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The 'pyrono route' to 4-hydroxy-2-quinolones and 4-hydroxy-2-pyridones

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Abstract

The condensation of *N*-substituted anilines **6**, azomethines or enamines **13** with two equivalents of diethyl malonate yields pyrono-quinolones **8**, **10–12** or pyrono-pyridones (for instance **15**, **20**, **23**, **30**, **34**) in high yields and on large scale preparations. These pyrono-quinolones and -pyridones are therefore excellent intermediates in the synthesis of a vast number of compounds, a number of which have potential biological activity.

Keywords: 4-Hydroxy-2-quinolones; 4-Hydroxy-2-pyridones; 3-Acyl-4-hydroxy-2-quinolones; 3-Acyl-4-hydroxy-2-pyridones; Dichloroacetyl-4-hydroxy-2-quinolones; Dichloroacetyl-4-hydroxy-2-pyridones; 3-Tetrazolylcarbonyl-4-hydroxy-quinolones

1. Introduction

4-Hydroxy-2(1*H*)-quinolone (**1**) is the fundamental ring system of a large number of alkaloids, usually containing additional methoxy groups. Some are prenylated or have anellated furo (e.g. dictamine) or pyrano rings (e.g. flinderisine). Many pharmacological active derivatives of **1** are known: recently 3-aryl-4-hydroxy-2(1*H*)-quinolones have been shown to be orally active and selective antagonists of the glycine site on the NMDA receptor [1,2], and also some chloro substituted 3-nitroso derivatives of **1** are highly potent in this respect [3].

Coumestrol **2** represents an estrogenic factor occurring naturally in forage crops. Note that the 4,4′-dihydroxy-*E*-stilbene moiety is present in this structure, as in diethyl stilbestrol. Synthetic nonsteroidal estrogens with structures similar to coumestrol have been developed for the treatment of breast cancer (for a literature survey see [4]). We and others have also synthesized 'aza coumestrol' derivatives by replacing the coumarin part against the 2-quinolone unit. Moreover, some azacoumetrols were found to possess antiosteoporotic activity, the most prominent example being **3**, KCA-098 (Fig. 1) [5,6]. The various synthetic pathways leading to coumestrols and azacoumestrols have been summarized [4]. We have mainly used two routes for the synthesis of azacoumestanes: the first one [4,7] employs a cyclodehydrogenation of 3-aryl-4-hydroxy-2-quinolones (**7**, $R^2 = Ar$, Scheme 1) with palladium, while the second method [4,7,8][1] employs 4-hydroxy-2-quinolones **10** which are unsubstituted in position 3 (and are readily obtained by the pyrono route, see below).

The 4-hydroxy-2(1*H*)-pyridone system **4** is noteworthy for several reasons: the basic structure can be found in many natural products, such as flavipucin [9], the long known and highly toxic ricinine [10,11], and the yellow pigments bassianin [12] and tellenin [13]. The

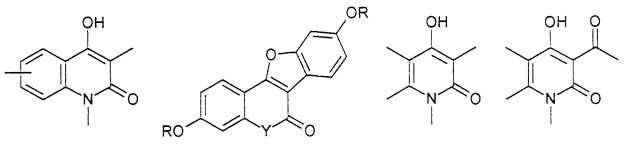

Fig. 1. Structures with biological interest.

[1] By this method 3-aryliodonium-ylids of 4-hydroxy-2-quinolones are prepared, rearranged to 4-aryloxy-3-iodo-2-quinolones, and subsequent Heck-reaction leads to azacoumestrols (see Ref. [7]) or coumestrols.

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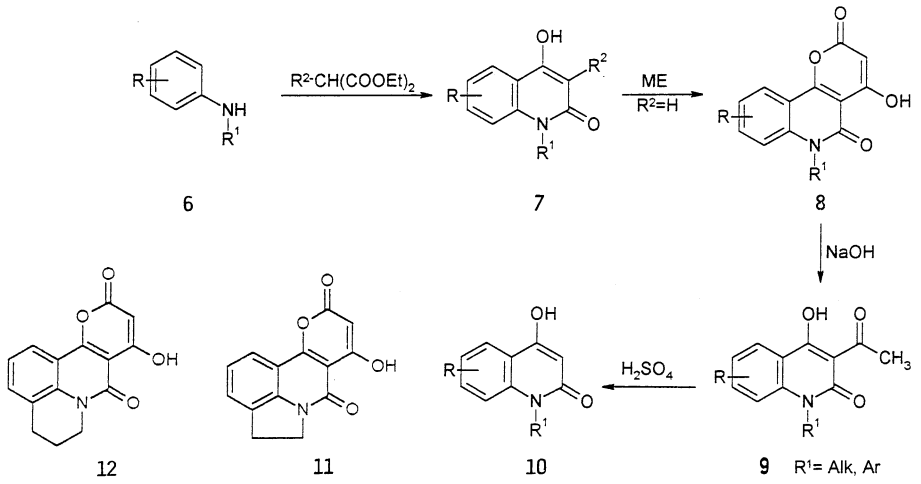


Scheme 1. Reaction of anilines with diethyl malonates and degradation of the pyrono structures to 4-hydroxy-2-quinolones.

latter two compounds have a 3-acyl-4-hydroxy-2-pyridone structure **5**, a structural moiety which is common in a large number of antibiotic substances, such as ilicicolin H [14], funiculosin [15], harzianopyridon [16], sambutoxin [17], mocimycin [18], and aurodox [18], produced by a variety of *Streptomyces* species. Moreover, substances with the general structure of type **5** belong to the large group of so-called 'cyclic tricarbonylmethane compounds' which play an important role in agricultural chemistry, whether they are carbocyclic or heterocyclic, oximated or not [19,20]. 4-Hydroxy-2-pyridone itself (also known as 'deazauracil') has also been used as a base in the synthesis of nucleosides [21]. Exchange of the hydroxy group in **4** against the arylthio moiety leads to compounds with potent HIV-1 reverse transcriptase inhibitory properties [22].

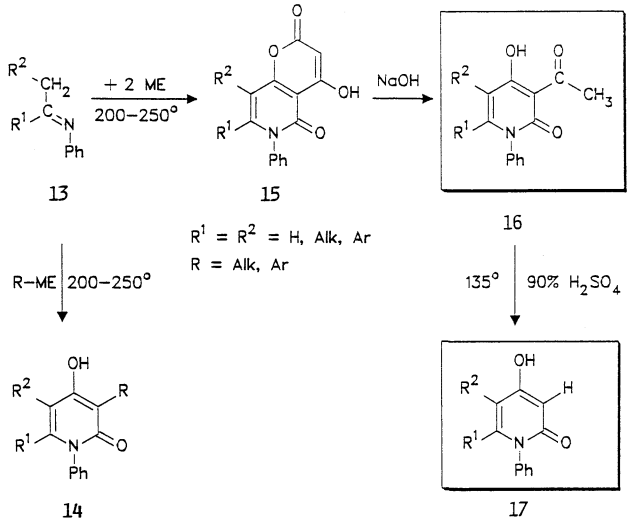
2. Chemistry

Heating anilines and their derivatives **6** with substituted dialkyl malonates in a 1:1 fusion reaction without solvent at temperatures of 250°C and above leads to 4-hydroxy-2-quinolones **7** substituted in position 3 in good yields [23,24]. However, if unsubstituted diethyl malonate (ME) is used in a 1:2 ratio then the hydroxypyrano-quinolones **8** are formed (Scheme 1). This reaction was first described by Bowman in 1958 using *N*-methylaniline as the starting material [25], and the method has been improved considerably by us [27,28], and extended to a variety of aromatic amines as substrates. The best results are obtained when this condensation reaction is carried out in boiling diphenyl ether [27,28]. Cyclic anilines, such as indoline and tetrahydroquinoline, lead to tetracyclic compounds, e.g. **11** [29] and **12** [30]. The pyronopyridones **8**, **11**, **12** are valuable intermediates for the synthesis of a number of quinolones having various functional groups in position 3 (see below), or for degradation to the basic ring system **10**.

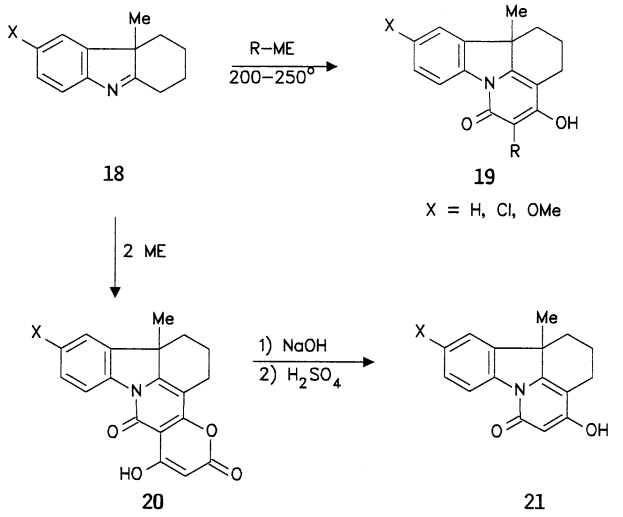
Enamines or azomethines react in the same manner as anilines; thus, compounds of type **13** react with substituted dialkyl malonates to yield 3-substituted 4-hydroxy-2(1*H*)-pyridones **14** [31], while unsubstituted malonates (ME = malonic esters) produce the hydroxypyrono-pyridones **15** [32] (Scheme 2).

Degradation of **15** with sodium hydroxide in boiling 1,2-dihydroxyethane leads to 3-acetyl derivatives **16** in nearly quantitative yields [27,28,32]. Cleavage of the acetyl group with 90% sulfuric acid at 135°C results in the formation of 3-unsubstituted pyridones **17** [32].

The reaction sequence can be performed with a broad variety of azomethines, especially those having a *N*-aryl substituent. Scheme 3 presents the results obtained with three tetrahydrocarbazoles **18** [33] (readily



Scheme 2. Reaction of azomethines with diethyl malonates and degradation of the pyrono derivatives to 4-hydroxy-2-pyridones.



Scheme 3. Reaction of tetrahydrocarbazoles with diethyl malonate.

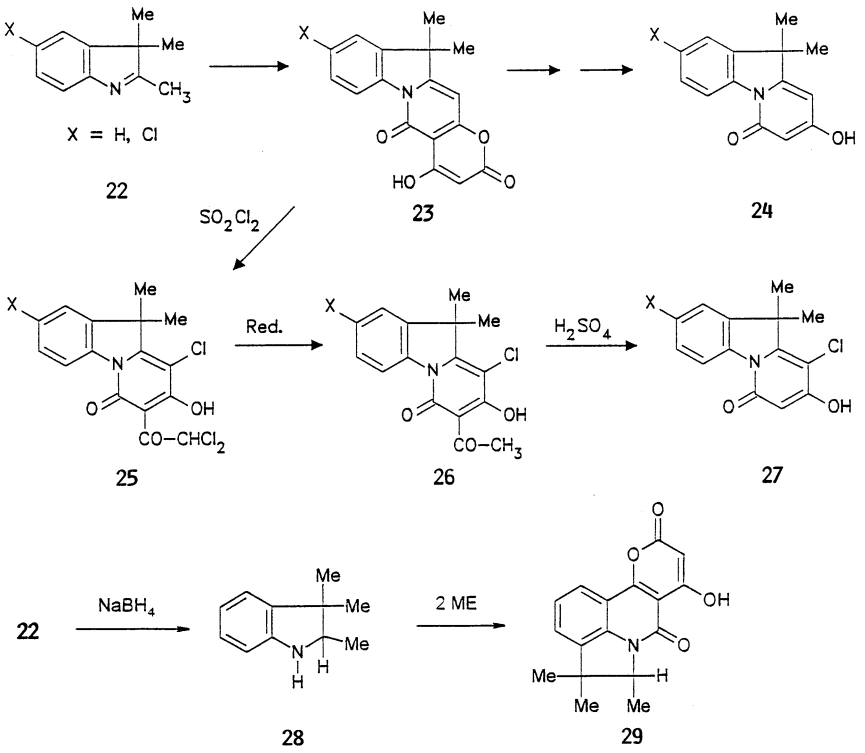
obtained by a Fischer indole synthesis from 2-methylcyclohexanone and the corresponding phenylhydrazine) [34]. It can be noted that compound **21** already contains rings A–D of the strychnine structure with the two oxygen atoms at the correct position.

Other indolenines react in the same manner [35]. Thus, 2,3,3-trimethyl-indolenines **22** react with diethyl malonate to yield **23** which, upon subsequent degradation with sodium hydroxide and sulfuric acid, yield the basic pyrido-indole structure **24** via the acetyl derivative (Scheme 4) [35].

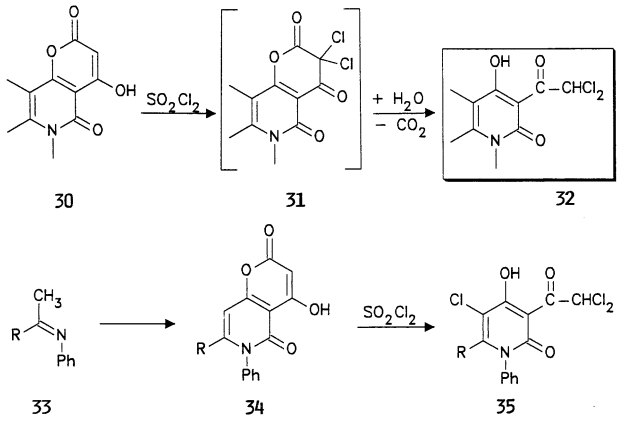
Reaction of **23** with sulfurylchloride in dioxane and aqueous work up leads to the dichloroacetyl compound **25** (another chloro atom has entered into the hydroxypyridone part of the molecule). Reduction with zinc powder in an ethanol/acetic acid mixture removes the two chloro atoms from the acetyl group but leaves the chloro atom at the sp^2-carbon atom unaffected, thus yielding **26**. Treatment of **26** with 90% sulfuric acid at 135°C leads to **27** which differs only from **24** by having an additional chloro substituent in the pyridone moiety. Dichloroacetyl compounds of this type are valuable intermediates (see below).

The indoline **28**, easily obtained by reduction of the indolenine **22**, behaves like a *N*-substituted aniline affording with two equivalents of ME the pyranoquinolone **29**, a trimethyl derivative of **11**, and starting material for the synthesis of sterically hindered *N*-substituted quinolones. Such derivatives with bulky groups at the *N*-atom were needed for a study of structure–activity relationship. Similarly, hydrogenation of the tetrahydrocarbazole **18** with sodium borohydride lead to 4a-methyl-hexahydrocarbazole (two diasteroisomers) which reacted with two MEs to form a pyronoquinolone [35].

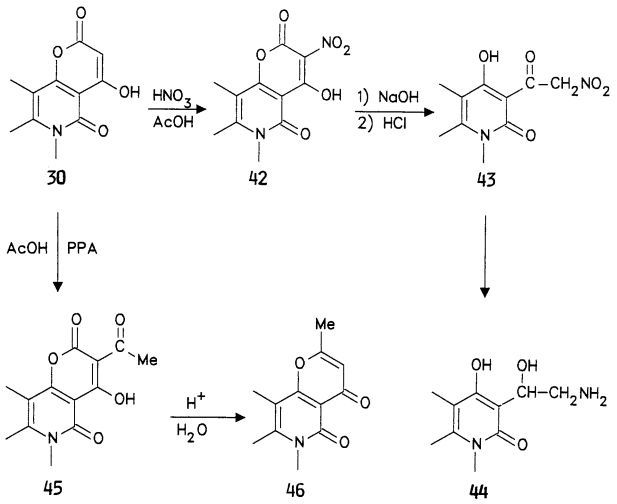
The generality of the chlorination of pyronoquinolones or -pyridones is summarized in Scheme 5 [26,28–30,32]. The intermediate 3,3-dichloro-pyran-2,4-dione (**31**) is hydrolyzed during aqueous work up to a β-keto acid which decarboxylates readily to the



Scheme 4. Reaction of 2,3,3-trimethylindolenin with diethyl malonate and degradation studies with pyrono derivatives.



Scheme 5. Degradation of pyrono-compounds with sulfurylchloride to dichloroacetyl derivatives.



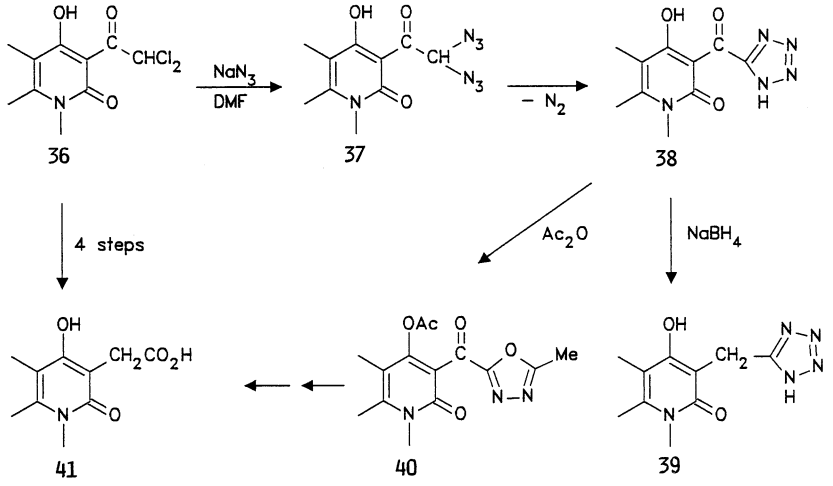
Scheme 7. Nitration and acylation of pyrono-compounds and their further reactions.

dichloroacetyl derivatives **32**. If the pyridone moiety is unsubstituted in position 5 this C-atom is also chlorinated. Thus, a pyrono-pyridone derived from a methyl ketone anil (e.g. acetophenone or picolone anil) affords a trichloro derivative such as **35** on chlorination. Compound **35** with R = Ph showed hypolipidemic activity. Therefore, we have prepared a number of analogs of this type of 3-dichloroacetyl-4-hydroxy-2-pyridones [32].

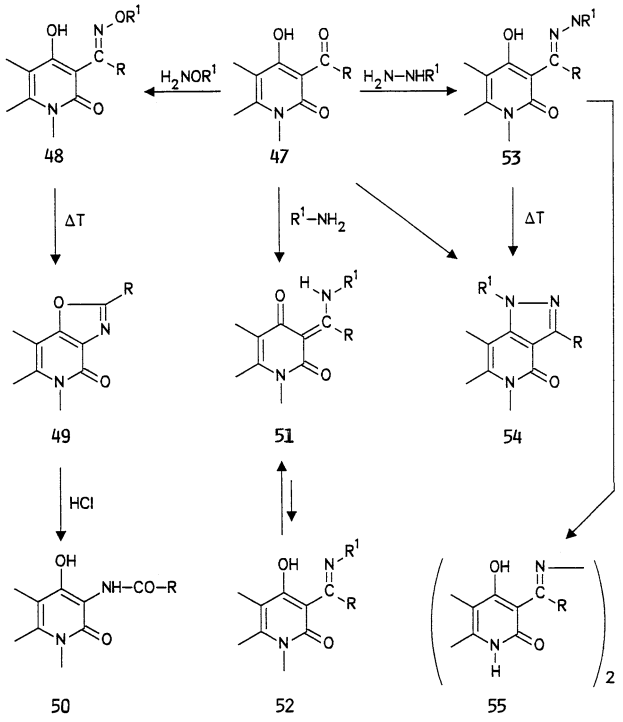
Compounds of type **32** or **35** are versatile intermediates for further functionalization of position 3 in 4-hydroxy-2-quinolines and 2-pyridones. Reactions with nucleophiles, such as sodium cyanide or morpholine, afford ring closure to furanone derivatives [26,37].

However, with sodium azide the tetrazolyl derivatives **38** [26,29,35,36] are formed, apparently via the geminal diazide **37** [38]. The carbonyl group in **38** is readily reduced with sodium borohydride to the CH_2 group of **39** [20,26,37]. Reaction of **38** with acetic anhydride not only acetylates the hydroxy group, but also converts the tetrazol moiety to the oxadiazole ring system **40** by a well-known mechanism [38,39]. Reduction of **40** with sodium borohydride and subsequent saponification leads to the heterocyclic acetic acid **41** [26]. Thus, the heterocyclic acetic acid **40** (a compound which is difficult to obtain by other methods) can be produced in four steps from the dichloroacetyl derivative **36** (Scheme 6).

Electrophilic substitutions, such as nitration, nitrosation, or coupling reactions of aromatic diazonium salts with hydroxy-quinolones and -pyridones **30** (**8**, **15**) take place at position 3 [28,29,32]. The compounds obtained by these reactions can be reduced to ethanolamines or ethylamines. Scheme 7 examplifies this reaction sequence with the nitration of **30** which firstly gives the 4-hydroxy-3-nitro-2-pyrono derivative **42**. Ring opening occurs in dilute sodium hydroxide, and after acidification the decarboxylated 4-hydroxy-3-nitro-2-quinolone or 2-pyridone **43** is obtained. Reduction leads to the



Scheme 6. Conversion of dichloroacetyl derivatives to tetrazolylcarbonyl compounds and further reaction to acetic acid derivatives.



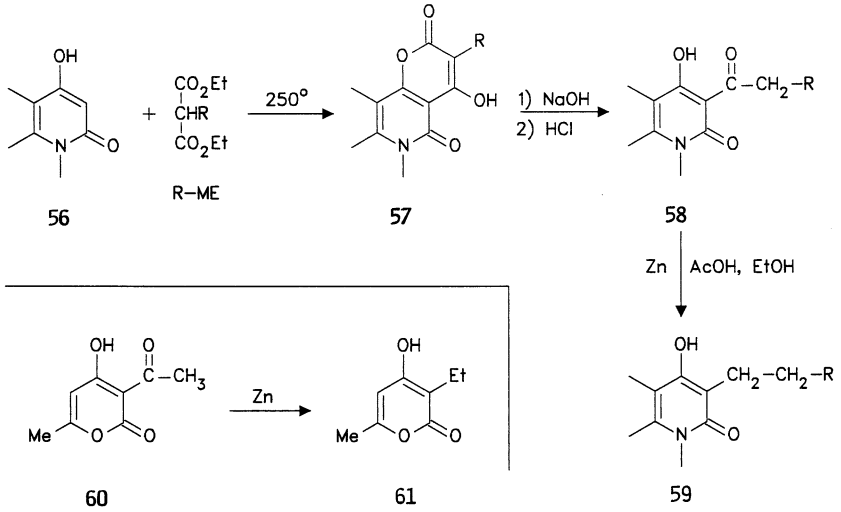
Scheme 8. Reaction of 3-acyl-4-hydroxy-2-quinolones and 2-pyridones with nitrogen bases.

ethanolamine **44**, and with palladium as catalyst the corresponding ethylamine can be obtained.

In Scheme 7 the acetylation of **30** using a mixture of acetic acid and polyphosphoric acid is depicted. The 3-acetyl derivative **45** can be rearranged with mineral acids to afford 2-methyl-4-pyrone derivatives of 4-hydroxy-2-quinolones and -pyridones **46** [44]. The method is noteworthy because using different conditions of the Pechmann condensation reaction of 4-hydroxy-2-quinolones **10** and -2-pyridones **17** with acetoacetic ester or β-amino-crotonic ester only the corresponding 4-methyl-2-pyrone derivatives can be obtained [45].

3-Acyl-4-hydroxy-2-quinolones and 2-pyridones of the general formula **47** react with a number of nitrogen bases. The reaction with hydroxylamine (and its *O*-alkyl derivatives), primary amines, and hydrazines is shown in Scheme 8. The oxime derivatives **48** are the most interesting species, because of their potential herbicidal activity [19]. Moreover, they can easily be concerted by a thermal Beckmann rearrangement to derivatives of 3-amino-4-hydroxy-2-quinolones and 2-pyridones [32,40,44]. Thus, heating **48** in ethylene glycol yields the oxazolo derivatives **49**, which are converted by acid hydrolysis to the acylamino derivatives **50**. Since the free amines are usually unstable, they are best stored in the form of **49** or **50** before using them for further transformations. Reaction of **47** with aliphatic or aromatic primary amines leads to aminomethylene derivatives **51** [32,40]. According to NMR studies this enamino–ketone structure is predominant over the imino–enol form **52** [39e]. Hydrazones **53** are obtained from hydrazine(s) and **47**. Substituted hydrazones **53** give upon heating, preferably in acetic acid, the pyrazoles **54**, which can also be obtained directly from **47** in this solvent. Hydrazones obtained with hydrazine itself (**53**, R = H) afford under these conditions the azines **55** [40].

The importance of the acyl derivatives of 4-hydroxy-2-quinolones and 2-pyridones should again be stressed [39e]. Firstly, they belong to an important class of natural products with potent biological properties (see Section 1). Secondly, these cyclic tricarbonylmethane derivatives can easily be converted to imines, oximes, and oxim-*O*-alkyl ethers (as shown in Scheme 8), which are of potential interest in agricultural chemistry [19,20,39,40]. The procedures outlined in Schemes 1–3 using unsubstituted ME lead only to the 3-acetyl



Scheme 9. Chain elongation of acetyl derivatives and their reduction to alkyl side chains.

derivatives. However, there are ways to convert them into longer chains or arylalkyl substituents. One method uses an aldol condensation of the acetyl group with an aldehyde, followed by reduction of the alkenoyl substituent [41]. In our favorite method (Scheme 9) [28] the basic structures **56** (**10**, **17**) are condensed with a substituted malonic ester (R–ME) which leads to a 3-substituted pyrono derivative **57,** which gives **58** (R = alkyl, aryl) upon alkaline hydrolysis. Interestingly, 3-acyl-4-hydroxy-2-quinolones and pyridones can be reduced with zinc dust [42] in acetic acid to the 3-alkyl derivatives **59** [43]. We have tested the generality of this reaction by also reducing 3-acyl-4-hydroxy-coumarins and 2-pyrones to their corresponding 3-alkyl derivatives; thus, dehydracetic acid **60** gives 3-ethyl-4-hydroxy-6-methyl-2-pyrone (**61**) under these conditions [43].

3. Conclusion

We have shown that the compounds depicted in Fig. 1 can be prepared easily via their pyrono derivatives. Moreover, intermediates in the degradation pathway are valuable intermediates for a vast number of 4-hydroxy-2-quinolones and 2-pyridones functionalized in position 3. The biological activity of a number of these intermediates has also encouraged us to prepare 3-aroyl-4-hydroxy-2-quinolones [20] and 2-pyridones [46] by anionic Fries rearrangement of the corresponding 4-aroyloxy derivatives. Furthermore, we have prepared sulfoxide analogs of the acyl compounds (e.g. compounds with –SO–R substituents in position 3) [47,48]. Needless to say, many of the starting 4-hydroxy-2-quinolones and 2-pyridones have been prepared via the 'pyrono route'.

References

[1] J.J. Kulagowski, R. Baker, N. Curtis, P.D. Leeson, I.M. Mawer, A.M. Mosely, M.P. Ridgilli, M. Rowley, I. Stansfield, A.C. Foster, S. Grimwood, R.G. Hill, J.A. Kemp, G.R. Marshall, K.L. Saywell, M.D. Tricklebank, J. Med. Chem. 37 (1994) 1402–1405.

[2] L.A. McQuaid, E.C.R. Smith, D. Lodge, E. Pralong, J.H. Wikel, D.O. Calligaro, P.J. O'Malley, J. Med. Chem. 35 (1992) 3423–3425.

[3] S.X. Cai, Z.L. Zhou, J.-C. Huang, E.R. Whittemore, Z.O. Egbuwoku, Y. Lü, J.E. Hawkinson, R.M. Woodward, E. Weber, J.F.W. Keana, J. Med. Chem. 39 (1996) 3248–3255.

[4] W. Stadlbauer, T. Kappe, Heterocycles 35 (1993) 1425–1440. Review on: 'Simple and effective approaches to coumestanes and azacoumestanes'.

[5] X. Rabasseda, N. Mealy, J. Castaner, Drugs Future, Prous Sci., Barcelona 20 (3) (1995) 235–237.

[6] T. Kamijo, A. Tsubaki, T. Yamaguchi, K. Hirata (Kissei Pharmaceutical Co., Ltd.), Jpn. Kokei JP 02,273,679; JP 02,273,680; JP 02,273,681 (1990); (Chem. Abstr. 114, 207237a, 207238b, 207239c; p. 829 (1991)).

[7] W. Stadlbauer, R. Laschober, T. Kappe, Liebigs Ann. Chem. (1990) 531–539.

[8] R. Laschober, T. Kappe, Synthesis (1990) 387–388.

[9] (a) P.S. White, J.A. Findlay, H.J. Tam, Can. J. Chem. 56 (1978) 1904. (b) N.N. Girotra, N.L. Wendler, Tetrahedron Lett. 50 (1979) 493. See Ref. [10]: no. F-00041, p. 437.

[10] I.W. Southon, J. Buckingham (Eds.), Dictionary of Alkaloids, 1st ed., Chapman and Hall, London, 1989, no. R-00072, p. 923.

[11] The Merck Index, 12th ed., Merck & Co., Inc., Rahway, NJ, 1996, no. 8377, p. 1412.

[12] See Ref. [10]: no. B-00056, p. 135. C.-K. Wat, A.G. Molnes, D.G. Smith, J.L.C. Wright, L.C. Vining, Can. J. Chem. 55 (1977) 4090.

[13] See Ref. [10]: no. T-00055, p. 1028. (a) D.R. Williams, S.Y. Sit, J. Org. Chem. 47 (1982) 2846. (b) R. Cox, D. O'Hagan, J. Chem. Soc., Perkin Trans. 1 (1991) 2537–2540.

[14] See Ref. [10]: no. I-00015, p. 560. M. Matsumoto, H. Minato, Tetrahedron Lett. 36 (1976) 3827.

[15] (a) K. Ando, I. Matsuura, Y. Nawata, H. Endo, H. Sasaki, T. Okutomi, T. Saeki, G. Tamura, J. Antibiot. 31 (1976) 533–538. (b) Y. Nawata, I. Matsuura, K. Ando, Y. Iitaka, Acta Crystallogr., Sect. C 46 (1990) 515–517.

[16] (a) F. Trecourt, M. Mallet, O. Mongin, G. Quegeuiner, J. Heterocycl. Chem. 32 (1995) 1117–1124. (b) H.G. Cutler, J.M. Jacyno, Agric. Biol. Chem. 55 (1991) 2629–2631.

[17] J.-C. Kim, Y.-W. Lee, H. Tamura, T. Yoshizawa, Tetrahedron Lett. 36 (1995) 1047–1050.

[18] Antibiotic MYC 8003; see Ref. [11]: no. 6308, p. 1065. H. Maehr, M. Leach, T.H. Williams, J.F. Blount, Can. J. Chem. 58 (1980) 501–526.

[19] I. Iwataki, in: W. Draber, T. Fijita (Eds.), Rational Approaches to Structure, Activity, and Ecotoxicology of Agrochemicals, CRC Press, Boca Raton, FL, 1992, pp. 397–426.

[20] T. Kappe, B. Schnell, J. Heterocycl. Chem. 33 (1996) 663–670.

[21] (a) P.D. Cook, R.T. Day, R.K. Robins, J. Heterocycl. Chem. 14 (1977) 1295–1298. (b) R.L. Stone, Tetrahedron Lett. 46 (1977) 4017–4020. (c) D.J. McNamara, P.D. Cook, L.B. Allen, M.J. Kehoe, C.S. Holland, A.G. Teepe, J. Med. Chem. 33 (1990) 2006–2011.

[22] V. Dollé, E. Fan, C.H. Nguyen, A.-M. Aubertin, A. Kirn, M.L. Andreola, G. Jamieson, L. Tarrago-Litvak, E. Bisagni, J. Med. Chem. 38 (1995) 4679–4686.

[23] W. Stadlbauer, R. Laschober, H. Lutschounig, G. Schindler, Monatsh. Chem. 123 (1992) 617–636. For earlier literature, see Ref. [24].

[24] (a) W. Stadlbauer, T. Kappe, Monatsh. Chem. 116 (1985) 1005–1015. (b) W. Stadlbauer, T. Kappe, Z. Naturforsch., Teil B 37 (1982) 1196–1200. (c) W. Stadlbauer, O. Schmut, T. Kappe, Monatsh. Chem. 111 (1980) 1005–1013. (d) P. Baumgarten, W. Kärgel, Ber. Dtsch. Chem. Ges. 60 (1927) 832.

[25] (a) R.E. Bowman, A. Campbell, E.M. Tanner, J. Chem. Soc. (1959) 444. (b) J.A. Bosson, M. Rasmussen, E. Ritchie, A.V. Robertson, W.C. Taylor, Aust. J. Chem. 16 (1963) 480.

[26] K. Faber, T. Kappe, J. Heterocycl. Chem. 21 (1984) 1881–1883.

[27] (a) P. Roschger, W. Stadlbauer, Liebigs Ann. Chem. (1990) 821. (b) P. Roschger, W. Fiala, W. Stadlbauer, J. Heterocycl. Chem. 29 (1992) 225.

[28] T. Kappe, R. Aigner, P. Hohengassner, W. Stadlbauer, J. Prakt. Chem. 336 (1994) 596–601.

[29] (a) C.O. Kappe, T. Kappe, J. Heterocycl. Chem. 26 (1989) 1555–1560. (b) B. Schuiki, Planned Masters Thesis, University of Graz, 1999.

[30] O. Schmut, R. Korchid-Zadeh, H. Stückler, B. Schuiki, T. Kappe, unpublished results.

[31] (a) S. Kafka, T. Kappe, Monatsh. Chem. 128 (1997) 1019–1031. (b) F. Frühwirth, P. Roschger, U. Bohdal, T. Kappe, unpublished results.
[32] Experimental results of T. Wolf (1974), H. Stückler (1981), A. Pfaffenschlager (1985), P. Roschger (1991), P. Hohengassner (1992), A. Danel (1993), B.P. Nikam (1994).
[33] (a) N.P. Buu-Hoi, P. Jaquinon, T.B. J. Chem. Soc. (1958) 738. (b) S. Sakai, M. Wakabayashi, M. Nishina, Yakugaku Zasshi 89 (1969) 1061; Chem. Abstr. 72 (1970) 3308d.
[34] A. Deeb, T. Kappe, unpublished results.
[35] P. Roschger, T. Kappe, unpublished results. (b) B. Schuiki, Planned Masters Thesis, University of Graz, 1999.
[36] T. Krivitchenko, Dissertation, University of Graz, 1999.
[37] B. Schnell, experimental results, 1998.
[38] For a review on the chemistry of heterocyclic geminal diazides see: T. Kappe, C.O. Kappe, in: H. Suschitzky, G.W. Gribble (Eds.), Progress in Heterocyclic Chemistry, vol. 8, Pergamon, Oxford, UK, 1996, pp. 1–13.
[39] (a) R. Huisgen, J. Sauer, H.J. Sturm, Angew. Chem. 70 (1968) 272. (b) R. Huisgen, J. Sauer, H.J. Sturm, J.H. Markgraf, Chem. Ber. 93 (1960) 2106. (c) R. Huisgen, Angew. Chem. 72 (1960) 364. (d) J. Sauer, R. Huisgen, H.J. Sturm, Tetrahedron Lett. (1960) 241. For the tautomeric behavior of 3-acyl-4-hydroxyquinolones and pyridones and their imine derivatives see: (e) P.E. Hansen, S. Bolvig, T. Kappe, J. Chem. Soc., Perkin Trans. 2 (1995) 1901–1909.
[40] T. Kappe, R. Aigner, M. Jöbstl, P. Hohengassner, W. Stadlbauer, Heterocycl. Commun. 1 (1995) 341–352.
[41] (a) C. Ukita, M. Matsumoto, Yakugaku Zhassi 72 (1952) 800. (b) Y. Rachedi, M. Hamdi, V. Speziale, Synth. Commun. 19 (1989) 3437.
[42] Zinc powder from Merck Co., No. 1.08789, particle size < 45 μm, has been employed.
[43] T. Kappe, R. Aigner, P. Roschger, B. Schnell, W. Stadlbauer, Tetrahedron 51 (1995) 12923–12928.
[44] P. Hohengassner, Masters Thesis, University of Graz, 1988.
[45] T. Kappe, C. Mayer, Synthesis (1981) 524.
[46] B. Schnell, T. Kappe, Monatsh. Chem. 129 (1998) 871–885.
[47] T. Kappe, B. Schnell, K. Georgieva, B. Jocham, A.E. Mayrhofer, B.P. Nikam, Y. Issac, K. Langhans, Posphorus Sulfur Silicon 95–96 (1994) 349–350.
[48] B. Schnell, Ph.D. Thesis, University of Graz, 1994.