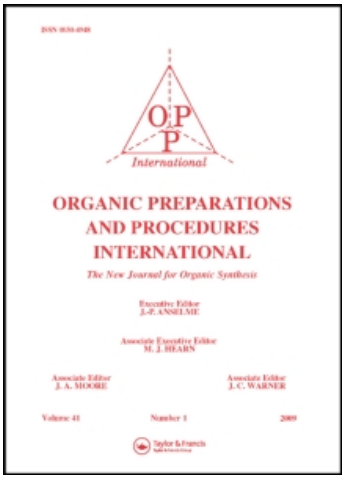


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

AMIDES OF (1-AZULYL)ACETIC AND (1-AZULYL)GLYOXYLIC ACIDS

Arthur G. Anderson Jr.[a]; Robert D. Breazeale[a]
[a] Department of Chemistry, University of Washington, Seattle, Washington

To cite this Article Anderson Jr., Arthur G. and Breazeale, Robert D.(1969) 'AMIDES OF (1-AZULYL)ACETIC AND (1-AZULYL)GLYOXYLIC ACIDS', Organic Preparations and Procedures International, 1: 3, 177 — 182
To link to this Article: DOI: 10.1080/00304946909458376
URL: http://dx.doi.org/10.1080/00304946909458376

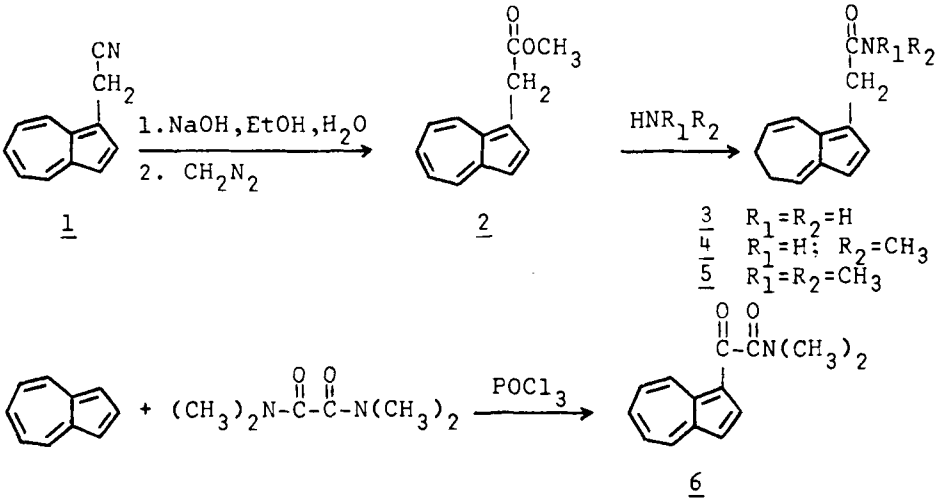
ORGANIC PREPARATIONS AND PROCEDURES 1(3), 177-182 (1969)

AMIDES OF (1-AZULYL)ACETIC AND (1-AZULYL)GLYOXYLIC ACIDS

Arthur G. Anderson, Jr. and Robert D. Breazeale

Department of Chemistry

University of Washington, Seattle, Washington 98105



The amides reported herein are new derivatives of azulene. 1-Cyanomethylazulene (1) was prepared by a modified procedure. Tetramethyloxamide has been prepared by a new method from the readily available oxalyl chloride and dimethylamine.[1]

Experimental[2]

1-Cyanomethylazulene(1).[3] Under anhydrous conditions a stirred solution of 981 mg (3 mmol) of 1-azulylmethyltrimethylammonium iodide and 735 mg (15 mol) of NaCN (dried by

heating over a flame) in 10 ml of CH_3OH (reagent grade dried over 4Å molecular sieves) was heated under reflux for 2 hours, then cooled and diluted with 100 ml of H_2O. The mixture was extracted with ether and the extract was washed twice with H_2O, once with saturated NaCl, and was then dried (Na_2SO_4). Chromatography over basic Al_2O_3 of the residue obtained after removal of the solvent and elution with 1:1 petroleum ether - CH_2Cl_2 gave a minor (30 mg) blue band thought to be 1-methoxymethylazulene[3] and then 360 mg (72%) of 1 as a blue oil having infrared, ultraviolet and visible spectra identical with those reported.[3]

(1-Azulyl)acetamide(3). A solution of 134 mg (0.803 mmol) of 1 in 10 ml of 0.6M NaOH in 50% aqueous ethanol was heated under reflux for 5.5 hr, then cooled (ice bath), diluted with 100 ml of H_2O, and extracted with ether. The pale green extract was discarded. The aqueous fraction was made slightly acidic with 6N hydrochloric acid and then extracted with ether. The extract was washed twice with H_2O, once with saturated NaCl, and was then dried (Na_2SO_4) before treatment with an excess of an ethereal solution of CH_2N_2 at room temperature for 10 min. Excess CH_2N_2 was decomposed with glacial acetic acid and the solution was then filtered through solid sodium carbonate. Chromatography over acidic Al_2O_3 of the residue obtained after removal of the solvent and elution with 1:1 petroleum ether-CH_2Cl_2 gave 143 mg (89%) of a blue oil thought to be methyl (1-azulyl)acetate (2): uv (cyclohexane) (Dmax) 232 (0.75), 275 (1.0), 285 (0.95), 298 (0.18), 342 (0.09), and 358 mμ (0.07); visible (cyclohexane) (Dmax)

570 (1.19), 591 (1.45), 617 (1.25), 645 (1.28), 680 (0.58), and 714 mμ (0.55).

A solution of 272 mg (1.36 mmol) of the product formulated as 2 in 20 ml of 1:1 CH_3OH-conc. NH_4OH was allowed to stand in a closed flask at room temperature for 40 hr, then diluted with 100 ml of H_2O and extracted with ether. The aqueous portion was somewhat blue after several extractions and so was made slightly acidic and then extracted further. This second, blue extract was washed with H_2O, dried (Na_2SO_4), and then treated with an excess of an ether solution of CH_2N_2. Concentration and chromatography as described above afforded 51 mg (15%) of material formulated as 2. The first extract (of the basic solution) was washed with H_2O, saturated NaCl, and dried (Na_2SO_4). Chromatography over basic Al_2O_3 (deactivated with 10% H_2O by weight) of the residue obtained by removal of the solvent gave a small amount of a red-violet oil (CH_2Cl_2 eluent) and then 159 mg (63%, 78% net) of 3 as a blue solid, mp 160-161°: uv (ethanol) (Dmax) 230 (0.81), 277 (0.94), 282 (0.86), 342 (0.09), and 357 mμ (0.05); visible (ethanol) (Dmax) 590 (0.67), 640 (0.55 sh), and 708 mμ (0.19 sh).

Anal. Calcd for $C_{12}H_{11}NO$: C, 77.84; H, 5.94; N, 7.57. Found: C, 77.92; H, 6.06; N, 7.49.

N-Methyl(1-azulyl)acetamide(4). A solution of 125 mg (0.625 mmol) of the intermediate formulated as 2, and obtained as described for the preparation of 3, in 10 ml of 1:1 CH_3OH - 40% aqueous CH_3NH_2 was allowed to stand at room temperature for 37 hr in a stoppered flask, then diluted with 100 ml of

H_2O and extracted with CH_2Cl_2. The extract was washed with saturated NaCl, dried (Na_2SO_4), and the solvent was removed. Chromatography over basic Al_2O_3 and elution with CH_2Cl_2 gave a trace of a violet oil. Ether then removed 109 mg (88%) of 4 which was obtained as blue needles, mp 111.5-113°: uv (ethanol) (Dmax) 230 (0.70), 278 (1.00), 282 (0.90), 342 (0.09), and 357 m (0.05); visible (ethanol) (Dmax) 589 (0.73), 640 (0.59, sh), and 708 mμ (0.20, sh).

Anal. Calcd for $C_{13}H_{13}NO$: C, 78.39; H, 6.53; N, 7.03. Found: C, 78.30; H, 6.62; N, 6.95.

N,N-Dimethyl(1-azulyl)acetamide(5). To a solution of 260 mg (1.3 mmol) of the material formulated as 2, and obtained as described for the preparation of 3, in 7 ml of CH_3OH at 0° was added 5 ml of dimethylamine. The stoppered flask was allowed to stand in a refrigerator for 86 hr and then, loosely stoppered, at room temperature for 24 hr. The mixture was worked up as described for 4 and the crude product chromatographed on basic Al_2O_3. Elution with 1:1 petroleum ether - CH_2Cl_2 removed 78 mg of 2, and then 9:1 CH_2Cl_2-ether gave 121 mg (44%, 63% net) of 5 as a blue oil: uv (ethanol) (Dmax) 233 (0.70), 278 (1.46), 282 (1.31), 342 (0.14), and 359 mμ (0.09); visible (ethanol) (Dmax) 592 (1.70), 644 (1.40), and 711 mμ (0.49).

Anal. Calcd for $C_{14}H_{15}NO$: C, 78.87; H, 7.04. Found: C, 78.86; H, 7.23.

N,N,N',N'-Tetramethyloxamide.[1] A solution of 20 ml (30 g, 0.236 mol) of oxalyl chloride in 30 ml of benzene was added dropwise to a stirred solution of 66 ml (45 g, 1.0 mol) of

anhydrous dimethylamine in 50 ml of benzene at -5° over a 3-hr period. Toward the end of this time the solution became so viscous that stirring was no longer possible. After an additional hour in the cold, 100 ml of H_2O was added carefully. The layers were separated and the aqueous fraction was washed with benzene.[4] The aqueous solution was made slightly basic with 10% NaOH and then extracted continuously with ether for one week. Removal of the ether solvent and recrystallization of the product from CH_2Cl_2 gave 20.5 g (60%) of tetramethyloxamide as colorless needles, mp 78-80° (lit.[1] mp 80°).

N,N-Dimethyl(1-azulyl)glyoxylamide(6). Under anhydrous conditions, to a cooled (0°), stirred solution of 1.28 g (10 mmol) of azulene and 2.88 g (20 mmol) of tetramethyloxamide in 15 ml of dry tetrahydrofuran was added dropwise 1.1 ml (12 mmol) of $POCl_3$. The mixture was stirred for 20 min at 0°, 30 min at room temperature, and then 3 hr under reflux. The cooled solution was poured into 100 ml of H_2O, made slightly basic with 10% KOH, and then extracted four times with CH_2Cl_2.[5] The red aqueous layer was continuously extracted with ether for 4 days and the residue from the dried (Na_2SO_4) extract was chromatographed over basic alumina. Elution with ether gave 459 mg (20%) of 6 as a red solid, mp 134-135°: uv (ethanol) (Dmax) 261 (0.21), 300 (0.33, sh), 310 (0.37), 380 (0.12), and 395 mμ (0.12); visible (ethanol) 512 mμ.

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 74.01; H, 5.72; N, 6.17. Found: C, 73.84; H, 5.81; N, 6.40.

Acknowledgments.

Support by a grant from the National Science Foundation and by a Weyerhaeuser Fellowship (to RDB in 1962-1963) are gratefully acknowledged.

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1. The earlier method utilized the reaction of N,N-dimethylcarbamoyl chloride with sodium: A.P.N. Franchimont and H. A. Rouffaer, Rec. Trav. Chim. Pays-Bas, 13, 331 (1895). A more recent preparation from ethyl oxalate and dimethylamine is reported to give 90.6% yield and would be more convenient if the pressure vessel required were available: J. K. Lawson, Jr. and J. A. T. Croom, J. Org. Chem., 28, (1963).
2. Yields for 1, 3, 4 and 5 are the optima achieved after several trial experiments; that for 6 is from one experiment.
3. For the earlier procedure, see A. G. Anderson, Jr., R. G. Anderson, and T. S. Fujita, J. Org. Chem., 27, 4535 (1962).
4. Concentration of the combined benzene fractions gave ca. 1 g of yellow semi-solid which was not investigated.
5. Chromatography of the residue from the CH_2Cl_2 extracts over basic alumina indicated the presence of an uncharacterized green material plus smaller amounts of azulene and 6, but a good separation was not obtained.

(Received April 3, 1969)