99. Heterocyclic Spiro-naphthalenones. Part V. Synthesis of Some 2-Benzazepines from 3,4-Dihydrospiro[furan-2-(5*H*),1′(2′*H*)-naphthalene]-2,5-dione[1])

by **Daniel Berney** and **Karlheinz Schuh**

Wander Research Institute (a *Sandoz* Research Unit), CH-3001 Berne, Switzerland

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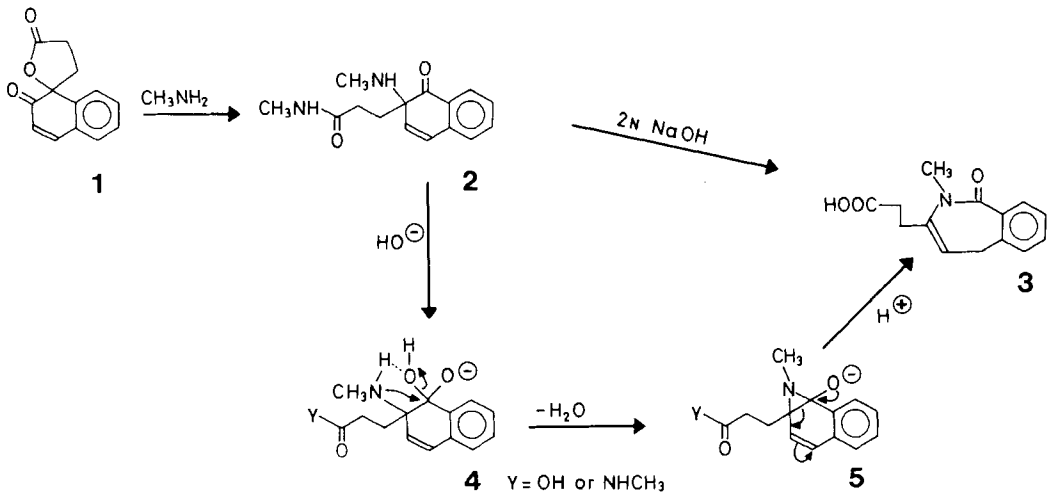
Summary

Compound **2** was rearranged on treatment with 2N NaOH to the 2-benzazepine-3-propanoic[2]) acid **3**. Some aspects of the chemistry of this acid were studied.

Introduction. – We have reported the rearrangement of the spirolactone **1** to the methylaminonaphthalenone **2** which was cyclized by 2N HCl to give a spirolactam [1]. We now report the rearrangement of **2** by 2N NaOH to the 2-benzazepine-3-propanoic acid **3**. A few transformations of **3** are also discussed.



1 2 3 4 5

[1]) This work was presented at the 7th International Congress of Heterocyclic Chemistry at Tampa (Fla.) USA, August 12–17, 1979.

[2]) See footnote 5) of the preceding paper.

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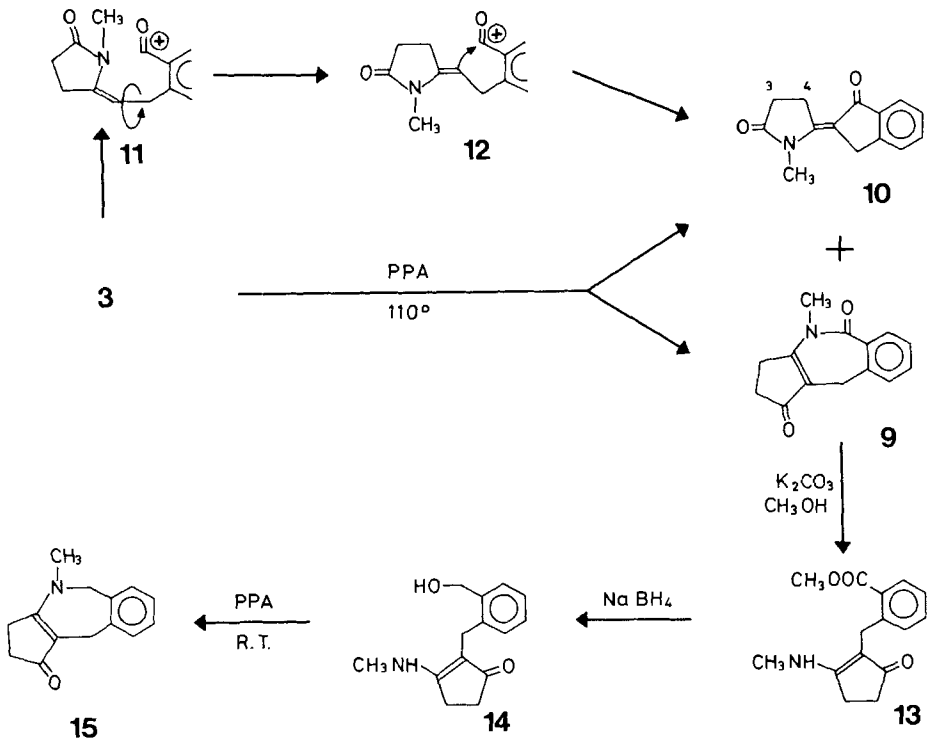
Results. – On treatment with 2N NaOH compound **2** gave the benzazepine **3**, probably through the intermediates **4** and **5**. The ^{1}H-NMR. spectrum of **3** shows a triplet at δ 5.7 ppm corresponding to the olefinic H–C(4)[3]).

Compound **3** was cyclized with polyphosphoric acid (PPA) to give a 4:1 ratio of the expected benzo[*e*]cyclopent[*b*]azepine-1,5-dione[4]) **9** and a product which presumably has structure **10**. The formation of **10** may be explained *via* **11** and **12**.



The NMR. spectrum of **9** is similar to that of **3** except for the absence of the signals corresponding to the olefinic proton and for a slight shift to lower field of the signals corresponding to the non-aromatic protons. The spectrum of **10**

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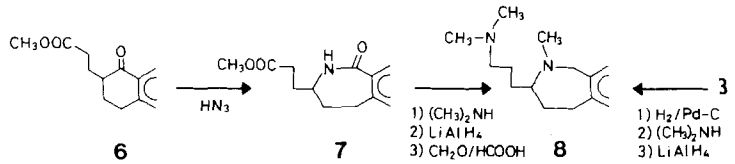
[3]) A rigorous structural proof of **3** was provided by the transformation of both compounds **3** and **6** into the 2-benzazepine-3-propanamine[5]) **8** dihydrochloride, m.p. 230–233°.



[4]) Cyclopenta[*c*][2]benzazepine-1,5-dione.

[5]) 2-Benzazepine-3-propylamine.

presents a similar pattern, but the chemical shifts are quite different from those of **3** and **9**, benzylic protons appearing at δ 4.1 ppm instead of at 3.2 and 3.5 ppm as in the spectra of **3** and **9**, respectively. This difference is in agreement with the structure of **10**, being strained and planar in contrast to those of **3** and **9**. The four protons of the cyclopentenone ring in structure **9** appear between 2.3 and 2.9 ppm, these shifts being comparable with those of 3-pyrrolidino-2-cyclopenten-1-one, the protons of which appear between 2.25 and 2.70 ppm [2].

In the spectrum of the planar structure **10**, the corresponding four protons, which are included in a type of vinylogous succinimide, appear as two sets of multiplets: one centered at 2.6 ppm which accounts for 2 H–C(3) and the other at 3.5 for 2 H–C(4), the latter pair being deshielded by the indanone carbonyl group. Compared to the less rigid isomer **9**, compound **10** has, as would be expected, a much higher m.p. and a much lower solubility.

The 2,3,4,10-tetrahydrobenzo[*e*]cyclopent[*b*]azepine-1,5-dione[6]) **9** was opened with $MeOH/K_2CO_3$ to give the methyl ester **13** which was then reduced with $NaBH_4$ to the benzylic alcohol **14**. The benzazepine **15** was obtained by cyclization of **14** in PPA.

We thank *A. Horisberger* for his excellent experimental assistance.

Experimental Part

For general remarks on ^{1}H-NMR. spectra see [3].

*2,5-Dihydro-2-methyl-1-oxo-1*H*-2-benzazepine-3-propanoic acid*[7]) (**3**). Compound **2** (20 g, 0.077 mol) was suspended in 2N NaOH (400 ml) and MeOH (40 ml). The mixture was heated 3 h under reflux, then cooled, acidified and extracted with $CHCl_3$. The organic extract was dried and evaporated to dryness. The residue was crystallized from $CHCl_3$/ether to give 16.5 g (87%) of the acid **3**; m.p. 128–132°. – ^{1}H-NMR.: 3.3 (*s*, CH_3N); other signals discussed in the text.

$C_{14}H_{15}NO_3$ (245.3) Calc. C 68.6 H 6.2 N 5.7% Found C 68.3 H 6.4 N 5.7%

2,3,4,10-Tetrahydro-4-methyl-benzo[e]cyclopent[b]azepine-1,5-dione[8]) (**9**) *and 5-(1,3-Dihydro-1-oxo-2*H*-inden-2-yliden)-1-methyl-2-pyrrolidinone*[9]) (**10**). Compound **3** (50 g, 0.2 mol) was heated 45 min at 110° in PPA (750 g). The mixture was poured into water and extracted with $CHCl_3$, and the extract was dried and evaporated to dryness. The residue crystallized from $CHCl_3$/ether to give 7.5 g (16%) of **10**; m.p. 282–285°. – ^{1}H-NMR.: 3.2 (*s*, CH_3N), other signals discussed in the text.

$C_{14}H_{13}NO_2$ (227.3) Calc. C 74.0 H 5.8 N 6.2% Found C 74.1 H 6.1 N 6.2%

The mother liquor was evaporated and treated with $CHCl_3$/petroleum ether to afford 35 g (76%) of **9**; m.p. 153–156°. – ^{1}H-NMR.: 3.5 (*s*, CH_3N), other signals discussed in the text.

$C_{14}H_{13}NO_2$ (227.3) Calc. C 74.0 H 5.8 N 6.2% Found C 74.0 H 5.9 N 6.2%

Methyl 2-[(2-(methylamino)-5-oxo-1-cyclopenten-1-yl)methyl]benzoate (**13**). Compound **9** (3 g, 13.2 mmol) was suspended in MeOH (200 ml) and a 50% aqueous solution of K_2CO_3 (20 ml) was added. The mixture was kept at RT. for 15 min, poured into water (500 ml) and extracted with CH_2Cl_2, and the extract was dried and evaporated. The residue was crystallized in ether at −20°; 2.4 g (70%) of **13**

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[6]) 2,3,4,10-Tetrahydrocyclopenta[*c*][2]benzazepine-1,5-dione.

[7]) 2-Methyl-1-oxo-2,5-dihydro-2-benzazepine-3-propanoic acid.

[8]) 4-Methyl-2,3,4,10-tetrahydrocyclopenta[*c*][2]benzazepine-1,5-dione.

[9]) 5-(1-Oxo-1,3-dihydro-2*H*-inden-2-yliden)-1-methyl-2-pyrrolidinone.

were collected; m.p. 141°. – ^{1}H-NMR.: 3.95 (*s*, CO_2CH_3); 3.7 (*s*, CH_2 benzylic); 2.9 (*d*, CH_3N, collapses to *s* after D_2O exchange); 2.5 (*s*, CH_2CH_2).

$C_{15}H_{17}NO_3$ (259.3) Calc. C 69.5 H 6.6 N 5.4% Found C 69.4 H 6.7 N 5.5%

2-([2-(Hydroxymethyl)phenyl]methyl)-3-(methylamino)-2-cyclopenten-1-one (**14**). Compound **13** (18 g, 0.069 mol) was dissolved in diglyme (400 ml), $NaBH_4$ (10.5 g, 0.28 mol) was added and the mixture was heated to 80° for 8 h. After 6 h at RT. the volume of solvent was reduced under reduced pressure, water was added and the mixture extracted with $CHCl_3$, and the extract was dried and evaporated to dryness. The residue crystallized from $CHCl_3$/ether to give 6.75 g (42%) of the benzylic alcohol **14**; m.p. 186–187°. – ^{1}H-NMR.: 4.7 (*s*, CH_2O); 3.5 (*s*, $ArCH_2C=$); 2.8 (*d*, CH_3N, collapses to *s* after D_2O exchange); 2.4 (*s*, CH_2CH_2).

$C_{14}H_{17}NO_2$ (231.3) Calc. C 72.7 H 7.4 N 6.1% Found C 72.7 H 7.4 N 6.1%

3,4,5,10-Tetrahydro-4-methyl-benzo[e]cyclopent[b]azepine-1(2H)one[10]) (**15**). Compound **14** (6.6 g, 0.029 mol) was stirred in PPA (70 g) at RT. for 5 h. The mixture was then poured into cold H_2O, made alkaline with NaOH, extracted with $CHCl_3$, and the extract was dried and evaporated to dryness. The residue crystallized from hexane to give 5.2 g (85%) of **15**; m.p. 126–128°. – ^{1}H-NMR.: 7.3 (*s*, 4 arom. H); 5.2 (*s*, CH_2N); 3.8 (*s*, $ArCH_2C=$); 3.2 (*s*, CH_3N); 2.4 (*s*, CH_2CH_2).

$C_{14}H_{15}NO$ (213.3) Calc. C 78.8 H 7.1 N 6.6% Found C 78.7 H 7.0 N 6.6%

REFERENCES

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[2] *E.J. Cone, R.H. Garner & W. Hayes*, J. org. Chemistry *37*, 4436 (1972).
[3] *D. Berney & K. Schuh*, Helv. *61*, 1262 (1978).

[10]) 4-Methyl-3,4,5,10-tetrahydro-2*H*-cyclopenta[*c*][2]benzazepine-1-one.