

RING TRANSFORMATION OF 1-AZADIBENZO[c,f]BICYCLO[3.3.1]NONA-3,6-DIENES:
NOVEL ROUTES TO DIBENZOPYRROLIZIDINE AND DIBENZOTROPANE

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Abstract— Base-induced reactions of N-methyl quaternary salts of 11b-methyl-7,11b-dihydro-5H-isoindolo[2,3-b]isoindole (4), which were effectively transformed from readily available 1-azadibenzo[c,f]bicyclo[3.3.1]nona-3,6-dienes (1), were examined and consequently, 5,12-dimethyl-5,10-imino-10,11-dihydro-5H-dibenzo[a,d]cycloheptens (6) and 6,10b-dimethyl-5,6,6a,10b-tetrahydrobenzo[3,4]cyclobut[1,2-c]isoquinolines (7) were obtained via Stevens rearrangement.

Recently we have developed a facile synthesis of 1-azadibenzo[c,f]bicyclo[3.3.1]nona-3,6-dienes (1)^{1a-c} optionally substituted at suitable positions and successfully transformed them into other heterocycles (isopavine², pavine³ alkaloids, and so on). We wish to describe here efficient and preparatively useful routes to isoindolo[2,3-b]isoindole (dibenzopyrrolizidine), 5,10-iminodibenzo[a,e]cycloheptene (dibenzotropane) and benzo[3,4]cyclobut[1,2-c]isoquinoline skeletons.

Reaction of N-methyl quaternary salt (2a) of 1a with t-BuOK in t-BuOH gave exo methylene compound (3a)^{1a, 2} as a sole product in 94% yield. Transannular reaction of 3a between double bond and nitrogen atom in refluxing acetic acid followed by treatment with perchloric acid gave crystalline N-methyl quaternary salt of 11b-methyl-7,11b-dihydro-5H-isoindolo[2,3-b]isoindole (4a) (X=ClO₄) in 84% yield [4a: mp 193-195°C, Anal. C₁₇H₁₈NC₁₀O₄, ¹H NMR (CF₃COOH) δ 2.03 (3H, s), 3.33 (3H, s), 4.89 (4H, s), 7.43 (8H, s)]⁴. Demethylation of quaternary salt

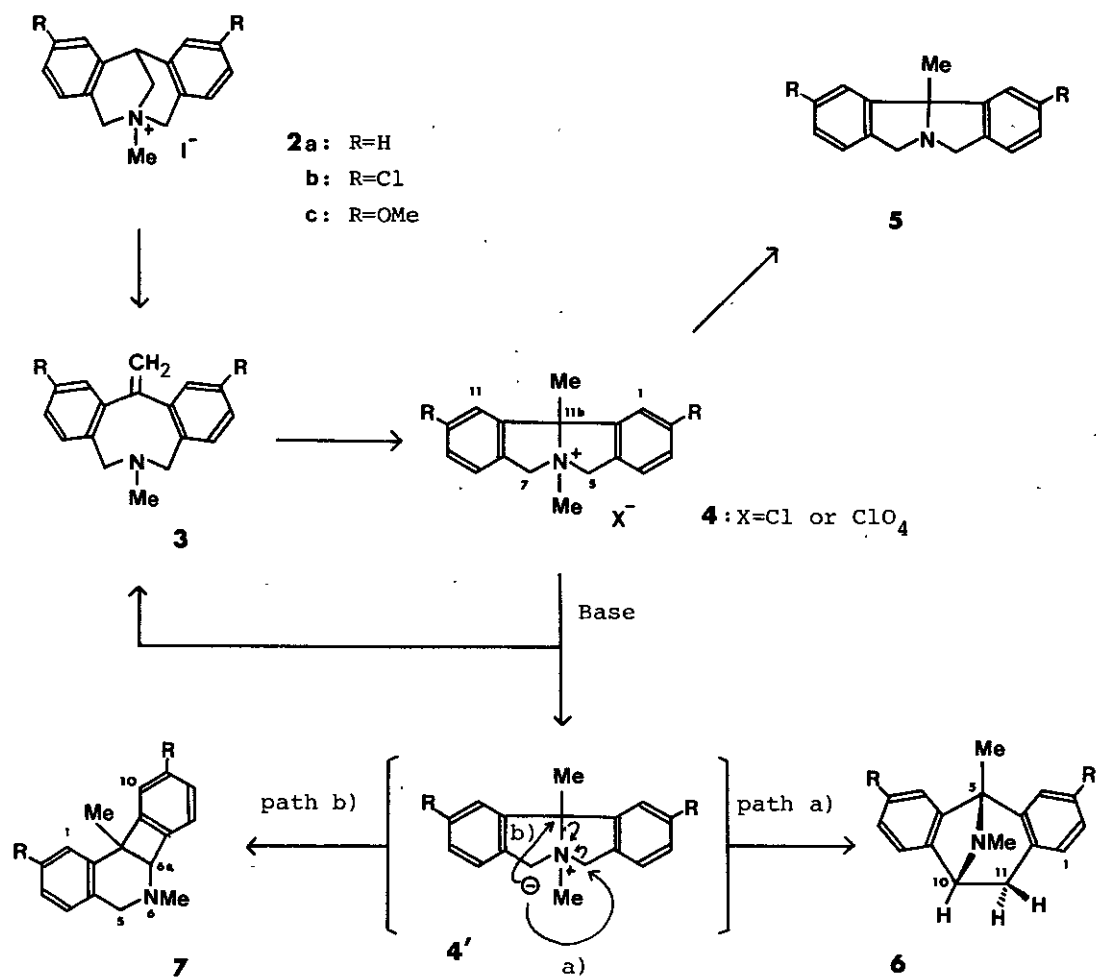


Table 1. Base-induced Reactions of **4a-c** in Dioxane

Entry	4 (R)	Base	Temp. (°C)	Time(h)	Yield(%)		
					6	7	3
1	a (H)	t-BuOK	80	2	57	23	1
2	b (Cl)	t-BuOK	80	2	40	43	0
3	c (OMe)	t-BuOK	80	2	39	16	40
4	a (H)	n-BuLi	r.t.	3	50	11	0
5	b (Cl)	n-BuLi	r.t.	3	30	38	0
6	c (OMe)	n-BuLi	r.t.	3	79	15	0

(4a) with triethylenediamine⁵ in DMF in sealed tube at 165°C for 3 h afforded tertiary amine (5a) in 94% yield [5a: mp 240-243°C (HCl salt), MS m/e 221 (M⁺), ¹H NMR (CDCl₃) δ 1.67 (3H, s), 3.90 and 4.51 (each 2H, d, J=15.0 Hz), 7.10-7.50 (8H, m)].

Further, base-induced reactions of 4 were examined, and pharmacologically active⁶ dibenzotropane derivative, namely, 5,12-dimethyl-5,10-imino-10,11-dihydro-5H-dibenzo[a,d]cycloheptene (6) and isoquinoline derivative containing four membered ring, namely, 6,10b-dimethyl-5,6,6a,10b-tetrahydrobenzo[3,4]cyclobut[1,2-c]isoquinoline (7) were obtained via Stevens rearrangement (path a and b). Structures of 6 and 7 were determined by its spectroscopic data⁷ [6a: mp 70-71°C, MS m/e 235 (M⁺), ¹H NMR (CDCl₃) δ 1.82 (3H, s), 2.35 (3H, s), 2.50 (1H, d, J=17.0 Hz, H-11α), 3.33 (1H, dd, J=17.0, 5.0 Hz, H-11β), 4.33 (1H, d, J=5.0 Hz, H-10), 6.80-7.40 (8H, m). 7a: oil, MS m/e 235 (M⁺), ¹H NMR (CDCl₃) δ 1.84 (3H, s), 2.60 (3H, s), 3.53 (2H, s, H-5), 4.29 (1H, s, H-6a), 6.90-7.65 (8H, m), ¹³C NMR (CDCl₃) δ 24.29 (q, C-CH₃), 42.08 (q, N-CH₃), 49.09 (s, C-10b), 53.11 (t, C-5), 73.52 (d, C-6a)].

In a typical experiment, compound (4a) (X=ClO₄) (1 mmol) in a solution of dioxane (7 ml) containing 1.5 eq. of t-BuOK was heated with stirring at 80°C for 3 h under argon atmosphere. After dilution with water, the reaction mixture was extracted with dichloromethane and the organic layer was dried over Na₂SO₄ and evaporated. The residue was chromatographed on silica gel using ethyl acetate-hexane (1:1) to give 6a (57%), 7a (23%), and trace amounts of Hofmann elimination product (3a) (1%).

Product ratios of the base-induced reactions of 4 were affected by the substituents on benzene ring (Table 1). Although two Stevens rearrangement products (6) and (7) were formed from common intermediate (4'), the data serve to indicate the general trend toward an increasing proportion of 6 (path a) in the order Cl < H < OMe for substituents. Furthermore, reaction of 4c (R=OMe) with t-BuOK in dioxane gave Hofmann elimination product (3c) mainly (entry 3), but reaction with n-BuLi gave selectively Stevens rearrangement products (6c) and (7c) (entry 6).

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- 4) **4b** (X=Cl): 90%, mp >300 °C, Anal. $C_{17}H_{16}NCl_3$.
4c (X=ClO₄): 88%, mp 208-209 °C, Anal. $C_{19}H_{22}NO_6Cl$.
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- 7) **6b**: 1H NMR (CDCl₃) δ 1.79 (3H, s), 2.33 (3H, s, N-CH₃), 2.45 (1H, d, J=17.5 Hz, H-11 α), 3.52 (1H, dd, J=17.5, 5.0 Hz, H-11 β), 4.34 (1H, d, J=5.0 Hz, H-10), 6.75-7.30 (6H, m); **6c**: 1H NMR (CDCl₃) δ 1.86 (3H, s), 2.35 (3H, s, N-CH₃), 2.40 (1H, d, J=17.0 Hz, H-11 α), 3.20 (1H, dd, J=17.0, 5.0 Hz, H-11 β), 3.70 and 3.74 (each 3H, s, OCH₃ X 2), 4.28 (1H, d, J=5.0 Hz, H=10), 6.50-7.25 (6H, m); **7b**: 1H NMR (CDCl₃) δ 1.81 (3H, s, C-CH₃), 2.56 (3H, s, N-CH₃), 3.42 and 3.55 (each 1H, d, J=13.8 Hz, H-5), 4.24 (1H, s, H-6a), 6.90-7.60 (6H, m), ^{13}C NMR (CDCl₃) δ 23.9 (q, C-CH₃), 41.9 (q, N-CH₃), 48.9 (s, C-10b), 52.3 (t, C-5), 72.6 (d, C-6a); **7c**: 1H NMR (CDCl₃) δ 1.82 (3H, s, C-CH₃), 2.58 (3H, s, N-CH₃), 3.50 (2H, s, H-5), 3.72 and 3.84 (each 3H, s, OCH₃ X 2), 4.22 (1H, s, H-6a), 6.50-7.30 (6H, m).

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