

1-PYRENYLMETHYL ESTERS, PHOTOLABILE PROTECTING GROUPS
FOR CARBOXYLIC ACIDS

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Summary: 1-Diazomethylpyrenes were prepared and reacted with
carboxylic acids to give 1-pyrenylmethyl esters. The fluorescent
esters were photolysed at 340 nm in methanol to form the starting
acids and the corresponding 1-methoxymethylpyrenes in high yield.

The formation and solvolysis of esters are one of the most important
processes in organic syntheses. A number of good protecting ester functions
and methods for their cleavage have been proposed for carboxylic acids.¹
Whereas some ester groups, e.g., benzyl, nitrophenyl and nitrobenzyl groups,
are susceptible to a photolytic cleavage, they are not necessarily
satisfactory as protecting groups.² We have found that 1-diazomethylpyrenes
2a-c are useful reagents for esterifying carboxylic acids, and describe here
the formation and photo-solvolysis of the 1-pyrenylmethyl esters. The latter
reactions allow the nearly complete recovery of the starting carboxylic acids
from the esters under neutral and mild conditions without any catalyst.

1-Diazomethylpyrenes **2a-c** were derived from the oxidation of the
corresponding hydrazones **1a-c** either with mercuric oxide or silver oxide in
ether in the presence of methanolic potassium hydroxide.³ They are dark-red
crystals which are stable in the dark and cold place, and can be stored without
decomposition for weeks in a refrigerator. The esterification of an acid was
carried out by adding the *N,N*-dimethylformamide solution of **2a-c** into the
solution of an acid in the same solvent until disappearance of wine-red color
stopped. The reaction conditions and yields are shown in Table 1 along with
the mp's of the corresponding *p*-toluates. During the reaction, the red color
of the diazo compounds disappeared in a few minutes at 50 °C for **2a**, 20 °C for
3b and 80 °C for **2c**. At room temperature, while the red color of **2a**
disappeared gradually, **2c** remained almost unchanged. From the data in Table 1,
2b is concluded to be the best esterifying reagent among the three.

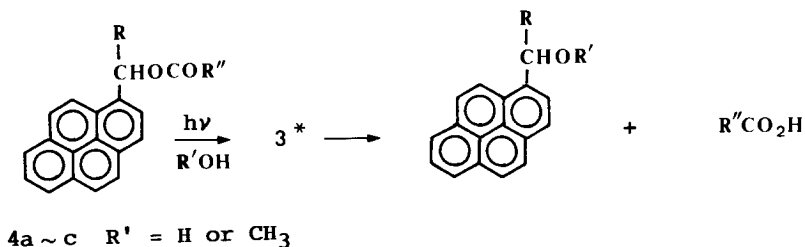
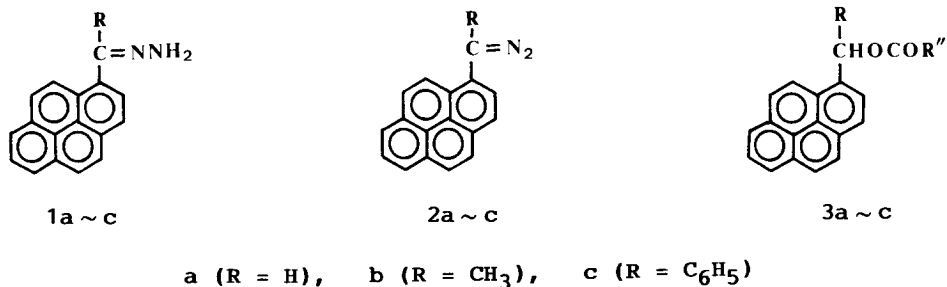


Table 1. 1-Diazomethylpyrenes **2** from **1**, and 1-pyrenylmethyl esters **3** from **2**

R	1-Diazomethylpyrene 2			1-Pyrenylmethyl p-toluoate 3		
	Oxidant	Yield/ %	mp/°C	React.temp./°C	Yield/ %	mp/°C
H	HgO	88	112	50	60	132-133
CH ₃	Ag ₂ O ^{a)}	66	-- ^{b)}	20	80	148-150
C ₆ H ₅	HgO	95	94-96	80	20	154-155

a) The oxidation with HgO was not successful.

b) Due to its instability, purification by recrystallization was difficult.

A 1-3 mM methanol solution of p-toluoate **3a** was irradiated under Argon with a high pressure mercury lamp in a Pyrex immersion cell. The analysis of the photolysed solution by means of HPLC showed two peaks which were assigned to the equimolar amounts of p-toluic acid and methyl 1-pyrenylmethyl ether **4a** ($\text{R}'=\text{CH}_3$). The NMR spectrum of the reaction mixture did not show any signal due to any other compound than those two. From the irradiation in aqueous dioxane, 1-pyrenylmethanol **4a** ($\text{R}'=\text{H}$) was obtained in place of the ether. The results of

Table 2. Photolyses of 1-pyrenylmethyl esters 3a

Carboxylic acid	Mp of the ester (°C)	% Photolysis ^{a)}	% Yields of the liberated acid
cyclohexane-carboxylic acid	81-82	90	100
p-toluic acid	130-132	95	100
phenylacetic acid	59-60	94	95
N-CBZ-L-phenyl-alanine	141-142	98	85
N-CBZ-L-leucine	82-84	98	80

a) Determined by HPLC after irradiation for 30 minutes.

the photolysis of the esters of series 3a are summarized in Table 2. For the esters of simple carboxylic acids, almost complete recovery of the starting acids was observed, while N-CBZ amino acids were recovered in slightly lower yields. It is noteworthy that only 1-pyrenylmethyl group was removed and the N-CBZ group was intact in the latter examples. Other methods of the cleavage of the ester groups such as hydrogenation or basic solvolysis usually take off both alcohol and CBZ groups. The irradiation of 3a-c at 340 ± 5 nm was also effective and gave similar results.

There are a number of merits for these 1-pyrenylmethyl esters. Firstly, they are generally good crystalline compounds and can be purified easily by recrystallization and/or chromatography. For a second, they are highly fluorescent under UV irradiation. For a third, since these esters have the absorption maxima at the longer wavelength region of 340-2 nm ($\epsilon:29,000$),⁴ they can be photolysed by the UV light at 340nm. For a fourth, it is the most unique feature of these esters that they are photolysed to give only the corresponding carboxylic acids and 4 without formation of any meaningful by-product. There are several examples of protecting ester groups which can be removed by photolysis. However, they often carry reactive substituents such as a nitro group that are susceptible to irradiation as well and to chemicals requiring the protection of the carboxyl group.

The application of 1-diazomethylpyrenes as the protecting reagents of the carboxyl groups in the amino acid and peptide syntheses is promising and now being studied in these laboratories.

References

- 1) For the tabulation and critical evaluation of protecting groups, see, for example, T. G. Greene, "Protective Groups in Organic Synthesis", Wiley, New York, N.Y. 1981.
- 2) J. A. Barltrop and P. Schofield, *Tetrahedron Lett.*, 1962, 697; D. H. R. Barton, Y. L. Chow, A. Cox and G. W. Kirby, *J. Chem. Soc.*, 1965, 3571; A. Patchornik, B. Amit and R. B. Woodward, *J. Am. Chem. Soc.*, 92, 6333(1970); L. D. Cama and B. G. Christenum, *J. Am. Chem. Soc.*, 100, 8006 (1978).
- 3) The hydrazone **1a** was prepared by the reaction of 1-formylpyrene with a large excess of hydrazine hydrate in anhydrous ether at 0 °C. Hydrazone **1b** was obtained by the reaction of 1-acetylpyrene with anhydrous hydrazine in refluxing n-butanol. Hydrazone **1c** was prepared by the action of anhydrous hydrazine, hydrazine dihydrochloride on 1-benzoylpyrene in dimethyl sulfoxide at 100 °C. This procedure of hydrazone formation gives satisfactory results for many resistant ketones and will be published elsewhere.
- 4) These 1-pyrenylmethyl esters show UV absorption spectra almost identical with that of pyrene itself.

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