Monatshefte für Chemie 122, 323–325 (1991)

Monatshefte für Chemie
Chemical Monthly

Printed in Austria

Short Communication

Transformation of Acridines and Azepines into the Corresponding 3-Oxo-heterocycles by Means of Hypervalent Aromatic Iodine Compounds

Roland Barret[1,*] and **Marc Daudon**[2]

[1] Laboratoire de Chimie Thérapeutique, Faculté de Pharmacie, 51 Rue Cognacq, Jay, F-51096 Reims Cedex, France
[2] Laboratoire de Chimie Organique, Faculté de Pharmacie, 8 Avenue Rockefeller, F-69373 Lyon Cedex 08, France

Summary. The acridines **3**, **5**, and **6**, as well as the dibenzo[b,f]-azepine **4** were converted into the 3-oxo-derivatives **7**–**10** using hypervalent iodine compounds (iodosylbenzene and bis-(trifluoroacetoxy)iodopentafluorobenzene).

Keywords. Bis-(trifluoroacetoxy)pentafluoroiodobenzene; Iodosylbenzene; Oxidation; Heterocycles.

Oxidation von Acridinen und Azepinen in ihre 3-Oxoderivate mit Hilfe von hypervalenten aromatischen Jodverbindungen (Kurze Mitt.)

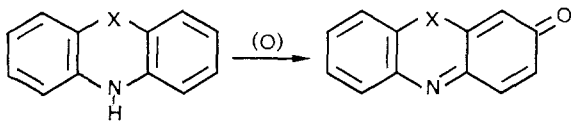
Zusammenfassung. Die Acridine **3**, **5** und **6** sowie das Dibenzo[b,f]azepin **4** wurden mit Hilfe der beiden hypervalenten Jod-Verbindungen Jodosobenzol (**1**) und Bis-trifluoroacetoxyiodbenzol (**2**) zu den entsprechenden 3-Acridinonen **7**, **9** und **10** sowie zum Dibenzoazepin-3-on **8** oxidiert.

Introduction

Hypervalent iodine compounds have been extensively studied for eighty years [1], but interest in their use as oxidant of amines is relatively new [1, 2]. The few reports of the synthesis of 3-oxo heterocycles from acridines and derivates prompted us to plan their preparation by oxidation of amines by hypervalent iodo compounds such as iodosylbenzene (C_6H_5IO, **1**) and bis(trifluoroacetoxy)pentafluoroiodobenzene [$C_6F_5I(OCOCF_3)_2$, **2**]; the latter compound was chosen for its high solubility in organic solvents. The reaction we report in this contribution is to our knowledge a new way to synthesize 3-oxo derivatives of acridines.

Results and Discussion

The reaction was carried out at room temperature with different heterocyclic amines in methanol as solvent with **1** and acetonitrile-water (2/1, *v/v*) with **2**. The results are summarized in Scheme 1.



Substrates		Products	
3	X = S	7	70% a , 80% b
4	X = CH=CH	8	20% a , 46% b
5	X = O	9	70% a , b
6	X = C(C_6H_5)$_2$	10	50% a , b

a: with **1** in CH_3OH

b: with **2** in CH_3CN-H_2O (2:1)

Under these conditions, phenothiazine (**3**) was converted into phenothiazin-3-one (**7**) with good yield with both oxidants **1** and **2**.

Dibenzo[b, f]azepine (**4**) led to dibenzo[b, f]azepin-3-one **8** [4] with a yield of 46% with **2**, whereas Fremy's salt and iodylbenzene in the presence of vanadyl-acetylacetonate formed 9-carbaldehyde acridine as a major product with only a minute quantity of 3-oxo derivative [4, 5].

Phenoxazin-3-one (**9**) [6] was obtained from **5** with identical yields with **1** and **2**. 9,9-Diphenylacridine **6** gave the 9,9-diphenylacridin-3-one **10** in better yields with **1** and **2** (50%), compared to Fremy's salt (20%).

The structures of the 3-oxo derivatives were determined from the spectroscopic data (IR and ^{1}H-NMR) and melting points after separation by chromatographic column and comparison with original samples obtained with Fremy's salt [7].

In conclusion, this reaction affords a convenient route to 3-oxo-heterocycles from acridine derivatives and azepines.

Experimental

Phenothiazine (**3**) and dibenzo[b, f]azepine (**4**) were purchased from EGA-Chemie, phenoxazine (**5**) from Janssen Chimica. All these products were purified by crystallization before use. Fremy's salt was prepared by Zimmer's procedure [7]. Iodosylbenzene and bis(trifluoroacetoxy)pentafluoroiodobenzene were obtained by literature procedures [8, 9]. 9,9-Diphenylacridine (**6**) was synthesized according to [10].

Infrared spectra were recorded on a Perkin-Elmer 1310 model and NMR spectra were taken on an H.P.E. 24 B spectrometer (60 MHz) or a Brucker (AC 300) (300 MHz). Melting points are given uncorrected as recorded with a Buchi melting-point apparatus.

Physical Data

7: M.p. 156–160°C (Lit. 161° [11]); IR (cm^{-1}): 1620, 1600; NMR ($CDCl_3$) 6.5–8 ppm.

8: M.p. 134°C (Lit. 134–136°C [4]); IR (cm^{-1}): 1640, 1620; NMR ($CDCl_3$): 6.6 ppm (1 H, d, J=2 Hz), 6.78 ppm (1 H, d, J=9 Hz), 6.9–7.0 ppm (2 H, m), 7.4–7.6 ppm (4 H, m), 7.92 ppm (1 H, dd, J=9 and 2 Hz).

9: M.p. 208 – 210°C (Lit. 215°C [6]); IR (cm^{-1}): 1 650, 1 620; NMR ($CDCl_3$) 6.2 ppm (1 H, d, J = 9 Hz), 7.6 – 7.2 ppm (6 H, m).

10: M.p. 172 – 173°C; IR (cm^{-1}) 1 635, 1 615; NMR ($CDCl_3$): 7.4 – 6.6 ppm (16 H, m), 5.8 ppm (1 H, s).

Oxidation of 9,9-Diphenylacridine (**6**) *with Fremy's Salt*

A solution of Fremy's salt (2.6 g, 9.7 mmol) and disodium phosphate (1.99 g, 14 mmol) in water (95 ml) was added to 9,9-diphenylacridine (1 g, 3 mmol) in acetone (70 ml). The solution was stirred for 20 min. The mixture was chromatographied on silicagel (hexane/ethylacetate 2/1). We obtained 603 mg. M.p. 171 – 173°C; IR (cm^{-1}): 1 636, 1 615; NMR (300 MHz, $CDCl_3$): 7.7 ppm (1 H, d, 8.5 Hz), 7.2 – 7.4 ppm (4 H), 6.9 – 7.0 ppm (10 H), 6.6 ppm (1 H, dd, 9 Hz and 2 Hz), 6.3 ppm (1 H, d, 2 Hz).

Oxidation of Heterocyclic Amines with Iodosylbenzene

Iodosylbenzene (120 mg, 0.524 mmol) was stirred in methanol (5 ml) for 5 min. Amines (0.250 mmol) dissolved into acetonitrile-water (3 ml, 2/1, *v/v*) was added. The reaction was monitored by TLC (silica, benzene/ethylacetate 9/1). The solution was extracted with ether and the products were purified by column chromatography.

Oxidation with Bis(trifluoroacetoxy)pentafluoroiodobenzene

0.250 mmol of amines in methanol (3 ml) was added to the oxidant (260 mg, 0.5 mmol) dissolved in acetonitrile/water (3 ml, 2/1, *v/v*) and stirred for 1 h. The solution was purified by column chromatography.

References

[1] Banks D. F. (1966) Chem. Rev. **66**: 243; Varvoglis A. (1984) Synthesis: 709; Moriarty R. M., Praksch O. (1986) Acc. Chem. Res. **19**: 244
[2] Varvoglis A. (1981) Chem. Soc. Rev. **10**: 377
[3] Moriarty R. M., Vaid R. K., Ducan M. P., Ochiai N., Inenaga N., Nagao Y. (1988) Tetrahedron Lett. **29**: 6913
[4] Haque K. E., Hardie K. H., Proctor G. R. (1972) J. Chem. Soc. Perkin I: 539
[5] Barret R., Daudon M. (in press) Synth. Comm.
[6] Bird C. W., Latif M. (1980) Tetrahedron **36**: 529
[7] Zimmer H., Lankin D. C., Horgan S. W. (1970) Chem. Rev. **70**: 229
[8] Lucas H. J., Formo M. W., Kennedy E. R. (1955) In: Horning E. C. (Ed.) Org. Synth. Coll., Vol. III. Wiley, New York, p. 483
[9] Lu F. H. H. (1984) Ph. D. Dissertation. Univ. Nebraska, Lincoln, Nebraska
[10] Golstein H., Huser G. (1944) Helv. Chim. Acta: 616
[11] Terdic M., Bodea C. (1968) Rev. Roum. Chim. **13**: 833

Received May 31, 1990. Revised October 15, 1990. Accepted November 9, 1990

Verleger: Springer-Verlag KG, Sachsenplatz 4-6, A-1201 Wien. — Herausgeber: Österreichische Akademie der Wissenschaften, Dr.-Ignaz-Seipel-Platz 2, A-1010 Wien, und Gesellschaft Österreichischer Chemiker, Eschenbachgasse 9, A-1010 Wien. — Redaktion: Währinger Straße 38, A-1090 Wien. — Hersteller: Adolf Holzhausens Nachfolger, Kandlgasse 19-21, A-1070 Wien. — Verlagsort: Wien. — Herstellungsort: Wien. — Printed in Austria.