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NEW SIMPLE WITTIG-TYPE CYCLIZATIONS TO FLAVONES, 4-QUINOLONES AND INDENONES[1]

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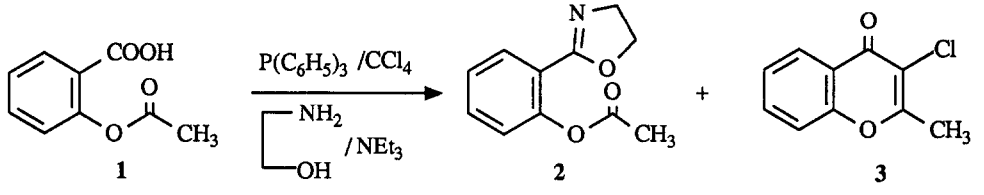
Abstract - 2-Acyloxy-, 2-phthalimido- or 2-benzoylbenzoic acids **4, 6** and **9** are readily cyclized in one step in up to 80% yield by excess triphenylphosphine/carbon tetrachloride in methylene chloride at 24°C to the corresponding 3-chloroflavones **5**, 3-chloroquinoline-4-ones **7** or 2-chloroindenones **10**. On employing trichloroacetonitrile instead of carbon tetrachloride and subsequent heating to 180°C 2-acetoxy-benzoic acid (aspirin) **1** is cyclized to 2-methyl-3-cyanoflavone **28**.

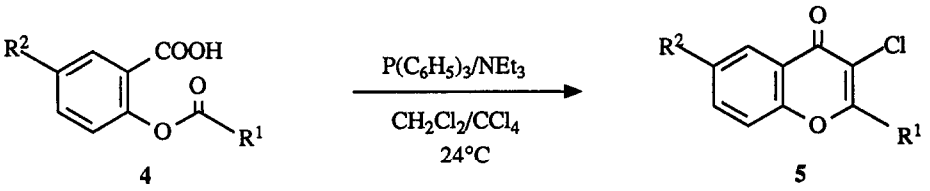
During studies on the conversion of the carboxylic groups of non-steroidal antiinflammatory agents into their corresponding 1,3-oxazolines, aspirin **1** afforded on treatment with 1,2-ethanolamine in the presence of triphenylphosphine, carbon tetrachloride (CCl_4) and triethylamine at room temperature,[2] besides the desired 1,3-oxazoline **2**,[3] small amounts of the known 2-methyl-3-chloroflavone **3**.[4]



1 2 3

When the reaction was repeated with aspirin **1** at 24°C, omitting the 1,2-ethanolamine and working with excess triphenylphosphine-CCl_4-methylene chloride (CH_2Cl_2), **3** was obtained in 60% yield. The analogous cyclizations of the O-aroylsalicylates **4** afforded the corresponding 3-chloroflavones **5** in similar yields.

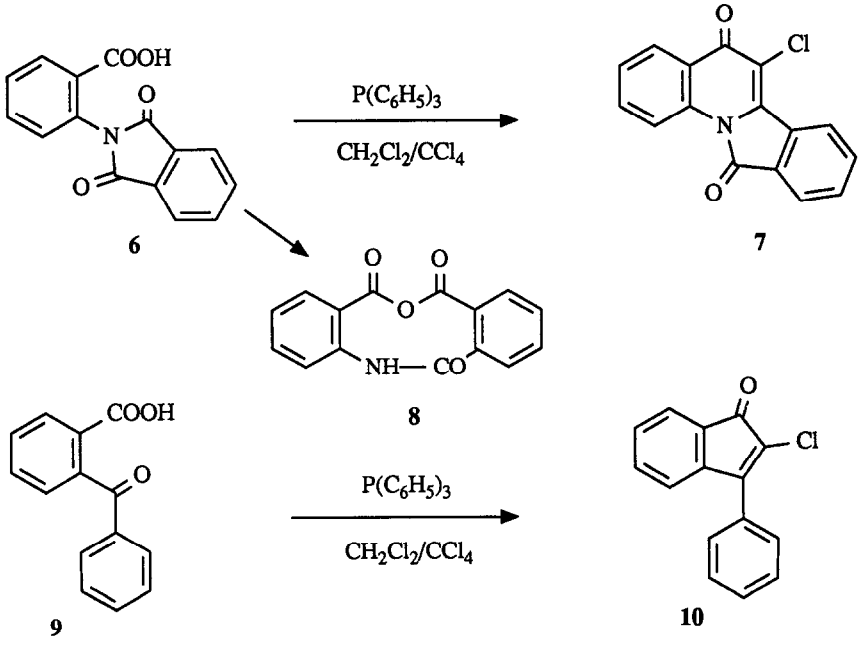
These one step Wittig-type cyclizations (see also the preparation of **28**) can probably still be improved and are much simpler to carry out than the procedures described in the literature, which demand the use of pre-formed Wittig-type reagents.[5,6,7] The scope of these cyclizations extends to other 2-substituted benzoic acids.



4 5

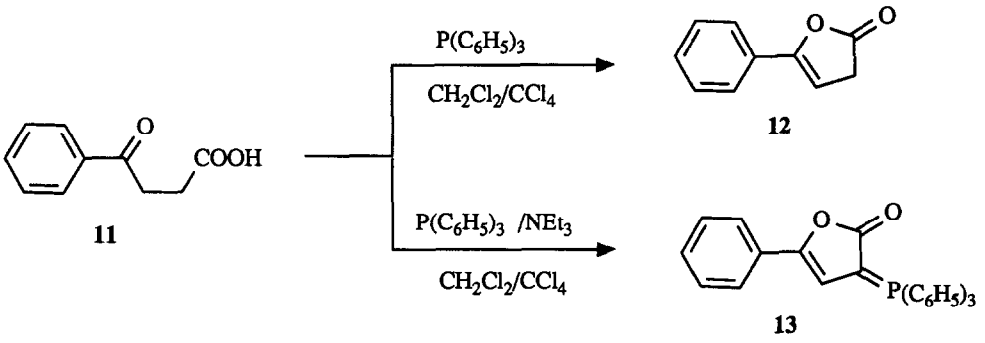
a	R^1 = Phenyl	R^2 = H	57%
b	R^1 = 4-Chlorophenyl	R^2 = H	43%
c	R^1 = 3-Pyridyl	R^2 = Cl	60%

Thus, 2-phthalimidobenzoic acid[8] **6** cyclized at 25°C in 84% yield to the substituted 4-quinolinone **7**. In the presence of triethylamine, however, besides 22% of **7** the cyclic anhydride **8** was formed in 39% yield. Analogously, 2-benzoylbenzoic acid **9** afforded in 37% yield the known 2-chloro-3-phenylindenone **10**.[9]



6 7 8 9 10

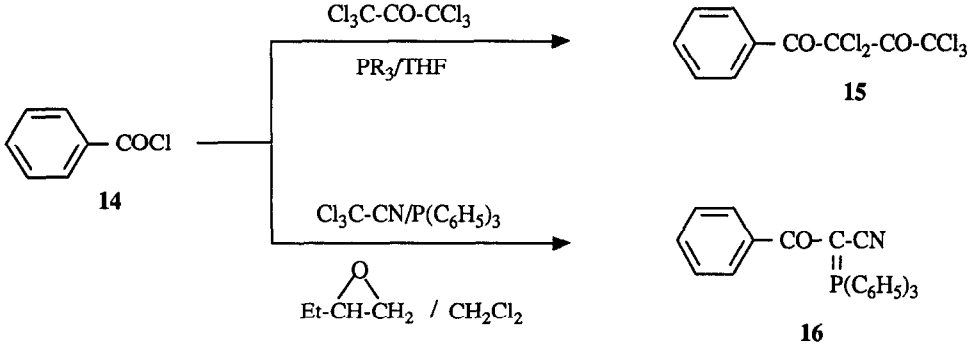
In contrast to **9**, the readily enolized ß-benzoylpropionic acid **11** cyclized at 24°C in 75% yield with triphenylphosphine-CCl_4 to the known enol lactone **12**.[10] In the presence of triethylamine, the reaction gave the enol lactone-ylid **13** in one step in 20% yield. The latter reaction, however, might still be improved.



To elucidate the mechanism of these cyclizations, we used the corresponding aromatic acid chlorides, as they are known to be the first intermediates in these reactions.[2] Therefore, we treated benzoyl chloride **14**, nicotinoyl chloride-hydrochloride **23** as well as 2-acetoxy-benzoyl chloride **25** with hexachloroacetone[11] and trichloroacetonitrile as well as benzoyl chloride **14** with ethyl trichloroacetate[12] in the presence of trivalent phosphorous compounds.

Reactions of benzoyl chloride **14** with hexachloroacetone[11] proceeded with tris(dimethylamino)-phosphine or tributylphosphine at -35°C in tetrahydrofuran to give in both cases ca. 75% yield of 2,2,4,4,4-pentachloro-1-phenyl-butane-1,3-dione **15**. With the less reactive triphenylphosphine at room temperature and triphenylphosphite at 65°C **15** was obtained in 72% and 47% yields, respectively. These reactions may proceed by attack of the pentachloroacetone anion on the carbonyl group of **14** with subsequent loss of chloride ion.

Reactions of benzoyl chloride **14** with trichloroacetonitrile, excess triphenylphosphine, and 1,2-butylene oxide (to remove triphenylphosphine dichloride) in CH_2Cl_2 gave the corresponding ylid **16** in 43% yield.

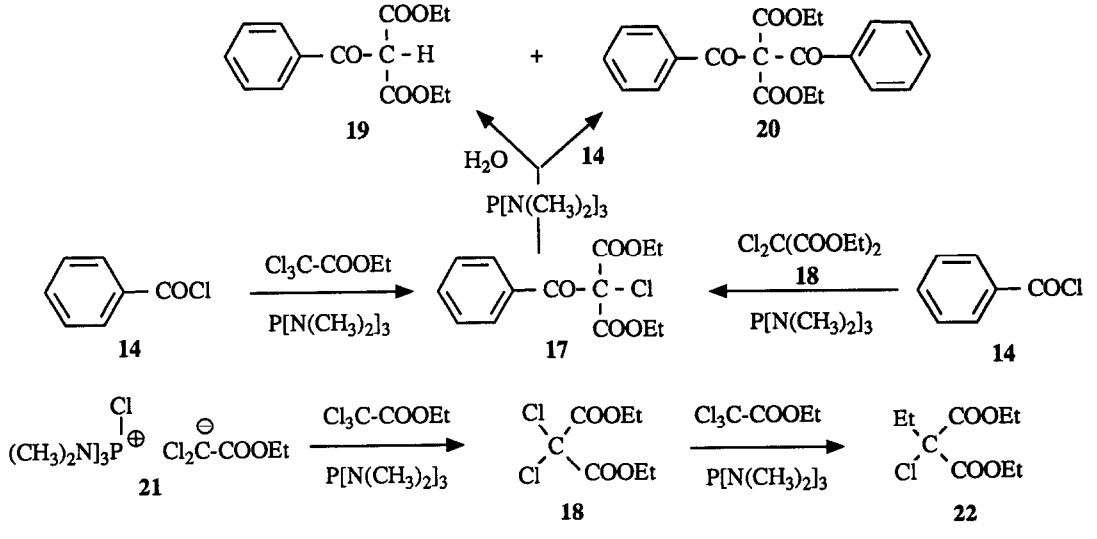


Surprisingly, benzoyl chloride **14** afforded with a prereacted mixture of 2 equivalents of ethyl trichloroacetate and 2 equivalents of tris(dimethylamino)phosphine at -35°C in tetrahydrofuran in 36% yield diethyl 2-benzoyl-2-chloromalonate **17**, which is however obtained in 68% yield on analogous

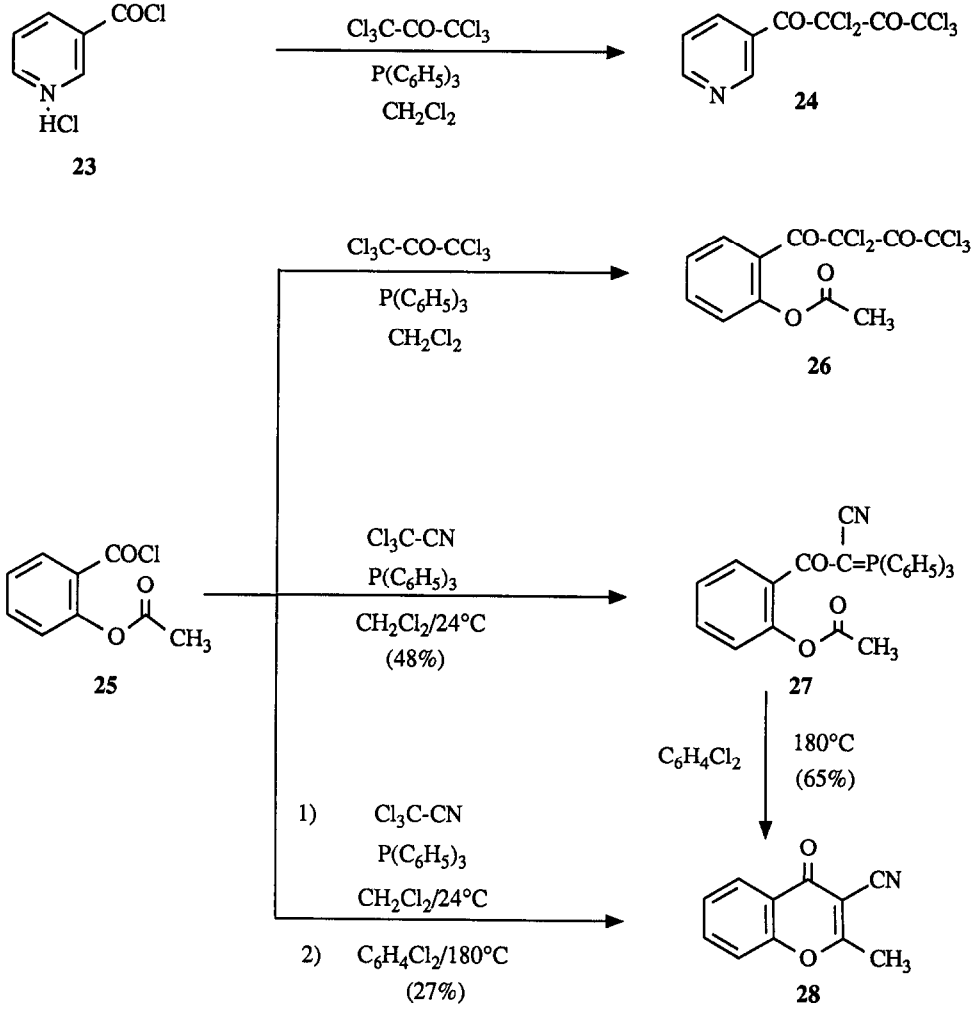
reaction of benzoyl chloride **14** with 2 equivalents each of tris(dimethylamino)phosphine and diethyl 2,2-dichloromalonate **18**. Thus **18** is therefore probably an intermediate in the reaction of ethyl trichloroacetate with tris(dimethylamino)phosphines. Treatment of benzoyl chloride **14** with a prereacted mixture of 2 equivalents of ethyl trichloroacetate and 3.5 equivalents of tris(dimethylamino)phosphine at -35°C afforded along with 32% of diethyl 2-benzoyl-2-chloromalonate **17** more polar products such as ca. 15% of diethyl 2,2-dibenzoylmalonate **20**. On reaction of diethyl 2-benzoyl-2-chloromalonate **17** with tris(dimethylamino)phosphine in tetrahydrofuran at -30°C diethyl 2-benzoylmalonate **19** is obtained in 83% yield after aqueous workup.

On treatment of ethyl trichloroacetate with tris(dimethylamino)phosphine the initially formed ethyl dichloroacetate[12] **21** apparently attacks the estercarbonyl groups of ethyl trichloroacetate to give the trichloromethyl anion and diethyl 2,2-dichloromalonate **18**. The latter compound can react further with excess tris(dimethylamino)phosphine to form the corresponding diethyl 2-chloromalonate anion, which is alkylated in the absence of benzoyl chloride **14** by excess ethyl trichloroacetate to form diethyl 2-chloro-2-ethylmalonate **22**. The analogous ethylation of the diethyl 2-chloromalonate anion by diethyl 2,2-dichloromalonate **18** does not seem to occur since chlorine is apparently preferentially abstracted from **18** to result in the same diethyl 2-chloromalonate anion. Whereas 2 equivalents of ethyl trichloroacetate and 1 equivalent of tris(dimethylamino)phosphine afforded according to GC/MS a mixture of ca. 20% of diethyl 2,2-dichloromalonate and ca. 30% of diethyl 2-chloro-2-ethylmalonate **22** as well as other products, the reaction of equimolar amounts of ethyl trichloroacetate, diethyl 2,2-dichloromalonate and tris(dimethylamino)phosphine gave rise to 27% of diethyl 2-chloro-2-ethylmalonate **22**.

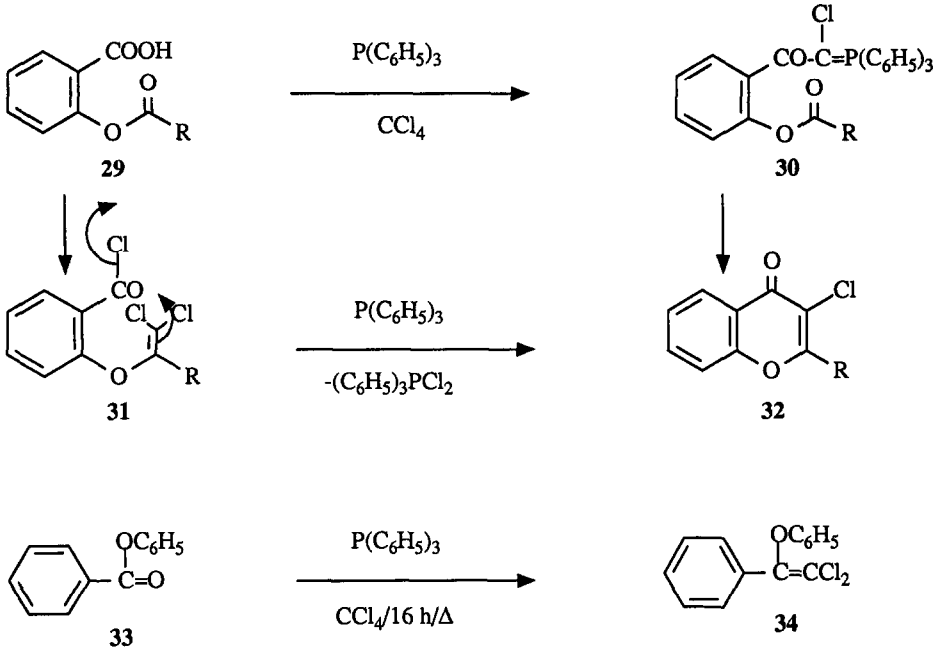
These reaction have to be carried out with very careful exclusion of humidity, since even traces of H_2O transform the intermediate diethyl 2-chloromalonate anion into diethyl 2-chloromalonate.



Nicotinoylchloride hydrochloride **23** was converted by hexachloroacetone and triphenylphosphine in 83% yield to **24**, and 2-acetoxy-benzoylchloride **25** gave 43% of the corresponding product **26**. Most importantly, 2-acetoxy-benzoylchloride **25** reacted with trichloroacetonitrile/triphenylphosphine in CH_2Cl_2 at 24°C, to furnish on chromatography the ylid **27** in 48% yield, which was cyclized on heating to 180°C in 1,2-dichlorobenzene in 65% yield to 2-methyl-3-cyanoflavone **28**.[14] The same reaction first at room temperature in CH_2Cl_2, followed by heating in 1,2-dichlorobenzene without isolating the intermediate **27**, afforded 2-methyl-3-cyanoflavone **28** in an overall yield of 27%. This moderate yield, however, might be increased on addition of 1,2-butylene oxide to remove any triphenylphosphine dichloride formed during the reaction.



These facile C-C bond formations described above, make it probable that 2-acyloxy-benzoic acids **29** are converted via their acid chlorides to the reactive chloro-ylid-intermediates **30**, which cyclize to the corresponding 3-chloroflavones **32**. Since phenyl benzoate **33** is only converted under forcing Suda conditions[15] by triphenylphosphine-CCl_4 in 44% yield into 1,1-dichloro-2-phenoxy-2-phenylethylene **34**, this Suda route of **29** via **31** to **32** appears to be less probable. The cyclizations of **6** to **7** and of **9** to **10** might follow analogous mechanistic pathways.



We hope to solve some remaining mechanistic problems and to extend these reactions to include other reactive perhalogenated compounds, as well as other ring systems, in the near future.

EXPERIMENTAL

The NMR spectra were recorded on Varian A 60 (60 MHz), Bruker WHX 90 (90 MHz) and Nicolet QE-300 (300 MHz) spectrometers, the EI and CI (NH_3) mass spectra on a V.G. 70 - 70 HS spectrometer. The melting points were taken on a Kofler hot stage microscope. The solvents and reagents were freshly distilled and carefully dried. Furthermore, all reactions were performed under nitrogen with exclusion of moisture. For column chromatography silica gel (SiO_2, E. Merck, Kieselgel 60, 0.040 - 0.063 mm) was used.

2-Methyl-3-chloroflavone 3:

To a stirred solution of 0.90 g (5 mmol) O-acetylsalicylic acid **1** in 90 ml CH_2Cl_2 and 30 ml CCl_4 a solution of 6.56 g (25 mmol) triphenylphosphine and 3.48 ml (25 mmol) triethylamine in 40 ml CH_2Cl_2 was added dropwise at 24°C within 3.5 h. The yellow solution kept overnight at 24°C, after which no starting material **1** was present anymore. Workup with 250 ml ice cold sat. $NaHCO_3$ solution, extraction of the aqueous phase with 3 x 50 ml CH_2Cl_2, and evaporation of the organic phase after drying (Na_2SO_4), gave 8 g crude product. Chromatography on a column of 250 g SiO_2 gave on elution with toluene-ethyl acetate 3 : 1 (1 l) 0.58 g (60%) 2-methyl-3-chloroflavone **3**, which was recrystallized from toluene to afford 0.56 g (58%) of analytically pure **3**, mp 128.2°C (Lit.[4] 127°C). ^{1}H-NMR ($CDCl_3$, 60 MHz) δ 2.6 (s, 3H), 7.3-7.9 (m, 3H), 8.2-8.4 (m, 1H), m/z (CI) 196 (M^+), 194; 166 (194-CO), 159, 131, 120, 92. Found: C, 61.84; H, 3.65; Cl, 18.15. $C_{10}H_7ClO_2$ (194.62) requires: C, 61.72; H, 3.62; C, 18.22%.

2-Phenyl-3-chloroflavone 5a and 2-(4-chlorophenyl)-3-chloroflavone 5b:

To a stirred solution of 11.15 ml (80 mmol) triethylamine in 50 ml CCl_4 was added dropwise a solution of 4.8 g (20 mmol) O-benzoylsalicylic acid **4a**[16] and 15.74 g (60 mmol) triphenylphosphine in 100 ml CH_2Cl_2 over 3 h whereupon the solution turned red-brown. After 18 h there was still some starting material **4a** left, so a further amount of 5.25 g (20 mmol) triphenylphosphine in 25 ml CH_2Cl_2 was added slowly over 3 h and the reaction was then complete. Workup as described above gave 9.86 g crude product, which was chromatographed on a column of 150 g SiO_2 to give on elution with toluene 3.06 g (57%) **5a**. Recrystallization from ethanol afforded analytically pure **5a**, mp 120.4°C (Lit.[17] 122-123°C). ^{1}H-NMR ($CDCl_3$, 60 MHz) δ 7.3-7.9 (m, 8H), 8.1-8.3 (m, 1H). Found: C, 70.16; H, 3.79; Cl, 13.97. $C_{15}H_9ClO_2$ (256.69) requires: C, 70.18; H, 3.53; Cl, 13.81%.

O-(4-Chlorobenzoyl)-salicylic acid **4b** gave analogously 43% of 2-(4-chlorophenyl)-3-chloroflavone **5b**, mp 165.8°C (EtOH) (Lit.[18] 165-166°C). ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 7.3-7.9 (m, 7H), 8.1-8.3 (m, 1H). Found: C, 61.91; H, 2.87; Cl, 24.34. $C_{15}H_8Cl_2O_2$ (291.14) requires: C, 61.88; H, 2.77; Cl, 24.36%.

O-(3-Nicotinoyl)-5-chlorosalicylic acid 4c:

25.9 g (0.15 mol) 5-Chlorosalicylic acid was dissolved in 100 ml abs. ether then 40 ml abs. pyridine and 26.7 g (0.15 mol) nicotinoylchloride-hydrochloride was added gradually with stirring and exclusion of moisture. After 18 h, the precipitated crystals were filtered and recrystallized from ethanol to give in two crops 4.69 g of O-(3-nicotinoyl)-5-chlorosalicylic acid **4c**, mp 223.7°C. On evaporation of the filtrate and recrystallization from methanol, further crops of **4c**, mp 233-236°C were obtained. Combined yield 14.72 g (35%).

2-(3-Pyridyl)-3,6-dichloroflavone 5c:

To a stirred suspension of 8.34 g (30 mmol) O-nicotinoyl-5-chlorosalicylic acid **4c** and 16.73 ml (120 mmol) triethylamine in 100 ml CCl_4, a solution of 23.6 g (90 mmol) triphenylphosphine in 120 ml abs. CH_2Cl_2 was added within 2 h. After 12 h, the crystals were filtered off and the mother liquor concentrated. The combined precipitated crystals were recrystallized from ethanol to give in several crops 5.28 g (60%) of 2-(3-pyridyl)-3,6-dichloroflavone **5c**, mp 222-223°C. ^{1}H-NMR ($CDCl_3$, 60 MHz) δ 1.3-7.8 (m, 3H), 8.0-8.4 (m, 2H); 8.7 (dd, J = 2+7 Hz, 1H), 9.1 (d, J = 3 Hz, 1H). Found: C, 56,09; H, 2,91; Cl, 12.95; N, 4.80. $C_{14}H_7Cl_2NO$ (292.13) requires: C, 56.23; H, 2.90; Cl, 12.77; N, 5.05%.

12-Chloro-5,11-dihydroisoindolo[2,1-a]quinoline-5,11-dione 7 and 1-oxa-5-aza-3,4,7,8-dibenzo-cyclononan-2,6,9-trione 8:

To a stirred suspension of 0.534 g (2 mmol) 2-phthalimido-benzoic acid[8] **6** in 90 ml CH_2Cl_2 and 30 ml CCl_4 a solution of 1.574 g (6 mmol) triphenylphosphine in 40 ml CH_2Cl_2 was added at 25°C over 4 h, whereupon everything passed into solution. As there was still starting material left after 18 h, a further amount of 3.148 g (12 mmol) triphenylphosphine was added within 4 h after which the reaction was complete. After evaporation, the crude product (10.2 g) was chromatographed with toluene-ethyl acetate (1:1) on a column of 120 g SiO_2. The first 500 ml eluted 0.47 g (84%) **7**, which was recrystallized from acetone to give the analytical sample, mp 205.1°C. ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 7.3-7.9 (m, 5H), 8.2 (dd, J = 2+8 Hz, 1H), 8.5 (dd, J = 2+8 Hz, 1H), 9.0 (dd, J = 1+8 Hz, 1H) m/z (EI) 283, 281 (M^+), 255, 253 (M^+-CO), 190 (M^+-COCOCl) Found: C, 68.17; H, 3.01; Cl, 12.60; N, 4.90 $C_{16}H_8ClNO_2$ (281.7) requires: C 68.22; H, 2.86; Cl, 12.59; N, 4.97%.

On performing the same reaction in the presence of 4 equivalents of triethylamine and 5 equivalents of 1,2-butylene oxide, colorless crystals were precipitated, then filtered and washed with a small amount of CH_2Cl_2 to give 1.053 g (39%) of **8**, mp 295°C. (The mother liquor was worked up and chromatographed as described above to give 0.61 g (22%) of the desired **7**) **8**: ^{1}H-NMR (DMSO-D_6, 300 MHz) δ 7.4-8.1 (m, 8H), 13 (br, NH), m/z (EI) 267 (M^+), 250, 223 (M^+-CO_2), 222, 195, 179, 167, 149, 104, 76. Found: C, 68.01; H, 3.24; N, 5.51 $C_{15}H_9NO_4$ (267.25) requires: C, 67.41; H, 3.39; N, 5.24%.

2-Chloro-3-phenylindenone 10:

To a stirred solution of 2.26 g (10 mmol) 2-benzoylbenzoic acid **9**, 2.78 ml (20 mmol) triethylamine, and 4.31 ml (50 mmol) 1,2-butylene oxide in 90 ml CH_2Cl_2 and 30 ml CCl_4, a solution of 15,74 g (60 mmol) triphenylphosphine in 150 ml CH_2Cl_2 was added over 3 h at 0°C. The mixture was then warmed up to 25°C. As the red-brown solution still contained some starting material after 18 h, a solution of 15.74 g (60 mmol) triphenylphosphine and 8.62 ml (100 mmol) 1,2-butylene oxide was added without resulting in any change in the reaction. After workup with saturated ice cold $NaHCO_3$ solution, drying (Na_2SO_4) and evaporation, the crude product was chromatographed on a column of 160 g SiO_2. Elution with 1 l toluene then 1 l toluene-ethyl acetate (1:1) gave 0.9 g (37.5%) of **10**, which was obtained analytically pure after recrystallization from hexane mp 99.2°C (Lit.[9] 99-100°C). ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 7.0-7.0 (m, 9H) m/z (EI) 242, 240, 205 (M^+-Cl), 176 (205-CHO), 151, 120, 103, 88, 75. Found: C, 74.43; H, 3.79; Cl, 14.83 $C_{15}H_9ClO$ (240.69) requires: C, 74,86; H, 3.77; Cl, 14.73%.

2-Hydroxy-5-phenylfuran 12:

To a stirred solution of 0.89 g (5 mmol) ß-benzoylpropionic acid **11** in 60 ml CH_2Cl_2 and 30 ml CCl_4 a solution of 3.93 g (15 mmol) triphenylphosphine was added over 5 h. The yellow solution was then treated with ice-cold saturated $NaHCO_3$ solution, the CH_2Cl_2 extracts dried (Na_2SO_4) and evaporated. The crude residue (4.56 g) was chromatographed on a column of 130 g SiO_2 and eluted with toluene (1 l) to afford 0.6 g (75%) 2-hydroxy-5-phenylfuran **12**, which on recrystallization from toluene gave the analytical sample, mp 90.5°C (Lit.[10] 90-91°C). ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 3.41 (d, J=4 Hz, 2H), 5.75 (t, J=4 Hz, 1H), 4.3-7.7 (m, 5H). Found: C, 74.98; H, 5.05 $C_{10}H_8O_2$ (160.17) requires: C, 74.99; H, 5.03%.

3-Triphenylphosphinylidene-Δ^4-5-phenylbutyrolactone 13:

A solution of 1.78 g (10 mmol) ß-benzoylpropionic acid and 10.49 g (40 mmol) triphenylphosphine in 150 ml CH_2Cl_2 was added dropwise over 4 h to a stirred solution of 8.3 ml (60 mmol) triethylamine in 76 ml CCl_4 at room temperature. After 16 h, the light brown, partially crystalline reaction product was concentrated and the brown residue chromatographed in CH_2Cl_2 on a column of 250 g Al_2O_3 (neutral, AIII). Whereas the first fractions (1 l) still contained some triphenylphosphine oxide, the subsequent fractions furnished after evaporation, recrystallization from methanol, and then from ethyl acetate two crops 0.828 g (20%) of light yellow **13**, mp 242-244°C. ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 5.8 (d, J = 2 Hz, 1H), 6.9-7.7 (m, 20H) m/z (EI) 421, 420 (M^+), 392, 391 (M^+-CO), 315 (M^+-C_6H_5CO), 288, 287 (M^+-C_6H_5, -CO), 262, 210, 183, 108. Found: C, 80.28; H, 5,07 $C_{28}H_{21}O_2P$ (420.43) requires: C, 79.9; H, 5.0%.

2,2,4,4,4-Pentachloro-1-phenyl-butane-1,3-dione 15:

a) A stirred solution of 9.94 g (30 mmol) hexachloroacetone in 180 ml abs. THF was cooled to -35°C and 10.77 g (66 mmol) of tris(dimethylamino)phosphine added dropwise within 15 min whereupon the solution turned red-brown and turbid. After 30 min at -35°C 4.22 g (30 mmol) benzoyl chloride **14**, in 50 ml abs. THF was added over 35 min and the reaction mixture was warmed up to 24°C, then stirred at this temperature for 1 h. The crude mixture containing a lot of precipitate was concentrated under reduced pressure. Then the residue was treated in 250 ml ether with ice-cold saturated $NaHCO_3$ solution to give an insoluble dark gum. The combined ether extracts were dried (Na_2SO_4), filtered and concentrated. The crude product was chromatographed in hexane on a column of 125 g SiO_2. After a for-run of 900 ml hexane, further elution with hexane (400 ml) then hexane-ether (9:1; 600 ml) gave 9.2 g product, which was distilled at 120°C/35 mtorr to furnish 8.2 g (74%) **15** as a yellowish oil.

b) The analogous reaction of benzoylchloride **14** with hexachloroacetone in the presence of tributylphosphine in THF at -45°C then warming up to 24°C gave 76% of **15**.

c) The reaction of benzoylchloride **14** with hexachloroacetone in the presence of triphenylphosphine proceeded in THF at 24°C to give 72% of **15**.

d) After heating 4.22 g (30 mmol) benzoylchloride **14** with 17.47 g (66 mmol) hexachloracetone and 20.48 g (66 mmol) triphenylphosphite in 100 ml THF for 16 h at 68°C, workup gave 5.2 g (47%) **15**. ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 7.4-7.8 (m, 4H), 8.1-8.3 (m, 3H) m/z (EI) 300, 299, 298, 139, 122, 105. Found: C, 35.84; H, 1.77; Cl, 52.53 $C_{10}H_5Cl_5O_2$ (334.43) requires: C,35.91; H, 1.51; Cl, 53.01%.

2-Triphenylphosphorylidene-3-oxo-3-phenylpropionitrile 16:

To 4.22 g (30 mmol) benzoylchloride **14** and 8.66 g (60 mmol) trichloroacetonitrile in 100 ml abs. CH_2Cl_2, a solution of 15.74 g (60 mmol) triphenylphosphine and 5.22 ml (60 mmol) 1,2-butylene oxide was added with stirring, over 5 h keeping the temperature at 24°C. After 18 h, the mixture was concentrated and the red-brown residue chromatographed in toluene-ethyl acetate (9:1) on a column of 200 g SiO_2. After a for-run of 700 ml, further elution with 1.4 l afforded 5.3 g (43%) of crystalline **16**, which gave on recrystallization from toluene, pure **16**, mp 205-207°C. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.35-7.75 (m, 18H), 8.0 (dd, J = 2+4 Hz, 2H) m/z (EI) 405 (M^+), 404, 328 (M^+-C_6H_5), 303, 277 (M^+-C_6H_5-C≡CCN-H), 262 [$P(C_6H_5)_3^+$], 201, 183, 152, 127 (C_6H_5-C≡C-CN^+), 77. Found: C, 79.25; H, 4.97; N, 3.76 $C_{27}H_{20}NOP$ (405.44) requires: C, 79.98; H, 4.97; N, 3.45%.

Diethyl 2-benzoyl-2-chloromalonate 17, diethyl 2-benzoylmalonate 19 and diethyl 2,2-dibenzoylmalonate 20:

1) To a solution of 12.64 g (66 mmol) ethyl trichloroacetate in 175 ml abs. THF at -35°C, 10.77 g (66 mmol) tris(dimethylamino)phosphine was added dropwise over 1 h and stirring was continued for 45 min at -32°C. A solution of 4.22 g (30 mmol) benzoyl chloride **14** in 50 ml abs. THF was then added at -35°C within 1 h and stirring continued for 3 h at -30°C. After allowing to warm up to 23°C and

stirring for 3 days at this temperature, evaporation, workup with ether and cold aqueous saturated $NaHCO_3$ solution gave, after drying (Na_2SO_4), 10.4 g crude product. Chromatography in toluene on acolumn of 200 g SiO_2 afforded 2.8 g (36%) diethyl 2-benzoyl-2-chloromalonate **17**, which on distillation at 130°C/12 mtorr yielded the analytical sample.

2) To a stirred solution of 5.04 g (22 mmol) diethyl 2,2-dichloromalonate **18** in 80 ml abs. THF at -35°C, 3.59 g (22 mmol) tris(dimethylamino)phosphine was added within 1 h and the thick yellowish suspension stirred for another hour at -35°C. A solution of 1.406 g (10 mmol) benzoyl chloride **14** in 25 ml abs. THF was then added over 1 h and stirring continued for 2 h at -30°C then 18 h at 24°C. The thick suspension was evaporated and the residue worked up with ether/ice-cold aqueous saturated $NaHCO_3$ solution. The combined ether-phase gave after drying (Na_2SO_4) and evaporation 5.27 g of crude product, which afforded, after chromatography in toluene on 120 g SiO_2 and Kugelrohr distillation, 2.03 g (68%) of crystalline colorless diethyl 2-benzoyl-2-chloromalonate **17**, mp 49.5°C. ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 1.3 (t, J = 7 Hz, 6H), 4.38 (q, J = 7 Hz, 4H), 7.3-7.65 (m, 3H), 7.5-7.65 (m, 1H), 7.85-7.95 (m, 2H) m/z (CI, NH_3) 299 (M^++1), 282, 265, 105. Found: C, 56.12; H, 5.35; Cl, 11.99 $C_{15}H_5ClO_5$ (298.73) requires: C, 56.29; H, 5.06; Cl, 11.87%.

3) To a solution of 0.3 g (1 mmol) diethyl 2-benzoyl-2-chloromalonate **17** was added at -35°C in THF 0.16 g (1 mmol) tris(dimethylamino)phosphine within 20 min. After 2 h at -35°C and warming up over night workup as described above gave 0.4 g crude product, which on chromatography on a column of 30 g SiO_2 in toluene-ethyl acetate (5:1) afforded 0.22 g (83%) of diethyl 2-benzoylmalonate **19**. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.25 (t, J = 7 Hz, 6H), 4.28 (q, J = 7 Hz, 4H), 5.3 (s, 1H), 7.4-7.65 (m, 4H), 8.1 (d, J = 8 Hz, 1H) identical with an authentic sample.[19]

4) On reaction of 3.83 g (20 mmol) ethyl trichloroacetate in 80 ml abs. THF, 5.39 g (33 mmol) tris(dimethylamino)phosphine were reacted for 1 h at -35°C, then 1.41 g (10 mmol) benzoyl chloride in 20 ml abs. THF was added and the mixture treated as described unter procedure 1. Chromatography of the crude product (4.2 g) on a column of 200 g SiO_2 gave on elution with toluene 0.96 g (32 %) diethyl 2-benzoyl-2-chloromalonate **17**. Further elution with toluene gave 0.56 g (15%) of diethyl 2,2-dibenzoylmalonate **20**. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1,3 (t, J = 7 Hz, 6H), 4.2 (q, J = 7 Hz, 4H), 7.35-7.65 (m, 8H), 8.1 (d, J = 8 Hz, 2H) identical with an authentic sample.[20]

Diethyl 2-chloro-2-ethylmalonate 22:

1) To a stirred solution of 2.87 g (15 mmol) ethyl trichloroacetate in 35 ml abs. THF at -35°C, 3.26 g (20 mmol) tris(dimethylamino)phosphine was added dropwise within 30 min. After stirring for further 2 h at -35°C and warming up to 25°C overnight, workup with ether - cold saturated aqueous citric acid followed by washing the ether phase with cold aqueous saturated $NaHCO_3$ solution and brine gave after drying (Na_2SO_4) and evaporation 1.34 g crude product, which acc. to GC-MS contained besides other minor products ca. 20% of diethyl 2,2-dichloromalonate **18** (m/z (EI) 229, 201, 155, 128, 110) as well as 30% of diethyl 2-chloro-2-ethylmalonate **22** (m/z (EI) 223, 194, 150, 122, 107, 69) identical with

the MS and IR of an authentic sample obtained by chlorination of diethyl ethylmalonate with SO_2Cl_2.[13]

2) To a stirred solution of 0.389 g (2 mmol) ethyl trichloroacetate and 0.46 g (2 mmol) diethyl 2,2-dichloromalonate **18** in 20 ml abs. THF at -35°C, 0.33 g (2 mmol) tris(dimethylamino)phosphine was added with a syringe within 30 min at -35°C. After warming up overnight to 24°C and workup with ice cold aqueous saturated $NaHCO_3$-solution and brine there was obtained after drying ($NaSO_4$) and evaporation 0.89 g crude product, which according to GC/MS contained 28% of diethyl 2-chloromalonate, 43% of diethyl 2,2-dichloromalonate **18** and 27% of diethyl 2-chloro-2-ethylmalonate **22.**

2,2,4,4,4-Pentachloro-1-(3-pyridyl)-1,3-butanedione 24:

A suspension of 5.34 g (30 mmol) of nicotinoylchloride-hydrochloride **23** in 150 ml abs. CH_2Cl_2 was treated with 4.18 ml (30 mmol) abs. triethylamine followed by 11.91 g (45 mmol) of hexachloroacetone. Addition of 11.8 g (45 mmol) of triphenylphosphine in 150 ml abs. CH_2Cl_2 at 18-26°C with stirring over 2.5 h and workup after 18 h gave 8.6 g crude product after chromatography in toluene on a column of 240 g SiO_2. Distillation in a Kugelrohr apparatus at 120°C/12 mtorr furnished 8.4 g (84%) of pure **24.** ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 7.4-7.6 (m, 1H), 8.3-8.5 (m, 1H), 8.9 (dd, J = 2+5 Hz, 1H), 9.5 (d, J = 2 Hz, 1H). Found: C, 31.95; H, 1.22; N, 4.38; Cl, 53.36 $C_9H_4Cl_5NO_2$ (335.42) requires: C, 32.23; H, 1.2; N, 4.18; Cl, 52.85%.

2,2,4,4,4-Pentachloro-1-(2-acetoxyphenyl)-1,3-butanedione 26:

To a stirred solution of 1.98 g (10 mmol) 2-acetoxybenzoyl chloride **25** and 2.65 g (10 mmol) hexachloroacetone in 40 ml abs. CH_2Cl_2, was added a solution of 6.56 g (25 mmol) triphenylphosphine in 40 ml abs. CH_2Cl_2 over 4 h. The dark solution was then stirred for another 20 h. After workup with ice-cold $NaHCO_3$ solution, the crude product was extracted with hot toluene and the solution chromatographed in toluene on a column of 125 g SiO_2 to give 1.7 g (43.4%) of colorless **26.** Recrystallization from hexane gave analytically pure **26**, mp 75°C. ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 2.35 (2, 3H), 7.1-7.8 (m, 3H), 8.1-8.3 (m, 1H) m/z (EI) 357 (M^+-Cl), 163, 121, 120, 92, 65. Found: C, 36.75; H, 1.83; Cl, 45.23 $C_{12}H_7O_4Cl_5$ (392.47) requires: C, 36,72; H; 1,80; Cl, 45.17%.

2-Triphenylphosphorylidene-3-oxo-3-(2-acetoxyphenyl)-propionitrile 27:

To a stirred solution of 0.379 g (2 mmol) 2-acetoxybenzoyl chloride **25** and 0.866 g (6 mmol) trichloroacetonitrile in 50 ml abs. CH_2Cl_2, a solution of 3.15 g (12 mmol) triphenylphosphine and 1.034 ml (12 mmol) 1,2-butylene oxide in 50 ml abs. CH_2Cl_2, was added over 4 h. The yellow solution was stirred for another 18 h, concentrated and the crude product chromatographed on a column of 150 g iron-free SiO_2. Elution with 3.5 l toluene-ethyl acetate (1:1) and CH_2Cl_2-ethyl acetate (1:1) gave 3.35 g crude product. Extraction with warm ethyl acetate removed the triphenylphosphine oxide to give 0.45 g (48%) **27**, which on recrystallization from toluene yielded pure **27** mp 239.3°C. ^{1}H-NMR ($CDCl_3$,

300 MHz) δ 2.05 (s, 3H), 7.1-7.85 (m, 19H) m/z (CI) 464 (M^+), 422, 391, 328, 302, 279, 255, 217, 183, 109, 91. Found: C, 75.29; H, 5.02; N, 2.93; P, 6.60 $C_{29}H_{22}NO_3P$ (464.49) requires: C, 75.15; H, 4.79; N, 3.02; P, 6.68%.

2-Methyl-3-cyanoflavone 28:

a) 0.34 g (0.73 mmol) of 2-triphenylphosphorylidene-3-oxo-3-(2-acetoxyphenyl)-propionitrile **27** was refluxed in 20 ml dry 1,2-dichlorobenzene for 30 h and the solution concentrated under reduced pressure. The crude product (0.34 g) was chromatographed in toluene on a column of 40 g SiO_2 to give 0.088 g (65%) of 2-methyl-3-cyanoflavone **28**, which on recrystallization from hexane-toluene furnished pure **28**, mp 192.3°C (Lit.[14] 195°C).

b) 0.794 g (4 mmol) 2-Acetoxybenzoyl chloride **25** in 50 ml abs. CH_2Cl_2 was treated at 24°C with 3.15 g (12 mmol) triphenylphosphine, 1.209 ml (12 mmol) trichloroacetonitrile and 1.034 ml (12 mmol) 1,2-butylene oxide in 50 ml CH_2Cl_2. After 18 h the mixture was evaporated and the crude product (6.1 g) heated in 30 ml 1,2-dichlorobenzene for 13 h at 180°C. Chromatography in toluene-ethyl acetate (4:1) on a column of 200 g SiO_2 afforded 0.2 g (27%) of **28**. υ_{max} ($CHCl_3$) 2238, 1662, 1641 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.75 (s, 3H) m/z (EI) 185 (M^+), 157, 120 (M-CH_3-C≡C-CN), 92. Found: C, 71.25; H, 3.90; N, 7.48 $C_{11}H_7NO_2$ (185.19) requires: C, 71.35; H, 3.81; N, 7.57%.

1,1-Dichloro-2-phenoxy-2-phenylethylene 34:

A solution of 1.99 g (10 mmol) phenyl benzoate **33** and 7.87 g (30 mmol) triphenylphosphine in 30 ml CCl_4 was stirred under reflux for 8 h. Then an additional amount of 5.25 g (20 mmol) triphenylphosphine was added and the reaction mixture refluxed for further 8 h. After evaporation, the residue (21.2 g) was filtered in hexane (3 l) and hexane-toluene (4:1, 3 l) over a column of 300 g SiO_2 to give 1.17 g (44%) of pure **34**, which was distilled at 125°C/40 mtorr to give the analytical sample. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.9-7.0 (m, 3H), 7.18-7.28 (m, 2H), 7.28-7.36 (m, 3H), 7.60-7.66 (m, 2H), m/z (EI) 264 (M^+), 228 (M-Cl), 194 (M-Cl_2), 171 (M-C_6H_5O), 138, 105, 77, 51. Found: C, 63.39; H, 4.05; Cl, 27.06 $C_{14}H_{10}Cl_2O$ (265.14) requires: C, 63.42; H, 3.80; Cl, 26.74%.

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