Russian Journal of Organic Chemistry, Vol. 40, No. 5, 2004, pp. 747–750. Translated from Zhurnal Organicheskoi Khimii, Vol. 40, No. 5, 2004, pp. 781–784.
Original Russian Text Copyright © 2004 by Vaganova, Shteingarts.

SHORT COMMUNICATIONS

Reductive Activation of Arenes: XVII.* Effect of Methyl Substituent in Anion-radicals of Tolunitriles on the Mechanism of Their Reaction with Alkyl Bromides in Liquid Ammonia

T.A. Vaganova[1] and V.D. Shteingarts[1,2]

[1] *Vorozhtsov Nobosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences, Novosibirsk, 630090 Russia*
e-mail: shtein@nioch.nsc.ru
[2] *Novosibirsk State University, Novosibirsk, Russia*

Received November 18, 2003

Earlier studies of factors governing the concurrent S_N and ET processes in reactions of arenecarbonitriles anion-radicals with alkyl halides established that the reaction of benzonitrile anion-radical (**Ia**) with primary alkyl halides in liquid ammonia furnished products corresponding to *ipso*-alkylation with respect to cyano group. Inasmuch as with a model reagent, cyclo-propylmethyl bromide, no alkyl fragment isomerisation in the course of the reaction was observed, the reaction was assigned S_N mechanism [2]. Introduction of an additional electron-attracting substituent , a second cyano group, into the *ortho*- or *para*-position of the anion-radical crucially alters the mechanism and associated with it orientation of alkylation: in reactions of terephthalonitrile and phthalonitrile anion-radicals with alkyl halides due to an electron transfer followed by recombination of the anion-radical with an alkyl radical occurs substitution of both cyano group and hydrogen atom.. Therefore among the products of reaction between the above anion-radicals and cyclopropylmethyl bromide are present compounds with isomerized alkyl fragment [3–5]. Incorporation of a methyl group into the *meta*- or *para*-position of benzonitrile anion-radical did not affect the orientation of alkylation in reactions of *m*-tolunitrile (**Ib**) [6] and *p*-tolunitrile (**Ic**) [1] with butyl bromide in liquid ammonia: the resulting products were butylarenes **IIb, c** and cyanobutylcyclohexadienes **IIIb, c** originating from cycnohexadienyl anion **IV** as the common precursor (see scheme).

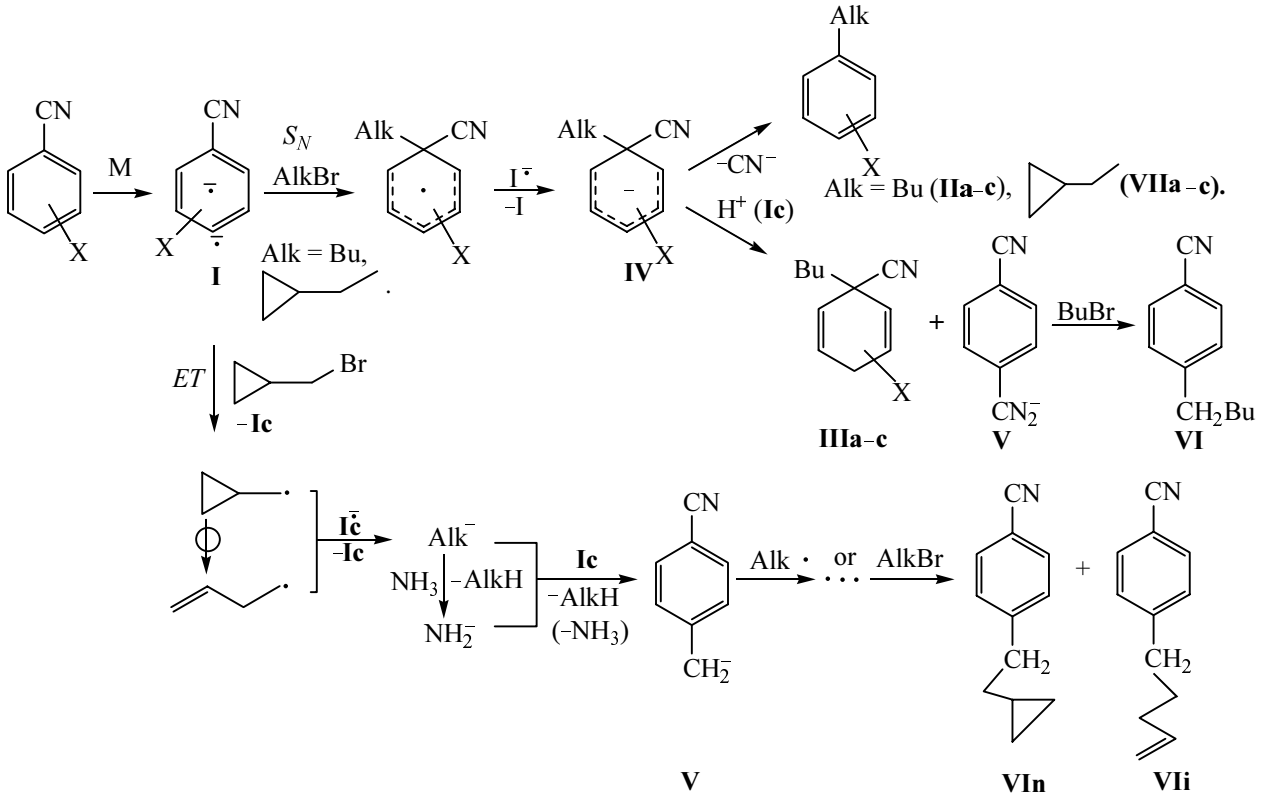
Besides with nitrile **Ic** due to its high CH-acidity formed a product of cyanobenzyl anion **V** alkylation, *p*-amylbenzonitrile (**VI**).

A similar orientation in reaction of nitrile **Ia** anion-radical with cyclopropylmethyl bromide affording benzylcyclopropane (**VIIa**) and in alkylation of anion-radicals from nitriles **Ib, c** with butyl bromide furnishing 1-butyl-substituted compounds **IIb, c** and **IIIb, c** is an indirect evidence of the fact that introducing a methyl group into *meta*- or *para*-position of the arenecarbonitrile anion-radical does not result in a replacement of S_N mechanism with ET one. On the other hand, on the force of electrochemical data it was formerly inferred that tolunitrile anion radicals in reactions with primary alkyl halides showed both nucleophilic (S_N mechanism) and electron-donating (ET mechanism) reactivity [7]. Yet these data do not allow a conclusion on the alkylation orientation inherent to each of concurrent mechanisms.

In extension of these investigations we report here on the study of reaction of anion-radicals generated by sodium action on nitriles **Ib, c** in liquid ammonia (Na–ArCN ratio 9:10, concentration $\leq 10^{-2}$ mol l^{-1}, –33°C), with cyclopropylmethyl bromide applied as a reagent for testing a mechanism. It was established that the reaction of nitrile **Ib** anion-radical gave rise to a product of cyano group replacement, *m*-methylbenzylcyclopropane (**VIIb**) isolated in ~35% yield (maximal possible yield 50%), and no compounds with isomerized alkyl fragment were detected. Taking into account the estimates of

* For communication XVI see [1].

Scheme.



I, X = H (**a**), *m*-CH_3 (**b**), *p*-CH_3 (**c**).

isomerization extent expected at realization of the ET mechanism [2–5] the above experimental data support the assumption [6] that the anion-radical of nitrile **Ib** reacts with the primary alkyl bromides as nucleophile.

In contrast the reaction of nitrile **Ic** anion-radical with cyclopropylmethyl bromide gave the *ipso*-alkylation product, *p*-methylbenzylcyclopropane (**VIIc**) in a low yield (≤3%), and the main products were *p*-(cyclopropylethyl)benzonitrile (**VIn**) (11%) and *p*-(4-pentenyl)benzonitrile (**VIi**) (15%). At a 5-fold increase in the anion-radical concentration the overall yield of nitriles **VIn, i** did not change, but the ratio **VIn/VIi** grew from 0.7 to 1.7. As mentioned before, in reaction of nitrile **Ic** anion-radical with butyl bromide the alkylation at the methyl group providing nitrile **VI** occured simultaneously with formation of diene **IIIc** generated due to protonation by the substrate of anion **IV** followed by alkylation of arising therewith cyanbenzyl anion **V**. Unlike that in the reaction mixture obtained from nitrile **Ic** and cyclopropylmethyl bromide diene of type **III** was lacking. The data obtained apparently suggest that the process takes another route and indicate that probably the S_N mechanism gives way to ET, firstly, in the reaction of anion-radical with cyclopropylmethyl bromide in going from nitriles **Ia, b** to **Ic** and, secondly, in reaction of nitrile **Ic** anion-radical with alkyl bromide in going from butyl bromide to cyclopropylmethyl bromide. In the first case the change in the mechanism is likely caused by the growing electron-attracting ability of the anion-radicals in nitrile series **Ia–c** (cf., for instance, the corresponding values of $-E°$ measured in DMF against standard calomel electrode: 2.23, 2.26, 2.34 [8]). In the second case the reason may be the easier reduction of cyclopropylmethyl bromide compared to butyl bromide due to overlapping of the p-orbital of the lone electron with the quasi-π-system of the cyclopropyl ring [9] in the cyclopropylmethyl radical. The latter arising by electron transfer from the nitrile anion-radical to cyclopropylmethyl bromide transforms further along two concurrent routes: by reaction with the initial anion-radical, and by isomerization into a 3-butenyl radical [10] that in its turn also reacts with the anion-radical. Yet in contrast to analogous reaction of terephthalonitrile anion-radical [3, 4] in this case the alkyl radicals do not undergo recombination with the nitrile **Ic** anion-radical but are reduced therewith giving the corresponding alkyl anions. This difference may originate from either higher

electron-donating capacity of nitrile **Ic** anion-radical compared to anion-radicals of dinitriles or the presence of a methyl group in its *para*-positin where the highest spin density is located [11]. The alkyl anions get protonated either by the initial nitrile **Ic** or more probably by ammonia producing amide anion. In both cases finally arises a cyclobenzyl anion **V** that on alkylation affords **VIn, i**.

We demonstrated by special experiment that anion **V** generated by treating nitrile **Ic** with sodium amide actually reacted with the cyclopropylmethyl bromide furnishing compounds **VIn, i**, and the ratio **VIn/VIi** increased from 17 to 65 at growing reagents concentration from 10^{-2} to 10^{-1} mol l^{-1}. The presence of product **VIi** containing an isomerized alkyl fragment indicates that reaction of anion **V** with cyclopropylmethyl bromide involves at least partially an electron transfer resulting in formation of cyclopropylmethyl radical that undergoes fast isomerization, and thus reaction occurs by S_{RN} mechanism. Examples of concurrent occurrence with the S_N2 mechanism of similar processes initiated by solvated electron are known for reactions with carbaniuons of a number of benzyl and alkyl halides activated by electron-attracting substituent [12]. The difference in the ratio **VIn/VIi** obtained in reaction of cyclopropylmethyl bromide with a specially prepared anion **V** and nitrile **Ic** anion-radical is presumably due to the conciderably lower concentration of anion **V** in the latter case and consequently with a higher degree of cyclopropyl radical isomerization.

Thus the results obtained evidence firstly in favor of mechanism S_N in the previously studied [1, 6] reaction of nitriles **Ib, c** anion-radicals with butyl bromide, and secondly reveal the difference in effects of methyl group from the *meta*- and *para*-positions of benzonitrile anion-radical on its reactivity due apparently to localization in the *para*-position of the main part of the electron density from the lone electron. Whereas in goimg from benzonitrile to *m*-tolunitrile the ratio of anion-radical reactivities with respect to S_N and ET mechanisms does not apparently significantly alter and it behaves as nucleophile in reactions with alkyl bromides, in going to *p*-tolunitrile the electron-donating activity of anion-radical relative its nucleophilic activity increases and thus in reaction with cyclopropylmethyl bromide possessing higher electron affinity than that of n-alkyl bromides the S_N mechanism is replaced by ET one. It was formerly shown that a similar change in mechanism occurred in going from benzonitrile to dicyanoarenes [3–5], and therefore a conclusion was done that the nucleophilic reactivity of anion-radical was stronder suppressed by electron-withdrawing substituent than electron-donating activity. The effect of methyl group discovered in this study suggests that the introduction of an electron-donating substituent increased stronger the activity of arenecarbonitrile anion-radical as one-electron reductant than as nucleophile.

The procedures for generating and alkylating anion-radical are similar to those described in [1, 5]. The cyanobenzyl anion was obtained by adding nitrile **Ic** to a dispersion of sodium amide in liquid ammonia.

Characteristics of individual compounds are as follows:

***p*-(Cyclopropylethyl)benzonitrile (VIn)**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: –0.02–0.06 m (2H), 0.37–0.47 m (2H), 0.53–0.73 m (1H, cyclo-C_3H_5), 1.51 q (2H, C^2H_2, J 8 Hz), 2.75 t (2H, C^1H_2, J 8 Hz), 7.27 d (2H, $H^{3,5}$, J_o 8 Hz), 7.51 d (2H, $H^{2,6}$). Found: M^+ 171.10472. $C_{12}H_{13}N$.. Calculated: M 171.10479.

***p*-(4-Pentenyl)benzonitrile (VIi).** ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.73 m (2H, C^2H_2), 2.08 m (2H, C^3H_2), 2.67 t (2H, C^1H_2, J 8 Hz), 4.94–5.07 m (2H, C^5H_2), 5.70–5.90 m (1H, C^4H), 7.28 d (2H, $H^{3,5}$, J_O 8 Hz), 7.52 d (2H, $H^{2,6}$). Found: M^+ 171.10472. $C_{12}H_{13}N$. Calculated: M 171.10479.

***m*-Methylbenzylcyclopropane (VIIb).** ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.17–0.23 m (2H), 0.46–0.53 m (2H), 0.86–0.96 m (1H, cyclo-C_3H_5), 2.33 s (3H, CH_3), 2.50 d (2H, CH_2, J 8 Hz), 6.98–7.22 m (4H, $H^{2,4,5,6}$). Found: M^+ 146.10966. $C_{11}H_{14}$.. Calculated: M 146.10954.

***p*-Methylbenzylcyclopropane (VIIc).** ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.14–0.20 m (2H), 0.45–0.52 m (2H), 0.81–0.91 m (1H, cyclo-C_3H_5); 2.31 s (3H, CH_3), 2.48 d (2H, CH_2, J 8 Hz), 7.09, 7.13 AB-system (4H, $H^{2,3,5,6}$). Found: M^+ 146.10963. $C_{11}H_{14}$. Calculated: M 146.10954.

^{1}H NMR spectra were registered on spectrometer Bruker WP-200SY, high resolution mass spectra were measured on Finnigan MAT-8200 instrument.

REFERENCES

1. Vaganova, T.A., Starokon', E.V., and Shteingarts, V.D., *Zh. Org. Khim.*, 2003, vol 39, p. 725.
2. Bil'kis, I.I., Vaganova, T.A., Bobyleva, V.I., and Shteingarts, V.D., *Zh. Org. Khim.*, 1991, vol. 27, p. 48.
3. Panteleeva, E., Vaganova, T., Shteingarts, V., and Bilkis, I., *Tetrahedron Lett*., 1995, vol. 36, p. 8465.
4. Bil'kis, I.I., Panteleeva, E.V., Tananakin, A.P., and Shteingarts, V.D., *Zh. Org. Khim.*, 1994, vol. 30, p. 882.
5. Bi'kis, I.I., Panteleeva, E.V., and Shteingarts, V.D., *Zh. Org.*

Khim., 1998, vol. 34, p. 1702.
6. Vaganova, T.A., Starokon', E.V., and Shteingarts, V.D., *Zh. Org. Khim.*, 2002, vol. 38, p. 865.
7. Occhialini, D., Kristensen, J.S., Daasbjerg, K., and Lund, H., *Acta Chem. Scand.*, 1992, vol. 46, p. 474.
8. Occhialini, D., Pedersen, S.U., and Lund, H., *Acta Chem. Scand.*, 1992, vol. 44, p. 715.
9. Walton, J., *Magn. Res. Chem.*, 1987, vol. 25, p. 998.
10. Newcomb, M. and Gurran, D.P., *Acc. Chem. Res.*, 1988, vol. 21, p. 206.
11. Rieger, P.H. and Fraenkel, G.K., *J. Chem. Phys.*, 1962, vol. 37, p. 2795; Rieger, P.H, Bernal, I., Reinmuth, W.H., and Fraenkel, G.K., *J. Am. Chem. Soc*., 1963, vol. 85, p. 683.
12. Rossi R.A. and de Rossi, R.H., *Aromatic Substitution by the $S_{RN}1$ Mechanism*, Washington, DC: Am. Chem. Soc., 1983.