295. Photochemische Reaktionen

92. Mitteilung [1]

Photochemistry of Imidazolides II. C_2-C_3 Cleavage of Carboxylic Acid Chains. A Convenient New Method for the Side-Chain Degradation of Bile Acids and of Lanosterol

by **Shigeo Iwasaki**[1])

Organisch-chemisches Laboratorium
der Eidgenössischen Technischen Hochschule, CH–8006 Zürich

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Summary. Irradiation of N-stearoylimidazole (**1**) gave hexadec-1-ene (**4**) in 45% yield, whereas irradiation of N-(4-methylstearoyl)imidazole (**13**) possessing a tertiary hydrogen atom γ to the carbonyl group led to 2-methylhexadec-1-ene (**14**) in 62% yield. These results are explained by a two-stage process: acyl migration, followed by *Norrish* Type II elimination. The reaction has been utilized for the side chain degradation of bile acids and of lanosterol, in which the second stage of the reaction was shown to proceed in up to 70% yield.

In the preceding paper [1] we reported the N→C acyl migration of N-acylimidazoles on irradiation with a low-pressure mercury lamp, leading to a mixture of isomeric 2- and 4- (or 5)-acylimidazoles in moderate yields. Certain other N-acylimidazoles have now been found to undergo photochemical fragmentation in good yields by a *Norrish* Type II process involving the acyl carbonyl group; and this type of reaction appears to constitute a convenient way of cleaving an alkanoic acid side chain between carbon atoms 2 and 3.

Results. – N-Stearoylimidazole (**1**), prepared from imidazole and stearoyl chloride, was irradiated in tetrahydrofuran for 24 hours using a low-pressure mercury lamp. This led to a mixture of 2-stearoylimidazole (**2**) (30%) and 4 (or 5)-stearoylimidazole (**3**) (25%), with 85% conversion of starting material. In addition, hexadec-1-ene (**4**) (25%), heptadecane (**5**) (2%), and 2-acetyl- (**6**) and 4 (or 5)-acetylimidazole (**7**) (each 10%) were obtained (see *Scheme 1*).

Under the same conditions but after 60 hours the yield of the mixture of hydrocarbons **4** and **5**, formed in the ratio 9:1, was raised to 45% with 95% conversion of starting material.

Since it appeared that compound **4** was formed as a result of a *Norrish* Type II reaction normally involving facile abstraction of a tertiary hydrogen atom by a photo-excited carbonyl group [2] it was decided to repeat this reaction with N-(4-methylstearoyl)imidazole (**13**) possessing such a hydrogen atom at a γ-position relative to the acyl carbonyl group. This compound was prepared starting from 1-bromo-

[1]) On leave from *Institute of Applied Microbiology*, University of Tokyo, Tokyo, Japan.

Scheme 1

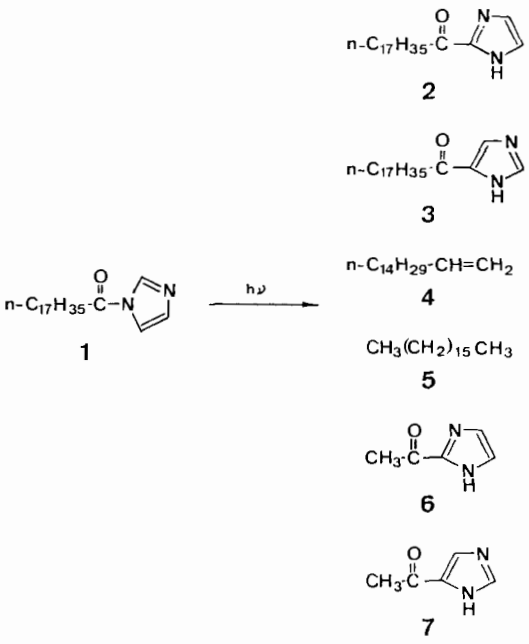
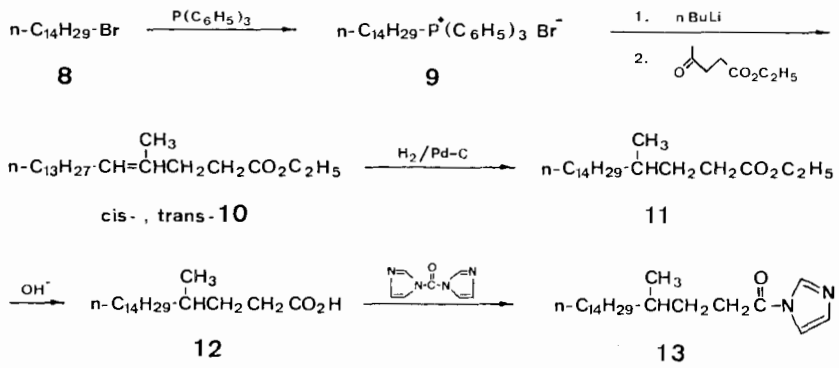


Table 1. *The results of UV. irradiation* [a]) *of 1-stearoylimidazole* (**1**)

Irradiation time (h)	Conversion (%)	Yields of the products (%) **2**	**3**	**4**	**5**	**6**	**7**
24	85	30	25	25	2	10	10
60	95	–	–	40	5	–	–

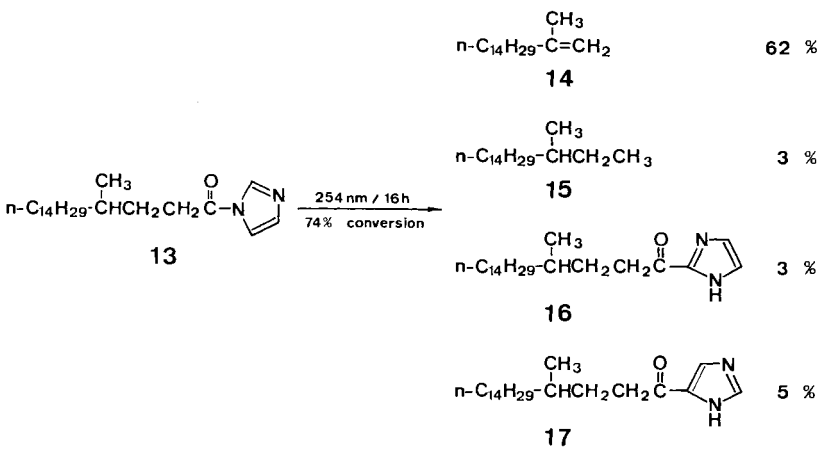
a) 254 nm light.

Scheme 2



tetradecane (**8**) *via* the corresponding triphenylphosphonium salt (**9**) followed by treatment of the derived ylide with ethyl levulinate. The resulting mixture of unsaturated esters **10** was hydrogenated and the product was hydrolysed with alkali. Treatment of the 4-methylstearic acid produced with N,N'-carbonyldiimidazole gave the desired imidazolide **13** in *ca.* 18% overall yield (not optimized). Irradiation of the latter now gave 2-methylhexadec-1-ene (**14**) and 3-methylheptadecane (**15**) in 62% and 3% yield respectively, as well as 2-(4-methylstearoyl)imidazole (**16**) (3%) and 4- (or 5)-(4-methylstearoyl)imidazole (**17**) (5%); the conversion of **13** was 74%.

Scheme 3



This type of reaction was now tried as a new method for degradation of the bile acid side chain. Treatment of 3β-acetoxy-5-cholenic acid (**19**) with N,N'-carbonyldiimidazole led to the derived imidazolide **18**. Irradiation of this as described above led to 83% conversion and to the formation of 20-methylene-5-pregnen-3β-ol acetate (**20**) (64%), of the 2-imidazoyl derivative **21** (6%) and of the 4-(or 5)-imidazoyl derivative **22** (5%). Irradiation of the crude imidazolide as formed *in situ* gave similar results: 62% of **20**, 8% of **21** and 8% of **22**.

The results of irradiation of a number of imidazolides derived from substituted cholic acids **23a–23d** are summarized in Table 2; the reaction being conducted in each case with the crude derivative as formed *in situ*. Yields of over 50% of the expected 2-methylenepregnane derivatives could be obtained[2]).

Some of these reactions were now repeated using a medium pressure mercury lamp with quartz immersion wells. From compound **1** (both pure and as prepared *in situ*), hydrocarbons **4** and **5** (9:1) were obtained in 45–50% yield, with complete conversion of starting material; and none of the substituted imidazoles **2** and **3** could

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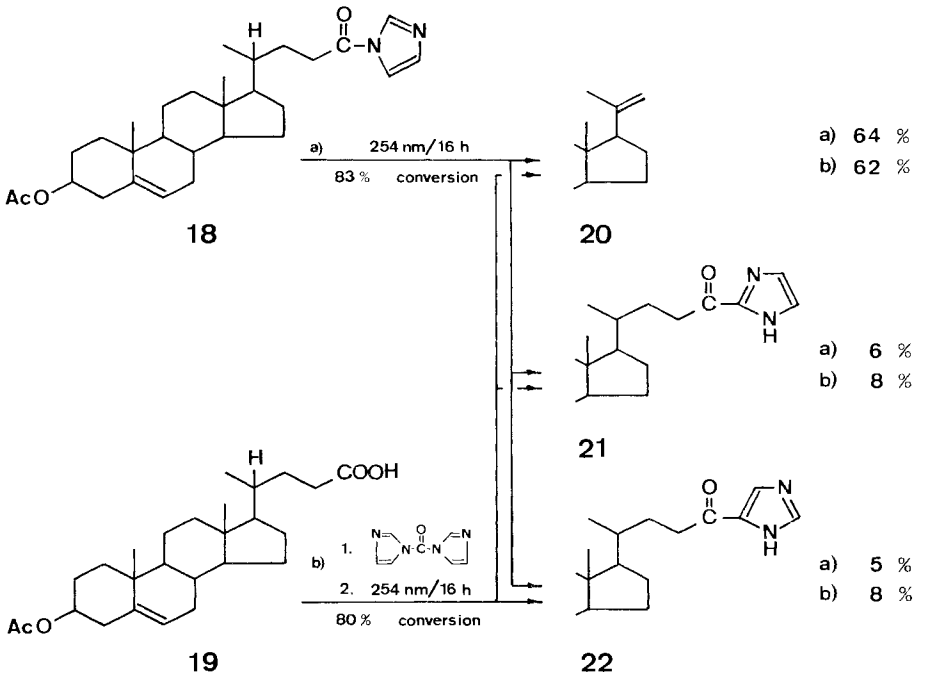
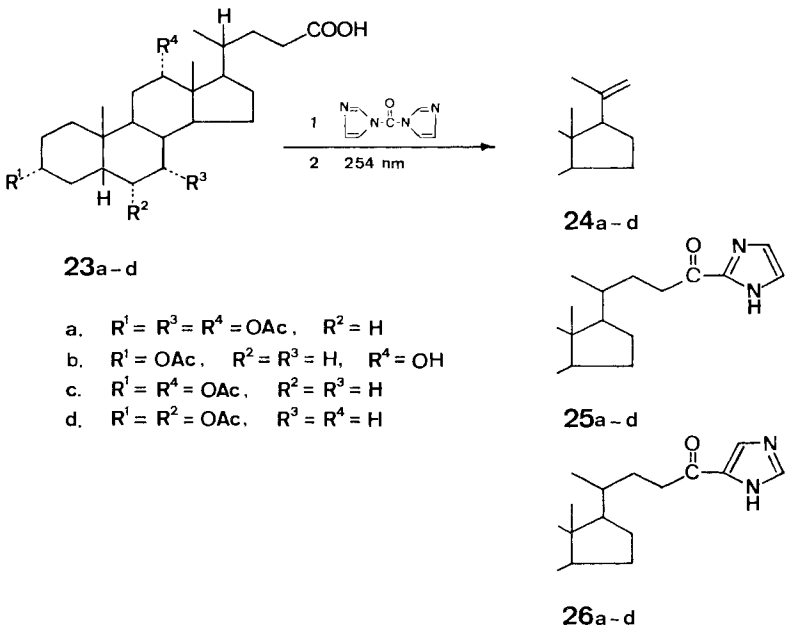
2) With some starting materials (**23**, $R^1 = R^3 = R^4 = OH$, $R^2 = H$), (**23**, $R^1 = R^4 = OH$, $R^2 = R^3 = H$) and (**23**, $R^1 = R^2 = OH$, $R^3 = R^4 = H$), the yields of 20-methylene derivatives were over 60% but the products were not obtained pure, apparently because of partial reaction of the 3α- or 6α-hydroxy groups with the excess of N,N'-carbonylimidazole present leading to partial formation of the corresponding alkoxycarbonylimidazoles (for this reaction, see reference [3]), and hence these results are not recorded.

Scheme 4



Scheme 5



a. $R^1 = R^3 = R^4 = OAc$, $R^2 = H$
b. $R^1 = OAc$, $R^2 = R^3 = H$, $R^4 = OH$
c. $R^1 = R^4 = OAc$, $R^2 = R^3 = H$
d. $R^1 = R^2 = OAc$, $R^3 = R^4 = H$

Table 2. *The results of UV. irradiation of bile acids* (**23a–d**)

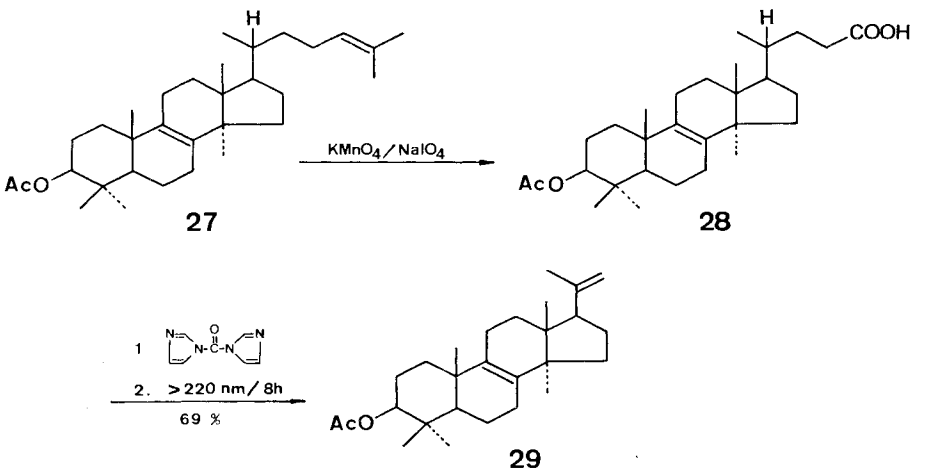
Irradiation of **23**				Yields of the products (%)			
Compound	Amount (g)	Irradiation time (h)	Conversion (%)	**24**	**25**	**26**	Total
a	1.65	16	82	65	4	4	73
b	2.0	16	70	65	7	7	79
c	2.5	15	70	50	19	8	77
d	2.4	20	76	63	9	6	78

be detected (by TLC.) during the entire reaction. Irradiation of the steroid derivative **18** under the same conditions (both pure and as prepared *in situ*) gave the 20-methylene-5-pregnene **20** in *ca.* 70% yield with complete conversion.

The mechanistic course of the reaction became apparent when the acyl rearrangement products **2** and **3** were irradiated. With both a low pressure and a medium pressure mercury lamp the mixture of hydrocarbons **4** and **5** (9:1) was formed rapidly in both cases. In the course of the reaction TLC. examination indicated the temporary appearance of acetylimidazoles **6** and **7**. Other products formed could not be identified.

The efficiency of this degradation method was also demonstrated in the case of lanosterol. 3β-Acetoxy-25,26,27-trinorlanost-8-en-24-oic acid (**28**), prepared from lanosterol-acetate (**27**) [4], was converted into the derived imidazolide, whose irradiation as formed *in situ* using a medium pressure lamp gave 3β-acetoxy-4,4,14,20-tetramethylpregna-8,20-diene (**29**) in 69% yield.

Scheme 6



Structures of photo-fragmentation products. – The structures of the products obtained from the above reactions are based on spectroscopic data. Olefin **4** was identical with an authentic specimen by comparison of spectra and chromato-

graphic behaviour. Hydrocarbon **5** was identified on spectral grounds together with comparison of its retention time with that of an authentic specimen. The structure of olefin **14** was confirmed by its NMR. spectrum (see exper. part). The co-occurence of hydrocarbon **15** was indicated by the mass spectrum of the hydrocarbon mixture and its analysis by gas chromatography.

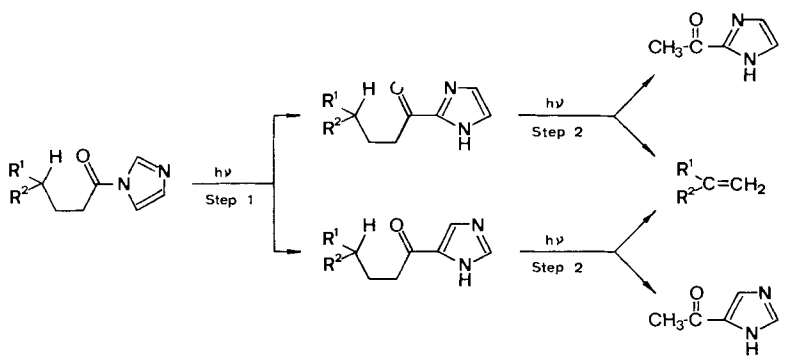
All the steroidal products obtained by the photo-fragmentation reactions show the IR. absorption and NMR. signals expected from the presence of the 20-methylene group. Compounds **20** and **29** were also found to have physical constants in agreement with those reported previously ([5] and [6] respectively). The structure of product **24a** was confirmed by its conversion to the known [7] 3α12α-diacetoxy-5β-pregnan-20-one (**30**) by ozonolysis. In these steroidal products the presence of traces of 20-ethylpregnane derivatives was indicated in the mass spectra of crude products such as of **20**, **24a–24d**, and **29**, but these impurities were not isolated.

The structure assignments of the acyl rearrangement products were based on their spectroscopic and chromatographic properties and relation of these to the imidazole substitution pattern as discussed in the previous paper [1].

Discussion. – The formation of hexadec-1-ene (**4**) by photolysis of N-stearoylimidazole (**1**) through a *Norrish* Type II elimination could arise by γ-hydrogen abstraction by an acyl carbonyl group, either directly from **1** or from rearrangement products **2** and **3**. The results of the photolysis of **1** with 254 nm light after two different reaction times appear to support the second alternative which would require the formation of *Norrish* Type II elimination products in greater relative yield after longer reaction times (with increasing consumption of acyl rearrangement products). This conclusion is further supported by the fact that both **2** and **3** were consumed more rapidly than **1**, giving product **4** in all cases, although the yield of the latter from **2** and **3** were unexpectedly low and comparable to that from **1**. The same tendency was observed in the case of the steroidal imidazole derivatives **21** and **22**.

The most likely mechanisms for these elimination reactions is therefore summarized as in *Scheme 7*, even though a dual mechanistic pathway involving elimination from both N-acylimidazoles and from their acyl rearrangement products cannot be ruled out.

Scheme 7



The photolysis of **1** with 254 nm light gave a 55% yield of acyl rearrangement products **2** and **3** and a 25% yield of *Norrish* Type II elimination product **4** (see *Scheme 1*). This means that in this particular case acyl migration should proceed to the extent of at least 80%, according to *Scheme 7*. A similar conclusion can be made from the results obtained with the steroidal imidazoles.

In conclusion, we have shown that (a) the N-acylimidazoles described in this paper exhibit N→C acyl rearrangement in at least 80% intermediate yield, (b) in the case of of N-stearoylimidazole (having a secondary hydrogen atom γ to the carbonyl group) and using 254 nm light the primary acyl migration step is faster than the second *Norrish* Type II elimination step, thus allowing for temporary accumulation of acyl migration products during the course of the reaction, whereas with a medium pressure lamp both steps appear to proceed at comparable rates, (c) in the case of N-acylimidazoles with tertiary hydrogen atom in the γ-position the second step appears to be much faster (with both low and medium pressure lamps).

There are previous examples in the literature of bile acid and lanosterol side chain degradations based on photochemical *Norrish* Type II processes [6] [8] [9]. However, these involve a number of experimental steps, and the reported yields of 20-methylene pregnane derivatives from the corresponding 24-oic acids do not exceed 24–35%. The procedure reported in this paper appears to offer a number of advantages both regarding yield and experimental simplicity.

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Experimental Part

General. See [1]. Optical rotations were measured in a 0.5 dm tube and are recorded as follows; $[\alpha]_D^{temp.}$ (% concentration, solvent). Gas-Chromatography (GC.) was carried out on *Varian* apparatus model 90-P. The column used was 15% SE-52 (silicon gum rubber) on chromosorb W (60/80 NAW).

Preparation of acylimidazoles. – *1-Stearoylimidazole* (**1**). 5.69 g (0.02 mol) of commercial stearic acid (*Fluka AG*, puriss) was dissolved in 15 ml of thionyl chloride and heated under reflux for 2 h. After complete removal of excess thionyl chloride under reduced pressure, the residual stearoyl chloride was dissolved in 100 ml of dry benzene. The solution was added to a suspension of 2.8 g (0.04 mol) of imidazole in 150 ml of dry benzene and stirred for 24 h at RT. Imidazole hydrochloride was removed by filtration. The filtrate was evaporated *i.V.* and the residue was recrystallized from acetonitrile to give colorless leaflets (6.4 g). M.p. 83–85°. – IR. (CCl_4): 3160 *w*, 3135 *w*, 3110 *w*, 2920 *s*, 2860 *s*, 1740 *s*, 1470 *s*, 1390 *s*, 1295 *m*, 1270 *m*, 1230 *s*, 1100 *m*, 1080 *w*, 1045 *w*, 960 *m*, 900 *w*, 720 *w*. – ^{1}H-NMR. ($CDCl_3$)[3]: 8.14 (br. *s*, H–C(2)); 7.46 (*t*, J = 1.0, H–C(5)); 7.08 *q*, J = 1.0, H–C(4)); 2.87 (*t*, J = 7.0, H_2CCO); 1.26 (*m*, 30H); 0.88 (*t*, J = 6.0, H_3C). – MS.: 334 (6, M^+), 306 (2), 284 (1), 267 (18), 249 (1), 185 (1), 149 (4), 137 (2), 123 (4), 111 (4), 110 (4), 109 (5), 98 (7), 97 (6), 95 (7), 85 (10), 83 (7), 81 (5), 69 (*100*), 68 (87), 60 (6), 57 (31), 55 (21), 43 (33), 41 (56).

$C_{21}H_{38}N_2O$ (334.53) Calc. C 75.39 H 11.45 N 8.37% Found C 75.27 H 11.34 N 8.21%

[3] The numbering are given for the imidazole ring protons.

Tetradecanyl triphenylphosphonium bromide (**9**). 11 g of 1-bromotetradecane and 11.3 g of triphenylphosphine was heated in 30 ml of benzonitrile at 145–150° for 3 h[4]). About one half of the solvent was removed under reduced pressure and the remainder was added into a 500 ml dry ether. The oil which separated solidified on further stirring. Filtration of the solid gave fine crystalline **9** which was washed with ether and dried. M.p. 87–89°. – IR. (CCl_4): 3060*w*, 3005*w*, 2920*s*, 2855*s*, 1587*w*, 1485*w*, 1467*m*, 1440*s*, 1110*s*, 993*m*, 713*m*, 687*s*.

Ethyl 4-methylstearate (**11**). To a suspension of 11 g of **9** in 100 ml dry ether was added 14 ml of *n*-BuLi in hexane (~2M, *Fluka AG*, pract.) and the whole was stirred for 2 h at –78°. To this solution was added 3 g of ethyl levulinate in 20 ml ether and the whole was stirred overnight at RT. and for 1 h under reflux. After cooling dilute sulfuric acid was added. The ether layer was separated, washed with water and dried over magnesium sulfate. Evaporation of the solvent i.V. gave an oil which was roughly chromatographed on 60 g silicagel. Elution with benzene/ethyl acetate 9:1 afforded 1.7 g of a mixture of *ethyl* cis- and trans-*4-methyl-4-octadecanoate* (**10**). The mixture was hydrogenated over Pd/C (10%) in 30 ml THF to give crude *ethyl 4-methylstearate* (**11**) which was purified by silicagel chromatography and eluted with benzene/hexane 1:1. 1.5 g of pure **11** was isolated as a gum. – IR. (CCl_4): 2930*s*, 2855*s*, 1740*s*, 1465*m*, 1380*m*, 1175*m*, 1035*w*. – ^{1}H-NMR. ($CDCl_3$): 4.13 (*q*, J = 7.0, H_2COCO); 2.30 (*t*, J = 7.0, 2H–C(2)); 1.8–1.16 (*m*, 32H); 1.0–0.8 (*m*, H_3C–C(4) and H_3C–C(17)). – MS.: 326 (9, M^+), 297 (2), 281 (6), 169 (23), 239 (8), 183 (1), 169 (2), 155 (2), 141 (2), 129 (8), 111 (4), 101 (*100*), 88 (56), 73 (14), 71 (14), 69 (16), 57 (24), 55 (24), 43 (33).

1-(4-Methylstearoyl)imidazole (**13**). 2.5 g of **11** was heated under reflux in 100 ml of 5% ethanolic sodium hydroxide for 3 h. After evaporation of ethanol the residue was added to dilute hydrochloric acid. The solid which separated was extracted with chloroform and the extract was washed with water and dried over magnesium sulfate. Evaporation of solvent gave crude *4-methylstearic acid* (**12**) as red brown crystals. This crude material was treated with 2 g of N,N'-carbonyldiimidazole in 30 ml of dry acetonitrile and the whole was heated to 60–70° to dissolve all the material. On standing at RT. crystals of **13** separated as leaflets (2.0 g), m.p. 65–66°. – IR. (CCl_4): 3160*w*, 3130*w*, 2920*s*, 2855*s*, 1740*s*, 1470*m*, 1380*m*, 1290*w*, 1270*m*, 1220*m*, 1205*w*, 1095*w*, 1075*w*, 950*w*. – ^{1}H-NMR. ($CDCl_3$)[3]): 8.14 (br.*s*, H–C(2)); 7.46 (*t*, J = 1.0, H–C(5)); 7.08 (*t*, J = 1.0, H–C(4)); 2.87 (*t*, J = 7.0, H_2CCO); 1.96–1.50 (*m*, $HCCH_2CH_2CO$); 1.26 (*m*, 28H); 1.0–0.8 (*m*, $2H_3C$). – MS.: 348 (24, M^+), 333 (1), 320 (1), 281 (22), 263 (7), 207 (1), 193 (1), 179 (1), 165 (1), 151 (3), 149 (2), 137 (3), 123 (18), 112 (10), 109 (10), 95 (15), 83 (11), 69 (*100*), 57 (22), 55 (17), 43 (25).

$C_{22}H_{40}N_2O$ (348.56) Calc. C 75.80 H 11.57 N 8.04% Found C 75.80 H 11.52 N 8.06%

1-(3β-Acetoxy-5-cholenoyl)imidazole (**18**). 4.2 g of *3β-acetoxy-5-cholenic acid* (**19**) was dissolved in 50 ml of dry THF and treated with 2.5 g of N,N'-carbonyldiimidazole. To this solution 100 ml of dry acetonitrile was added and the solution was concentrated to *ca.* 80 ml by distillation. On keeping at RT. crystals of **18** separated (3.9 g), m.p. 95–98°. – IR. (CCl_4): 2940*s*, 2905*w*, 2870*w*, 2850*w*, 1740*s*, 1470*m*, 1385*m*, 1375*m*, 1365*w*, 1270*w*, 1240*s*, 1095*w*, 1075*w*, 1033*m*, 955*w*. – ^{1}H-NMR. ($CDCl_3$)[5]): 8.14 (br.*s*, H–C(2')); 7.46 (*t*, J = 1.0, H–C(5')); 7.08 (*q*, J = 1.0, H–C(4')); 5.38 (*m*, H–C(6)); 4.6 (*m*, H–C(3)); 3.0–2.7 (*m*, H–C(23)); 2.03 (*s*, H_3CCOO); 1.02 (*s*, H–C(19)); 1.05 (*d*, J = 6.0, H–C(20)); 0.70 (*s*, H–C(18)). – MS.: 466 (1, M^+), 406 (13), 338 (6), 323 (1), 310 (1), 295 (1), 283 (1), 253 (2), 239 (1), 228 (1), 213 (3), 199 (2), 189 (1), 185 (1), 173 (2), 159 (4), 145 (8), 133 (5), 121 (6), 119 (6), 105 (11), 91 (10), 81 (13), 69 (*100*), 55 (13), 43 (11).

$C_{29}H_{42}N_2O_3$ (466.64) Calc. C 74.69 H 9.07 N 6.00% Found C 74.61 H 9.11 N 5.90%

Photolysis of imidazolides. – *General procedure.* a) Irradiation as in [1]. After irradiation the solvent was removed *i. V.* and the residual mixture was separated by silicagel column chromatography, normally eluting with $CHCl_3$/MeOH 9:1 or 19:1. The reaction and the separation were followed by TLC. (developed either with $CHCl_3$/MeOH 5:1 or with benzene/MeOH 2:1).

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4) According to the method of synthesizing lauryl triphenylphosphonium bromide [10].

5) The numbering 2', 4' and 5' are given for the protons on imidazole ring, the others are according to the steroid numbering.

b) The carboxylic acid was mixed with excess N,N'-carbonyldiimidazole (1.5–2 equiv.) in 30–40 ml of dry THF and the mixture allowed to stand for a few h at RT. protected from moisture with occasional shaking. It was then diluted to 500 ml with THF and irradiated as in method a. The irradiation mixture after evaporation of solvent was extracted with ethyl acetate and washed with water to remove imidazole and other water soluble substances. When lamp B was used especially as in method b, the use of a 'circulating thin film apparatus' was found advisable in order to avoid the adhesion of insoluble material to the surface of the immersion well.

Photolysis of 1-stearoylimidazole (**1**). 1) 3.34 g of **1** was irradiated (lamp A) for 24 h. The irradiation mixture was passed through a column of 100 g of silicagel, and the products were eluted with hexane/benzene 4:1 to give 520 mg of a mixture of **4** and **5** (9:1 as determined by GC.). The residual material adsorbed in the column was eluted using $CHCl_3$/MeOH 1:1, and the mixture obtained was separated by repeated column chromatography affording 850 mg of **2**, 710 mg of **3** and 80–90 mg each of **6** and **7** with a recovery of 420 mg of stearic acid.

2) 2.0 g of **1** was irradiated (lamp A) for 60 h. 580 mg of a mixture of **4** and **5** (9:1) was separated by a procedure as described above with a recovery of *ca.* 70 mg of stearic acid.

3) 2.0 g of **1** was irradiated (lamp B) for 10 h, 610 mg of a mixture of **4** and **5** (9:1) was isolated.

4) 1.7 g of stearic acid was treated with 1.7 g of N,N'-carbonyldiimidazole and the reaction mixture was irradiated (lamp B) for 10 h, 540 mg of a mixture of **4** and **5** (9:1) was isolated.

2-Stearoylimidazole (**2**). M.p. 110–111° (from CCl_4). – UV. (THF): 279 (13750). – IR. ($CHCl_3$): 3440*m*, 3280*m*, 2925*s*, 2855*s*, 1675*s*, 1470*m*, 1420*m*, 1393*m*, 1088*m*, 950*w*, 915*w*. – ^{1}H-NMR. ($CDCl_3$)[3]): 8.30–8.18 (*m*, H—C(4) and H—C(5)); 3.12 (*t*, J = 7.0, H_2CCO); 1.26 (*m*, 30H); 0.88 (*t*, J = 7.0, H_3C). – MS.: 334 (*100*, M^+), 306 (8), 291 (2), 278 (8), 263 (7), 249 (3), 235 (5), 221 (3), 207 (5), 193 (6), 186 (3), 179 (5), 165 (5), 151 (9), 149 (15), 137 (15), 123 (15), 110 (72), 95 (22), 82 (23), 69 (35), 57 (13), 55 (14), 43 (25).

$C_{21}H_{38}N_2O$ (334.53) Calc. C 75.39 H 11.45 N 8.37% Found C 75.31 H 11.39 N 8.28%

4(or 5)-Stearoylimidazole (**3**). M.p. 118–119° (from CCl_4). – UV. (THF): 260 (13200). – IR. ($CHCl_3$): 3440*m*, 3250*w*, 2920*s*, 2855*s*, 1675*s*, 1550*w*, 1464*m*, 1410*w*, 1380*m*, 1320*w*, 1305*w*, 1140*w*, 1120*w*, 1100*w*, 953*m*, 863*m*. – ^{1}H-NMR. ($CDCl_3$)[3]): 7.80 (*s*, H—C(2)); 7.74 (*s*, H—C(4 or 5)); 2.86 (*t*, *J* = 7.0, H_2CCO); 1.26 (*m*, 30H); 0.88 (*t*, *J* = 6.0, H_3C). – MS.: 334 (20, M^+), 319 (1), 316 (1), 306 (2), 291 (1), 277 (1), 263 (1), 249 (1), 235 (1), 221 (1), 207 (1), 193 (1), 186 (2), 179 (1), 165 (1), 149 (4), 137 (3), 123 (13), 110 (*100*), 95 (22), 82 (3), 69 (7), 57 (6), 55 (7).

$C_{21}H_{38}N_2O$ (334.53) Calc. C 75.39 H 11.45 N 8.37% Found C 75.54 H 11.40 N 8.40%

Hexadec-1-ene (**4**). Liquid: Separated by GC. – IR. (CCl_4): 3080*w*, 2920*s*, 2850*s*, 1640*m* 1467*m*, 990*m*, 910*m*. – ^{1}H-NMR. ($CDCl_3$): 5.88–5.52 (*m*, H—C(2)); 4.98 and 4.84 (*m*, 2H—C(1)); 1.28 (*m*, 24H); 0.89 (*t*, *J* = 6.0, H_3C). – MS.: 224 (8, M^+), 196 (4), 182 (2), 168 (2), 154 (5), 140 (8), 139 (8), 125 (20), 111 (41), 97 (78), 83 (90), 69 (75), 57 (90), 55 (97), 43 (*100*), 41 (88).

$C_{16}H_{32}$ (224.42) Calc. C 85.63 H 14.37% Found C 85.52 H 14.43%

n-*Heptadecane* (**5**). Liquid: Separated by GC. – IR. (CCl_4): 2960*s*, 2920*s*, 2850*s*, 1465*m*, 1380*w*.

Photolysis of 1-(4-methylstearoyl)imidazole (**13**). 1.9 g of **13** was irradiated (lamp A) for 16 h. The irradiation mixture was worked up as in the case of **1** and afforded 640 mg of a mixture of **14** and **15** (19:1 as determined by GC.), 40 mg of **16** and 70 mg of **17** with a recovery of 420 mg of **12**.

2-Methyl-hexadec-1-ene (**14**). Liquid: Separated by GC. – IR. (CCl_4): 3075*w*, 2920*s*, 2855*s*, 1650*m*, 1470*m*, 1373*m*, 887*m*. – ^{1}H-NMR. ($CDCl_3$): 4.65 (br.*s*, 2H—C(1)); 2.05 (br.*t*, *J* = 7.0, H—C(3)); 1.72 (br.*s*, H_3C—C(2)); 1.26 (*m*, 28H); 0.88 (*t*, *J* = 6.0, H_3C—C(15)). – MS.: 238 (9, M^+), 223 (2), 210 (4), 195 (1), 182 (4), 167 (1), 154 (1), 149 (1), 139 (2), 125 (5), 97 (16), 83 (19), 69 (38), 56 (*100*), 43 (36), 41 (46).

3-Methylheptadecane (**15**) was identified only by GC. retention time and mass spectrum.

2-(4-Methylstearoyl)imidazole (**16**). M.p. 78–79° (from hexane). – UV. (THF): 278 (13350). – IR. (CCl_4): 3450*m*, 3275*m*, 2925*s*, 2855*s*, 1660*s*, 1465*m*, 1417*m*, 1160*w*, 1115*w*, 1080*w*, 950*w*. –

^{1}H-NMR. ($CDCl_3$)[3]: 7.30–7.18 (*m*, H—C(4) and H—C(5)); 3.14 (*t*, J = 7.0, H_2CCO); 2.0–1.4 (*m*, $HCCH_2CH_2CO$); 1.25 (*m*, 28H); 1.0–0.8 (*m*, $2H_3C$). – MS.: 348 (33, M^+), 333 (2), 320 (2), 305 (1), 292 (5), 263 (6), 249 (2), 235 (3), 221 (3), 207 (4), 193 (3), 179 (3), 165 (3), 151 (11), 123 (31), 110 (*100*), 98 (7), 95 (22), 82 (22), 69 (35), 55 (15), 43 (21).

$C_{22}H_{40}N_2O$ (348.56) Calc. C 75.80 H 11.75 N 8.04% Found C 75.70 H 11.51 N 8.08%

4(or 5)-(4-Methylstearoyl)imidazole (**17**). M.p. 72–74° (from hexane). – UV. (THF): 259 (13900). – IR. (CCl_4): 3360–3000*m*, 2925*s*, 2855*s*, 1670*s*, 1470*m*, 1460*m*, 1380*m*, 1135*m*, 850*w*. – ^{1}H-NMR. ($CDCl_3$)[3]: 7.80 (*s*, H—C(2)); 7.75 (*s*, H—C(4 or 5)); 2.87 (*t*, J = 7.0, H_2CCO); 1.9–1.4 (*m*, $HCCH_2CH_2CO$); 1.26 (*m*, 28H); 1.0–0.76 (*m*, $2H_3C$). – MS.: 348 (1, M^+), 297 (4), 282 (1), 268 (4), 240 (21), 226 (1), 212 (1), 198 (1), 184 (1), 156 (1), 149 (3), 142 (2), 129 (4), 123 (4), 110 (17), 100 (22), 83 (9), 72 (*100*), 59 (82), 43 (30).

$C_{22}H_{40}N_2O$ (348.56) Calc. C 75.80 H 11.57 N 8.04% Found C 75.70 H 11.51 N 8.08%

Photolysis of 1-(3β-acetoxy-5-cholenoyl)imidazole (**18**). 1) 2.24 g of **18** was irradiated (lamp A) for 16 h. The irradiation mixture was separated by column chromatography affording 910 mg of **20**, 110 mg of **21** and 90 mg of **22** with a recovery of 340 mg of 3β-acetoxy-5-cholenic acid (**19**).

2) 2 g of **19** was mixed with 2 g of N,N'-carbonyldiimidazole in 50 ml of dry THF and the mixture was kept standing at RT. for 1 h. It was diluted to a 500 ml with THF and irradiated (lamp A) for 16 h. The irradiation mixture was separated by column chromatography affording 850 mg of **20**, 140 mg of **21** and 140 mg of **22** with a recovery of 400 mg of acid **19**.

3) 2 g of **18** was irradiated (lamp B) for 8 h. Chromatographic separation afforded 1.09 g of **20**.

4) 1.64 g of **19** was treated with 1.5 g of N,N'-carbonyldiimidazole and the solution was irradiated (lamp B) for 8 h. Chromatography of the irradiation mixture afforded 950 mg of **20**.

20-Methylene-5-pregnen-3β-ol acetate (**20**). M.p. 129–130° (from $CHCl_3$/MeOH, (lit. [5] 128.5–129°). $[\alpha]_D^{22}$: −61.2° (*c* = 0.49, $CHCl_3$) (lit. [5] $[\alpha]_D^{27}$: −72° (*c* = 1.62, $CHCl_3$)). IR. (CCl_4): 3080*w*, 2950*s*, 2905*w*, 2877*w*, 2855*w*, 1735*s*, 1643*w*, 1470*w*, 1440*w*, 1380*m*, 1370*m*, 1245*s*, 1140*w*, 1035*m*, 905*w*, 893*m*. – ^{1}H-NMR. ($CDCl_3$): 5.38 (br.*d*, J = 5.0, H—C(6)); 4.86 and 4.72 (2br.*s*, H_2C=C(20)); 4.6 (*m*, H—C(3)); 2.38 (br.*s*, 1H); 2.30 (br.*s*, 1H); 2.06 (*s*, H_3CCOO); 1.80 (*s*, H—C(21)); 1.05 (*s*, H—C(19)); 0.62 (*s*, H—C(18)). – MS.: 356 (1, M^+), 312 (14), 296 (*100*), 281 (29), 253 (8), 239 (2), 228 (11), 213 (19), 211 (12), 199 (6), 197 (7), 191 (3), 189 (3), 185 (4), 171 (5), 158 (8), 149 (12), 145 (13), 143 (12), 133 (6), 131 (7), 119 (6), 105 (12), 91 (13), 81 (14), 67 (10), 55 (10), 43 (15).

$C_{24}H_{36}O_2$ (356.53) Calc. C 80.85 H 10.18% Found C 80.57 H 10.17%

2-(3β-acetoxy-5-cholenoyl)imidazole (**21**). M.p. 216–218° (from benzene). – UV. (THF): 278 (13440). – IR. (CCl_4): 3450*m*, 3280*m*, 2940*s*, 2875*m*, 1732*s*, 1675*s*, 1420*m*, 1245*s*, 1035*m*. – ^{1}H-NMR. ($CDCl_3$)[5]: 7.35–7.20 (*m*, H—C(4') and H—C(5')); 5.37 (br.*d*, J = 5.0, H—C(6)); 4.6 (*m*, H—C(3)); 3.25–3.0 (*m*, H—C(23)); 2.37 (br.*s*, 1H); 2.29 (br.*s*, 1H); 2.07 (*s*, H_3CCOO); 1.04 (*s*, H—C(19)); 0.99 (*d*, J = 5.0, H—C(21)), 0.70 (*s*, H—C(18)). – MS.: 466 (1, M^+), 451 (1), 436 (1), 423 (1), 406 (*100*), 391 (12), 378 (2), 373 (3), 350 (5), 301 (2), 296 (2), 285 (6), 267 (2), 256 (4), 228 (2), 213 (5), 199 (2), 185 (2), 171 (2), 159 (4), 145 (5), 123 (12), 110 (33), 95 (9), 81 (7), 69 (17), 55 (12), 43 (15).

4(or 5)-(3β-acetoxy-5-cholenoyl)imidazole (**22**). M.p. 159–161° (from acetone). – UV. (THF): 259 (13700). – IR. ($CHCl_3$, sparingly soluble): 3440–3000*m*, 2950*s*, 1735*s*, 1660*s*, 1250*s*. – ^{1}H-NMR. ($CDCl_3$)[5]: 7.82 (br.*s*, H—C(2')), 7.77 (br.*s*, H—C(4' or 5')); 5.38 (br.*d*, J = 5.0, H—C(6)); 4.6 (*m*, H—C(3)); 3.0–2.7 (*m*, H—C(23)); 2.39 (br.*s*, 1H); 2.30 (br.*s*, 1H); 2.06 (*s*, H_3COO); 1.04 (*s*, H—C(19)); 1.01 (*d*, J = 5.0, H—C(21)); 0.71 (*s*, H—C(18)). – MS.: 466 (1, M^+), 424 (1), 406 (*100*), 391 (5), 373 (5), 296 (10), 286 (3), 281 (4), 267 (4), 253 (3), 228 (3), 213 (8), 199 (3), 185 (2), 175 (3), 159 (8), 145 (12), 123 (19), 110 (48), 95 (56), 81 (18), 67 (15), 55 (18), 43 (32).

Photolysis of imidazolides of cholic acids **23a–d**. Cholic acids **23a–d** were treated with excess amounts of N,N'-carbonyldiimidazole in THF and were photolyzed (lamp A). The yields of the

resulting 20-methylene-pregnane derivatives **24a–d**, 2-cholanoylimidazoles **25a–d** and 4(or 5)-cholanoylimidazoles **26a–d** are listed in Table 2 together with conversion rates. The structure determination of acyl rearrangement products **25a–d** and **26a–d** by spectroscopic data and estimation of their yields were made using the crude products.

20-Methylene-5β-pregnane-3α,7α,12α-triol triacetate (**24a**). This could not be obtained crystalline. $[\alpha]_D^{22}$: +79.0° (*c* = 1.65, $CHCl_3$). – IR. (CCl_4): 3080*w*, 2960–2940*s*, 2870*m*, 1735*s*, 1645*w*, 1470*m*, 1450*m*, 1440*m*, 1378*s*, 1365*s*, 1250–1230*s*, 1147*w*, 1065*m*, 1050*m*, 1023*s*, 963*m*, 937*m*, 890*m*. – ^{1}H-NMR. ($CDCl_3$): 4.94 (*m*, H–C(7) and H–C(12)); 4.88 and 4.67 (2br.*s*, H_2C=C(20)); 4.6 (*m*, H–C(3)); 2.60 (*t*, *J* = 10.0, H–C(17)); 2.15, 2.09 and 2.04 (*s*, 3 H_3CCO); 1.67 (*s*, H–C(21)); 0.92 (*s*, H–C(19)); 0.64 (*s*, H–C(18)). – MS.: 474 (1, M^+), 414 (1), 372 (1), 370 (1), 354 (27), 339 (1), 312 (1), 310 (1), 294 (28), 279 (9), 226 (13), 211 (14), 187 (7), 171 (2), 169 (2), 157 (7), 149 (9), 119 (3), 107 (4), 105 (5), 93 (4), 83 (*100*), 67 (5), 55 (6), 47 (25), 43 (16).

20-Methylene-5β-pregnane-3α,12α-diol 3-acetate (**24b**). M.p. 151–152° (from acetone/hexane). $[\alpha]_D^{22}$: +64.6° (*c* = 0.90, $CHCl_3$). – IR. (CCl_4): 3630*w*, 3600–3400*w*, 3080*w*, 2940*s*, 2875*m*, 1737*s*, 1643*w*, 1450*m*, 1380*m*, 1365*m*, 1245*s*, 1090*w*, 1030*m*, 890*m*. – ^{1}H-NMR. ($CDCl_3$): 4.88 and 4.75 (2br.*s*, H_2C=C(20)); 4.7 (*m*, H–C(3)); 3.88 (*m*, H–C(12)); 2.04 (*s*, H_3CCOO); 1.83 (*s*, H–C(21)); 0.94 (*s*, H–C(19)); 0.61 (*s*, H–C(18)). – MS.: 374 (7, M^+), 356 (35), 314 (23), 296 (58), 285 (34), 281 (19), 253 (10), 232 (11), 229 (12), 217 (10), 213 (11), 203 (16), 187 (14), 171 (9), 161 (9), 159 (10), 147 (21), 134 (61), 121 (20), 107 (24), 93 (25), 81 (27), 78 (*100*), 67 (23), 55 (28), 43 (36).

$C_{24}H_{38}O_3$ (374.54) Calc. C 76.96 H 10.23% Found C 77.04 H 10.29%

20-Methylene-5β-pregnane-3α,12α-diol diacetate (**24c**). M.p. 124.5–125.5° (from hexane). $[\alpha]_D^{22}$: +110.4° (*c* = 0.91, $CHCl_3$). – IR. (CCl_4): 3080*w*, 2940*s*, 2870*m*, 1735*s*, 1640*w*, 1450*m*, 1375*m*, 1363*m*, 1240*s*, 1195*w*, 1030*m*, 893*m*. – ^{1}H-NMR. ($CDCl_3$): 4.94 (*m*, H–C(12)); 4.86 and 4.67 (2br.*s*, H_2C=C(20)); 4.7 (*m*, H–C(3)); 2.56 (*t*, *J* = 10.0, H–C(17)); 2.13 and 2.04 (*s*, 2 H_3CCOO); 1.67 (*s*, H–C(21)); 0.92 (*s*, H–C(19)); 0.64 (*s*, H–C(18)). – MS.: 416 (3, M^+), 374 (8), 356 (77), 341 (8), 312 (13), 296 (*100*), 281 (33), 253 (16), 228 (27), 213 (23), 187 (15), 171 (12), 159 (12), 147 (20), 134 (54), 119 (20), 105 (27), 93 (27), 81 (20), 67 (15), 55 (17), 43 (54).

$C_{26}H_{40}O_4$ (416.58) Calc. C 74.96 H 9.68% Found C 74.82 H 9.54%

180 mg of **24c** was ozonized in CH_2Cl_2 at –78°, and the ozonide was decomposed with zinc dust and acetic acid. After column chromatography 170 mg of *3α,12α-diacetoxy-5β-pregnane-20-one* (**30**) was isolated. M.p. 111.5–112.5° (lit. [7] m.p. 122–123°), $[\alpha]_D^{22}$: +173.4° (*c* = 1.01, $CHCl_3$) (lit. [7] $[\alpha]_{5461}^{25}$: +190.4°). – IR. (CCl_4): 2940*s*, 2865*m*, 1737*s*, 1708*s*, 1450*m*, 1360*m*, 1240*s*, 1190*w*, 1025*s*, 970*w*. – ^{1}H-NMR. ($CDCl_3$): 5.16 (*t*, *J* = 3.0, H–C(12)); 4.72 (*m*, H–C(3)); 2.98 (*t*, *J* = 9.0, H–C(17)); 2.18, 2.04 and 2.03 (*s*, 3 H_3CCOO); 0.92 (*s*, H–C(19)); 0.70 (*s*, H–C(19)). – MS.: 418 (<1, M^+), 403 (<1), 375 (10), 358 (62), 343 (3), 315 (13), 298 (*100*), 283 (16), 255 (44), 244 (4), 240 (4), 231 (6), 213 (6), 199 (2), 188 (4), 173 (4), 159 (5), 145 (6), 131 (5), 119 (4), 105 (6), 93 (7), 81 (8), 67 (6), 55 (6), 43 (33).

$C_{25}H_{38}O_5$ (418.55) Calc. C 71.74 H 9.15% Found C 71.68 H 9.10%

20-Methylene-5β-pregnane-3α,6α-diol diacetate (**24d**). This could not be obtained crystalline. $[\alpha]_D^{22}$: +10.4° (*c* = 0.77, $CHCl_3$). – IR. (CCl_4): 3080*w*, 2950*s*, 2875*m*, 1740*s*, 1645*w*, 1455*m*, 1365*m*, 1240*s*, 1030*s*, 955*w*, 890*m*. – ^{1}H-NMR. ($CDCl_3$): 5.16 (*m*, H–C(6)); 4.86 and 4.72 (2br.*s*, H_2C=C(20)); 4.7 (*m*, H–C(3)); 2.05 and 2.03 (*s*, 2 H_3CCOO); 1.78 (*s*, H–C(21)); 0.95 (*s*, H–C(19)); 0.57 (H–C(18)). – MS.: 416 (1, M^+), 374 (2), 356 (44), 341 (4), 314 (13), 296 (28), 281 (15), 153 (7), 241 (8), 227 (26), 213 (18), 199 (8), 185 (24), 171 (7), 159 (10), 149 (11), 145 (5), 133 (6), 131 (8), 119 (8), 105 (13), 95 (10), 93 (11), 91 (11), 78 (*100*), 52 (23), 43 (23).

24d was hydrolysed with 5% ethanolic NaOH giving crystalline *20-methylene-5β-pregnane-3α,6α-diol*, m.p. 195–197° (from $CHCl_3$). $[\alpha]_D^{22}$: –5.7° (*c* = 0.53, $CHCl_3$). – IR. ($CHCl_3$): 3610*m*, 2940*s*, 2870*m*, 1640*w*, 1455*m*, 1380*m*, 1030*s*, 890*m*. – ^{1}H-NMR. ($CDCl_3$): 4.85 and 4.71 (2br.*s*, H_2C=C(20)); 4.06 (*m*, H–C(6)); 3.63 (*m*, H–C(3)); 1.77 (*s*, H–C(21)); 0.92 (*s*, H–C(19)); 0.56 (*s*, H–C(18)). – MS.: 332 (33, M^+), 314 (*100*), 299 (33), 296 (24), 258 (11), 245 (21), 232 (23),

227 (16), 213 (22), 199 (10), 185 (8), 173 (8), 159 (10), 149 (10), 145 (10), 95 (25), 81 (16), 69 (14), 55 (21), 43 (21).

$C_{22}H_{36}O_2$ (332.51) Calc. C 79.41 H 10.92% Found C 79.57 H 10.70%

Photolysis of the imidazolide of 3β-acetoxy-25,26,27-trinorlanost-8-en-24-oic acid (**28**). **28** was prepared from commercial lanosterol (**27**) by the method reported in [4]. 770 mg of **28** was treated with 350 mg of N,N'-carbonyldiimidazole in THF and the mixture was irradiated (lamp B) for 8 h. Chromatographic separation afforded 460 mg of *3β-acetoxy-4,4,14,20-tetramethylpregna-8,20-diene* (**29**), m.p. 166–168° (from MeOH). (lit. [6a] m.p. 168–170°; [6b] m.p. 164–168°), $[\alpha]_D^{22}$: +58.9° (*c* = 0.73, $CHCl_3$) (lit. [6a] $[\alpha]_D$: +45.5°). – IR. (CCl_4): 3080*w*, 2960*s*, 2950*s*, 2875*m*, 2830*w*, 1735*s*, 1640*w*, 1455*m*, 1373*m*, 1245*s*, 1025*m*, 1010*w*, 980*w*, 885*m*. – ^{1}H-NMR. ($CDCl_3$): 4.85 and 4.74 (2br.*s*, H_2C=C(20)); 4.51 (*q*, J_1 = 10.0, J_2 = 5.0, H–C(3)); 2.48 (*t*, *J* = 8.0, H–C(17)); 2.05 (*s*, H_3CCOO); 1.78 (*s*, H–C(21)); 1.05 (*s*, H_3C); 0.93 (*s*, H_3C); 0.89 (*s*, $2H_3C$); 0.60 (*s*, H_3C). – MS.: 398 (43, M^+), 383 (45), 355 (5), 339 (8), 330 (13), 323 (60), 316 (40), 301 (5), 289 (37), 273 (17), 255 (*100*), 241 (12), 229 (43), 215 (23), 201 (16), 185 (22), 173 (17), 159 (90), 145 (30), 135 (23), 133 (24), 119 (53), 107 (30), 95 (28), 81 (18), 69 (31), 55 (35), 43 (67).

$C_{27}H_{42}O_2$ (398.61) Calc. C 81.35 H 10.62% Found C 81.22 H 10.61%

Photolysis of 2- (2) and 4(or 5)-stearoylimidazole (3). – *Photolysis of 2-stearoylimidazole* (2). 334 mg of **2** in 45 ml of THF was irradiated (lamp B) for 30 min. The irradiation mixture was passed through a column packed with 10 g of silicagel and the products were eluted with hexane giving 114 mg of a hydrocarbon mixture (**4** and **5**, 9:1).

Photolysis of 4(or 5)-stearoylimidazole (**3**). 334 mg of **3** was irradiated similarly but for 90 min. A similar work-up as above afforded 100 mg of the above hydrocarbon mixture.

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