

Iffland's Reaction with Methyl Ketone Oximes of Adamantane Series

N. V. Makarova, I. K. Moiseev, and M. N. Zemtsova

Samara State Technical University, Samara, 443010 Russia

Received December 13, 2000

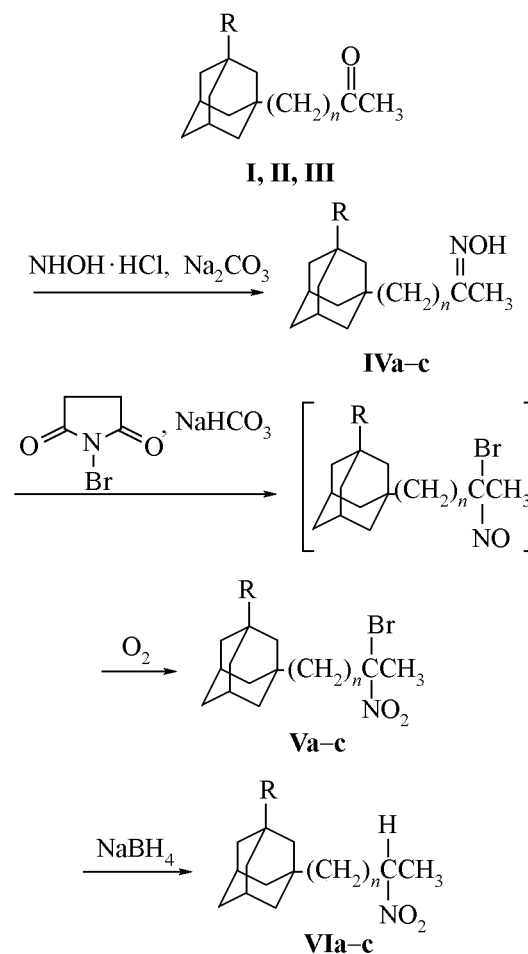
Abstract—Along Iffland's reactions from 1-adamantyl methyl ketone, (1-adamantyl)acetone, 3-hydroxy-1-adamantyl methyl ketone and *N*-bromosuccinimide were obtained the corresponding bromonitro derivatives that on reduction with sodium borohydride afforded 1-(1-adamantyl)-1-nitroethane, 1-(1-adamantyl)-2-nitropropane, and 1-(3-hydroxy-1-adamantyl)-1-nitroethane.

The described syntheses of adamantyl compounds with a nitro group in the side chain are scanty: only reaction of trinitromethyl compounds with 1-adamantyl radical arising on thermolysis of *tert*-butyl 1-adamantylcarboxylates [1] and alkylation of 1-bromoadamantane and its derivatives with trinitromethane silver salt [2] can be cited.

Our previous reports concerned the transformation of aliphatic and alicyclic ketones into chloronitro [3] and dinitro [4, 5] compounds. The best results with sterically hindered oximes were obtained by Iffland's reaction that afforded previously unavailable nitro derivatives of cycloalkanes [6-8]. Iffland's reaction was successfully applied to the synthesis of 2-nitroadamantane and 2,6-dinitroadamantane from 2-adamantanone oximes and 2,6-adamantanedione dioxime [9].

In order to prepare nitro compounds of adamantane series with a nitro group in the side chain we carried out Iffland's reaction with 1-adamantyl methyl ketone (**I**), (1-adamantyl)acetone (**II**), and 3-hydroxy-1-adamantyl methyl ketone (**III**). In the first stage of the process we boiled the original ketones **I-III** with hydroxylamine hydrochloride in 50% aqueous ethanol in the presence of a water solution of Na_2CO_3 to obtain the corresponding oximes **IVa-c** of high purity and in quantitative yield. In the second stage the oximes **IVa-c** were treated with *N*-bromosuccinimide and sodium bicarbonate in 50% aqueous dioxane at 20°C to yield bromonitroso compounds that without isolation were oxidized in air to furnish bromonitro compounds: 1-(1-adamantyl)-1-bromo-1-nitroethane (**Va**), 1-(1-adamantyl)-2-bromo-2-nitropropane (**Vb**), and 1-(3-hydroxy-1-adamantyl)-1-bromo-1-nitroethane (**Vc**). The last stage consisted in reduction of compounds **Va-c** with sodium borohydride in 95%

aqueous methanol at 20°C yielding the following nitro derivatives of adamantane: 1-(1-adamantyl)-1-nitroethane (**VIa**), 1-(1-adamantyl)-2-nitropropane (**VIb**), and 1-(3-hydroxy-1-adamantyl)-1-nitroethane (**VIc**).



$n = 0$, $R = \text{H}$ (**a**); $n = 1$, $R = \text{H}$ (**b**); $n = 0$, $R = \text{OH}$ (**c**).

Table 1. Physical properties of oximes **IVa–c**, bromonitro compounds **Va–c**, and nitro compounds **VIa–c**

Compd. no.	mp, °C	Yield, %	R_f	IR spectrum, ν , cm^{-1}	
				CH_2Ad	other
IVa	181–182	95	0.29 ^a	2900, 2850	1610 (C=N)
IVb	82–84	89	0.71 ^b	2900, 2850	1600 (C=N)
IVc	180–182	95	0.20 ^c	2900, 2850	3300 (OH), 1620 (C=N)
Va	103–105	67	0.49 ^b	2910, 2860	1540, 1350 (NO_2)
Vb	120–121	77	0.72 ^c	2900, 2850	1550, 1350 (NO_2)
Vc	135–136	77	0.52 ^c	2920, 2860	3260 (OH), 1530, 1335 (NO_2)
VIa	40–41	65	0.64 ^c	2910, 2860	1530, 1360 (NO_2)
VIb	n_D^{20} 1.4985	91	0.73 ^d	2900, 2850	1570, 1340 (NO_2)
VIc	72–73	30	0.46 ^d	2910, 2860	3290 (OH), 1520, 1360 (NO_2)

Solvent: ^a acetone; ^b hexane–chloroform–acetone, 1 : 1 : 1; ^c acetone– CCl_4 , 1 : 2; ^d acetone– CCl_4 , 1 : 6.

Table 2. ¹H NMR spectra of bromonitro **Va–c** and nitro compounds **VIa–c**, δ , ppm

Compd. no.	$\text{CH}_2(\text{Ad})$	$\text{CH}(\text{Ad})$	CH_3	CHNO_2	Other protons
Va	1.65–1.75 d (12H)	1.98 s (3H)	2.28 s (3H)	–	–
Vb	1.60–1.70 d (12H)	1.90 s (3H)	2.35 s (3H)	–	3.12 s (2H, CH_2)
Vc	1.50–1.58 d (12H)	1.65 s (2H)	2.25 s (3H)	–	4.42 s (1H, OH)
VIa	1.60–1.75 d (12H)	1.80 s (3H)	2.05 d (3H)	4.25 q (1H)	–
VIb	1.65–1.75 d (12H)	1.95 s (3H)	2.10 d (3H)	4.15 m (1H)	3.00 d (2H, CH_2)
VIc	1.55–1.60 d (12H)	1.75 s (2H)	2.18 d (3H)	4.32 q (1H)	4.50 s (1H, OH)

Table 3. Elemental analyses of oximes **IVa–c**, bromonitro **Va–c** and nitro compounds **VIa–c**

Compd. no.	Found, %			Formula	Calculated, %		
	C	H	N		C	H	N
IVa	–	–	–	$\text{C}_{12}\text{H}_{19}\text{NO}$	–	–	–
IVb	–	–	–	$\text{C}_{13}\text{H}_{21}\text{NO}$	–	–	–
IVc	–	–	–	$\text{C}_{12}\text{H}_{19}\text{NO}_2$	–	–	–
Va	50.01	6.00	5.02	$\text{C}_{12}\text{H}_{18}\text{BrNO}_2$	50.01	6.30	4.86
Vb	52.08	6.33	4.49	$\text{C}_{13}\text{H}_{20}\text{BrNO}_2$	51.67	6.67	4.64
Vc	47.50	5.99	4.47	$\text{C}_{12}\text{H}_{18}\text{BrNO}_3$	47.38	5.97	4.61
VIa	69.01	8.99	6.81	$\text{C}_{12}\text{H}_{19}\text{NO}_2$	68.87	9.15	6.69
VIb	69.99	9.50	6.11	$\text{C}_{13}\text{H}_{21}\text{NO}_2$	69.92	9.48	6.27
VIc	64.17	8.52	6.10	$\text{C}_{12}\text{H}_{19}\text{NO}_3$	63.98	8.50	6.22

If the reaction mixture in the last stage is neutralized with acetic acid, the aci forms of nitro compounds **VI** are cleaved into original ketones **I–III**, whereas the use of a milder agent, hydroxylamine hydrochloride, provides nitro compounds **VI** in high yield. Physical properties of compounds **IV–VI** syn-

thesized and their spectral characteristics are presented in Tables 1–3.

Thus we for the first time performed Iffland's reaction with oximes **IV** of methyl ketones belonging to the adamantane series and synthesized nitro derivatives of adamantane **VI**.

EXPERIMENTAL

¹H NMR spectra were registered on spectrometer Bruker AC-300 (300.13 MHz) in DMSO, internal reference HMDS. IR spectra were obtained on spectrometer Specord M-80 from samples pelleted with KBr. The purity of compounds was checked by TLC on Silufol UV-254 plates, development in iodine vapor.

General procedure for oximes IVa-c synthesis.

To a solution of 5.6 mmol of ketone **Ia-III** and 0.43 g (6.2 mmol) of hydroxylamine hydrochloride in 10 ml of ethanol was added a solution of 0.3 g (2.8 mmol) of Na₂CO₃ in 5 ml of water. The reaction mixture was boiled till complete precipitation of oxime, then cooled, the precipitate was filtered off, washed with water, dried, and recrystallized from ethanol.

General procedure for synthesis of bromonitro compounds Va-c.

In 10 ml of 59% aqueous dioxane was dissolved 5.2 mmol of oxime **IV**, and to the solution was added by portions 2.58 g (14.5 mmol) of bromosuccinimide and 1.22 g (14.5 mmol) of NaHCO₃. The reaction mixture turned blue. The mixture was evaporated, the reaction products were extracted into ether, the ether was evaporated till dryness, the precipitate was filtered off and recrystallized from ethanol.

General procedure for synthesis of nitro compounds VIa-c. To a solution of 3.5 mmol of bromonitro compound **V** in 10 ml of methanol was added by small portions 0.45 g (11.9 mmol) of sodium borohydride. After 12 h hydroxylamine hydrochloride was added till neutral reaction, the mixture was diluted with water, the precipitate was filtered off, dried, and recrystallized from ethanol.

REFERENCES

1. Medzhinskii, V.L. and Golod, E.L., *Zh. Org. Khim.*, 1994, vol. 30, no. 5, pp. 699-703, 704-706.
2. Luk'yanov, O.A., Savost'yanova, I.A., Gorelik, V.P., Shlykova, N.I. and Tartakovskii, V.A., *Izv. Akad. Nauk, Ser. Khim.*, 1992, no. 8, pp. 1798-1803.
3. Moiseev, I.K., Mratkuzina, T.A., and Makarova, N.V., *Zh. Obshch. Khim.*, 1999, vol. 69, no. 11, pp. 1855-1857.
4. Moiseev, I.K., Nafikov, G.F., and Makarova N.V., *Zh. Obshch. Khim.*, 1998, vol. 68, no. 4, pp. 645-646.
5. Moiseev, I.K., Mratkuzina, T.A., Balenkova E.S., and Makarova, N.V., *Zh. Org. Khim.*, 1999, vol. 35, no. 6, pp. 863-865.
6. Iffland, D.C., Criner, G.X., and Koral M., *J. Am. Chem. Soc.*, 1953, vol. 75, no. 16, pp. 4044-4046.
7. Iffland, D.C. and Criner, G.X., *J. Am. Chem. Soc.*, 1953, vol. 75, no. 16, pp. 4047-4048.
8. Iffland, D.C. and Ten-Fu, Yen, *J. Am. Chem. Soc.*, 1954, vol. 76, no. 16, pp. 4083-4085.
9. Archibald, T.G. and Baum, K., *J. Org. Chem.*, 1988, vol. 53, no. 20, pp. 4645-4650.