were isolated by column chromatography both in LTA and PID oxidations. In LTA oxidations of hydrazones **10**, diacylbenzenes **12** were isolated by crystallisation from chloroform/petroleum ether (Table 1).

Table 1. Transformation of hydroxyl by a carbonyl group *via* phenyliodoso diacetate oxidation[a,b]

Substrate	PID oxidation				LTA oxidation			
Hydrazone	Product	Yield %	Isolation	Ref.	Product	Yields %	Isolation	Ref.
10[a]	**12a-d, f, k-o**[c]	60-97	B	32	**12a-j**	68-95	A	3
20[b]	**21a-m**[d]	68-95	B	34	**21a-e**	60-90	B	14
40[b]	**42**	68	B	20	**42**	73	B	20
41[b]	**43**	50	B	20	**43**	55	B	20
45[b]	**46a-f**	55-79	B	35	**46a-f**	68-95	B	21
52[b]	**53a-l**	62-90	B	24	**53a-l**	65-90	B	23,24
55[b]	**56e**	60	B	27	**56a-f**	60-73	B	27

[a]Oxidation conditions: $Ph[I(OAc)_2]/CH_2Cl_2$/25ºC/0.33-44h. [b]Oxidation conditions: $Ph[I(OAc)_2]/CH_2Cl_2$/25ºC/2h. [c]k: R^1=Me, R^2=R^3=R^4=H, R^5= *p*-$MeOC_6H_4$; l: R^1=Me R^2=R^3=R^4=H, R^5= *p*-MeC_6H_4; m: R^1=Me, R^2=R^3=R^4=H, R^5=2-furyl; n: R^1=Me, R^2=R^3=R^4=H, R^5=2-thienyl; o: R^1=Et, R^2=R^3=R^4=R^5=H. [d]g: R^1=R^2=Me, R^3=H, R^4=Et; h: R^1=R^2=R^3=Me, R^4=Et; i: R^1=Me, R^2=Cl, R^3=H, R^4=Et; j: R^1=Me, R^2=Br, R^3=H, R^4=Et; k: R^1=*p*-HOC_6H_4, R^2=R^3=H, R^4=Et; l: R^1=Me, R^2=R^3=H, R^4= CH_2Ph; m: R^1=Et, R^2=R^3=H, R^4=CH_2Ph.
A: Crystalisation by treatment with chloroform/pet. ether
B: Column chromatography

8. The Transformation of Hydroxyl into a Carbonyl Group *via* Sodium Hypochlorite Oxidation

Sodium hypochlorite is also a mild oxidizing agent and has the advantages of being less toxic and less costly. Treatment of *o*-hydroxyacetophenone *N*-benzoylhydrazone **10b** with sodium hypochlorite for two hours at room temperature led to the formation of 1-acetyl-2-benzoylbenzene **12b** in 52% yield.[36] Thus, the transformation of phenolic hydroxy to an acyl

group was successful. However, the generality of this reaction as well as the optimisation of the yield should be further investigated.

9. Conclusions

The transformation of a hydroxyl into an acyl group works smoothly in several carbocyclic and heterocyclic substrates and gives the ability for the synthesis of *ortho*-diacylsubstituted carbocyclic and heterocyclic compounds respectively which were previously unavailable. Despite the difficulties for their preparation, both *o*-acylbenzaldehydes[37] or *o*-diacylbenzenes[12] have been shown to be useful starting materials in the synthesis of various compounds such as 1,3-diarylisobenzofurans, isoindoles, phthalimidines, isoindoloquinazolines, indanes, naphthols, olefins and they could be promising tools in organic synthesis in the future. The products could further serve also as useful intermediates to the synthesis of various derivatives with possible pharmaceutical properties.

The simplicity of the experimental procedure, the generality, the high yields and the low cost of the reagents add to the synthetic value of the method.

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Antigoni Kotali was born in Thessaloniki, Greece and studied chemistry at the Aristotle University of Thessaloniki where she obtained her B.Sc. in 1981 and her Ph.D. in 1986 under the supervision of Professor V. P. Papageorgiou. Since 1981 she has been working in the University of Thessaloniki first as research assistant, then as a lecturer and later as an assistant professor. Her present position is an Associate Professor. In 1989-1990 she worked in Professor A R. Katritzky's group at the University of Florida, Gainesville, FL and later in 1994 in Professor S. W. Baldwin's group at Duke University, Durham, NC, on a sabbatical. Her scientific interests are mainly in organic synthesis, in particular, oxidations of nitrogen derivatives of carbonyl compounds and synthesis of molecules with biological activity.