ISSN 1070-4280, Russian Journal of Organic Chemistry, 2012, Vol. 48, No. 4, pp. 605–606. © Pleiades Publishing, Ltd., 2012. Original Russian Text © A.M. Magerramov, I.A. Aliev, U.F. Askerova, I.M. Akhmedov, S.F. Farzaliev, 2012, published in Zhurnal Organicheskoi Khimii, 2012, Vol. 48, No. 4, pp. 607–608.

SHORT COMMUNICATIONS

A New Synthesis of Methanoisoindoles

A. M. Magerramov, I. A. Aliev, U. F. Askerova, I. M. Akhmedov, and S. F. Farzaliev

Baku State University, ul. Z. Khalilova 23, Baku, AZ-1148 Azerbaijan e-mail: idrismecid@yahoo.com, rayten507@mail.ru

Received April 25, 2011

DOI: 10.1134/S1070428012040264

Isoindoles occupy a particular place in the chemistry of heterocyclic compounds [1, 2]. Some isoindole derivatives were found to exhibit antihypertensive, antidiabetic, and antibacterial activity [3, 4]. Polymeric composite materials based on isoindoles and methanoisoindoles are used in optoelectronics as fluorescent sensors and laser dyes [5, 6]. Aromatic character and high reactivity of isoindoles make them convenient model substrates for theoretical studies [7].

Among isoindole derivative, methanoisoindoles have been studied relatively poorly, and available data on these compounds are contradictory [7]. Lebedev et al. [4] described a procedure for the synthesis of 4-aryl-4-azatricyclo[5.2.1.0^{2,6}]deca-2,5,8-trienes II in 62-65% yield by reaction of amines with cyclopentadiene adduct I with *cis/trans*-isomeric 2,5-dimethoxy-2,5-dihydrofurans in glacial acetic acid at 70–100°C (Scheme 1). However, we failed to reproduce this procedure. Kobayashi et al. [7] also failed to obtain compound II under the conditions described in [4]. The authors [7] developed a four-step procedure for the synthesis of **II** via reaction of aromatic amine with 3-(diethoxymethyl)bicyclo[2.2.1]hepta-2,5-diene-2carbaldehyde (adduct of cyclopentadiene with 4,4-diethoxybut-2-ynal), followed by reduction of the products to amines and cyclization of the latter to the corresponding methanoisoindoles. However, the yields were relatively poor (18-22%).

Scheme 1.



We succeeded in obtaining compound **IIa** in 55– 60% yield by treatment of adduct **I** with 2 N aqueous HCl at 75°C over a period of 0.5 h (as described in [8]) and subsequent addition of a mixture of 5 equiv of aniline and AcONa \cdot 7H₂O in CHCl₃. Presumably, initial hydrolysis of compound **I** gives intermediate dialdehyde **A** which then reacts with amine according to Paal–Knorr to afford compounds **II** (Scheme 2).



The properties of compound **IIa** were fully consistent with those reported in [7]. The structure of **IIa** and **IIb** was confirmed by their ¹H and ¹³C NMR spectra and elemental analysis. The ¹H NMR spectrum of 4-phenyl-4-azatricyclo[5.2.1.0^{2,6}]deca-2,5,8-triene (**IIa**) contained two doublets at δ 2.29 (J = 6.85 Hz) and 2.44 ppm (J = 6.85 Hz) from protons in the methylene bridge with an intensity ratio of 1:1. Magnetically equivalent (in pairs) 3-H/5-H protons in the pyrrole ring and 1-H/7-H and 8-H/9-H in the norbornene fragment resonated as singlets at δ 6.72, 3.80, and 6.78 ppm, respectively. Signals from protons in the 27.20 Hz), 7.26 (J = 7.55 Hz), and 7.32 ppm (J = 7.26 Hz) with an intensity ratio of 1:2:2.

Initial compound **I** was synthesized according to the procedure described in [9].

Compounds IIa and IIb (general procedure). A mixture of 1 mmol of adduct I and 3.5 ml of 0.2 N hydrochloric acid was stirred for 0.5 h at 75°C and cooled to room temperature, 7.1 mmol of AcONa[•] $7H_2O$, 5 mmol of aniline or benzylamine, and 15 ml of chloroform were added, and the mixture was heated for 24 h under reflux. The progress of the reaction was monitored by TLC (Silufol UV-254, hexane–ethyl acetate, 8:2). The mixture was washed with a saturated solution of sodium hydrogen carbonate, the organic phase was separated and dried over MgSO₄, the solvent was distilled off, and the residue was subjected to column chromatography on KSK silica gel (O-70MK) using hexane–ethyl acetate (8:2) as eluent.

4-Phenyl-4-azatricyclo[**5.2.1.0**^{2,6}]**deca-2,5,8-triene (IIa).** Yield 0.10 g (50%), mp 91–95°C (from hexane); published data [7]: mp 91–92°C. ¹H NMR spectrum, δ , ppm: 2.29 d (1H, CH, J = 6.85 Hz), 2.44 d (1H, CH, J = 6.85 Hz), 3.80 s (2H, CH), 6.72 s (2H, 3-H, 5-H), 6.78 s (2H, 8-H, 9-H), 7.10 t (1H, H_{arom}, J =7.20 Hz), 7.26 t (2H, H_{arom}, J = 7.55 Hz), 7.32 t (2H, H_{arom}, J = 7.26 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 44.40, 68.60, 110.52, 120.00, 123.82, 129.32, 138.50, 141.52, 142.50. Found, %: C 87.12; H 6.51; N 6.85. C₁₅H₁₃N. Calculated, %: C 86.99; H 6.32; N 6.76.

4-Benzyl-4-azatricyclo[5.2.1.0^{2,6}]**deca-2,5,8-triene (IIb).** Yield 0.14 g (62%), yellow oily substance. ¹H NMR spectrum, δ , ppm: 2.28 d and 2.42 d (1H each, 10-H, *J* = 6.80 Hz), 3.83 s (2H, CH), 5.10 s (2H, PhCH₂), 6.68 s (2H, 3-H, 5-H), 6.74 s (2H, 8-H, 9-H), 6.84 m (2H, H_{arom}), 7.22 m (3H, H_{arom}). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 15.00, 44.32, 68.64, 110.80, 120.10, 124.00, 129.34, 138.55, 141.58, 142.52. Found, %: C 86.94; H 6.70; N 6.41. Calculated, %: C 86.88; H 6.78; N 6.33.

The ¹H and ¹³C NMR spectra were recorded on a Bruker 400FT spectrometer at 400 and 100 MHz, respectively, using CDCl₃ as solvent and tetramethylsilane as internal reference.

REFERENCES

- Babichev, F.S. and Kovtunenko, V.A., *Khimiya izoindolov* (Chemistry of Isoindoles), Kiev: Naukova Dumka, 1983, p. 267.
- Kovtunenko, V.A. and Voitenko, Z.V., Usp. Khim., 1994, vol. 63, p. 1064.
- Feldhoff, U., Grevels, F.W., Kreher, R.P., Angermund, K., and Krueqer, C., *Chem. Ber.*, 1986, vol. 119, p. 1919.
- Lebedev, A.A., Markushina, I.A., Marnicheva, G.E., Merkulova, T.B., and Bazhmina, M.Yu., *Khim. Farm. Zh.*, 1981, p. 38.
- 5. Ito, S., Murashima, T., Uno, H., and Ono, N., *Chem Commun.*, 1998, p. 1661.
- Wada, M., Ito, S., Uno, H., Murashima, T., Ono, N., Urano, T., and Urano, Y., *Tetrahedron Lett.*, 2001, vol. 42, p. 6711.
- Kobayashi, T., Suda, H., Takase, H., Iriye, R., and Kato, H., Bull. Chem. Soc. Jpn., 1995, vol. 68, p. 3269.
- 8. Merz, A. and Meyer, T., Synthesis, 1999, p. 94.
- 9. Alder, K., Betzing, H., and Heimbach, K., Justus Liebigs Ann. Chem., 1960, vol. 638, p. 187.