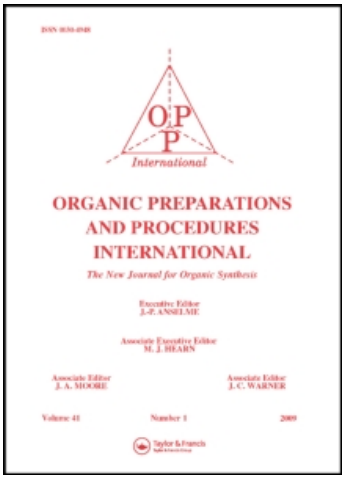


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

AN IMPROVED SYNTHESIS OF 4,8,9,10-TETRAARYL-1,3-DIAZAADAMANTANES

S. Sivasubramanian[a]; M. Sundaravadivelu[a]; N. Arumugam[a]
[a] Department of Organic Chemistry, Madurai Kamaraj University, Madurai, INDIA

To cite this Article Sivasubramanian, S. , Sundaravadivelu, M. and Arumugam, N.(1990) 'AN IMPROVED SYNTHESIS OF 4,8,9,10-TETRAARYL-1,3-DIAZAADAMANTANES', Organic Preparations and Procedures International, 22: 5, 645 — 648
To link to this Article: DOI: 10.1080/00304949009356342
URL: http://dx.doi.org/10.1080/00304949009356342

Pharmazie, 37, 251 (1982).

5. C. C. Cheng, Prog. Med. Chem., 25, 35 (1988).

6. G. E. Davies and J. S. Lowe, Adv. Exptl. Med. Biol., 8, 453 (1970).

7. P. L. Compagnon and M. Miocque, Ann. Chim., 23 (1970).

****

AN IMPROVED SYNTHESIS OF 4,8,9,10-TETRAARYL-1,3-DIAZAADAMANTANES

Submitted by (05/30/89) S. Sivasubramanian*, M. Sundaravadivelu and N. Arumugam

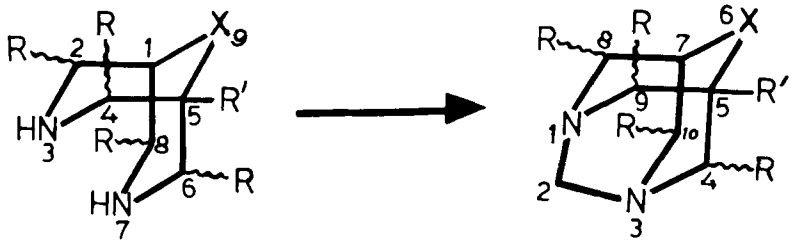
Department of Organic Chemistry
Madurai Kamaraj University
Madurai-625 021, INDIA

In continuation of our ^{1}H nmr spectral studies on 2,6-diphenylpiperidones and their bicyclic derivatives, viz. 3-azabicyclo[3.3.1]nonan-9-ones,[1,2] we were interested in the ^{1}H nmr spectra of 4,8,9,10-tetraaryl-1,3-diazaadamantane systems.[3] The synthesis of several 1,3-diazaadamantanes and their derivatives is reported here.

The most important and versatile route to the above tetraaryl-1,3-diazaadamantane system involves the preparation of the corresponding 2,4,6,8-tetraaryl-3,7-diazabicyclo[3.3.1]- nonane and connecting the two nitrogen functions in this system through a methylene group. Although Quast and Muller[4] adopted this route to prepare some of the above compounds, one of their procedures [Method A] involves refluxing a solution of the 3,7-diazabicyclo[3.3.1]nonane in tetrachloromethane with excess of paraformaldehyde for 6 hrs, the addition of paraformaldehyde being sequential [i. e. 1/4th was added initially followed by another 1/4th of the total quantity of paraformaldehyde being added after 1.5, 3.0 and 4.5 hrs] followed by work-up. With method B,[4] the 3,7-diazabicyclo[3.3.1]nonan-9-one in dichloromethane was boiled with excess paraformaldehyde for 3-4 hrs. The solution was filtered hot and worked up.

In our method, to a solution of the 3,7-diazabicyclo[3.3.1]nonan-9-one in hot dimethyl sulfoxide, paraformaldehyde was added slowly over a period of 10 min. and the mixture was heated for another 5 min. Water was then added and the resulting adamantanone was extracted into chloroform to give, after drying and evaporation, the corresponding 1,3-diazaadamantanone. Thus

the whole procedure is shorter than previously reported methods by at least 1 hr. Moreover, it was sufficient to use equal amount of paraformaldehyde compared to the excess used in earlier methods, and the yield ranged between 75-80%; compounds 3, 4 and 5 are unreported to our knowledge.



Cmpd	R	R'	X	Cmpd	R	R'	X
1	C_6H_5	H	CO	6	C_6H_5	H	CH_2
2	4-$CH_3C_6H_4$	H	CO	7	4-$CH_3C_6H_4$	H	CH_2
3	4-ClC_6H_4	H	CO	8	C_6H_5	H	CHOH
4	4-$CH_3OC_6H_4$	H	CO	9	4-ClC_6H_4	H	CHOH
5	C_6H_5	CH_3	CO				

Diazaadamantanones 1 and 2 were reduced by the Wolf-Kishner reaction[5] to yield the corresponding 4,8,9,10-tetraaryldiazaadamantanes 6 and 7 respectively, while sodium borohydride reduction[6] yielded the corresponding alcohols 8 and 9. All these tetracyclics have been identified through elemental analysis (Table 1), IR and ^1H nmr data (Table 2).

TABLE 1. Yields and Physical Constants of 1-9

Cpd	Yields (%)	mp. (°C)	Elemental Analysis Calculated C	H	N	Found C	H	N
1	80	228[a]	84.21	6.14	6.14	84.11	6.08	6.05
2	75	200[b]	84.38	7.03	5.47	84.21	7.10	5.41
3	78	284	64.65	4.04	4.71	64.78	4.11	4.68
4	80	185	75.05	6.25	4.86	74.68	6.20	4.77
5	80	260	84.26	6.38	5.96	84.18	6.45	6.10
6	60	272[c]	86.88	6.78	6.33	86.50	6.75	6.21
7	58	260[d]	86.75	7.63	5.62	86.65	7.52	5.51
8	90	255	83.84	6.55	6.11	83.75	6.41	6.13
9	85	282	68.79	4.14	4.46	68.91	4.24	4.35

a) Lit.[4] mp. 227°; b) Lit.[4] mp. 208°; c) Lit.[4,8] mp. 251-253° and 268-269°; d) Lit.[4] mp. 251-253°

TABLE 2. ^1H NMR Data ($CDCl_3$, δ)

Cmpd	Aromatic Hydrogens		Benzylic Hydrogens		C_2-H	C_5-H and C_7-H	Others
	axial	equat.	axial	equat.			
1	6.72-7.20	7.30-7.80	4.85	4.75	4.45	4.00	-
2	6.70-7.15	7.30-7.75	4.80	4.64	4.40	3.90	2.35($ArC\underline{H}_3$)
3	6.80-7.15	7.30-7.70	4.65 to 4.90		4.40	3.90	-
4	6.25-7.70(16H)		4.80	4.65	4.35	3.85	3.70($ArOC\underline{H}_3$)
5	6.60-7.85(20H)		4.85	4.70	4.30	5.55	1.35($C_5C\underline{H}_3$)
6	7.10-7.90(20H)		4.55	4.40	4.30	2.80	2.40(2H,C_6-H)
7	7.10-7.60(16H)		4.55	4.35	4.25	2.75	2.30(2H,C_6-H)
8	7.07.70(20H)		4.50 to 4.00		4.30	2.85	1.80(OH), 4.10(C<u>H</u>OH)
9	6.90-7.70(16H)		4.45 to 4.85		4.20	3.25	1.75(OH), 4.10(C<u>H</u>OH)

EXPERIMENTAL SECTION

Mps. are uncorrected. IR spectra were recorded on a Perkin 577 spectrophotometer. ^1H NMR spectra were determined in $CDCl_3$ using 90 MHz Perkin Elmer spectrometer with TMS as internal standard. The 2,4,6,8-tetraaryl-3,7-diazabicyclo[3.3.1]nonan-9-ones were prepared by the methods described in literature.[4,7]

<u>4,8,9,10-Tetraaryl-1,3-diazaadamantan-6-ones</u>. <u>Typical Procedure</u>.- The 2,4,6,8-tetraaryl-3,7-diazabicyclo[3.3.1]nonan-9-ones (2 g) were dissolved in dimethyl sulfoxide (20 ml) in a 100 ml conical flask by heating the mixture on a hot plate. To this hot solution, paraformaldehyde (2 g) was added slowly and heated for another five minutes. About 50 ml of water was added to this solution and the resulting adamantanone was extracted with chloroform. The chloroform layer was dried over anhydrous sodium sulfate. Evaporation of the solvent gave the 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-ones which were crystallized from chloroform.

<u>4,8,9,10-Tetraaryl-1,3-diazaadamantanes by Wolf-Kishner Reduction</u>. <u>Typical Procedure</u>.- A mixture of 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-one (2 g), triethylene glycol (75 ml) and hydrazine hydrate (90% solution, 10 ml) was kept at 100° for 1 hr. The mixture was allowed to cool and dry powered potassium hydroxide (2 g) was added. The excess of hydrazine was distilled off, the resulting solution heated slowly to 200° and kept at that temperature for 1 hr. The mixture was then cooled and poured into water. The tetraaryl-1,3-diazaadamantane which precipitated was collected and crystallized from chloroform.

<u>6-Hydroxy-4,8,9,10-tetraaryl-1,3-diazaadamantanes by Sodium Borohydride Reduction</u>. <u>Typical Procedure</u>.- To sodium borohydride (2 g) dissolved in a minimum amount of water, were added 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-one (2 g) in isopropanol (20 ml). The mixture was refluxed

on a steam-bath for about 3 hrs. Then about 5 ml of 6N sodium hydroxide solution and a boiling chip were added to the reaction mixture which was boiledgently on the steam-bath for another 10 min. The reaction mixture was then poured onto crushed ice and the resulting 6-hydroxy-4,8,9,10-tetraaryl-1,3-diazaadamantane was collected and crystallized from chloroform.

Acknowledgements.- One of us (H. S.) thanks the UGC, New Delhi for the award of the Junior research fellowship. We thank VHNSN college, Virudhunagar for the microanalytical data and University Services and Instrumentation centre, Madurai Kamaraj University for the spectra.

REFERENCES

1. S. Sivasubramanian et al., Indian J. Chem., 20B, 239, 878 (1981); 23B, 280 (1984).
2. S. Sivasubramanian, M. Sundaravadivelu, N. Arumugam and D. A. Wilson, Mag. Resonance Chem., 25, 869 (1987).
3. M. Sundaravadivelu, Ph.D. Thesis, Madurai Kamaraj University, Madurai, INDIA, June 1982.
4. H. Quast and B. Muller, Chem. Ber., 113, 2559 (1980).
5. Huang-Minlon, J. Am. Chem. Soc., 68, 2487 (1946).
6. H. C. Brown and H. M. Hess, J. Org. Chem., 34, 2206 (1969).
7. H. Quast, B. Muller, E. M. Peters, K. Peters and H. G. von Schnening, Chem. Ber., 115, 3631 (1982).
8. S. Chiavarelli, G. Settimj and F. M. Rabagliati Canessa, Gazz. Chim. Ital., 90, 311 (1960).

****

AN IMPROVED OZONOLYTIC APPROACH TO 6-OXOHEPTANAL

Submitted by (02/22/90)

M. R. Karim and P. Sampson*

Department of Chemistry
Kent State University
Kent, OH 44242

As part of a program aimed at the construction of macrocyclic lactone and medium-sized carbocyclic rings,[1] we required access to 6-oxoheptanal (1). The most direct literature approaches to 1 involve the ozonolysis of 1-methylcyclohexene (2) followed by the use of various reductive work-up procedures.[2,3] However, a number of these reports provide no experimental details and the yields of 1 (or products derived from crude 1) are often poor or notreported. In contrast, McMurry reported