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SYNTHESIS OF ANTI-[2,2] (2,6) AZULENOPHANE FROM 5-METHYLTROPOLONE

Nobuo Kato, Yoshimasa Fukazawa and Shô Itô*

Department of Chemistry, Tohoku University

Sendai 980, Japan

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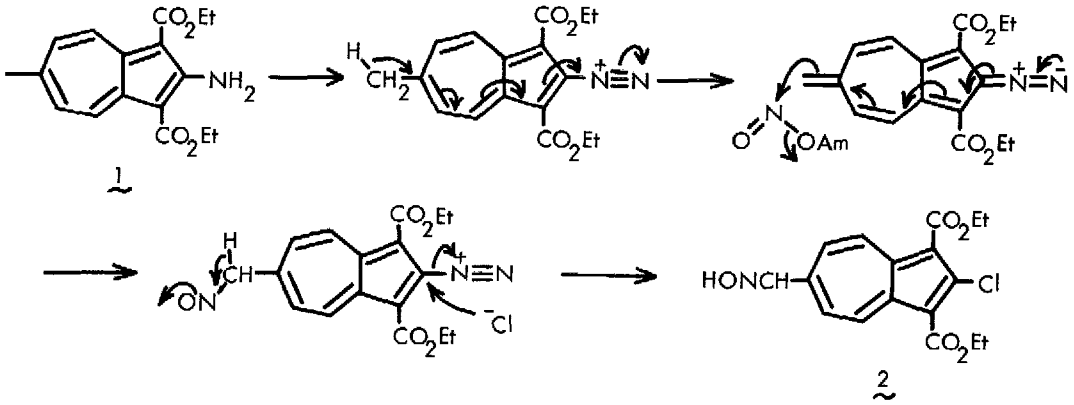
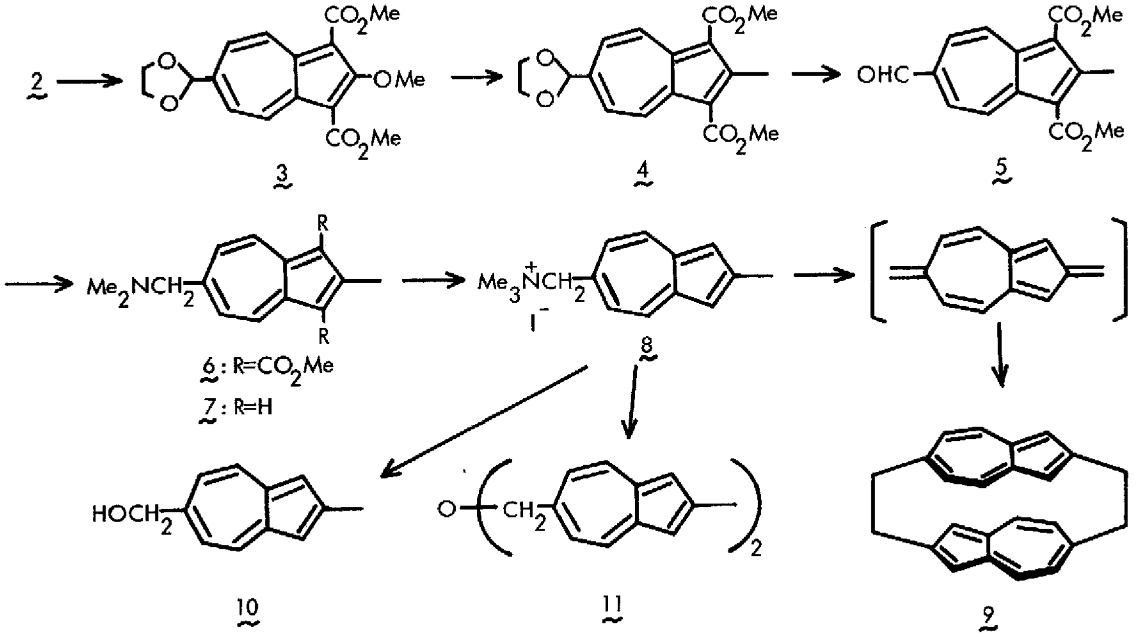
Transannular interaction between two benzene rings in cyclophanes attracted much attention and many papers appeared concerning the synthesis of phanes incorporating various benzenoid and heteroaromatic rings (1). Interested in the possible transannular *interaction in [2,2] azulenophane, in which two dipolar* azulene rings are facing each other, we have completed the synthesis starting from 5-methyltropolone (2), utilizing the Nozoe's azulene synthesis (3). Although the synthesis was reported very recently by Luhowy and Keehn (4), we present herein our result because the approach is different from theirs and involves some interesting transformation in azulene chemistry.

The methyl group in 2-amino-1,3-diethoxycarbonyl-6-methylazulene 1 (5) was functionalized by 2 moles of isoamyl nitrite to result in the chloroaldoxime 2, reddish violet needles, m.p. 226-227° (dec.) in 74% yield (6). Elimination of methyl hydrogen should have been facilitated by the three electron-attractive groups present in the 5-membered ring.





2 was converted (i NaOMe/MeOH, ii CH_2N_2, iii H^+, iv $HO(CH_2)_2OH$) to the 2-methoxy acetal 3, red plates, m.p. 89-90°, in 65% yield.

Reaction of methylmagnesium iodide with 3 afforded the 2-methylazulene 4, dark red granules, m.p. 114-115° in 65% yield (7), which on acid hydrolysis yielded the formyl azulene 5, dark green needles, m.p. 187-188° (96% yield). 5 was converted (i $NaBH_4$, CH_3NH_2, ii HCO_2H, HCHO) to the 6-dimethylaminomethyl derivative 6, orange scales, m.p. 105-106°, in 77% yield, which on treatment with phosphoric acid (at 120° for 30 min.) afforded 6-dimethylaminomethyl-2-methylazulene 7, violet plates, m.p. 39-40° in 85% yield. Methylation of 7 to 8, blue needles, d.p. 220° (95% yield) and the subsequent Hofmann degradation (ion-exchange resin, Δ) yielded, after recrystallization from $CHCl_3$, or SiO_2 chromatography, the desired azulenophane 9, greenish blue prisms, m.p. >300° in 11% yield. The spectral properties of 9 are identical with those reported by Luhowy and Keehn (4). Furthermore, the fact that the PMR spectrum, particularly AA'BB' pattern due to the bridging methylenes is unchanged at higher temperature, reinforces the evidence reported for structure assignment of 9. The other products in the last reaction were 6-hydroxymethyl-2-methylazulene 10, violet scales, m.p. 134-135° (20% yield) and the corresponding diazulenylmethylether **11**, violet microcrystals, m.p. 189-192° (14% yield), probably formed by the direct nucleophilic substitution.

All the compounds described in this paper gave correct elemental analyses and properly characterized by UV, IR and PMR spectra as well as mass spectra. Some of them are recorded below (8).

Thus, this route constitutes the second synthesis of anti-[2,2] (2,6) azulenophane.

2: m/e 349, 351 (3:1, M$^+$), 332 (b.p.), ν 3335, 3000, 1665, 1445, 1212 cm^{-1}, λmax 239 nm (log ε 4.45), 269 (4.11), 326 (4.76), 360 (4.21), 383 (4.15), 520 (2.83), δ (DMSO-d$_6$) 12.22 (1H, br.s), 9.25 (2H, br.d, J=11.5), 8.39 (1H, br.s), 8.09 (2H, br.d, J=11.5), 4.42 (4H, q, J=7.2), 1.42 (6H, t, J=7.2).

3: m/e 346 (M$^+$, b.p.), ν 2950, 2900, 1676, 1442, 1202 cm^{-1}, λmax 237 nm (log ε 4.44), 265 (4.24), 297 sh (4.67), 309 (4.78), 345 (3.85), 362 sh (3.78), 476 (2.58), δ 9.45 (2H, br.d, J=11.5), 7.83 (2H, br.d, J=11.5), 5.94 (1H, br.s), 4.17 (3H, s), 4.13 (4H, m), 4.00 (6H, s).

4: m/e 330 (M$^+$, b.p.), ν 2950, 2880, 1675, 1441, 1197 cm^{-1}, λmax 238 nm (log ε 4.49), 271 (4.33), 297 (4.68), 308 (4.79), 344 (3.89), 355 sh (3.79), 370 (3.77), 503 (2.65), δ 9.52 (2H, br.d, J=11.5), 7.83 (2H, br.d, J=11.5), 5.96 (1H, br.s), 4.15 (4H, br.s), 4.00 (6H, s), 3.03 (3H, br.s).

5: m/e 286 (M$^+$), 255 (b.p.), ν 2960, 1702, 1680, 1440, 1201 cm^{-1}, λmax (CHCl$_3$) 252 nm (log ε 4.50), 309 (4.73), 320 (4.86), 350 sh (3.86), 367 (3.99), 570 (2.59), δ 10.21 (1H, s), 9.63 (2H, br.d, J=11.5), 8.13 (2H, br.d, J=11.5), 4.03 (6H, s), 3.05 (3H, br.s).

6: m/e 315 (M$^+$), 272 (b.p.), ν 2960, 2830, 2770, 1677, 1443, 1200 cm^{-1}, λmax 236.5 nm (log ε 4.48), 272 (4.35), 298 (4.67), 309 (4.78), 346 (3.92), 355 (3.85), 371 (3.79), 494 (2.70), δ (CCl$_4$) 9.41 (2H, br.d, J=11.5), 7.67 (2H, br.d, J=11.5), 3.93 (6H, s), 3.58 (2H, br.s), 2.95 (3H, br.s), 2.26 (6H, br.s).

7: m/e 199 (M$^+$), 58 (b.p.), ν 2945, 2760, 1580, 1505, 1404, 1021, 822 cm^{-1}, λmax 238 nm (log ε 4.23), 267 sh (4.56), 276 (4.88), 281 sh (4.86), 285 (4.95), 305 (3.82), 333 (3.73), 348 (3.82), 360 sh (2.95), 565 (2.46), 610 sh (2.38), δ (CCl$_4$) 8.03 (2H, br.d, J=11.5), 7.14 (2H, br.d, J=11.5), 7.03 (2H, br.s), 3.47 (2H, br.s), 2.62 (3H, br.s), 2.23 (6H, s).

9: m/e 308 (M$^+$), 154 (b.p.), ν 2910, 2850, 1567, 1400, 877, 800, 618 cm^{-1}, λmax (CHCl$_3$) 278 nm (log ε 4.89), 310 sh (4.02), 345 sh (3.50), 367 (3.48), 606 (2.65), δ 7.58 (4H, dd like), 6.40 (4H, s), 6.38 (4H, dd like), 3.18 (8H, AA'BB').

10: m/e 172 (M$^+$, b.p.), ν 3275, 2850, 1582, 1415, 1011, 825 cm^{-1}, λmax 235 nm (log ε 4.16), 266 sh (4.44), 276 (4.80), 282 (4.78), 286 (4.87), 304 sh (3.79), 332 (3.63), 348 (3.73), 358 sh (3.08), 555 (2.49), 594 sh (2.44), δ 8.16 (2H, br.d, J=11), 7.27 (2H, s), 7.10 (br.d, J=11), 5.07 (2H, br.s), 2.63 (3H, br.s).

11: m/e 326 (M^+), 155 (b.p.), ν 2910, 2830, 1583, 1411, 1340, 1141, 830 cm^{-1}, λmax ($CHCl_3$) 279 nm sh (log ε 4.85), 286 sh (4.93), 297 (5.07), 335 (3.99), 350 (4.10), 362 sh (3.58), 556 (2.79), 596 sh (2.74), δ 8.16 (2H, br.d, J=11), 7.35 (2H, s), 7.07 (br.d, J=11), 5.04 (2H, br.s), 2.62 (3H, br.s).

References and Notes

1) Cf. R.W. Griffin, Jr., *Chem. Rev.*, **63**, 45 (1963). B.H. Smith, "Bridged Aromatic Compounds", Academic Press, New York (1964). D.J. Cram and J.M. Cram, *Accounts Chem. Res.*, **4**, 204 (1971). F. Vögtle, *Angew. Chem. Intern. Ed.*, **11**, 73 (1972). *Idem, Synthesis,* 85 (1973). D.J. Cram, R. B. Hornby, E.A. Truesdale, H.J. Reich, M.H. Delton and J.M. Cram, *Tetrahedron*, **30**, 1757 (1974). S. Misumi, *Kagaku no Ryoiki* (Japanese), **28**, 927 (1974).

2) S. Seto and K. Ogura, *Bull. Chem. Soc. Japan*, **32**, 493 (1959).

3) T. Nozoe, S. Seto and S. Matsumura, *Proc. Japan Acad.*, **28**, 438 (1959). T. Nozoe, S. Matsumura, Y. Murase and S. Seto, *Chem. and Ind.*, 1257 (1955). T. Nozoe, S. Seto, S. Matsumura and Y. Murase, *Bull. Chem. Soc. Japan*, **35**, 1179 (1962). T. Nozoe, K. Takase and N. Shimazaki, *Ibid.*, **37**, 1644 (1964). T. Nozoe, K. Takase, T. Nakazawa and S. Fukuda, *Tetrahedron*, **27**, 3357 (1971).

4) R. Luhowy and P.M. Keehn, *Tetrahedron Letters*, 1043 (1976).

5) H. Akino, *Sci. Rept. Fac. Lit. Sci., Hirosaki Univ.*, **11**, 18 (1964). We have synthesized this compound in 62% yield from 5-methyltropolone via 2-fluoro-5-methyltropone, colorless needles, m.p. 55-55.5°.

6) This reaction was also disclosed by K. Takase and T. Morita. (Prof. Takase, Tohoku University, private communication).

7) Replacement of methoxy group at C-2 by an alkyl or a phenyl group has been reported. N. Abe, Ph.D. Thesis, Tohoku University (1974). Also see N. Abe and K. Takase, *Tetrahedron Letters*, 4739, (1973).

8) The spectra were recorded under the following conditions unless otherwise stated. IR (ν): KBr disk, UV(λmax): methanol solution, PMR (δ): $CDCl_3$ solution.