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 (isopavine[2], pavine[3] 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=ClO_4) in 84% yield [**4a**: mp 193-195°C , Anal. $C_{17}H_{18}NClO_4$, ^{1}H NMR (CF_3COOH) δ 2.03 (3H, s), 3.33 (3H, s), 4.89 (4H, s), 7.43 (8H, s)][4]. Demethylation of quaternary salt

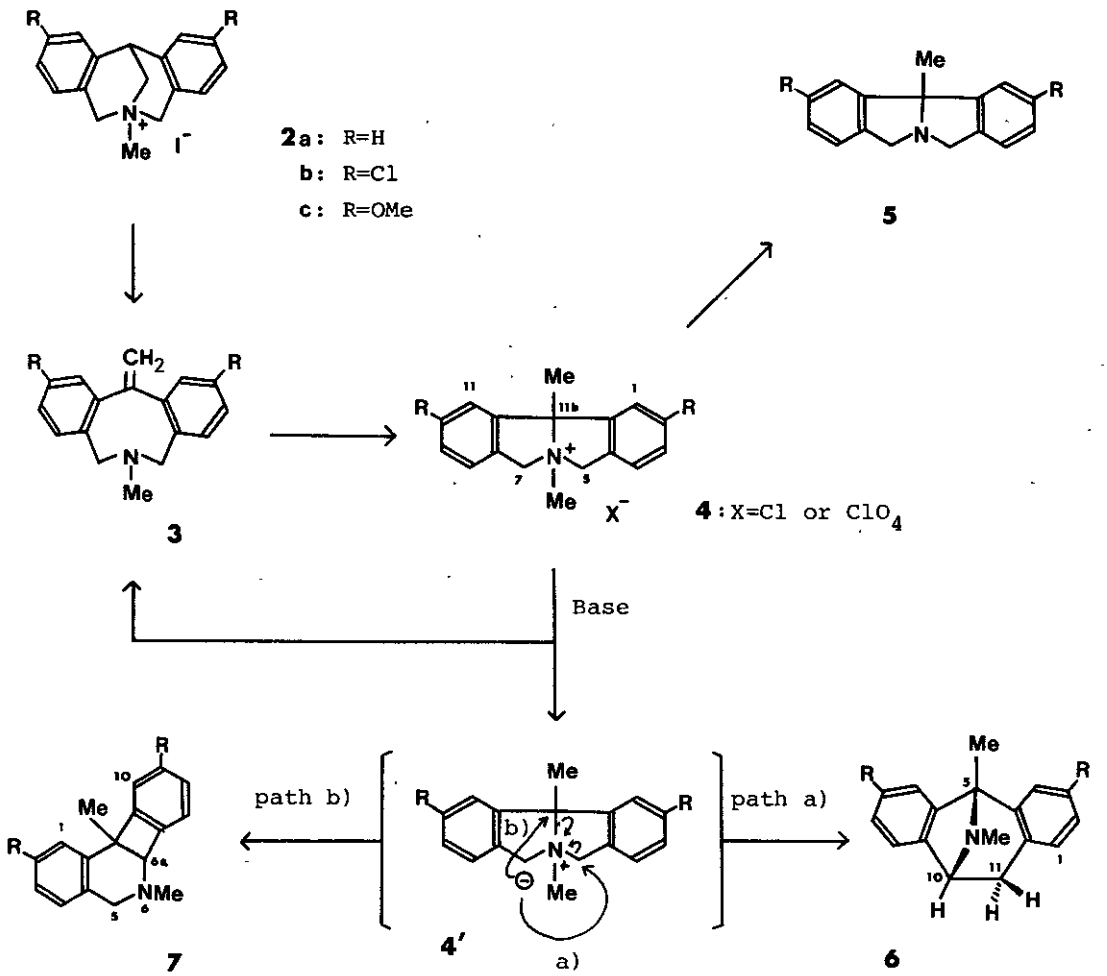

Table 1. Base-induced Reactions of **4a-c** in Dioxane

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 triethylenediamine[5] 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 ($CDCl_3$) 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 active[6] 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 data[7][**6a**: mp 70-71°C , MS m/e 235 (M^+), ^1H NMR ($CDCl_3$) 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 ($CDCl_3$) 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), ^{13}C NMR ($CDCl_3$) δ 24.29 (q, C-CH_3), 42.08 (q, N-CH_3), 49.09 (s, C-10b), 53.11 (t, C-5), 73.52 (d, C-6a)].

In a typical experiment, compound (**4a**) (X=ClO_4) (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 Na_2SO_4 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).

REFERENCES

1) a) H. Takayama, M. Takamoto, and T. Okamoto, Tetrahedron Lett., 1978, 1307. b) H. Takayama, T. Suzuki, M. Takamoto, and T. Okamoto, Heterocycles, 1978, **9**, 1429. c) H. Takayama, T. Suzuki, and T. Nomoto, Chem. Lett., 1978, 856.

2) H. Takayama, T. Nomoto, T. Suzuki, M. Takamoto, and T. Okamoto, Heterocycles, 1978, **9**, 1545.

3) T. Nomoto and H. Takayama, J. Chem. Soc., Chem. Commun., 1982, 1113.

4) **4b** (X=Cl): 90%, mp >300 °C , Anal. $C_{17}H_{16}NCl_3$.
4c (X=ClO_4): 88%, mp 208-209 °C , Anal. $C_{19}H_{22}NO_6Cl$.

5) T-L. Ho, Synthesis, 1972, 702.

6) M. E. Christy, P. S. Anderson, S. F. Britcher, C. D. Colton, B. E. Evans, D. C. Remy, and E. L. Engelhardt, J. Org. Chem., 1979, **44**, 3117 and references cited therein.

7) **6b**: ^{1}H NMR ($CDCl_3$) δ 1.79 (3H, s), 2.33 (3H, s, N-CH_3), 2.45 (1H, d, J=17.5 Hz, H-11α), 3.52 (1H, dd, J=17.5, 5.0 Hz, H-11β), 4.34 (1H, d, J=5.0 Hz, H-10), 6.75-7.30 (6H, m); **6c**: ^{1}H NMR ($CDCl_3$) δ 1.86 (3H, s), 2.35 (3H, s, N-CH_3), 2.40 (1H, d, J=17.0 Hz, H-11α), 3.20 (1H, dd, J=17.0, 5.0 Hz, H-11β), 3.70 and 3.74 (each 3H, s, OCH_3 X 2), 4.28 (1H, d, J=5.0 Hz, H=10), 6.50-7.25 (6H, m); **7b**: ^{1}H NMR ($CDCl_3$) δ 1.81 (3H, s, C-CH_3), 2.56 (3H, s, N-CH_3), 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 ($CDCl_3$) δ 23.9 (q, C-CH_3), 41.9 (q, N-CH_3), 48.9 (s, C-10b), 52.3 (t, C-5), 72.6 (d, C-6a); **7c**: ^{1}H NMR ($CDCl_3$) δ 1.82 (3H, s, C-CH_3), 2.58 (3H, s, N-CH_3), 3.50 (2H, s, H-5), 3.72 and 3.84 (each 3H, s, OCH_3 X 2), 4.22 (1H, s, H-6a), 6.50-7.30 (6H, m).

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