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# 3,3-Dialkylindolin-2-ones and 3,3-Dialkylisoindolin-1-ones. 1. Hofmann Hypohalite Degradation of 4,4-Dialkyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolines (4,4-Dialkylhomophthalimides)

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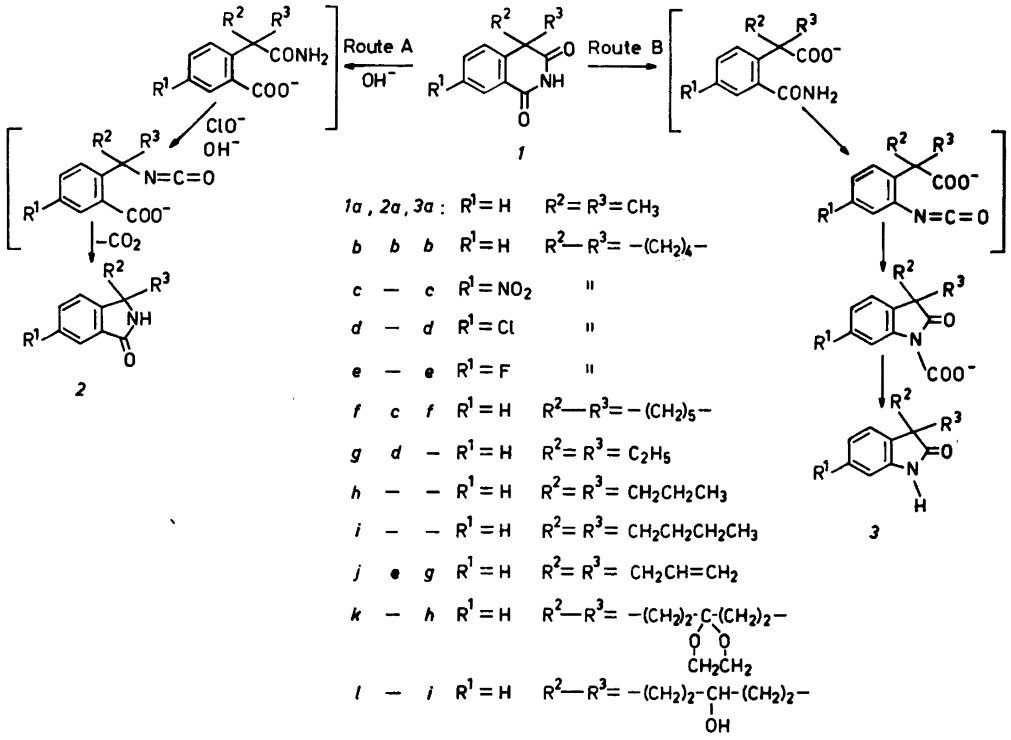
Hofmann hypohalite degradation of certain 4,4-dialkyl substituted homophthalimides has been found to give a high yield of the corresponding 3,3-dialkylindolin-2-ones. If these homophthalimides are subjected to alkaline hydrolysis prior to treatment with hypohalite, isoindolin-1-ones are produced together with the indolin-2-ones.

In the course of an investigation on certain types of biologically active compounds, we required a number of 3,3-dialkylisoindolin-1-ones. Of the limited number of such compounds described in the literature, the 3,3-dimethyl derivative had been prepared by zinc dust distillation of "1,1-dimethyl-3-amino-$\psi$-isoindole"[1] and its *N*-phenyl derivative was reportedly formed when 3,3-dimethylphthalide was heated with aniline.[2] Hauser *et al.*[3] reported that a number of *o*-(*N*-alkylcarbamoyl)benzyl alcohols, including the α,α-pentamethylene derivatives, undergo ring-closure to isoindolinones when treated with strong acids. A reinvestigation of the structures of these reaction products by Bailey and De Grazia,[4] however, revealed that some of them are iminophthalides rather than isoindolinones. New routes had therefore to be developed for the preparation of our intermediates.

Since isoindolin-1-ones may be regarded as lactams of *o*-aminomethylbenzoic acids, our interest became focussed on the means of preparation of such acids dialkylated at the methylene carbon atom. Of the large number of methods generally available for the preparation of amines, very few are adaptable to the synthesis of derivatives fully alkylated at the α-carbon atom. Methods involving nucleophilic replacement reactions generally fail because eliminations prevail, many other methods fail because of the steric hindrance exerted by the α-substituents. The Hofmann degradation of amides,[5] however, is an exception and permits the synthesis of this sort of amine in high yields from amides of α,α-dialkyl fatty acids. One route to the desired isoindolin-1-ones would therefore use *o*-carboxy-α,α-dialkylphenylacetamides as intermediates. The facile preparation of 4,4-dialkylhomophthalimides from the readily available homophthalimide [6,7] or from suitably substituted homophthalic acids induced us to investigate the possibilities of this type of compound as start material for the acetamide derivatives. Although it has been reported [8] that homophthalimide itself is hydrolysed to *o*-carbamoylphenylacetic acid rather than to *o*-carboxyphenylacetamide (however, *cf.* Ref. 9) it was felt that because of the steric hindrance exerted by the alkyl groups in the *geminally* alkylated homologues the formation of phenylacetamide derivatives from these compounds would be favoured. Hofmann degradation of these acetamide derivatives followed by ring closure would then afford the desired products, according to the sequence outlined in Scheme 1, Route A.

For our investigation of this type of reaction, we used mainly 1′,3′-dioxo-1′,2′,3′,4′-tetrahydrospiro(cyclopentane-1,4′-isoquinoline), (4,4-




*Scheme 1.*

tetramethylenehomophthalimide*) (*1b*) as our model compound, since this derivative could be readily prepared in good yield [7] and also proved to be eminently suited for the isolation of the products of reaction with little loss.

Hydrolysis experiments with the homophthalimide derivative *1b* soon showed that whereas the unsubstituted homophthalimide could be completely hydrolysed within 3 days at room temp.[8], the 4,4-dialkyl derivatives were apparently very resistant to alkaline hydrolysis even at elevated temperatures. Thus when a solution of *1b* in excess of 2 N sodium hydroxide was kept at room temp. for various times up to 25 days and subsequently treated with hypochlorite solution, the maximum yield of the expected 1′-oxospiro(cyclopentane-1,3′-isoindoline) (*2b*) that could be isolated was about 35 %. An interesting observation was the fact that almost maximum yields were obtained already within the first few days, after which the rise in yield was almost imperceptible (Fig. 1). Using elevated temperatures (60° and 95°) did not improve the yield of *2b*, indeed, it became lower, probably because of the secondary hydrolysis of the amide group, as indicated by a distinct smell of ammonia noticeable at the higher temp.

In order to recover start material supposed to be present in the mother liquor after *2b* had been filtered off, the filtrate was acidified. Vigorous evolution of carbon dioxide ensued and a material precipitated out which was subsequently identified as the known 2′-oxospiro(cyclopentane-1,3′-indoline) (*3b*). When the alkaline reaction mixture was cooled strongly instead of being acidified, a sodium salt precipitated which, according to elemental analysis, was apparently sodium 2′-oxospiro(cyclopentane-1,3′-indoline)-1′-carboxylate. The structure was confirmed by esterification with dimethyl sulphate followed by pyrolysis to the known 1′-methylspiro(cyclopentane-1,3′-indolin)-2′-one.

* For convenience, the compounds are named as derivatives of homophthalimide when this can be done without risk of misunderstanding.

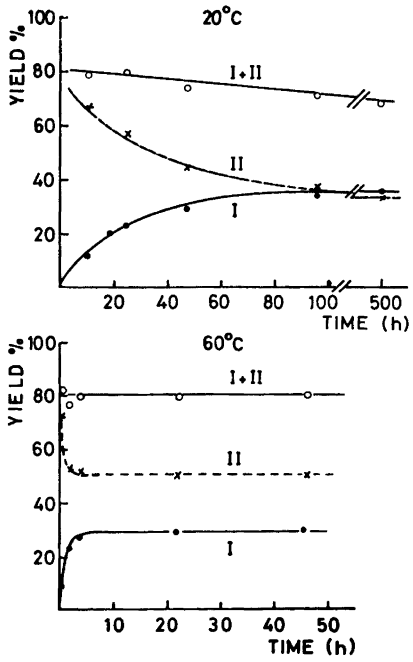



*Fig. 1.* Semiquantitative determination of the yields of 1′-oxospiro(cyclopentane-1,3′-isoindoline), I, and 2′-oxospiro(cyclopentane-1,3′-indoline), II, as functions of time and temp.

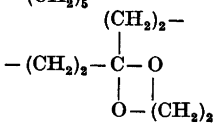
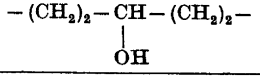
We later found that *3b* could be obtained in 89 % yield if the homophthalimide derivative was dissolved in aqueous alkali and immediately treated with the hypochlorite solution, even if the reaction was allowed to proceed at room temp. for as short a time as 1/2 h; under these conditions, none of the isoindolinone *2b* could be detected. This reaction, when applied to a variety of *geminally* disubstituted homophthalimides, afforded in high yields the disubstituted indolinones listed in Table 1, and thus offers a convenient route to several 3,3-dialkylated indolinones unsubstituted at the nitrogen atom, a class of compounds which has hitherto only been available through lengthy procedures and in unsatisfactory yields.[10–13]

When the reaction was carried out with 4,4-diallylhomophthalimide (*1j*) much longer reaction times were required (of the order of 24 h) and a mixture of the indolinone and the isoindolinone derivatives was isolated together with unreacted start material. 4,4-Diethylhomophthalimide failed to give any 3,3-diethylindolin-2-one but afforded up to 36 % of 3,3-diethylisoindolin-1-one when the homophthalimide derivative was allowed to react with alkaline hypochlorite solution for 3 days at room temp. 4,4-Dipropyl- and 4,4-dibutylhomophthalimide failed to react under any of the conditions tried. It thus appears that increasing steric hindrance prevents progressively first the reaction leading to an indolinone derivative and then that leading to an isoindolinone. Unsubstituted homophthalimide appears to give halogenated products with no indication of any rearrangement when treated with hypohalite solution.

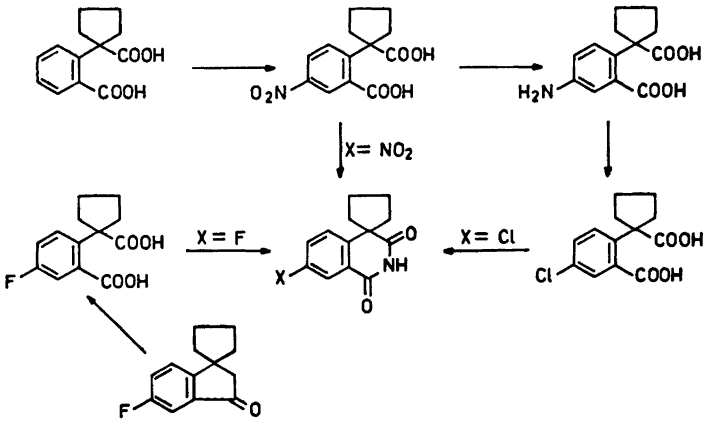
Some comments on the modes of formation of the indolinones seem to be of interest. Although other mechanisms have been suggested [14] it is generally accepted [5,15,16] that the Hofmann degradation of imides is preceded by a hydrolytic opening of the imide ring to produce an "amic" acid intermediate which then rearranges. The formation of the isoindoline and indoline derivatives after pretreatment with alkali seems to be readily explicable by such ring opening mechanisms, Scheme 1. It is interesting that the yield of the isoindolinone *2b* levels off at about 35 % despite the fact that very little further hydrolysis to the dicarboxylic acid occurs, as is evident from Fig. 1. A possible explanation for this would be that the two hydrolysis routes, A and B in Scheme 1, compete with each other, finally resulting in an equilibrium mixture containing approx. 35 % of 1-(2-carboxyphenyl)cyclopentanecarboxamide.

However, it is much more difficult to envisage the mechanism by which the indolinones are formed when the homophthalimides are treated with alkaline hypochlorite solution without prehydrolysis. Since, under these conditions, the indolinones are formed very rapidly in almost quantitative yields, in contrast to the presumably very slow hydrolysis of the homophthalimide derivatives, it is extremely difficult to reconcile the rearrangement reaction with a mechanism involving a conventional ring opening of the homophthalimide derivative to the intermediate *o*-carbamoylphenylacetic acid. Because of this, we undertook a more extensive investigation of the mechanism

*Table 1.*

| No. | $R^1$ | $R^2$ | $R^3$ | Formula | M.p. °C | Yield % | Analyses Found C | H | N | O | Calculated C | H | N | O |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *3a* | H | $CH_3$ | $CH_3$ | $C_{10}H_{11}NO$ | 150–151 [19] | 84.5 | 74.3 | 6.9 | 8.6 | 10.3 | 74.5 | 6.9 | 8.7 | 9.9 |
| *b* | H | $-(CH_2)_4-$ | | $C_{12}H_{13}NO$ | 114–113 [11] | 89 | 77.0 | 7.0 | 7.5 | 9.0 | 77.0 | 7.0 | 7.5 | 8.6 |
| *c* | $NO_2$ | » | | $C_{12}H_{12}N_2O_3$ | 228–230 | 84.5 | 61.7 | 5.2 | 11.9 | 20.8 | 62.1 | 5.2 | 12.1 | 20.7 |
| *d* | Cl | » | | $C_{12}H_{12}ClNO$ | 143–145 (128[a]) | 73 | 65.2 | 5.6 | 6.3 | 7.4 Cl 15.7 | 65.0 | 5.5 | 6.3 | 7.2 Cl 16.0 |
| *e* | F | » | | $C_{12}H_{12}FNO$ | 124 | 81.5 | 70.4 | 5.9 | 6.9 | F 9.3 | 70.2 | 6.0 | 6.8 | F 9.3 |
| *f* | H | $-(CH_2)_5-$ | | $C_{13}H_{15}NO$ | 120–124 [11] | 52 | | | | | | | | |
| *h* | H |  | | $C_{15}H_{17}NO_3$ | 211 | 88 | 69.3 | 6.68 | 5.35 | 18.9 | 69.5 | 6.61 | 5.40 | 18.9 |
| *i* | H |  | | $C_{13}H_{15}NO_2$ | 191 | 71 | 71.4 | 7.0 | 6.4 | 15.2 | 71.9 | 7.0 | 6.5 | 14.7 |

*a** Unstable isomorph.




*Scheme 2.*

of this reaction, which will be the subject of a forthcoming paper.

Several of the substituted homophthalimides used as start material have been described in the literature.[6,7] The syntheses of the new compounds are described in the Experimental Part. The halogenated derivatives of 4,4-tetramethylenehomophthalimide were prepared according to Scheme 2.

The structures of the rearranged products were established by means of IR-, UV-, and NMR-spectroscopy. Especially the UV and NMR spectra were found to be very informative. In methanolic solution, all the indolinones investigated had a strong absorption band at 245 – 250 nm and only weak absorption around 225 nm. The isoindolinones, on the other hand, had a very strong, complex peak around 225 nm, almost no absorption around 250 nm but two small peaks at about 270 and 280 nm (cf. Ref. 20). In the NMR spectra of the indolinones the aromatic hydrogen atom *ortho* to the amino group is clearly distinguishable at $\tau$ 2.8 – 3.0 ppm ($CDCl_3$ solution), the corresponding atom appearing at $\tau$ 2.0 – 2.2 ppm in the isoindolinones. The IR spectra (in KBr) are less informative but there is a trend towards a shifting of the carbonyl frequences to higher values in the isoindolinones. (Thus the diallylindolinone derivative *3g* has two C=O absorption bands at 1675 and 1715 $cm^{-1}$, the corresponding bands in the isoindolinone derivative *2e* appearing at 1650 and 1700 $cm^{-1}$).

## EXPERIMENTAL PART

Melting points were taken on a Heraeus Fus-O-Mat melting point apparatus. The structures of the compounds were determined by elemental analyses and by IR-, UV-, and NMR-spectroscopy. The microanalyses were carried out by Prof. K. J. Karrman, University of Lund, Lund, Sweden, and by Dr. Alfred Bernhardt, Mikroanalytisches Laboratorium, Elbach über Engelskirchen, Germany.

### A. Preparation of homophthalic acid derivatives

*1-(2-Carboxy-4-nitrophenyl)cyclopentanecarboxylic acid.* 1-(2-Carboxyphenyl)cyclopentanecarboxylic acid [17] (355 g; 1.53 mol) was added portionwise to fuming nitric acid (sp. gr. 1.52; 1100 ml) under vigorous stirring, the temp. being kept at 5 – 10° by external cooling. After being stirred for 3 h, the mixture was poured onto crushed ice, the product was collected, washed copiously with water and dried, affording 400 g (93.5 %) of white crystals, m.p. *ca.* 200° (rapid heating). A sample crystallized from methanol-petroleum ether had m.p. 210°. (Found: C 55.7; H 4.72; N 5.00; O 34.4. $C_{13}H_{13}NO_6$ requires: C 55.9; H 4.70; N 5.02; O 34.4). If the reaction is carried out at 20°, the corresponding *anhydride* is obtained in 90 % yield, m.p. 132° (from benzene). (Found: C 59.9; H 4.17; N 5.36; O 30.4. $C_{13}H_{11}NO_5$ requires: C 59.8; H 4.24; N 5.36; O 30.6).

*1-(4-Amino-2-carboxyphenyl)cyclopentanecarboxylic acid.* The foregoing nitro compound (56 g; 0.2 mol) was dissolved in 150 ml of methanol, Raney nickel (20 g wet weight) was added and the mixture shaken in an atmosphere of hydrogen at an initial pressure of about

4 kg/cm². After 4 h, by when the theoretical quantity of hydrogen had been consumed, the grey precipitate was filtered off and sucked dry, the product was dissolved in conc. ammonia (50 ml), the solution filtered, cooled and neutralised with dil. hydrochloric acid. After acidification with acetic acid, the precipitate was collected, washed with cold water and dried, affording 46 g (92 %) of a grey-white powder of indefinite m.p. Recrystallization from water gave a product containing 1 mol of water. (Found: C 57.6; H 6.43; N 5.19; O 30.4. $C_{13}H_{15}NO_4.H_2O$ requires: C 58.4; H 6.41; N 5.24; O 29.9). Recrystallization from acetic acid gave the corresponding anhydride. (Found: C 67.1; H 5.64; N 5.84; O 21.4. $C_{13}H_{13}NO_3$ requires: C 67.4; H 5.67; N 6.06; O 20.8).

Note: It is important to observe that the starting material in this reaction contains no anhydride and that the reaction temp. is not allowed to rise to a level that will cause the diacid to be converted to the anhydride. If this is not rigorously followed, considerable quantities of polymeric products resulting from reaction between the anhydride and amino acid will be obtained.

*1-(2-Carboxy-4-chlorophenyl)cyclopentanecarboxylic acid.* The foregoing amino acid (31.8 g; 0.15 mol) in a mixture of 35 ml of conc. hydrochloric acid and 200 g of ice was diazotised at 5 – 10° with sodium nitrite (10.5 g; 0.15 mol) in 75 ml of water. After addition, the mixture was stirred for about 15 min and then added portionwise with vigorous stirring to an ice-cold solution of freshly prepared cuprous chloride (from 195 g of $CuSO_4.5H_2O$; 0.75 mol) in conc. hydrochloric acid (400 ml). This reaction should be carried out in a 3 litre beaker since copious effervescence occurs. After standing at ambient temp. for about 2 h the precipitate was collected, washed with dilute hydrochloric acid and water, and dried, giving 28.2 g (69.5 %) of a cream coloured product of indeterminable m.p. A sample warmed with acetic anhydride afforded an orange coloured product which was purified by column chromatography on alumina and subsequently crystallized from benzene-petroleum ether, affording the corresponding *anhydride* as bright orange crystals, m.p. 120 – 122°. (Found: C 62.9; H 4.38; Cl 13.5; O 19.2. $C_{13}H_{11}ClO_3$ requires: C 62.3; H 4.42; Cl 14.1; O 19.1).

*1-(2-Carboxy-4-fluorophenyl)cyclopentanecarboxylic acid.* 5'-Fluorospiro(cyclopentane-1,1'-indan)-3'-one [18] (41 g; 0.2 mol) in 0.5 N sodium hydroxide solution (800 ml; 0.4 mol) was warmed to 95° and treated portionwise with potassium permanganate (90 g; 0.55 mol) under stirring. After addition, the mixture was stirred on a water-bath for about 15 min by when the permanganate colour had become discharged. The mixture was filtered hot, the manganese dioxide cake was washed with hot water, the filtrate was cooled and acidified with conc. hydrochloric acid till crystals began to appear. Sodium bicarbonate was added, the mixture was warmed, filtered, cooled and acidified. The precipitate was collected, washed and dried giving 34 g (67.5 %) of crude diacid, m.p. 130 – 140°, with conversion to the *anhydride*, m.p. 83°. For analysis, a sample of the diacid was recrystallized from diisopropyl ether-petrol. ether and then melted at *ca.* 140°. (Found: C 61.9; H 5.20; F 7.53. $C_{13}H_{13}FO_4$ requires: C 61.9; H 5.19; F 7.53).

## B. Preparation of homophthalimide derivatives

*1',3'-Dioxo-7'-nitro-1',2',3',4'-tetrahydrospiro-(cyclopentane-1,4'-isoquinoline)* (1c). 1-(2-Carboxy-4-nitrophenyl)cyclopentanecarboxylic acid (28 g; 0.1 mol) was treated with conc. ammonia (30 ml) and the mixture heated in an open flask over an open flame. The mixture darkened and eventually became converted to a high melting solid. On further heating, it melted with effervescence. Heating was continued until a clear dark melt was obtained which, after solidification, was pulverised and crystallized from 100 ml of dioxane, yielding 19.9 g (76.5 %) if the imide *1c*, m.p. 227°. (Found: C 59.9; H 4.65; N 10.7; O 24.6. $C_{13}H_{12}N_2O_4$ requires: C 60.0; H 4.65; N 10.8; O 24.6).

The following two compounds were prepared in a similar manner.

*7'-Chloro-1',3'-dioxo-1',2',3',4'-tetrahydrospiro-(cyclopentane-1,4'-isoquinoline)* (1d), hair-like needles from ethanol, m.p. 215 – 216°. Yield almost 100 %. (Found: C 62.7; H 4.87; Cl 13.8; N 5.63; O 13.2. $C_{13}H_{12}ClNO_2$ requires: C 62.5; H 4.87; Cl 14.2; N 5.61; O 12.8).

*1',3'-Dioxo-7'-fluoro-1',2',3',4'-tetrahydrospiro(cyclopentane-1,4'-isoquinoline)* (1e), white hair-like crystals from ethanol, m.p. 213°, yield 87 %. (Found: C 67.0; H 5.19; F 8.82; N 6.10; O 13.6. $C_{13}H_{12}FNO_2$ requires: C 66.9; H 5.19; F 8.15; N 6.01; O 13.7).

*Ethylene glycol ketal of 1',3',4-trioxo-1',2',3',4'-tetrahydrospiro(cyclohexane-1,4'-isoquinoline)* (1k). 1',3',4-Trioxo-1',2',3',4'-tetrahydrospiro-(cyclohexane-1,4'-isoquinoline) [17] (4.9 g; 0.02 mol) in toluene (250 ml) was treated with ethylene glycol (52 ml) and *p*-toluenesulphonic acid (200 mg). The mixture was distilled slowly from an oil-bath during 20 h, the volume of the reaction mixture being kept approximately constant by the periodic addition of dry toluene. After about 200 ml of distillate had been collected the mixture was cooled, the crystals were collected, washed with petroleum ether and water, and dried, giving 5.5 g (96 %) of stout, pale-yellow crystals, m.p. 220°. Crystallization from ethanol afforded a white product melting at 223 – 224°. (Found: C 66.1; H 6.10; N 4.89;

O 22.3. $C_{16}H_{17}NO_4$ requires: C 66.9; H 5.96; N 4.88; O 22.3).

*1',3'-Dioxo-4-hydroxy-1',2',3',4'-tetrahydrospiro(cyclohexane-1,4'-isoquinoline)* (11). 1',3',4-Trioxo-1',2',3',4'-tetrahydrospiro(cyclohexane-1,4'-isoquinoline) [17] (7.3 g; 0.03 mol) in abs. ethanol was treated at room temp. with sodium borohydride (0.6 g; 0.015 mol) under vigorous stirring. After 1.5 h, the clear yellow solution was treated with 2.0 ml of acetic acid, the volatile matter was removed under vacuum and the residual syrup was triturated with diisopropyl ether, causing it to become crystalline. The product was collected (8.2 g, m.p. *ca.* 170°) and crystallized from 100 ml of 50 % methanol, affording 4.8 g (64 %) of white crystals, m.p. 189 – 190°. (Found: C 68.6; H 6.16; N 5.70; O 19.7. $C_{14}H_{15}NO_3$ requires: C 68.6; H 6.16; N 5.71; O 19.6). The NMR spectrum in $(CD_3)_2SO$ reveals 1 aromatic H at $\tau$ 1.8 – 1.9 ppm, 3 aromatic H centered around $\tau$ 2.2 ppm. From the mother liquor there was isolated 0.75 g of white crystals melting at 247° after crystallization from dioxane, which gave a correct analysis for a *dihydro derivative* of compound 11. (Found: C 67.8; H 7.03; N 5.65; O 19.8. $C_{14}H_{17}NO_3$ requires: C 68.0; H 6.93; N 5.66; O 19.4). The IR-spectrum of this compound indicates two different hydroxyl groups. The NMR spectrum in $(CD_3)_2SO$ reveals 4 aromatic H centered around $\tau$ 2.9 ppm, indicating reduction of the aromatic carboxyl group. The compound thus is *1',4-dihydroxy-3'-oxo-1',2',3',4'-tetrahydrospiro(cyclohexane-1,4'-isoquinoline)*.

## C. Simultaneous preparation of isoindolin-1-one and indolin-2-one derivatives

*Spiro(cyclopentane-1,3'-isoindolin)-1'-one* (2b) *and spiro(cyclopentane-1,3'-indolin)-2'-one* (3b). A stock solution of 1',3'-dioxo-1',2',3',4'-tetrahydrospiro(cyclopentane-1,4'-isoquinoline) [7] (65 g; 0.3 mol) in 2 N sodium hydroxide solution (600 ml; 1.2 mol) was prepared and stored at room temp. At regular intervals, an aliquot corresponding to 0.03 mol was withdrawn and treated with 1.08 M sodium hypochlorite solution (32 ml; 0.033 mol). After standing for 2 h, the solution was heated on a water bath for 15 min, cooled, and the precipitated spiro(cyclopentane-1,3'-isoindolin)-1'-one filtered off, washed and dried. The compound was analytically pure and melted at 179°. (Found: C 77.2; H 6.98; N 7.34; O 8.85. $C_{12}H_{13}NO$ requires: C 77.0; H 7.00; N 7.48; O 8.55). The filtrate from above was acidified with acetic acid, whereupon evolution of carbon dioxide ensued and a viscous oil fell out which gradually solidified on cooling. Recrystallization from aqueous methanol afforded spiro(cyclopentane-1,3'-indolin)-2'-one as colourless crystals, m.p. 114° (Lit.[11] m.p. 113°). The yields of these lactams varied as a function of time in the manner depicted in Fig. 1. The results of a similar series of experiments performed at 60° are likewise presented in Fig. 1.

*3,3-Dimethylisoindolin-1-one* (2a), *and 3,3-dimethylindolin-2-one* (3a). When the above reaction was carried out with 4,4-dimethylhomophthalimide at approximately 20°, yields of 3,3-dimethylisoindolin-1-one ranging from 10 % to 17 % and of 3,3-dimethylindolin-2-one ranging from 60 % to 44 % were obtained, the times of reaction with alkali varying from 18 to 67 h. Compound *3a* melted at 150° (Lit.[19] m.p. 150 – 151°), compound *2a* melted at 158 – 162° (Lit.[1] m.p. 162°).

*3,3-Diallylisoindolin-1-one* (2e) *and 3,3-diallylindolin-2-one* (3i). When a solution of 4,4-diallylhomophthalimide [6] in alkaline sodium hypochlorite solution was allowed to stand at room temp. for about 24 h, *3,3-diallylisoindolin-1-one* precipitated out in yields up to 43 %. Crystallization of the crude product from dilute ethanol gave beige crystals, m.p. 112°. (Found: C 78.3; H 7.06; N 6.57; O 7.79. $C_{14}H_{15}NO$ requires: C 78.8; H 7.09; N 6.57; O 7.50). When the alkaline filtrate was acidified, a crystalline precipitate was obtained which, after washing with dilute sodium hydroxide solution and water, afforded *3,3-diallylindolin-2-one*, m.p. 96° after crystallization from dilute ethanol. Yield 16 – 28 %. (Found: C 78.2; H 7.04; N 6.55; O 7.93. $C_{14}H_{15}NO$ requires: C 78.8; H 7.09; N 6.57; O 7.50).

*3,3-Diethylisoindolin-1-one* (2d). 4,4-Diethylhomophthalimide [6] was allowed to react with sodium hydroxide solution for 3 days at 20° and then treated with hypochlorite as described. The titel compound separated from the solution and was collected. White crystals from ethanol, m.p. 171 – 172°. Yield 36 %. (Found: C 76.2; H 8.01; N 7.31; O 18.1. $C_{12}H_{15}NO$ requires: C 76.2; H 7.99; N 7.40; O 18.5). When the alkaline filtrate was acidified, only unreacted start material was recovered with no evidence of any formation of the indolinone derivative.

*Note:* When 4,4-dipropyl- and 4,4-dibutylhomophthalimide were submitted to this treatment only unreacted start material could be recovered from the reaction mixtures even when the temp. in the hydrolysis step was as high as 90°.

## D. Preparation of indolin-2-one derivatives unaccompanied by formation of isoindolin-1-one derivatives

The following procedure, used in the preparation of spiro(cyclopentane-1,3'-indolin)-2'-one, illustrates the method that was used for the synthesis of the indolin-2-ones listed in Table 1. 4,4-Dipropyl- and 4,4-dibutylhomophthalimide failed to react under these conditions and the start materials were recovered.

Sodium hypochlorite (1.08 M, 31 ml; 0.033 mol) was added to a cold solution of 1',3'-dioxo-1',2',3',4'-tetrahydrospiro(cyclopentane-1,4'-isoquinoline)[7] (6.5 g; 0.03 mol) in 2 N sodium hydroxide (60 ml; 0.12 mol) and the mixture stood at room temp. for 2 h. The clear solution was then warmed on a water bath for 15 min, cooled, and acidified with acetic acid, whereupon brisk evolution of carbon dioxide ensued and a viscous oily material fell out which became crystalline on cooling and scratching. The crystals were collected, washed with dilute sodium hydroxide and water and dried, affording 5.0 g (89 %) of the title compound *3b*, m.p. 114°. (Lit.[11] m.p. 113°).

*Sodium 2'-oxospiro(cyclopentane-1,3'-indoline)-1'-carboxylate* and *1'-methylspiro(cyclopentane-1,3'-indolin)-2'-one.* When the reaction mixture prepared as above was cooled strongly with ice-water before acidification with acetic acid, a white crystalline precipitate, approximately analysing for $C_{13}H_{12}NO_3Na$ and apparently consisting of *sodium 2'-oxospiro(cyclopentane-1,3'-indoline)-1'-carboxylate*, was isolated in about 50 % yield. This salt (7.6 g; 0.03 mol) was dissolved in water (40 ml) and the stirred solution treated dropwise with dimethyl sulphate (6.5 ml; 0.06 mol) at room temp. Dilute sodium hydroxide was added simultaneously at such a rate as to maintain an alkaline pH. The mixture was extracted with chloroform, the extract was washed with sodium bicarbonate solution and water, dried and the solvent evaporated, affording 6.1 g (83 %) of an oil assumed to be *methyl 2'-oxospiro(cyclopentane-1,3'-indoline)-1'-carboxylate.* Distillation at 110 – 120°/1.0 Torr caused decomposition and the product isolated was *1'-methylspiro(cyclopentane-1,3'-indolin)-2'-one,* m.p. 57 – 59° after crystallization from hexane (Lit.[21] m.p. 63°). (Found: C 77.1; H 7.50; N 6.96; O 7.72. $C_{13}H_{15}NO$ requires: C 77.6; H 7.51; N 6.96; O 7.95).

*2',4-Dioxospiro(cyclohexane-1,3'-indoline).* The ketal *3h* (1.04 g; 0.004 mol) was dissolved in a mixture of acetic acid (5 ml) and 2 N hydrochloric acid (5 ml) and the solution heated over a free flame for some minutes. After cooling, the product was collected, affording 0.66 g (78 %) of white crystals, m.p. 200 – 201°. (Found: C 72.2; H 6.11; N 6.45; O 15.1. $C_{13}H_{13}NO_2$ requires: C 72.5; H 6.09; N 6.51; O 14.9).

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